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A G E N D A
CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA
Orlando, FL
Friday, February 21, 2020, 12:15 pm – 2:15 pm

Co-Chair:	**Ryotaro Nakamura, MD, City of Hope** **Phone: 713-745-3055; Email: rnakamura@coh.org**
Co-Chair:	**Ronald Sobecks, MD, Cleveland Clinic** **Phone: 216-445-4626; Email: sobeckr@ccf.org**
Co-Chair:	**Bart Scott, MD, Fred Hutchinson Cancer Research Center** **Phone: 206-667-1990; Email: bscott@fredhutch.org**
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1. **Introduction**
   a. **Minutes and overview plan from February 2019 meeting** (Attachment 1)
   b. **Instructions for sign-in and voting**
   c. **Outgoing Chair: Ronald Sobecks**
   d. **Incoming Chair: Betul Oran**
2. **Accrual summary** (Attachment 2)
3. **Presentations, Published or Submitted Papers**
   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. **CK15-03** 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**.

d. **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.**

e. **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. **Submitted.**

f. **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. **Submitted**.

4. Studies in Progress (Attachment 3)

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) **Manuscript Preparation**

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. **CK16-02b** 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) **Submitted**

e. **CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome. (A Nazha) **Submitted**

f. **CK17-02** Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. (B Oran) **Manuscript Preparation**

g. **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**

h. **CK18-03** Impact of donor age on the outcomes of allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome (G Murthy) **Analysis**

i. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley) **Data File Preparation**

j. **CK18-02** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/ R Nakamura/ R Pillai) **Data File Preparation**

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) **Protocol Development**

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

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) (Attachment 4)
b. **PROP 1911-36** Clinical results of allogeneic hematopoietic stem cell transplantation for hairy cell leukemia (Chihara/Kreitman/Pavletic) (Attachment 5)
c. **PROP 1911-143** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime. (Murthy/ Saber) (Attachment 6)
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) (Attachment 7)
e. **PROP 1911-245** Outcomes of allogenic hematopoietic stem cell transplantation for patients with B-cell prolymphocytic leukemia. (Grover) (Attachment 8)
f. **PROP 1909-06/PROP1911-04** Combined proposal: Transplant outcomes for patients with large granular lymphocyte (LGL) leukemia. (Attachment 9)
Transplant outcomes for patients with T- and Natural Killer (NK)-cell large granular lymphocyte (LGL) leukemia (Shah/Go/Alkhateeb) (Attachment 9a) Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Large Granular Lymphocytic Leukemia. (Abdul-Hay/Al-Homsi/Kharfan-Dabaja) (Attachment 9b)
g. **PROP1911-129/PROP1911-173/PROP1911-66/PROP1811-28/1811-123** Combined proposal: Haploidentical allogeneic stem cell transplantation in patients with myelofibrosis and its comparison to full-matched donor allogeneic stem cell transplantation. (Attachment 10)
Outcomes With Haploidentical Allogeneic Stem Cell Transplantation In Patients With Myelofibrosis (Jain/Jones) (Attachment 10a) Comparison of Outcomes With Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation In Patients With Myelofibrosis (Jain/Jones) (Attachment 10b) Comparison of outcomes following allogeneic stem cell transplantation for myelofibrosis with HLA-haploidentical versus matched donors (Keyzner/Mascarenhas/Tremblay) (Attachment 10c) Outcomes of haploidentical transplantation for myelofibrosis. (Nadiminti) Comparison of outcomes in myelofibrosis after alternative types of allogeneic hematopoietic stem cell transplant. (Yazan)

Dropped proposed studies

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*.

6. Study results presentations

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA
Houston, Tx
Saturday, February 23, 2019, 2:45 p.m. – 4:45 p.m.

Co-Chair:	**Uday Popat, MD, MD Anderson Cancer Center**
	Telephone: 713-745-3055; Email: upopat@mdanderson.org
Co-Chair:	**Ronald Sobecks, MD, Cleveland Clinic Foundation**
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Co-Chair:	**Bart Scott, MD, Fred Hutchinson Cancer Research Center**
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1. Introduction

The Chronic Leukemia Working Committee (CKWC) met on Wednesday, February 23, 2018 at 2:45 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 one of the chairs of the CKWC, Dr. Uday Popat welcomed the attendees on behalf of the working committee leadership and gave the introduction presentation, introducing each member of the working committee leadership, how to gain and maintain membership, the goals, expectations and limitations of the working committee, the rules of authorship as well as the voting process. Dr. Wael Saber welcomed the incoming chair, Dr. Ryotaro Nakamura, from City of Hope, and thanked the departing chair, Dr. Uday Popat, for his leadership and guidance to the working committee in the past 3 years.

Dr. Popat emphasized that each proposal was given 5 minutes for presentation and 5 minutes for discussion, and the voting scores will be used as a critical recommendation to the leadership. Minutes from the 2018 Tandem meeting in Salt Lake City were approved by the attendees.

2. Accrual summary

The accrual summary was reference by Dr. Popat for review but not formally presented. The full accrual summary was available online as part of the attachments.

