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2021 STATUS REPORT
CHRONIC LEUKEMIA WORKING COMMITTEE

Working Committee Leadership	
Co-Chair:	Bart Scott; Fred Hutchinson Cancer Research Center; bscott@fredhutch.org
Co-Chair:	Ryotaro Nakamura; City of Hope; rnakamura@coh.org
Co-Chair:	Betul Oran; M.D. Anderson Cancer Center; boran@mdanderson.org
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INTRODUCTION

a. Minutes and overview plan from 2020 TCT meeting (Attachment 1)

PROPOSALS MOVING FORWARD FOR SCORING (click here to cast your score)

a. PROP 2010-104 Does melphalan dosing prior to allogeneic transplant affect outcomes in myeloid malignancies (Andrew Portuguese/ Bart Lee Scott/ Betul Oran). (Attachment 2)

b. PROP 2010-38; 2010-185 Haploidentical donor transplantation versus matched donor allogeneic hematopoietic cell transplantation outcomes in patients with myelofibrosis (Tania Jain/ Queralt Salas). (Attachment 3)

PROPOSALS DROPPED BECAUSE THEY OVERLAP WITH EXISTING STUDIES OR ARE NOT FEASIBLE DUE TO LIMITATIONS OF AVAILABLE PATIENTS OR DATA

a. PROP 2010-150 Utilization and outcomes of matched related and matched unrelated donor transplantation for myelofibrosis (Vaibhav Agrawal/ Sally Arai/ Laura Johnston).

b. PROP 2010-188 Outcomes of patients undergoing allogeneic stem cell transplantation for BCR-ABL1 negative chronic myeloid leukemia and chronic neutrophilic leukemia (Tania Jain/ Richard Jones).

c. PROP 2010-213 Outcomes with post-transplant cyclophosphamide for haploidentical vs. matched unrelated donor for myelodysplastic syndrome (Shukaib Arslan/ Monzr M. Al Malki).

d. PROP 2010-326 Impact of pre-transplant ruxolitinib in primary or secondary myelofibrosis on outcome of allogeneic hematopoietic stem cell transplant (Carrie Yuen).

e. PROP 2010-39 Impact of pre-alloHCT ruxolitinib in the incidence of GVHD and transplant related complications in patients with myelofibrosis (Marcio Andrade Campos/ Queralt Salas/ Vikas Gupta/Rajat Kumar).

f. PROP 2010-41 Late relapses in survivors of hematopoietic cell transplantation for myelofibrosis (Rachel Salit/ H. Joachim Deeg).

g. PROP 2010-199 Mutational predictors of outcomes following allogeneic blood or marrow transplantation for myelofibrosis (Hany Elmariah/ Nelli Bejanyan/ Taiga Nishihori).

PROPOSALS NOT ACCEPTED FOR CONSIDERATION AT THIS TIME DUE TO RELATIVE SCIENTIFIC IMPACT COMPARED TO ONGOING STUDIES AND/OR OTHER PROPOSALS

a. PROP 2009-05 Decitabine versus 5-azacytidine prior to hematopoietic cell transplant in patients with TP53 mutated myelodysplastic syndrome (Matt Kalaycio).

b. PROP 2009-06 Hematopoietic stem cell transplantation in patients with myelodysplastic syndrome after hypomethylating agents failure (Marielle Beckers/Johan Maertens).

c. PROP 2010-02 Predictors of therapy related MDS/AML in autologous stem cell transplantation in patients with lymphoma (Dave Raj Gupta/ Amelia A. Langston).

d. PROP 2010-35 Impact of ABO mismatch on outcomes of allogeneic stem cell transplant in patients with myelofibrosis (Sharat Damodar/ Stacey Goodman/Bipin Savani).

e. PROP 2010-43 Clinical outcomes after allogeneic hematopoietic cell transplantation in chronic lymphocytic leukemia patients previously treated with novel therapies (Talha Badar/ Mohamed Kharfan Dabaja).

f. PROP 2010-86 Outcomes of allogeneic transplant for CLL in the BTK/BCR inhibitor era (Maxwell M. Krem/ Chaitanya Iragavarapu/ Bipen Savani/ Gerhard C. Hildebrandt).

g. PROP 2010-223 Allogeneic stem cell transplant for chronic myelogenous leukemia (CML) using post-transplant cyclophosphamide as GVHD prophylaxis: An analysis from the CIBMTR database (Rajneesh Nath/ Zheng Zhou/ Aileen Go).

h. PROP 2010-247 Outcomes of patients with myelodysplastic/myeloproliferative neoplasm post-allogeneic hematopoietic stem cell transplantation (Rory M. Shallis/ Lohith Gowda/ Amer M. Zeidan).

i. PROP 2010-251 Exploring the impact of frontline therapy intensity in higher-risk myelodysplastic syndromes or chronic myelomonocytic leukemia on post-allogeneic stem cell transplant outcomes (Rory M. Shallis/ Lohith Gowda/ Amer M. Zeidan/ Andrew Artz).

j. PROP 2010-300 The effect of pre transplant chemotherapy on outcomes of high risk MDS patients presenting with marrow blasts <5% (Usama Gergis).

k. PROP 2010-334 Outcomes of allogeneic hematopoietic cell transplantation in patients with myelodysplastic syndrome with ring sideroblasts and MDS/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (Shukaib Arslan/ Raju Pillai/ Ryotaro Nakamura).

Due to the virtual nature of the 2021 Transplant and Cell Therapy (TCT) Meetings, the CIBMTR leadership changed the Working Committee process for this year. The details were sent previously in a broadcast email to WC members. In summary, each WC could select a maximum of 2 proposals to put forward for voting and only 10 – 15 proposals total from all WC will be presented with only 5 – 10 accepted for this coming year. Within the CKWC, we received 21 proposals. After considering feasibility, novelty, as well as impact, we chose two outstanding proposals but we recognize that several excellent proposals cannot move forward this year due to the maximum number of proposals that were permitted.

STUDIES IN PROGRESS

a. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. Status: Deferred. Dr. Lucy Godley's lab is finishing sequencing DNA samples, once completed data will be incorporated to the datafile and proceed with Multivariable analysis. Goal: Analysis.

b. **CK17-01** Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation. Status: Analysis. Analysis was completed by the PhD statistician analysis will be circulated to the Writing Committee. Goal: Submit.

c. **CK18-02** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. Status: Analysis. Multivariable analysis was completed by PhD statistician. Analysis will be presented at the statistical meeting. Goal: Submit.

d. **CK19-01a** Outcomes after hematopoietic cell transplants for rare chronic leukemias: Evaluating outcomes of allogeneic hematopoietic cell transplantation in T-cell prolymphocytic leukemias. Status: Manuscript Preparation. Manuscript sent for Writing committee review. Goal: Submit.

e. **CK-19-01b** Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. Status: Data File Preparation. Protocol presented at statistical meeting; supplemental data request sent to centers. EBMT collaborative study. Goal: Data File Preparation.

f. **CK20-01** Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. Status: Protocol Development. Protocol presented at Statistical meeting. Goal: Data File Preparation.