3. Presentations, Published or Submitted Papers

Dr. Popat mentioned the published or submitted papers in 2018, as well as abstracts that have been presented at various conferences, mentioning that it was a very productive year and emphasized the high metrics of the committee. Due to the full agenda, the papers were not presented. At the time, one study was published, two studies were submitted and four abstracts were presented or accepted for presentation. These include:

a. **CK15-02**. Chhabra S, Ahn KW, Hu Z-H, Jain S, Assal A, Cerny J, Copelan EA, Daly A, DeFilipp Z, Gadalla SM, Gale RP, Ganguly S, Hamilton BK, Hildebrandt GC, Hsu JW, Inamoto Y, Kanate AS, Khoury HJ, Lazarus HM, Litzow MR, Nathan S, Olsson RF, Pawarode A, Ringden O, Rowe JM, Saad A, Savani BN, Schouten HC, Seo S, Shah NN, Solh M, Stuart RK, Ustun C, Woolfrey AE, Yared JA, Alyea EP, Kalaycio ME, Popat U, Sobecks R, Saber W. Myeloablative vs reduced-intensity conditioning allogeneic hematopoietic cell transplantation for chronic myeloid leukemia. ***Blood Advances.*** **2018 Nov. In Press.**

b. **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. **Submitted.**

c. **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. **Submitted.**

d. **CK15-01** Gowin K, Bellen 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. ***60th ASH annual meeting and Exposition.*** **Poster.**

e. **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. ***60th ASH annual meeting and Exposition***. **Oral**.

f. **CK15-03** 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. ***2019 Transplantation and Cellular Therapy Meeting***. **Poster**.

g. **CK18-01** Nazha A, Hu Z-H, Tao W, Hamilton B, Majhail N, Lindsley C, Sobecks R, Popat U, Scott B, Saber W. A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome. ***60th ASH annual meeting and Exposition***. **Oral**.

4. Studies in Progress

Due to the full agenda, studies in progress were not presented at the meeting. Dr. Popat 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) **Manuscript Preparation**
b. **CK15-01** Comparison of transplant vs. non-transplant therapies for myelofibrosis. (K Ballen/RA Mesa/KL Gowin) **Manuscript Preparation**
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. **CK16-02b** 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) **Manuscript Preparation**
e. **CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome. (A Nazha) **Manuscript Preparation**
f. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley) **Data File Preparation**
g. **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) **Data File Preparation**
h. **CK17-02** Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. (B Oran) **Data File Preparation**
i. **CK18-02** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/ R Nakamura/ R Pillai) **Protocol Development**
j. **CK18-03** Impact of donor age on the outcomes of allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome (G Murthy) **Protocol Development**

5. Future/Proposed Studies

Dr. Popat thanked the investigators whose proposals were submitted but not selected for presentation, emphasizing that the majority were dropped due to overlaps with current studies and data availability issue. Also emphasized the voting process based on the scientific impact of the proposal. Dr. Bart Scott then announced the presenters for the first 3 proposals.

a. **PROP 1810-12** Impact of conditioning regimen on outcomes for patients with previously treated CLL who underwent allogeneic hematopoietic transplantation. (H Kim)

   Dr. Ronald Sobecks presented the proposal on behalf of Dr. Kim. The goal of the proposal was to compare outcomes after MAC-TBI and MAC-Flu/Bu to NST-TBI/Flu, NST-Flu/Cy, RIC-Flu/Bu, and RIC-Flu/Mel in previously treated CLL patients who underwent allogeneic transplantation. The hypothesize that non-TBI based MAC has the advantage of TBI-based MAC (low relapse) while maintaining low NRM. There were 758 CLL patients between 2008-2014, of which 606 had RIC/NMA and 152 patients had received MAC.

   A question was raised on whether the researcher was going to compare MAC vs other conditioning regimens. Another question raised on how many patients took rituximab as part of the conditioning regimen and how many patients are going to have an allogeneic transplant in the future years. A comment was made on whether the proposal would be relevant given the decline in the use of allo-HCT for CLL. Lastly, an attendee suggested to look for center effect.

b. **PROP 1811-27** Graft failure, donor lymphocyte infusion, and second transplant after allogeneic hematopoietic cell transplant for myelofibrosis. (S Kunte/A Gerds)

Dr. Siddarth Kunte presented the combined proposal. The goals of the proposal were to describe the rate and risk factors of allo-HCT for patients with myelofibrosis (MF), and to describe outcomes of DLI and second transplant as salvage treatment. The hypothesis of this is that graft source, conditioning intensity, and degree of marrow fibrosis will be associated with graft failure. Also, they hypothesized that DLI and second transplant are feasible options for restoring hematopoiesis in patients who experience graft failure. Between 2000 and 2017, there were 1239 MF adult patients, of which 169 had a graft failure vs 1070 which didn't have a graft failure. Dr. Kunte emphasized that allo-HCT remains the only curative therapy for MF. He indicated, that there are few dedicated analyses for graft failure and none in the JAK-inhibitor era.

Comments on the availability of spleen size and splenectomy were received. Dr. Scott replied by saying that the CIBMTR have the data. Another comment made by the audience was on why use cord blood in this study, suggesting it should be eliminated have a homologous population. Another comment was made on the availability on stem cell and CD34+ data, Dr. Saber replied that the CIBMTR doesn't collect the stem cell boost data but does have CD34+ data.

c. **PROP 1811-47/PROP 1811-54/ PROP 1711-111** Evaluating the efficacy of allogeneic hematopoietic cell transplantation for T cell prolymphocytic leukemia (H Murthy/B Dholaria/M Kharfan), Outcomes of patients with T cell prolymphocytic leukemia undergoing allogeneic stem cell transplantation (S Bal/C Sauter), Allogeneic stem cell transplant for prolymphocytic leukemias (L Gowda/F Foss/M Kalaycio/H Alkhateeb)

Dr. Susan Bal presented the proposal. The goal of the proposal was to describe clinical outcomes following allo HCT in patients with T-cell prolymphocytic leukemia. The hypothesis of this study is that alloHCT is an effective therapy for T-cell PLL. There were 289 patients diagnosed with PLL, which only 55 were on the CRF track between 2000 and 2016. Dr. Bal emphasized that the CIBMTR would represent the largest observational study in PLL and due to the rarity of the disease this study could help clinical decision making for an allo-HCT.

Comments on the availability of minimal residual disease (MRD) and complete remission (CR) data were received. The committee replied that CIBMTR doesn't have the data on MRD but has CR/PR data available. Another question was raised asking on availability of therapy, Dr. Saber replied that CIBMTR has that information available.

Dr. Sobecks announced the presenters for the next 3 proposals.

d. **PROP 1811-51** Alternative donor vs HLA matched donor hematopoietic cell transplantation in patients with myelodysplastic syndrome (R Mehta)

Dr. Rohtesh Mehta presented the proposal. The goal of the proposal was to compare the outcomes of patients with MDS according to the type of donor type. The hypothesis of this study is that the survival of adult patients with de novo or secondary MDS who underwent haploidentical HCT with post-cy would be similar to patients with HLA-matched HCT and better than HLA- mismatched unrelated donor. Between 2000 and 2016, there were 1310 MSD patients, 8/8 URD patients, 131 haploidentical with post-Cy and 267 cord bloods. Dr. Mehta

emphasized that there is a lack of studies evaluating haploidentical transplantation with post-Cy on MDS patients and other donor types.

Comments were made on limiting the study years from 2008 onwards where haploidentical cases with post-Cy became a practice, to make a better comparison. A question was raised asking what additional information this study could provide versus other BMT/CTN studies. Dr. Saber emphasized that the CIBMTR has a very different population to those other studies. Lastly a question was raised on whether CIBMTR had information for Haploidentical donors; Dr. Saber replied that we have the data available.

e. **PROP 1811-72** Precision model to predict outcomes of myelofibrosis using artificial intelligence techniques. (S Hashmi/A Tefferi/N Gangat)

Dr. Sharukh Hashmi presented the proposal. The goal of the proposal was to develop a model for prediction of clinical outcomes post-allogeneic transplantation for primary myelofibrosis using machine learning algorithms. The hypothesis of this study is that machine learning algorithms can create a reliable prognostic model for predicting prognosis in myelofibrosis from complex data. There were 887 adult patients who underwent allo-HCT between 2000 and 2016 for primary MF, and that had survived 2 years post-HCT. Dr. Hashmi emphasized that there is a need of a new predictive model for MF that combines genomics and other modifiable factors such as smoking.

Comments on the study design and genomics data for this study were received. Dr. Saber replied that CIBMTR has JAK2 genomics information as YES/NO questions. Dr. Hashmi also replied that he would use Mayo Clinic and Cleveland Hospital data on genomics for the study. A question was made on what would be CIBMTR role on this study and how the datasets would be merged. Comments on why the investigator excluded the MDS patients in this proposal were received. Dr. Hashmi replied that the Mayo Clinic genomic database only contains patients with Primary Myelofibrosis (PMF). A question was raised on how CIBMTR collected therapy prior transplant and response was received. Another comment was made by the committee that there was a concern with the sample size needed to perform the machine learning technique. Audience also pointed out that extensive genomic data was only available on a minority of patients.

f. **PROP 1711-171** Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. (B Dholaria/B Savani/M Kharfan)

Dr. Bhagi Dholaria presented the proposal. The goal of the proposal was to evaluate outcomes of patients with CNL who underwent allo-HCT. There were 30 CNL patients between 2000 and 2017. Only 10 patients were from the CRF track, while 20 patients were TED track. Dr. Dholaria emphasized that there are not enough patients to conduct prospective studies and there aren't too many studies about this rare disease. He emphasized that even with this small number of patients this would be the largest cohort of CNL patients and results could eventually define the role of allo-HCT and management of the disease.

A suggestion made by an EBMT member was to merge their data base to CIBMTR. Another attendee suggested to include children in the study, since it is a rare disease. A question was raised asking if the CIBMTR had certainty about the diagnosis of CNL. Dr. Scott responded that it is acknowledged that there is misclassification error across centers. Dr. Saber added that CIBMTR has auditors to verify the diagnosis and classification reported by the centers. Another suggestion made by an attendee was to contact centers to get the mutation and other

important information from these patients. Another attendee suggested to include atypical CML patients into this study.