PUBLICATIONS, SUBMITTED PAPERS, PRESENTATIONS

a. **CK15-03b** Gupta V, Kim S, Hu Z-H, Liu Y, Aljurf M, Bacher U, Beitinjaneh A, Cahn J-Y, Cerny J, Copelan E, Gadalla SM, Gale RP, Ganguly S, George B, Gerds AT, Gergis U, Hamilton BK, Hashmi S, Hildebrandt GC, Kamble RT, Kindwall-Keller T, Lazarus HM, Liesveld JL, Litzow M, Maziarz RT, Nishihori T, Olsson RF, Rizzieri D, Savani BN, Seo S, Solh M, Szer J, Verdonck LF, Wirk B, Woolfrey A, Yared JA, Alyea EP, Popat UR, Sobecks RM, Scott BL, Nakamura R, Saber W. Comparison of outcomes of HCT in blast phase of BCR-ABL1-MPN with de novo AML and with AML following MDS. Blood Advances. 2020 Oct 13; 4(19):4748-4757. doi:10.1182/bloodadvances.2020002621. Epub 2020 Oct 2. PMC7556156.

b. **CK18-01** Nazha A, Hu Z-H, Wang T, Lindsley RC, Abdel-Azim H, Aljurf M, Bacher U, Bashey A, Cahn J-Y, Cerny J, Copelan E, DeFilipp Z, Diaz MA, Farhadfar N, Gadalla SM, Gale RP, George B, Gergis U, Grunwald MR, Hamilton B, Hashmi S, Hildebrandt GC, Inamoto Y, Kalaycio M, Kamble RT, Kharfan-Dabaja MA, Lazarus HM, Liesveld JL, Litzow MR, Majhail NS, Murthy HS, Nathan S, Nishihori T, Pawarode A, Rizzieri D, Sabloff M, Savani BN, Schachter L, Schouten HC, Seo S, Shah NN, Solh M, Valcárcel D, Vij R, Warlick E, Wirk B, Wood WA, Yared JA, Alyea E, Popat U, Sobecks R, Scott BL, Nakamura R, Saber W. A personalized prediction model for outcomes after allogeneic hematopoietic cell transplant in myelodysplastic syndromes patients. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2020.08.003. Epub 2020 Aug 8.

c. **CK12-01** Hu B, Lin X, Lee HC, Huang X, Slack Tidwell RS, Ahn KW, Hu Z-H, Jabbour E, Verstovsek S, Ravandi F, Garcia-Manero G, Kharfan-Dabaja MA, Hossain NM, Marks DI, Kamble RT, Inamoto Y, Kindwall-Keller T, Saad A, Litzow MR, Savani BN, Hale GA, Bacher U, Gerds AT, Liesveld JL, Ustun C, Olsson RF, Daly A, Grunwald MR, Sohl M, DeFilipp Z, Aljurf M, Wirk B, Akpek G, Nishihori T, Cerny J, Seo S, Hsu JW, Champlin R, De Lima M, Alyea E, Popat U, Sobecks R, Scott BL, Kantarjian H, Cortes J, Saber W. Timing of allogeneic hematopoietic cell transplantation (alloHCT) for chronic myeloid leukemia (CML) patients. Leukemia & Lymphoma. doi:10.1080/10428194.2020.1783444. Epub 2020 Jul 14. 32662346.

d. **CK15-01** Gowin K, Ballen K, Ahn KW, Hu Z-H, Ali H, Arcasoy MO, Devlin R, Coakley M, Gerds AT, Green M, Gupta V, Hobbs G, Jain T, Kandarpa M, Komrokji R, Kuykendall AT, Luber K, Masarova L, Michaelis LC, Patches S, Pariser AC, Rampal R, Stein B, Talpaz M, Verstovsek S, Wadleigh M, Agrawal V, Aljurf M, Angel Diaz M, Avalos BR, Bacher U, Bashey A, Beitinjaneh AM, Cerny J, Chhabra S, Copelan E, Cutler CS, DeFilipp Z, Gadalla SM, Ganguly S, Grunwald MR, Hashmi SK, Kharfan-Dabaja MA, Kindwall-Keller T, Kröger N, Lazarus HM, Liesveld JL, Litzow MR, Marks DI, Nathan S, Nishihori T, Olsson RF, Pawarode A, Rowe JM, Savani BN, Savoie ML, Seo S, Solh M, Tamari R, Verdonck LF, Yared JA, Alyea E, Popat U, Sobecks R, Scott BL, Nakamura R, Mesa R, Saber W. Survival following allogeneic transplant in patients with myelofibrosis. Blood Advances. 2020 May 12; 4(9):1965-1973. doi:10.1182/bloodadvances.2019001084. Epub 2020 May 8. PMC7218417.

e. **CK16-02b** Schmidt S, Liu Y, Hu Z-H, Williams KM, Lazarus HM, Vij R, Kharfan-Dabaja MA, Ortí G, Wiernik PH, Weisdorf D, Kamble RT, Herzig R, Wirk B, Cerny J, Bacher U, Chaudhri NA, Nathan S, Farhadfar N, Aljurf M, Gergis U, Szer J, Seo S, Hsu JW, Olsson RF, Maharaj D, George B, Hildebrandt GC, Agrawal V, Nishihori T, Abdel-Azim H, Alyea E, Popat U, Sobecks R, Scott BL, Holter Chakrabarty J, Saber W. The role of donor lymphocyte infusion (DLI) in post-hematopoietic cell transplant (HCT) relapse for chronic myeloid leukemia (CML) in the tyrosine kinase inhibitor (TKI) era. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2020 Jun 1; 26(6):1137-1143. doi:10.1016/j.bbmt.2020.02.006. Epub 2020 Feb 14. PMC7367282.

f. **CK15-03a** Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of philadelphia-negative myeloproliferative neoplasm. *Submitted.*

g. **CK17-02** Reduced-intensity conditioning transplantation in older myelodysplastic syndrome: The effect of specific conditioning regimens on transplant outcomes. *Submitted.*

h. **CK18-03** Impact of donor age on the outcomes of allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome. *Poster presentation at the ASH 2020 Annual Meeting.*

i. **CK19-01a** Outcomes after hematopoietic cell transplants for rare chronic leukemias: Evaluating outcomes of allogeneic hematopoietic cell transplantation in T-cell prolymphocytic leukemias. *Poster presentation at the ASH 2020 Annual Meeting.*

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA
Orlando, FL
Friday, February 21, 2019, 12:15 p.m. – 2:15 p.m.

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1. Introduction

The Chronic Leukemia Working Committee (CKWC) met on **Friday**, **February 21, 2019** at 12:15 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 and presented Dr. Ronald Sobecks, who will present the welcome slides. Dr. Sobecks began by introducing each member of the working committee leadership. Dr. Sobecks welcomed the incoming chair, Dr. Betul Oran, from MD Anderson Cancer Center, and thanked the committee, for the opportunity to serve as a co-chair over the past 5 years. Dr. Sobecks continued the presentation explaining how to gain and maintain membership, the goals, expectations and limitations of the working committee, emphasizing the rules of authorship as well as the voting process and voting prioritization. Dr. Sobecks reiterated that each proposal was given 5 minutes for presentation and 5 minutes for discussion, and that voting scores will be used as an important aspect of deciding which proposals should be accepted. He also mentioned that a maximum of 2 proposals could be accepted.

Dr. Sobecks also emphasized that during this past year the baseline and follow-up forms for MDS and MPN disorders were divided into two sets of forms and were substantially updated for use in the future years.