Dr. Sobecks mentioned that the proposals below were submitted and dropped for the listed reason below:

a. **PROP 1802-01** The role of allogeneic stem cell transplantation for chronic lymphocyte leukemia in the era of novel agents. *Dropped due to lack of long-term follow-up and insufficient number of eligible cases*.
b. **PROP 1805-01** BMT CTN ancillary study proposal utilizing biospecimens. *Dropped due to overlapping with existing project.*
c. **PROP 1810-05** Clinical outcome after allogeneic hematopoietic cell transplantation in chronic lymphocytic leukemia patients previously treated with novel therapies. *Dropped due to lack of long-term follow-up and insufficient number of eligible cases*.
d. **PROP 1811-24** Outcomes of haploidentical transplant in patients with MDS/MPN over the age of 50. *Dropped due to insufficient number of eligible cases.*
e. **PROP 1811-26** Use of maintenance/consolidation therapy post SCT in AML/MDS/MPN and effect on outcome. *No data on maintenance/ consolidation therapy for MDS*
f. **PROP 1811-28** Outcomes of haploidentical transplantation for myelofibrosis. *Dropped due to insufficient number of eligible cases.*
g. **PROP 1811-33** Evaluation the role of pre-HCT JAK inhibition in post-transplant outcomes in myelofibrosis. *Dropped due to overlapping with CK17-01.*
h. **PROP 1811-36** Allogeneic stem cell transplantation for chronic lymphocytic leukemias in the era of novel agents. *Dropped due to lack of long-term follow-up and insufficient number of eligible cases*.
i. **PROP 1811-107** Impact of fludarabine and melphalan dose on transplant outcomes in patients with myelodysplastic syndrome or AML undergoing RIC alloHCT. *Dropped due to overlapping with CK17-02.*
j. **PROP 1811-123** Comparison of outcomes in myelofibrosis after alternative types of allogeneic hematopoietic stem cell transplant. *Dropped due to insufficient number of eligible cases.*
k. **PROP 1811-134** Comparing outcomes between post-ET and post-PV myelofibrosis and primary myelofibrosis after allogeneic stem cell transplantation. *Dropped due to overlapping with CK17-01.*
l. **PROP 1811-145** Upfront vs. pre-transplant cytoreductive therapy prior to hematopoietic cell transplantation in adult patients with myelodysplastic syndrome. *Dropped due to overlapping with BMT-CTN study/not feasible using HCT registry data.*
m. **PROP 1811-178** Mutational predictors of outcomes following allogeneic blood or marrow transplantation for myelofibrosis. *Dropped due to lack of data on mutational predictors.*
n. **PROP 1811-187** Impact of prior ruxolitinib on post-hematopoietic stem cell transplant outcomes in myelofibrosis with splenomegaly. *Dropped due to overlapping with CK17-01.*

6. Study Results Presentations

Dr. Saber presented the PI's of these 4 committee studies which accomplished an important landmark during the past year.

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

Dr. Karen Ballen presented on behalf of Dr. Krisstina Gowin. Dr. Ballen pointed out the main objective of this study was to compare outcomes for patients with MF receiving HCT vs other

non-transplant therapies. The main conclusion found in the study was that there was a survival advantage found in HCT patients with DIPPS scores: Int-1, Int-2 and high-risk disease. Another finding seen was that there was an upfront TRM and a survival advantage was only seen after 14 months. These results may be practice changing for patients with Int-1 disease.

A comment was made on the banana shape survival curves and the intersecting curves. Dr. Saber replied that the change in the slope is what matters. Another comment was made on time of diagnosis to transplant. Comment was made on patients that where on the non-transplant group and the comparability between the groups. A comment was made on the low use of Jakafi in the transplant arm, Dr. Ballen replied that this was due to the timing of the approval and use of Jakafi.

b. **CK15-03** Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm. (V Gupta).

Dr. Saber presented on behalf of Dr. Viktas Gupta. The study compared patients with MPN-BP with de novo AML and post MDS-AML. The main finding was a very high relapse rate observed in the MPN-BP cohort, also the MPN-BP patients with blasts<5% had a higher relapse rate compared to de novo AML and post MDS AML with blasts <5%. The was no difference in relapse between cohorts with active leukemia. Also, no difference was found in NRM. The study also found that adverse cytogenetics is the only predictor for inferior survival and increased relapse in MPN-BP.

No comments were made by the audience.

c. **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).

Dr. George Selby presented on behalf of Dr. Sarah Schmidt. The purpose of this study was to evaluate the impact of primary DLI (DLI without TKI), primary TKI (TKI without a DLI), and the impact of a combination therapy (DLI+TKI) on CML patients that relapsed post HCT. The main conclusions of this study were: that the use of TKI containing regimen afforded the best OS. In relapse patients the presence of maintenance therapy afforded the higher survival. The presence of GVHD prior relapse showed no impact on survival. TKI salvage therapy affords superior survival over cellular therapy.

No comments were made by the audience.

d. **CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome. (A Nazha).

Dr. Betty Hamilton presented on behalf of Dr. Aziz Nazha. The main purpose of this study was to build a model that incorporates clinical/ mutational data to predict outcomes after HCT in patients with MDS using machine learning. Conclusions from this study was that this personalized prediction model could predict outcomes post HCT and provides probability of survival and relapse at different time points.

Comments were made on the individualized prediction for patients with rare mutations, Dr. Hamilton acknowledges that she couldn't quantify based on the data and it is a limitation. Another comment made was that it seemed that machine learning technique doesn't add much in compared to other old models. A question was raised on whether this was an adaptative model, in which we could add more data and variables.