2. Accrual summary

The accrual summary was referenced for review, but not formally presented. 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 2019 were referenced, as well as abstracts that have been presented at various conferences. Dr. Sobecks mentioned that it was a very productive year and emphasized the high metrics of the committee. He mentioned that CK16-02b was the most recent publication. At the time, three studies were published, one accepted to journal recently and two abstracts were presented or accepted for presentation. These include:

a. **CK14-02** Kim HT, Ahn KW, Hu Z-H, Davids MS, Volpe VO, Antin JH, Sorror ML, Shadman M, Press O, Pidala J, Hogan W, Negrin R, Devine S, Uberti J, Agura E, Nash R, Mehta J, McGuirk J, Forman S, Langston A, Giralt SA, Perales M-A, Battiwalla M, Hale GA, Gale RP, Marks DI, Hamadani M, Ganguly S, Bacher U, Lazarus H, Reshef R, Hildebrandt GC, Inamoto Y, Cahn J-Y, Solh M, Kharfan-Dabaja MA, Ghosh N, Saad A, Aljurf M, Schouten HC, Hill BT, Pawarode A, Kindwall-Keller T, Saba N, Copelan EA, Nathan S, Beitinjaneh A, Savani BN, Cerny J, Grunwald MR, Yared J, Wirk BM, Nishihori T, Chhabra S, Olsson RF, Bashey A, Gergis U, Popat U, Sobecks R, Alyea E, Saber W, Brown JR. Prognostic score and cytogenetic risk classification for reduced intensity conditioning allogeneic HCT in CLL patients: a CIBMTR report. ***Clinical Cancer Research*. August 2019.**

b. **CK16-02a** DeFilipp Z, Ancheta R, Liu Y, Hu Z-H, Gale RP, Snyder D, Schouten HC, Kalaycio M, Hildebrandt GC, Ustun C, Daly A, Ganguly S, Inamoto Y, Litzow M, Szer J, Savoie ML, Hossain N, Kharfan-Dabaja MA, Hamadani M, Reshef R, Bajel A, Schultz KR, Gadalla S, Gerds A, Liesveld J, Juckett MB, Kamble R, Hashmi S, Abdel-Azim H, Solh M, Bacher U, Lazarus H, Olsson R, Cahn J-Y, Grunwald MR, Savani BN, Yared J, Rowe JM, Cerny J, Chaudhri NA, Aljurf M, Beitinjaneh A, Seo S, Nishihori T, Hsu JW, Ramanathan M, Alyea E, Popat U, Sobecks R, Saber W. Maintenance tyrosine kinase inhibitors following allo-HCT for chronic myeloid leukemia: a CIBMTR Study. ***BBMT*. Epub: October 2019.**

c. **CK16-02b** Schmidt SA, Chakrabarty JH, Liu Y, Hu Z-H, Williams K, Alyea E, Popat U, Sobecks R, Scott B, Saber W. Tyrosine kinase inhibitors with or without donor lymphocyte infusion continue to provide long-term survival after relapse of chronic myeloid leukemia following hematopoietic cell transplantation. ***BBMT***. **Epub: February 2020.**

d. **CK15-03b** Gupta V, Liu Y, Hu Z-H, Ahn KW, Alyea E, Popat U, Sobecks R, Scott B, Saber W. Comparison of outcomes of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia (AML) with antecedent history of Philadelphia-negative myeloproliferative neoplasm with de novo AML and with AML arising from myelodysplastic syndrome: a study from the CIBMTR. ***2020 Transplantation and Cellular Therapy Meeting***. **Oral**.

e. **CK17-02** Oran B, Ahn KW, Fretham C, Shah M, Nakamura R, Scott B, Sobecks R, Popat U, Saber W. Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. ***ASH Annual Meeting and Exposition*. Oral.**

f. **CK15-01** Gowin K, Ballen K, Ahn KW, Hu Z-H, Liu Y, Masarova L, Verstovsek S, Coakley M, Jain T, Kuykendall A, Komrokji R, Wadleigh M, Patches S, Arcasoy M, Green M, Kandarpa M, Talpaz M, Ali H, Gupta V, Devlin R, Michaelis L, Hobbs G, Stein B, Pariser A, Gerds A, Luber K, Rampal R, Alyea E, Popat U, Sobecks R, Scott B, Mesa R, Saber W. Survival advantage to allogeneic transplant in patients with myelofibrosis with intermediate-1 or higher DIPSS score. **In Press.**

4. Studies in Progress

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

a. **CK12-01** Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era. (B Hu/H Lee) **Submitted**

b. **CK15-01** Comparison of transplant vs. non-transplant therapies for myelofibrosis. (K Ballen/RA Mesa/KL Gowin) **In Press**

c. **CK15-03** Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm. (V Gupta) **Manuscript Preparation**
d. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley) **Data File Preparation**
e. **CK16-02b** In the era of tyrosine kinase inhibitors (TKIs), TKIs are superior to donor lymphocyte infusion for relapse of chronic myeloid leukemia post hematopoietic cell transplantation. (S Schmidt) **In Press**
f. **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) **Analysis**
g. **CK17-02** Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. (B Oran) **Manuscript Preparation**
h. **CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome. (A Nazha) **Submitted**
i. **CK18-02** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/ R Nakamura/ R Pillai) **Data File Preparation**
j. **CK18-03** Impact of donor age on the outcomes of allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome (G Murthy) **Analysis**
k. **CK19-01a** Outcomes after HCT for rare chronic leukemias: Evaluating outcomes of Allogeneic hematopoietic cell transplantation in T-cell prolymphocytic leukemias. (H Murthy/B Dholaria/M Kharfan/ S Bal/C Sauter/ L Gowda/F Foss/M Kalaycio/H Alkhateeb) **Data File Preparation**
l. **CK19-01b** Outcomes after HCT for rare chronic leukemias: Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. (B Dholaria/B Savani/M Kharfan) **Protocol Development**

5. Future/Proposed Studies

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

Dr. Bart Scott 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.

a. **PROP 1911-08** Myelodysplastic/ myeloproliferative neoplasms unclassifiable- Transplant outcomes and factors predicting survival- Retrospective analysis of chronic leukemia working party of CIBMTR. (Patnaik/Sheth/Mangaonkar)

Dr. Abhishek Mangaonkar presented the proposal. The goals of the proposal are: 1) to perform outcome analysis related on non-relapse mortality, relapse incidence, leukemia-free survival and overall survival, engraftment and GVHD; 2) to assess the relevance of IPSS/IPSS-R, CPSS and DRI scores as prognostic scores after an allogeneic HCT and compare models. We identified 281 patients with a reported diagnosis of MDS/MPN-U, above 18 years of age which received an allo-HCT from an HLA-identical sibling or unrelated donor from 97 centers between years 2012 to 2019 with a median follow-up of 24 months. Dr. Mangaonkar emphasized the importance of using CIBMTR data due to the relative rarity of this disease, which would prohibit the conduct of randomized prospective trials or large retrospective studies. Therefore, we aim to utilize the unique resources of CIBMTR to answer these important clinical questions.

The proposal was opened for comments and questions. Dr. Scott raised a concern on the misclassification at diagnosis with other syndromes. A member asked if there is molecular data available to classify these patients. Dr. Saber replied we did not have information on molecular data, but we should have path reports attached. A concern was raised on low number of patients to have a study

on prognostic risk factors. Lastly, a member of the audience suggested to combine efforts with EBMT working party to have a larger dataset.

b. **PROP 1911-36** Clinical results of allogeneic hematopoietic stem cell transplantation for hairy cell leukemia (Chihara/Kreitman/Pavletic)
Dr. Dai Chihara presented the proposal. The goals of the proposal are: 1) to estimate the probabilities of PFS and OS, as well as the cumulative incidences of relapse, NRM, grade II-IV and III-IV acute graft-vs-host disease (aGVHD), and chronic GVHD (cGVHD) for patients with HCL undergoing allo-HCT between 1983-2018 and descriptively describe outcomes; 2) to evaluate variables that may be associated with differences in HCT outcomes as a risk factor analysis, if power allows it. Between 1983 to 2018 a total of 26 allo-HCT patients were identified in the CIBMTR database; of which 22 patients were first allo-HCT transplants and 4 received a second allo-HCT. Dr. Chihara proposed a collaborative study with the EBMT-Chronic Malignancies Working Party. The EBMT cohort consists of 23 patients. Dr. Chihara emphasized that there is an unmet need for better and curative treatments in HCL patients. Due to the rarity of allogeneic hematopoietic cell transplant for HCL, a collaboration between CIBMTR and EBMT would potentially be the most appropriate way to obtain information for these patients to provide reference and guidelines.
Th proposal was opened for comments and questions. Dr. Oran commented on the study years' timeline being too wide on this study, explaining that practices have changed over the years, and suggested a stratified analysis by incremental years. Another comment was made concerning the low number of patients and trying to contact centers for cytogenetic reports for this study would be challenging and time consuming. A concern was raised on a possible selection bias in this study due to sicker patients being selected for transplant. Lastly, Dr. Nakamura commented on the limitations on small sample and how clinicians/researchers would use the study results in their practice and transplant/non-transplant research.

c. **PROP 1911-143** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime. (Murthy/ Saber)
Dr. Guru Murthy presented the proposal. The goals of the proposal is to determine the overall survival (OS), disease free survival (DFS), non-relapse mortality (NRM), engraftment, graft failure, relapse rate, incidence of acute graft versus host disease (GVHD) and chronic GVHD based on the choice of conditioning regimen used in MAC and RIC setting, for patients with MF undergoing allo-HCT. They hypothesize that the outcomes of patients with myelofibrosis (MF) who undergo allogeneic hematopoietic cell transplantation (allo-HCT) might be differ based on the choice of individual conditioning regimen used, both with myeloablative conditioning (MAC) and reduced intensity conditioning (RIC). Between years 2000 to 2018, 1161 patients allo-HCT for primary MF or post ET MF or post PV MF with MAC/RIC were identified. Dr. Murthy emphasized that the proposed study would provide information about the differences in outcomes of allo-HCT for MF based on the individual conditioning regimen utilized.
The proposal presentation was then opened for comments and questions. One comment was regarding that there had been a similar EBMT study. It was also suggested to include only more recent years of transplants. A member of the audience suggested to exclude the other regimens category or to make a stratified analysis. A comment was made that this would be a challenging study since transplant regimens are patient and center dependent. Dr. Murthy replied that we could factor in disease risk and

center effect in the multivariable analysis. Lastly, a member of the audience suggested trying to use EBMT regimen classification vs the CIBMTR standard regimen definition.

d. **PROP 1911-225** The Impact of Somatic Mutations on Allogeneic Hematopoietic Cell Transplant Outcomes in Patients with Low and Intermediate Risk Myelodysplastic Syndrome (Arslan/Khaled/Nakamura)
Dr. Shukaib Arslan presented the proposal. The goals of the proposal are: 1) to evaluate HCT outcomes in patients with "lower-risk" MDS who underwent allogeneic HCT; 2) to identify clinical risk factors for HCT outcomes; 3) characterize the mutation profile in the "lower-risk" MDS and examine potential impact of somatic mutations on HCT outcomes. They hypothesized that in patients with "lower-risk" myelodysplastic syndrome (MDS) allogeneic hematopoietic cell transplantation (HCT) is a highly effective therapy with long-term survival, and somatic mutations have prognostic relevance. Dr. Arslan emphasized that this proposed study will be the first to describe the landscape of somatic mutations in this specific patient population and will also provide a unique opportunity to re-classify the risk category (IPSS-R very low/low/intermediate) in these patients using the new criteria incorporating somatic mutations. For this purpose, they propose to assay recurrent somatic mutations using biologic samples from the NMDP repository. They plan to fund this assay using philanthropic funds dedicated for MDS research at City of Hope. A total of 621 patients with very low, low, and intermediate risk MDS with biorepository samples from 2001 through 2016 that contained bio-samples. Around 41% of the identified patients for this proposal are overlap cases from Dr. Lindsley Coleman's study. Dr Arslan mentioned that he will collaborate with Dr. Coleman to be consistent with previous publications.
The proposal presentation was opened for comments and questions. A member of the audience commented on the study not considering differences in allelic frequencies. Another comment was made on a possible selection bias in this study since patients that were transplanted may be sicker. A question was made on how many cord bloods and haploidentical transplant patients were excluded. Dr. Arslan replied that we would have to look at the data. Another member commented that Dr. Coleman's publication did not stratify IPSS. Lastly, a question was made on the possibility of adding a non-transplant arm for comparison.
Dr. Nakamura announced the presenters for the next 3 proposals.

e. **PROP 1911-245** Outcomes of allogeneic hematopoietic stem cell transplantation for patients with B-cell prolymphocytic leukemia. (Grover)
Dr. Punita Grover presented the proposal. The goals of the proposal are: 1) to determine the outcomes of HCT for B-PLL including PFS, OS, non-relapse mortality and cumulative incidence of relapse; 2) to identify patient, disease and transplant variables associated with outcomes. They hypothesize that allogeneic HCT is associated with long term PFS and OS in patients with B-PLL. For this proposal 71 patients with B-Cell PLL from 2000-2018 were identified, 17% of these patients were from the CRF track. Dr. Grover emphasized that there is a need to determine the patient population most likely to benefit from transplant and the CIBMTR would provide the largest cohort for this purpose.
The proposal presentation was opened for comments and questions. A member of the audience asked on how the PI planned to confirm real cases of the disease. Dr. Saber replied that we could provide available pathology reports for the PI to evaluate diagnosis of B-cell PLL. Another comment was made on the low numbers of patients on the CRF track which contains detailed information for studying prognostic factors. Dr. Saber replied that could make a study of prognostic factors at diagnosis and transplant that we collect on the TED track. Another member asked if any CAR-T is used for treating these patients and if CIBMTR would collect this data. Dr. Saber replied we should collect patients that received any cellular therapy.

f. **PROP 1909-06/PROP1911-04** Combined proposal: Transplant outcomes for patients with large granular lymphocyte (LGL) leukemia.

Dr. Mithun Shah presented the proposal on behalf of the groups who submitted similar concepts. The goals of the proposal are: 1) to study the patient- and transplant related characteristics in LGL leukemia patients undergoing stem cell transplant and 2) analyze transplant outcomes including relapse-free (RFS), transplant-related mortality (TRM), overall survival (OS), and cumulative incidence of graft-*vs*-host disease (GVHD). They hypothesize that stem cell transplant is a safe and effective treatment modality for patients with T- and natural killer (NK)-cell large granular lymphocyte (LGL) leukemia. This study would include 145 LGL leukemia patients undergoing HSCT between 2000 and 2018. Dr. Shah emphasized that this would be the largest cohort of LGL leukemia patients. The largest experience currently, is from EBMT consisting of 15 heterogenous patients.

The proposal was opened for comments and questions. A member on the audience asked about the accuracy of this diagnosis that has been reported to the CIBMTR and expressed concern regarding possible misclassification of the disease. Another member suggested a collaboration with the EBMT working party to have a bigger dataset which may then allow an evaluation of prognostic factors. Another member in the audience asked if bone marrow reports are submitted to the CIBMTR. Another suggestion was made with regards to limiting to the proposal to only patients who received allogeneic transplants.

g. **PROP 1911-129/PROP 1911-173/PROP 1911-66/PROP 1811-28/1811-123** Combined proposal: Haploidentical allogeneic stem cell transplantation in patients with myelofibrosis and its comparison to full-matched donor allogeneic stem cell transplantation.

Dr. Tania Jain presented the proposal on behalf of the groups who submitted similar concepts. The goals of the proposal are: 1) to determine clinical outcomes of patients who undergo HCT using a haploidentical related donor and determine patient, donor and HCT related factors that influence these outcomes and 2) compare clinical outcomes of patients who undergo haploidentical HCT using PTCy with matched related/unrelated HCT. The hypotheses for this study are: 1) that allogeneic HCT using a haploidentical related donor and PTCy based GVHD prophylaxis in myelofibrosis results in long-term remission; and 2) outcomes with haploidentical PTCy based HCT are comparable to matched related/unrelated donor HCT. Dr. Jain emphasized the importance of using CIBMTR, which contains the largest dataset of HCT for myelofibrosis. She mentioned that haploidentical donors are a small fraction of these transplants and this is a limitation regarding how best to guide physicians of the use of such transplants for MF. For this proposal we identified 515 PTCy haploidentical HCT adult patients from years 2013 to 2018 diagnosed with primary myelofibrosis, post-polycythemia myelofibrosis, post-essential thrombocythemia myelofibrosis.