7. Other Business

The meeting was adjourned at 4:40 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 the proposals using the provided voting sheets. Based on the voting results, 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. **PROP 1811-47/1811-54/1711-111** 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)
b. **PROP 1811-51** Alternative donor vs HLA matched donor hematopoietic cell transplantation in patients with myelodysplastic syndrome (R Mehta)
c. **PROP 1811-171** Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. (B Dholaria/B Savani/M Kharfan)

Working Committee Overview Plan for 2019-2020

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2019	Hours allocated 7/1/2019-6/30/2020	Total Hours allocated
CK12-01 Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era	Manuscript Preparation	Submitted – July 2019	10	10	10	10	20
CK14-02 Prognostic score and cytogenetic risk classification for chronic lymphocytic leukemia patients who underwent reduced intensity conditioning allogeneic HCT: a CIBMTR report	Submitted	Published – July 2019	0	0	0	0	0
CK15-01 Comparison of transplant versus non-transplant therapies for myelofibrosis	Manuscript Preparation	Submitted – July 2019	50	50	50	10	60
CK15-02 Comparison of outcomes after myeloablative versus reduced intensity conditioning for allogeneic hematopoietic stem cell transplant for chronic myeloid leukemia	Published	Published – July 2019	0	0	0	0	0
CK15-03 Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm	Manuscript Preparation	Submitted – July 2019	70	70	70	10	80
CK16-01 Identification of germline predisposition mutations in young myelodysplastic syndrome patients	Data File Preparation	Manuscript Preparation– July 2019	130	80	80	50	130
CK16-02a Contemporary role of maintenance tyrosine kinase inhibitors following allogeneic hematopoietic cell transplantation for chronic myeloid leukemia: a CIBMTR analysis	Submitted	Published – July 2019	0	10	0	10	10

CK16-02b The benefit of donor lymphocyte infusion in the tyrosine kinase inhibitors era in chronic myeloid leukemia post allogeneic hematopoietic cell transplantation	Manuscript Preparation	Submitted – July 2019	40	10	40	10	50
CK17-01 Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation	Data File Preparation	Analysis– July 2019	200	50	50	150	200
CK17-02 Reduced-intensity conditioning transplantation in older myelodysplastic syndrome: the effect of specific conditioning regimens on transplant outcomes	Data File Preparation	Manuscript Preparation– July 2019	160	90	90	70	160
CK18-01 A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes	Manuscript Preparation	Submitted – July 2019	70	70	70	10	80
CK18-02 The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia	Data File Preparation	Data File Preparation- July 2019	260	10	10	180	190
CK19-01 Outcomes after HCT for rare chronic leukemias	Protocol Pending	Data File Preparation- July 2020	330	100	0	100	100
CK19-02 Alternative donor versus HLA-matched donor hematopoietic cell transplantation in patients with myelodysplastic syndrome	Protocol Pending	Data File Preparation- July 2020	330	100	0	100	100

Working Assignments for Working Committee Leadership (March 2019)

Ronald Sobecks	**CK14-02** Validation of DFCI prognostic score for previously treated chronic lymphocytic leukemia patients who underwent reduced intensity conditioning allogeneic HSCT.
	CK15-02 Comparison of outcomes after MA vs. RIC for allogeneic HCT for CML.
	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.
Bart Scott	**CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes.
	CK18-02 The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia.
	CK17-01 Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation.
Ryotaro Nakamura	**PROP 1811-47/1811-54/1711-111/1811-171** Outcomes after HCT for rare chronic leukemias.
	PROP 1811-51 Alternative donor vs HLA matched donor hematopoietic cell transplantation in patients with myelodysplastic syndrome.
Wael Saber	**SC11-06** Assessment of allogeneic hematopoietic stem cell transplantation in Medicare beneficiaries with myelodysplastic syndrome and related disorders.

Accrual Summary for the Chronic Leukemia Working Committee

Characteristics of recipients undergoing allogeneic HCT for MDS reported to the CIBMTR between 1995 and 2019