The proposal presentation was opened for comments and questions. A member on the audience asked on the possible profile change for MF patients with the introduction of Jakafi in recent years. The PI suggested we could stratify by Jakafi use if possible. Dr. Saber asked PI what is the expected difference that Dr. Jain expects. Dr. Jain replied that she expected between 10-15% differences. Dr. Saber stated that PhD Statistician had run power calculations and the study is currently underpowered for comparisons and proposed a descriptive study. Lastly, a member in the audience asked why include unrelated donors. Dr. Jain was open to eliminate this group.

2 additional proposals were submitted but not presented as listed below:

a. **PROP 1911-116** Identifying the Optimal Allogeneic Transplantation Strategy for Primary and Secondary Myelofibrosis. (Patel/Prchal/Couriel) *Dropped due to overlap with CK17-01 study*.

b. **PROP 1911-214** Retrospective Analysis of Transplant Outcomes in Patients with T-cell Prolymphocytic Leukemia (T-PLL) Treated with Allogeneic or Autologous Stem Cell Transplant (Saba/Hajja/Safah/Socola) *This proposal was triaged to the Acute Leukemia WC and dropped due to overlap with CK19-01a study*.

6. Study Results Presentations

Dr. Saber asked our incoming chair Dr. Betul Oran to present the results of study CK17-02 "Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes" which she presented at the 2019 ASH meeting. The goal of this study was to compare outcomes between Fludarabine/Melphalan (FM) and Fludarabine/Busulfan (FluBu) based RIC for older MDS patients (60>=) between 2007-2016. The study concluded that FM led to a lower incidence of relapse compared with FluBu, which continued to be appreciated within different MDS risk groups by CIBMTR risk score. Also, that treatment related mortality (TRM) was higher in patients with FM within the first 4 months after transplant compared to FluBu. After 5 months of transplant, TRM was comparable between the groups. Another finding was an increase in aGVHD grade II-IV, but not in aGVHD grade III-IV incidence with the use of FM compared with FluBu. Lastly, FM was associated with superior DFS and overall survival compared with FluBu due to reduced RI despite higher TRM in older MDS patients.

7. 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, each attendee had the opportunity to vote on the proposals using the provided voting sheets. 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:

a. **(CK20-02): PROP 1911-143** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime.
b. **(CK20-02): PROP 1911-129/PROP 1911-173/PROP 1911-66/PROP 1811-28/1811-123** Combined proposal: Haploidentical allogeneic stem cell transplantation in patients with myelofibrosis.

Working Committee Overview Plan for 2020-2021

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2020	Hours allocated 7/1/2020-6/30/2021	Total Hours allocated
CK12-01: Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era	Submitted	Published – July 2020	0	0	0	0	0
CK15-01: Comparison of transplant versus non-transplant therapies for myelofibrosis	In Press	Published – July 2020	0	0	0	0	0
CK15-03a: Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm	Manuscript Preparation	Published – July 2021	50	60	50	10	60
CK15-03b: Impact of genetic mutations on the outcomes of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent myeloproliferative neoplasm	Manuscript Preparation	Published – July 2021	30	30	30	10	40
CK16-01: Identification of germline predisposition mutations in young myelodysplastic syndrome patients	Deferred	Submitted – July 2021	130	130	0	0	130
CK16-02b: The benefit of donor lymphocyte infusion in the tyrosine kinase inhibitors era in chronic myeloid leukemia post allogeneic hematopoietic cell transplantation	In Press	Published – July 2020	0	0	0	0	0

CK17-01: Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation	Deferred	Deferred-2021	150	0	0	0	0
CK17-02: Reduced-intensity conditioning transplantation in older myelodysplastic syndrome: the effect of specific conditioning regimens on transplant outcomes	Manuscript Preparation	Published–July 2021	70	80	70	10	80
CK18-01: A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes	Submitted	Published – July 2020	10	10	10	0	10
CK18-02: The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia	Sample Typing	Submitted – July 2021	150	150	20	130	150
CK19-01a: Evaluating outcomes of Allogeneic hematopoietic cell transplantation in T-cell prolymphocytic leukemias.	Data File Pep	Submitted – 2021	180	180	50	130	180
CK19-01b: Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation	Deferred	Deferred – July 2021	180	0	0	0	0
CK20-01: Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime.	Protocol Pending	Data File Prep – July 2021	330	100	0	100	100
CK20-02: Haploidentical allogeneic stem cell transplantation in patients with myelofibrosis	Protocol Pending	Data File Prep – July 2021	330	100	0	100	100

Working Assignments for Working Committee Leadership (March 2020)

Bart Scott	**CK15-03** Outcome of allo-HCT for AML with history of Ph- MPN
	CK16-01 Identification of germline predisposition mutations in young MDS patients.
	CK16-02a Contemporary role of tyrosine kinase inhibitors post allogeneic hematopoietic stem cell transplantation for advanced phase chronic myeloid leukemia.
	CK16-02b Donor lymphocyte infusion vs. tyrosine kinase inhibitors in chronic myeloid leukemia post allogeneic hematopoietic cell transplantation.
	CK18-02 The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia.
Ryotaro Nakamura	**CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes.
	CK17-01 Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation.
	CK19-01a Outcomes after HCT for rare chronic leukemias: Evaluating outcomes of Allogeneic hematopoietic cell transplantation in T-cell prolymphocytic leukemias.
	CK19-01b Outcomes after HCT for rare chronic leukemias: Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation.
Betul Oran	**CK20-01** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime.
	CK20-02 Haploidentical allogeneic stem cell transplantation in patients with myelofibrosis.

Proposal: 2010-104

Title:
Does Melphalan Dosing prior to Allogeneic Transplant affect Outcomes in Myeloid Malignancies

Andrew Portuguese, MD, aportugu@uw.edu, Fred Hutchinson Cancer Research Center (Junior investigator)
Bart Lee Scott, MD, bscott@fhcrc.org, Fred Hutchinson Cancer Research Center
Betul Oran, MD, BOran@mdanderson.org, MD Anderson Cancer Center

Research hypothesis:
There is an optimal dose of melphalan that offers the most anti-myeloid activity but without excessive toxicity. This optimal dose is determined based upon disease specific and patient specific factors. Knowing this optimal dose will result in improved outcomes for patients who receive a melphalan based conditioning regimen.

Specific aims:
- Determine optimal dose of Melphalan based upon disease status and Comorbidity Index

Scientific impact:
This is a key clinical question following the randomized BMT CTN 0901 trial.[1] Most centers have replaced 2 day busulfan with melphalan for the patients who cannot tolerate ablative dosing of busulfan

Scientific justification:
Several retrospective studies from the CIBMTR have identified melphalan as a superior regimen compared to 2 day busulfan.[2-4] In addition, there appears to be a lower relapse incidence with melphalan. This is at the expense of a higher TRM.[2] To date, there has been no study addressing the optimization of melphalan dosing based upon disease risk factors and patient related risk factors. One prior study from the Japanese registry evaluated the impact of melphalan dose but with limited patient centric and disease risk data.[5] We will also consider the potential impact of co-administration total body irradiation.

Study population:
- Patients with AML or MDS who underwent their first allogeneic stem cell transplantation between January 2007 to December 2018.
- Conditioning regimen with fludarabine and intravenous melphalan (FM).
- Use of matched related or unrelated donor.
- Disease status at transplant complete remission for AML patients.
- Disease status at transplant with bone marrow blast count <5% for MDS patients.

Study end points and definitions:
Study end-points of interest are 3-year incidence of disease progression, TRM at day 100, 1-year and 3-years after transplant, 3-year DFS and OS. Time to neutrophil recovery and acute GVHD grade 2 to 4 in addition to chronic GVHD will also be studies.

Variables to be analyzed:

Patient related variables:

- Age at transplantation (continuous)
- Gender: Female vs. male
- Karnofsky performance score: < 80% vs. ≥ 80%
- Previous history of autologous stem cell transplant
- Hematopoietic comorbidity index (HCT-CI) with each specific category of organ dysfunction.