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	7867	1333	5734	5215
No. of centers	191	153	191	252
Age, median (range) - median (min-max)	60.94 (0.45-83.42)	44.61 (0.34-76.54)	54.34 (0.01-80.79)	50.84 (0.32-79.67)
Age, years - no. (%)				
< 10	244 (3.1)	113 (8.5)	209 (3.6)	234 (4.5)
10-19	280 (3.6)	110 (8.3)	283 (4.9)	309 (5.9)
20-29	229 (2.9)	140 (10.5)	266 (4.6)	402 (7.7)
30-39	356 (4.5)	194 (14.6)	432 (7.5)	577 (11.1)
40-49	734 (9.3)	260 (19.5)	916 (16)	979 (18.8)
50-59	1842 (23.4)	314 (23.6)	1920 (33.5)	1384 (26.5)
60-69	3255 (41.4)	181 (13.6)	1564 (27.3)	1213 (23.3)
≥ 70	927 (11.8)	21 (1.6)	140 (2.4)	116 (2.2)
Missing	0	0	4 (0.1)	1 (0)
Sex - no. (%)				
Male	4882 (62.1)	809 (60.7)	3374 (58.8)	3146 (60.3)
Female	2985 (37.9)	523 (39.2)	2360 (41.2)	2063 (39.6)
Missing	0	1 (0.1)	0	6 (0.1)
Disease at diagnosis - no. (%)				
MDS unclassifiable, NOS	1272 (16.2)	138 (10.4)	1429 (24.9)	907 (17.4)
Refractory anemia (RA)	766 (9.7)	287 (21.5)	559 (9.7)	680 (13)
Refractory anemia excess blasts (RAEB)	3357 (42.7)	575 (43.1)	2218 (38.7)	2203 (42.2)
Chronic myelomonocytic leukemia (CMML)	746 (9.5)	132 (9.9)	515 (9)	453 (8.7)
Acquired idiopathic sideroblastic anemia (RARS)	314 (4)	38 (2.9)	197 (3.4)	131 (2.5)
Refactory anemia with multilineage dysplasia (RCMD)	995 (12.6)	100 (7.5)	616 (10.7)	606 (11.6)
Refactory anemia with dysplasia and ringed sideroblasts (RCMD/RS)	55 (0.7)	1 (0.1)	33 (0.6)	28 (0.5)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
5q- syndrome	99 (1.3)	4 (0.3)	81 (1.4)	40 (0.8)
Other MDS, specified	263 (3.3)	58 (4.4)	86 (1.5)	167 (3.2)
Graft source - no. (%)				
Bone marrow	1558 (19.8)	416 (31.2)	1231 (21.5)	1195 (22.9)
Peripheral blood	5745 (73)	830 (62.3)	4229 (73.8)	3809 (73)
Cord blood	546 (6.9)	87 (6.5)	205 (3.6)	116 (2.2)
Missing	18 (0.2)	0	69 (1.2)	95 (1.8)
Donor type - no. (%)				
HLA-identical sibling	1818 (23.1)	572 (42.9)	2335 (40.7)	2414 (46.3)
Haplo	388 (4.9)	46 (3.5)	213 (3.7)	36 (0.7)
Unrelated donor	4769 (60.6)	454 (34.1)	2548 (44.4)	2330 (44.7)
Cord blood	546 (6.9)	87 (6.5)	205 (3.6)	116 (2.2)
Other/missing	346 (4.4)	174 (13.1)	433 (7.6)	319 (6.1)
Year of transplant - no. (%)				
1995-1996	153 (1.9)	82 (6.2)	176 (3.1)	196 (3.8)
1997-1998	181 (2.3)	93 (7)	202 (3.5)	259 (5)
1999-2000	195 (2.5)	147 (11)	203 (3.5)	322 (6.2)
2001-2002	289 (3.7)	145 (10.9)	225 (3.9)	348 (6.7)
2003-2004	353 (4.5)	149 (11.2)	278 (4.8)	399 (7.7)
2005-2006	470 (6)	169 (12.7)	308 (5.4)	382 (7.3)
2007-2008	562 (7.1)	86 (6.5)	335 (5.8)	353 (6.8)
2009-2010	573 (7.3)	78 (5.9)	609 (10.6)	547 (10.5)
2011-2012	808 (10.3)	27 (2)	747 (13)	655 (12.6)
2013-2014	1236 (15.7)	122 (9.2)	637 (11.1)	526 (10.1)
2015-2016	1368 (17.4)	127 (9.5)	674 (11.8)	489 (9.4)
2017-2018	1298 (16.5)	89 (6.7)	945 (16.5)	572 (11)
2019	381 (4.8)	19 (1.4)	395 (6.9)	167 (3.2)

Characteristics of recipients undergoing allogeneic HCT for myelofibrosis reported to the CIBMTR between 1995 and 2019

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	1811	406	1385	1246
No. of centers	131	91	131	165
Age, median (range) - median (min-max)	59.79 (0.59-78.91)	53.79 (1.75-73.52)	57.83 (0.45-76.08)	54.97 (1.78-74.52)
Age, years - no. (%)				
< 10	10 (0.6)	3 (0.7)	16 (1.2)	10 (0.8)
10-19	11 (0.6)	7 (1.7)	10 (0.7)	24 (1.9)
20-29	12 (0.7)	10 (2.5)	20 (1.4)	32 (2.6)
30-39	48 (2.7)	25 (6.2)	53 (3.8)	106 (8.5)
40-49	238 (13.1)	98 (24.1)	214 (15.5)	251 (20.1)
50-59	608 (33.6)	153 (37.7)	517 (37.3)	459 (36.8)
60-69	751 (41.5)	107 (26.4)	507 (36.6)	343 (27.5)
≥ 70	133 (7.3)	3 (0.7)	48 (3.5)	21 (1.7)
Sex - no. (%)				
Male	1041 (57.5)	263 (64.8)	826 (59.6)	775 (62.2)
Female	770 (42.5)	143 (35.2)	559 (40.4)	471 (37.8)
Disease at diagnosis - no. (%)				
Polycythemia vera (PV)	234 (12.9)	45 (11.1)	181 (13.1)	93 (7.5)
Essential or primary thrombocythemia (ET)	291 (16.1)	49 (12.1)	196 (14.2)	147 (11.8)
Chronic myelofibrosis	1286 (71)	312 (76.8)	1008 (72.8)	1006 (80.7)
Graft source - no. (%)				
Bone marrow	183 (10.1)	81 (20)	130 (9.4)	191 (15.3)
Peripheral blood	1579 (87.2)	317 (78.1)	1230 (88.8)	1035 (83.1)
Cord blood	45 (2.5)	8 (2)	17 (1.2)	9 (0.7)
Missing	4 (0.2)	0	8 (0.6)	11 (0.9)
Donor type - no. (%)				
HLA-identical sibling	475 (26.2)	158 (38.9)	612 (44.2)	572 (45.9)
Haplo	87 (4.8)	12 (3)	38 (2.7)	4 (0.3)
Unrelated donor	1114 (61.5)	199 (49)	640 (46.2)	600 (48.2)
Cord blood	45 (2.5)	8 (2)	17 (1.2)	9 (0.7)
Other/missing	90 (5)	29 (7.1)	78 (5.6)	61 (4.9)
Year of transplant - no. (%)				