Disease related variables at diagnosis and treatment prior to allo-HCT

- Diagnosis date
- De novo or therapy related MDS/AML
- Histological subtype at diagnosis for MDS patients
- Cytogenetics at diagnosis (G banding and FISH)
- Bone marrow blast count at diagnosis
- Molecular information at diagnosis
- Number of lines of therapy prior to allogeneic stem cell transplantation.

Disease related variables prior to allo-HSCT (before initiation of conditioning regimen)

- Blood counts (Hb, ANC and platelet)
- Blast count in the peripheral blood
- Blast count in the bone marrow
- Cytogenetic test results from the bone marrow (G banding and FISH)
- Flow cytometry from bone marrow
- Disease status at stem cell transplantation
- Pre-transplant fungal infection

Transplant related variables:

- Donor type: HLA matched sibling vs. HLA matched unrelated donor (matched for HLA –A, B, C, DRB1)
- Conditioning regimen: fludarabine with melphalan (MEL) total dose ≤ 150 mg/m^2
    - Total melphalan dose
    - TBI (yes/no)
        - Dose of TBI
- Source of stem cells: Bone marrow (BM) vs. peripheral blood stem cell (PBSC)
- Donor-recipient CMV serostatus: -/- vs. -/+ vs. +/- vs. +/+
- GVHD prophylaxis: CSA or FK plus MTX vs. MMF+others vs. ex vivo T cell depletion vs. others
- Alemtuzumab (yes/no) and ATG (yes/no)

Data requirements:

None

Sample requirements:

None

Study design:
This is a retrospective cohort analysis to compare transplant outcomes in AML/MDS patients based upon melphalan exposure. First, based on the distribution of melphalan doses used, different treatment groups will be defined.
One may expect that there will be two major groups based on most commonly used melphalan doses as FM100 or FM140. The classification will be subject to change based on the observation from the CIBMTR database.
Then the treatment groups will be compared for patient and disease characteristics. Differences between categorical covariates will be tested using Fisher's exact test, and differences between continuous covariates will be compared using Wilcoxon's rank-sum test.
If baseline patient and disease characteristics are similarly distributed in treatment groups then they will be compared for transplant outcomes.
If the treatment groups have different distribution of disease and patient characteristics, then propensity score matching will be considered for to outcome comparisons to be performed.
After the treatment groups are deemed to be comparable (with our without propensity socre matching), then outcome comparisons will be performed. The incidence rates of neutrophil engraftment, TRM, disease progression, and GVHD will be estimated using the cumulative incidence method to account for competing risks. Disease progression or death attributable to persistence disease will be considered competing risks for TRM, TRM will be considered a competing risk for disease progression, and disease progression or death before GVHD will be considered competing risks for GVHD.
Actuarial OS and DFS will be estimated using the Kaplan-Meier method.
The use of TBI will be treated as a confounding variable and included in the cox regression analysis as a binomial variable.

Conflicts of interest:
None

References:
1. Scott BL, et al. *J Clin Oncol.* 2017;35:1154-1161
2. Eapen et al. *Blood Adv*. 2018;2;2095-2103
3. Oran et al. BBMT manuscript submitted
4. Zhou et al. *Blood Adv.* 2020
5. Harada et al. *Leuk Lymph* 2018; 60:1493-1502

Table 1. Baseline characteristics of AML and MDS patients undergoing 1st allo-HCT with Flu/Mel conditioning regimen, between 2008 and 2018

Characteristic	AML	MDS
No. of patients	905	993
No. of centers	105	89
Age - no. (%)		
Median (min-max)	61.77 (18.11-76.38)	66.29 (20.09-76.67)
18-29	32 (4)	5 (1)
30-39	33 (4)	11 (1)
40-49	86 (10)	19 (2)
50-59	222 (25)	146 (15)
60-69	444 (49)	644 (65)
70-80	88 (10)	168 (17)
Sex - no. (%)		
Male	490 (54)	636 (64)
Female	415 (46)	357 (36)
Race - no. (%)		
White	748 (83)	904 (91)
Black or African American	51 (6)	28 (3)
Asian	63 (7)	33 (3)
Native Hawaiian or other Pacific Islander	3 (0)	1 (0)
American Indian or Alaska Native	3 (0)	1 (0)
Other	1 (0)	0
More than one race	4 (0)	2 (0)
Missing	32 (4)	24 (2)
Karnofsky score - no. (%)		
90-100	443 (49)	500 (50)
< 90	453 (50)	483 (49)
Missing	9 (1)	10 (1)
HCT-CI - no. (%)		
0	169 (19)	142 (14)
1	111 (12)	102 (10)
2	87 (10)	120 (12)
3+	409 (45)	594 (60)
TBD, review needed for history of malignancies	0	1 (0)
TBD, inconsistencies between parent and sub-questions	6 (1)	3 (0)
NA, f2400 (pre-TED) not completed	100 (11)	26 (3)
Missing	23 (3)	5 (1)
Therapy related (AML/MDS) - no. (%)		
No	776 (86)	742 (75)

Characteristic	AML	MDS
Yes	100 (11)	227 (23)
Missing	29 (3)	24 (2)
Cytogenetic score - no. (%)		
Favorable	39 (4)	399 (40)
Intermediate	491 (54)	94 (9)
Poor	254 (28)	396 (40)
TBD (needs rev.)	86 (10)	79 (8)
Not tested	9 (1)	9 (1)
Missing	26 (3)	16 (2)
Disease status at time of HCT (AML) - no. (%)		
PIF	166 (18)	0
CR1	502 (55)	0
CR2	121 (13)	0
≥CR3	7 (1)	0
Relapse	89 (10)	0
Missing	20 (2)	993
Disease risk at HCT (MDS) - no. (%)		
MDS early	0	377 (38)
MDS advanced	0	609 (61)
Other	0	7 (1)
Missing	905	0
Blast in marrow prior to HCT - no. (%)		
< 5%	663 (73)	840 (85)
5-10%	72 (8)	62 (6)
11-20%	30 (3)	31 (3)
> 20%	44 (5)	0
Missing	96 (11)	60 (6)
Hb count prior to HCT - no. (%)		
≥ 100 g/L	465 (51)	437 (44)
< 100 g/L	374 (41)	556 (56)
Missing	66 (7)	0
ANC prior to HCT - no. (%)		
≥ 1500 /uL	458 (51)	329 (33)
< 1500 /uL	315 (35)	616 (62)
Missing	132 (15)	48 (5)
Platelet count prior to HCT - no. (%)		
≥ 100 x 10/L	462 (51)	433 (44)
< 100 x 10/L	374 (41)	560 (56)
Missing	69 (8)	0
Time from diagnosis to HCT - median (min-max)	5.66 (0.3-214.7)	8.78 (0.63-690.3)