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
1995-1996	15 (0.8)	8 (2)	11 (0.8)	19 (1.5)
1997-1998	22 (1.2)	11 (2.7)	13 (0.9)	36 (2.9)
1999-2000	31 (1.7)	22 (5.4)	19 (1.4)	44 (3.5)
2001-2002	52 (2.9)	21 (5.2)	33 (2.4)	81 (6.5)
2003-2004	54 (3)	30 (7.4)	46 (3.3)	99 (7.9)
2005-2006	76 (4.2)	43 (10.6)	77 (5.6)	100 (8)
2007-2008	124 (6.8)	38 (9.4)	74 (5.3)	116 (9.3)
2009-2010	125 (6.9)	30 (7.4)	175 (12.6)	188 (15.1)
2011-2012	38 (2.1)	5 (1.2)	307 (22.2)	159 (12.8)
2013-2014	193 (10.7)	45 (11.1)	235 (17)	131 (10.5)
2015-2016	286 (15.8)	46 (11.3)	236 (17)	98 (7.9)
2017-2018	561 (31)	85 (20.9)	111 (8)	143 (11.5)
2019	234 (12.9)	22 (5.4)	48 (3.5)	32 (2.6)

Characteristics of recipients undergoing allogeneic HCT for CML reported to the CIBMTR between 1995 and 2019

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	4095	2946	4476	8418
No. of centers	178	194	203	275
Age, median (range) - median (min-max)	39.92 (1.14-76.82)	35.66 (1.11-75.96)	42.89 (0.3-76)	36.82 (0.26-75.45)
Age, years - no. (%)				
< 10	85 (2.1)	69 (2.3)	65 (1.5)	197 (2.3)
10-19	363 (8.9)	306 (10.4)	271 (6.1)	670 (8)
20-29	585 (14.3)	618 (21)	526 (11.8)	1671 (19.9)
30-39	1021 (24.9)	878 (29.8)	1018 (22.7)	2504 (29.7)
40-49	1171 (28.6)	700 (23.8)	1318 (29.4)	2244 (26.7)
50-59	715 (17.5)	320 (10.9)	924 (20.6)	978 (11.6)
60-69	139 (3.4)	53 (1.8)	322 (7.2)	143 (1.7)
≥ 70	16 (0.4)	1 (0)	23 (0.5)	4 (0)
Missing	0	1 (0)	9 (0.2)	7 (0.1)
Sex - no. (%)				
Male	2388 (58.3)	1803 (61.2)	2656 (59.3)	5046 (59.9)
Female	1707 (41.7)	1143 (38.8)	1813 (40.5)	3335 (39.6)
Missing	0	0	7 (0.2)	37 (0.4)
Graft source - no. (%)				
Bone marrow	2553 (62.3)	1703 (57.8)	2022 (45.2)	4649 (55.2)
Peripheral blood	1358 (33.2)	1164 (39.5)	2239 (50)	3366 (40)
Cord blood	183 (4.5)	74 (2.5)	138 (3.1)	102 (1.2)
Missing	1 (0)	5 (0.2)	77 (1.7)	301 (3.6)
Donor type - no. (%)				
HLA-identical sibling	874 (21.3)	1609 (54.6)	2636 (58.9)	5419 (64.4)
Haplo	56 (1.4)	14 (0.5)	102 (2.3)	6 (0.1)
Unrelated donor	2821 (68.9)	968 (32.9)	1108 (24.8)	2347 (27.9)
Cord blood	183 (4.5)	74 (2.5)	138 (3.1)	102 (1.2)
Other/missing	161 (3.9)	281 (9.5)	492 (11)	544 (6.5)
Year of transplant - no. (%)				
1995-1996	711 (17.4)	498 (16.9)	656 (14.7)	1344 (16)
1997-1998	754 (18.4)	547 (18.6)	723 (16.2)	1741 (20.7)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
1999-2000	676 (16.5)	629 (21.4)	616 (13.8)	1775 (21.1)
2001-2002	357 (8.7)	391 (13.3)	277 (6.2)	1204 (14.3)
2003-2004	408 (10)	370 (12.6)	252 (5.6)	742 (8.8)
2005-2006	318 (7.8)	270 (9.2)	176 (3.9)	428 (5.1)
2007-2008	238 (5.8)	54 (1.8)	133 (3)	215 (2.6)
2009-2010	247 (6)	54 (1.8)	159 (3.6)	273 (3.2)
2011-2012	52 (1.3)	14 (0.5)	388 (8.7)	258 (3.1)
2013-2014	126 (3.1)	44 (1.5)	328 (7.3)	161 (1.9)
2015-2016	114 (2.8)	40 (1.4)	324 (7.2)	112 (1.3)
2017-2018	69 (1.7)	23 (0.8)	345 (7.7)	115 (1.4)
2019	25 (0.6)	12 (0.4)	99 (2.2)	50 (0.6)

Characteristics of recipients undergoing allogeneic HCT for CLL reported to the CIBMTR between 1995 and 2019