Characteristic	AML	MDS
Conditioning regimen - no. (%)		
TBI/Mel	58 (6)	41 (4)
Flu/Mel	847 (94)	952 (96)
Donor type - no. (%)		
HLA-identical sibling	240 (27)	261 (26)
Well-matched unrelated (8/8)	529 (58)	625 (63)
Partially-matched unrelated (7/8)	136 (15)	107 (11)
Donor/recipient sex match - no. (%)		
M-M	331 (37)	436 (44)
M-F	258 (29)	212 (21)
F-M	157 (17)	197 (20)
F-F	157 (17)	144 (15)
Missing	2 (0)	4 (0)
Donor/recipient CMV serostatus - no. (%)		
+/+	323 (36)	341 (34)
+/-	96 (11)	97 (10)
-/+	294 (32)	285 (29)
-/-	173 (19)	262 (26)
Missing	19 (2)	8 (1)
Graft source - no. (%)		
Bone marrow	116 (13)	91 (9)
Peripheral blood	789 (87)	902 (91)
GVHD prophylaxis - no. (%)		
No GVHD prophylaxis	6 (1)	9 (1)
Ex-vivo T-cell depletion	0	1 (0)
CD34 selection	1 (0)	1 (0)
Post-CY + other(s)	37 (4)	49 (5)
TAC + MMF ± other(s) (except post-CY)	165 (18)	159 (16)
TAC + MTX ± other(s) (except MMF, post-CY)	354 (39)	440 (44)
TAC + other(s) (except MMF, MTX, post-CY)	94 (10)	165 (17)
TAC alone	57 (6)	48 (5)
CSA + MMF ± other(s) (except post-CY)	43 (5)	28 (3)
CSA + MTX ± other(s) (except MMF, post-CY)	93 (10)	49 (5)
CSA + other(s) (except MMF, MTX, post-CY)	19 (2)	10 (1)
CSA alone	19 (2)	7 (1)
Other(s)	12 (1)	20 (2)
Missing	5 (1)	7 (1)
ATG/Campath - no. (%)		
ATG + CAMPATH	1 (0)	0
ATG alone	182 (20)	194 (20)

Characteristic	AML	MDS
CAMPATH alone	106 (12)	94 (9)
No ATG or CAMPATH	611 (68)	698 (70)
Missing	5 (1)	7 (1)
Year of HCT - no. (%)		
2007	107 (12)	25 (3)
2008	87 (10)	17 (2)
2009	58 (6)	22 (2)
2010	12 (1)	11 (1)
2011	18 (2)	49 (5)
2012	28 (3)	76 (8)
2013	94 (10)	97 (10)
2014	128 (14)	108 (11)
2015	123 (14)	127 (13)
2016	120 (13)	186 (19)
2017	77 (9)	144 (15)
2018	53 (6)	131 (13)
Follow-up - median (min-max)	59.84 (3.29-146.94)	47.99 (3.42-147.27)

Combined Proposal: 2010-38; 2010-185

Title:
Haploidentical Donor Transplantation versus Matched Donor Allogeneic Hematopoietic Cell Transplantation Outcomes In Patients With Myelofibrosis

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Hypothesis:
Allogeneic hematopoietic cell transplantation (HCT) using a haploidentical related donor and post-HCT cyclophosphamide (PTCy) based graft versus host disease (GVHD) prophylaxis results in similar clinical outcomes compared to matched sibling donor (MSD) or matched unrelated donor (MUD) HCT.

Primary aim:
- To explore the impact of donor type on overall survival of patient undergoing HCT for myelofibrosis.

Secondary aims:
- To compare clinical outcomes i.e. cumulative incidence of relapse, non-relapse mortality, acute GVHD, chronic GVHD, GVHD-free and relapse-free survival (GRFS), time to engraftment and primary graft failure between haploidentical versus MSD or MUD HCTs.
- To evaluate the impact of donor type on patients with myelofibrosis undergoing HCT using a PTCy platform for GVHD prophylaxis.

Scientific impact and innovation:
Despite recent advances in treatment options, HCT remains the only potentially curative treatment in myelofibrosis. Alternative donors have been used for HCT in myelofibrosis, like other malignancies, using HLA-haploidentical matches or less frequently, cord blood [1,2]. Historically, superior outcomes have been seen with full matched donors compared with partially mismatched donors for HCTs done between 1997 and 2010 [3]. Since then however, the use of haploidentical donor HCT using PTCy has been described and increasingly used especially as an alternate donor option [4].
Our multi-center study, including data from 12 centers across United States of America and Canada, has shown long term remissions in patients with myelofibrosis using haploidentical donors with PTCy platform as GVHD prophylaxis [1]. At 1 year and 2 years, overall survival 71% and 69%, relapse-free survival was 66% and 52%, non-relapse mortality was 25% and 27% while cumulative incidence of relapse was 9% and 21%, respectively. Estimate for grade 3-4 acute GVHD at 3 months was 10% and for chronic GVHD at 1 year was 26%. Another retrospective study conducted by European Society for Blood and Marrow Transplantation showed similar outcomes using haploidentical donor HCT in patients with myelofibrosis [2]. This has provided encouraging data to allow for the use of haploidentical donor for HCT in myelofibrosis. However, a knowledge gap and a clinical dilemma remains for donor selection when more than possibility is available. This is especially important, as myelofibrosis patients are often older and likely to have older siblings.
Several studies led by Center International Blood and Marrow Transplant Research (CIBMTR) working

committees have successfully elucidated and compared outcomes with haploidentical donor HCTs with MSD or MUD HCTs for acute myeloid leukemia and lymphomas [5-7]. However, such data is not yet available for patients who undergo HCT for myelofibrosis and leaves a 'no-evidence zone' while making clinical decisions.
Hence, we propose to compare clinical outcomes of HCT in these settings in patients undergoing HCT for myelofibrosis. This will help guide clinical practice for this rare condition where low numbers limits single institution studies. A data registry such as CIBMTR registry is the most suitable way to conduct this study.

Patient eligibility population:
Adult patients who underwent first HCT for myelofibrosis [primary, post-essential thrombocythemia (ET) or post-polycythemia vera (PV)] using haploidentical donor/ PTCy based GVHD prophylaxis and MSD or MUD in the recent years i.e. January 2013 through December 2019.

Inclusion criteria:

- Adults diagnosed with primary, post-ET or post-PV myelofibrosis, age ≥18 years, undergoing first HCT between 2013 and 2019.
- Eligible donors include: haploidentical donors with PTCy, MUDs, MSDs.
- Donor source: Peripheral blood and bone marrow will be permitted.
- Conditioning regimens: Myeloablative and reduced intensity conditioning regimen will be permitted.

Exclusion criteria:

- Disease phase: Patients who transformed to acute myeloid leukemia prior to HCT.
- Donor source: Umbilical donor HCTs as that is not usually preferred donor option in myelofibrosis (N=18 between 2013 and 2019 in the CIBMTR registry).
- GVHD prophylaxis: Patients who received in-vivo T cell depletion.

Data requirements:

Type of data	Data point	Specific data
Patient Specific	**Patient specific characteristics**	Age at diagnosis Age at transplant Gender Country of transplant Karnofsky performance score HCT-CI Myelofibrosis subtype: Primary, post-ET and post-PV Interval from diagnosis to transplant Disease Characteristics at the time of HCT: Cytogenetics risk stratification per Tefferi *et al*, Leukemia, 2018[8] Molecular profile (JAK2/CALR/MPL positive or negative where available) Percentage of blasts in peripheral blood Hemoglobin level

		WBC count Platelet count Transfusion dependence Constitutional symptoms Dynamic International Prognostic Scoring System Score Prior use of Ruxolitinib. Spleen size (if available). Pre-HCT splenectomy yes/no.
	Transplant date	HCT date
	Transplant information	Donor type HLA match -mismatch degree Donor-recipient gender match Donor-recipient ABO mismatch Donor age (if available)
	Conditioning regimen	Myeloablative vs Reduced-intensity Conditioning regimen description
	GVHD prophylaxis	Calcineurin based PTCy based Others
	Graft characteristic	Source of graft (peripheral blood stem cells or marrow) CD34+ cell dose (PBSC) / Nucleated cell dose (BM) CD3+ cell dose (if available)
Outcome Measures	**Engraftment**	Neutrophil engraftment date Platelet engraftment date Graft failure Date of the graft failure
	Post-transplant complications	VOD: Yes/No. Grade if available. Resolved: Yes/no CMV reactivation: yes/no. EBV reactivation: yes/no.
	GVHD	Acute GVHD overall percentages and according to grade Cumulative incidence of grade II-IV and grade III-IV acute GVHD Chronic GVHD overall percentages and according to grade Cumulative incidence of moderate/severe chronic GVHD Chronic GVHD requiring systemic therapy
	Relapse	Disease status after HCT Relapse/Progression Date of relapse/progression Donor lymphocyte infusion use
	Last follow/up or death	Disease status last follow-up Death yes/no Date of death Cause of Death

Study design:

The impact of donor type will be explored in the entire cohort of patients. Results among patients undergoing haploidentical donor HCT will be compared independently with the cohort of patients who underwent HCT using 8/8 MUD and with the cohort of patients who underwent HCT using HLA matched sibling donor.

The proposed study is a retrospective study using HCT data from CIBMTR registry. Baseline patient, disease and transplant related factors would be compared using standard statistical tests for categorical (chi-squared test) and continuous variables (Mann-Whitney test). The main variable of interest will be donor type (haploidentical vs MSD or MUD) and the main outcome variable will be overall survival. Kaplan Meier curve estimates would be used to generate probability of overall survival, progression-free survival and GRFS; and impact of variables assessed via Log-rank test. Cumulative incidence can be used to calculate probabilities of relapse, nonrelapse mortality, acute or chronic GVHD and graft failure. Cumulative incidence analysis will be done utilizing the cumulative incidence procedure to account for competing risks (relapse or death), and comparison will be performed utilizing the Fine-Gray test. Prognostic variables will be evaluated for their impact on overall survival and relapse-free survival using univariate and multivariate analysis by cox proportional hazards analysis. All *P*-values will be 2-sided and for the statistical analyses, $P < 0.05$ will be considered to indicate a statistically significant result. Donor type will be included in the multivariate model irrespective of the *P* value found in the univariate analysis

Lastly, given the recent report from CIBMTR analysis demonstrating differences in outcomes of patients undergoing HCT with PTCy platform using MUD versus haploidentical donor in reduced intensity conditioning regimen setting [9], we seek to identify those differences in this population since a majority (60-70%) patients in this overall cohort received reduced intensity conditioning. Hence, we will also conduct similar comparison in clinical outcomes of patients who underwent HCT with PTCy platform and used haploidentical donors (N=177) versus a combined cohort of matched related/unrelated donors (n=120).

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Table 1: Characteristics of patients undergoing HCT for myelofibrosis

Characteristic	HLA-identical sibling	Haplo	URD 8/8
No. of patients	542	177	921
No. of centers	141	73	138
track - no. (%)			
TED	190 (35)	32 (18)	217 (24)
CRF	352 (65)	145 (82)	704 (76)
Patients age - median (min-max)	59.92 (20.93-74.65)	62.07 (19.6-74.82)	62.37 (28.5-77.9)
Age - no. (%)			
18-29	3 (1)	1 (1)	1 (0)
30-39	13 (2)	4 (2)	20 (2)
40-49	60 (11)	24 (14)	80 (9)
50-59	196 (36)	47 (27)	261 (28)
60-69	257 (47)	82 (46)	463 (50)
≥ 70	13 (2)	19 (11)	96 (10)
Sex - no. (%)			
Male	325 (60)	107 (60)	541 (59)
Female	217 (40)	70 (40)	380 (41)
Race - no. (%)			
Caucasian	426 (79)	120 (68)	799 (87)
African-American	24 (4)	22 (12)	25 (3)
Asian	32 (6)	11 (6)	17 (2)
Pacific islander	7 (1)	1 (1)	5 (1)
Native American	2 (0)	1 (1)	3 (0)
More than one race	1 (0)	1 (1)	3 (0)
Missing	50 (9)	21 (12)	69 (7)
HCT-CI - no. (%)			
0	149 (27)	42 (24)	185 (20)
1	70 (13)	32 (18)	137 (15)
2	74 (14)	24 (14)	149 (16)
3+	240 (44)	77 (44)	435 (47)
TBD, inconsistencies between parent and sub-questions	8 (1)	2 (1)	14 (2)
Missing	1 (0)	0	1 (0)
Karnofsky score - no. (%)			
90-100	306 (56)	94 (53)	464 (50)
< 90	226 (42)	83 (47)	444 (48)
Missing	10 (2)	0	13 (1)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
Subdisease - no. (%)			
Primary Myelofibrosis	413 (76)	130 (73)	696 (76)
Polycythemia vesa	60 (11)	24 (14)	103 (11)
Essential thrombocythemia	69 (13)	23 (13)	122 (13)
Graft type - no. (%)			
Bone marrow	23 (4)	25 (14)	48 (5)
Peripheral blood	519 (96)	152 (86)	873 (95)
Time from diagnosis to HCT - no. (%)			
<6	64 (12)	9 (5)	77 (8)
6-11	85 (16)	34 (19)	160 (17)
≥12	359 (66)	131 (74)	636 (69)
Missing	34 (6)	3 (2)	48 (5)
Donor/recipient sex match - no. (%)			
M-M	178 (33)	71 (40)	392 (43)
M-F	102 (19)	31 (18)	268 (29)
F-M	147 (27)	36 (20)	149 (16)
F-F	115 (21)	39 (22)	111 (12)
Missing	0	0	1 (0)
Donor age at donation - no. (%)			
0-17	2 (0)	6 (3)	0
18-29	4 (1)	56 (32)	550 (60)
30-39	14 (3)	59 (33)	238 (26)
40-49	79 (15)	39 (22)	92 (10)
50-59	223 (41)	15 (8)	32 (3)
60-69	185 (34)	2 (1)	2 (0)
70-79	17 (3)	0	0
Missing	18 (3)	0	7 (1)
Donor age at donation, median (range), yr - median (min-max)	57.5 (0-75.8)	34.2 (16.2-63)	28 (-39.67-68.1)
Conditioning as reported by center - no. (%)			
MAC	219 (40)	51 (29)	339 (37)
RIC/NMA	318 (59)	126 (71)	581 (63)
Missing	5 (1)	0	1 (0)
Conditioning regimen - no. (%)			
TBI/Cy	1 (0)	0	6 (1)
TBI/Cy/Flu	11 (2)	75 (42)	7 (1)
TBI/Mel	11 (2)	28 (16)	18 (2)
TBI/Flu	22 (4)	19 (11)	85 (9)
TBI/other(s)	0	0	1 (0)
Bu/Cy	69 (13)	14 (8)	72 (8)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
Bu/Mel	0	2 (1)	1 (0)
Flu/Bu/TT	5 (1)	17 (10)	12 (1)
Flu/Bu	250 (46)	11 (6)	398 (43)
Flu/Mel/TT	1 (0)	4 (2)	4 (0)
Flu/Mel	157 (29)	4 (2)	299 (32)
Cy/Flu	8 (1)	3 (2)	6 (1)
Mel alone	1 (0)	0	0
Treosulfan	0	0	3 (0)
TLI	1 (0)	0	3 (0)
Other(s)	4 (1)	0	5 (1)
None	1 (0)	0	1 (0)
GHVD-prophylaxis - no. (%)			
PTcy + CNIs + MMF	18 (3)	157 (89)	46 (5)
PTcy + CNIs + MTX	0	1 (1)	1 (0)
PT-Cy + others	21 (4)	19 (11)	32 (3)
PT-Cy alone	1 (0)	0	1 (0)
CNI + MMF	75 (14)	0	136 (15)
CNI + MTX	376 (69)	0	616 (67)
CNI + others	41 (8)	0	72 (8)
CNI alone	10 (2)	0	16 (2)
Missing	0	0	1 (0)
TX year - no. (%)			
2013	50 (9)	4 (2)	83 (9)
2014	62 (11)	8 (5)	98 (11)
2015	77 (14)	7 (4)	94 (10)
2016	76 (14)	14 (8)	112 (12)
2017	91 (17)	38 (21)	156 (17)
2018	96 (18)	44 (25)	186 (20)
2019	90 (17)	62 (35)	192 (21)
Follow-up - median (min-max)	27.6 (3.03-73.95)	23.42 (3.22-76.88)	24.7 (3.16-81.41)