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	1497	395	1911	1432
No. of centers	126	83	135	148
Age, median (range) - median (min-max)	55.35 (11.67-75.16)	53.64 (1.68-73.05)	56.53 (7.31-80.45)	53.47 (3.91-74.1)
Age, years - no. (%)				
< 10	0	1 (0.3)	2 (0.1)	3 (0.2)
10-19	3 (0.2)	1 (0.3)	2 (0.1)	0
20-29	12 (0.8)	1 (0.3)	15 (0.8)	23 (1.6)
30-39	65 (4.3)	34 (8.6)	81 (4.2)	77 (5.4)
40-49	340 (22.7)	102 (25.8)	352 (18.4)	380 (26.5)
50-59	645 (43.1)	168 (42.5)	833 (43.6)	657 (45.9)
60-69	398 (26.6)	85 (21.5)	579 (30.3)	282 (19.7)
≥ 70	34 (2.3)	3 (0.8)	47 (2.5)	10 (0.7)
Sex - no. (%)				
Male	1113 (74.3)	289 (73.2)	1385 (72.5)	1038 (72.5)
Female	383 (25.6)	106 (26.8)	525 (27.5)	392 (27.4)
Missing	1 (0.1)	0	1 (0.1)	2 (0.1)
Disease at diagnosis - no. (%)				
Chronic lymphocytic leukemia, NOS	710 (47.4)	132 (33.4)	573 (30)	604 (42.2)
Chronic lymphocytic leukemia, B-cell	783 (52.3)	263 (66.6)	1327 (69.4)	822 (57.4)
Chronic lymphocytic leukemia, T-cell	4 (0.3)	0	11 (0.6)	6 (0.4)
Graft source - no. (%)				
Bone marrow	300 (20)	61 (15.4)	254 (13.3)	161 (11.2)
Peripheral blood	1108 (74)	320 (81)	1617 (84.6)	1219 (85.1)
Cord blood	87 (5.8)	13 (3.3)	33 (1.7)	17 (1.2)
Missing	2 (0.1)	1 (0.3)	7 (0.4)	35 (2.4)
Donor type - no. (%)				
HLA-identical sibling	412 (27.5)	225 (57)	972 (50.9)	783 (54.7)
Haplo	43 (2.9)	2 (0.5)	60 (3.1)	1 (0.1)
Unrelated donor	891 (59.5)	140 (35.4)	722 (37.8)	559 (39)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Cord blood	87 (5.8)	13 (3.3)	33 (1.7)	17 (1.2)
Other/missing	64 (4.3)	15 (3.8)	124 (6.5)	72 (5)
Year of transplant - no. (%)				
1995-1996	61 (4.1)	29 (7.3)	46 (2.4)	34 (2.4)
1997-1998	57 (3.8)	22 (5.6)	63 (3.3)	41 (2.9)
1999-2000	85 (5.7)	36 (9.1)	87 (4.6)	101 (7.1)
2001-2002	108 (7.2)	44 (11.1)	125 (6.5)	163 (11.4)
2003-2004	179 (12)	49 (12.4)	121 (6.3)	164 (11.5)
2005-2006	210 (14)	55 (13.9)	165 (8.6)	184 (12.8)
2007-2008	258 (17.2)	33 (8.4)	181 (9.5)	146 (10.2)
2009-2010	115 (7.7)	24 (6.1)	392 (20.5)	186 (13)
2011-2012	56 (3.7)	14 (3.5)	426 (22.3)	233 (16.3)
2013-2014	175 (11.7)	48 (12.2)	156 (8.2)	101 (7.1)
2015-2016	96 (6.4)	20 (5.1)	56 (2.9)	41 (2.9)
2017-2018	88 (5.9)	19 (4.8)	77 (4)	29 (2)
2019	9 (0.6)	2 (0.5)	16 (0.8)	9 (0.6)

Characteristics of recipients undergoing autologous HCT for CLL reported to the CIBMTR between 1995 and 2019

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	84	41	273	244
No. of centers	42	14	67	58
Age, median (range) - median (min-max)	51.86 (33.18-73.05)	49.78 (38.37-67.23)	53.13 (19.07-80.79)	52.09 (27.39-71.92)
Age, years - no. (%)				
10-19	0	0	1 (0.4)	0
20-29	0	0	2 (0.7)	4 (1.6)
30-39	12 (14.3)	3 (7.3)	14 (5.1)	12 (4.9)
40-49	25 (29.8)	18 (43.9)	81 (29.7)	76 (31.1)
50-59	26 (31)	18 (43.9)	113 (41.4)	114 (46.7)
60-69	19 (22.6)	2 (4.9)	57 (20.9)	37 (15.2)
≥ 70	2 (2.4)	0	5 (1.8)	1 (0.4)
Sex - no. (%)				
Male	61 (72.6)	33 (80.5)	191 (70)	194 (79.5)
Female	23 (27.4)	8 (19.5)	82 (30)	49 (20.1)
Missing	0	0	0	1 (0.4)
Disease at diagnosis - no. (%)				
Chronic lymphocytic leukemia, NOS	21 (25)	24 (58.5)	85 (31.1)	48 (19.7)
Chronic lymphocytic leukemia, B-cell	62 (73.8)	17 (41.5)	183 (67)	195 (79.9)
Chronic lymphocytic leukemia, T-cell	1 (1.2)	0	5 (1.8)	1 (0.4)
Graft source - no. (%)				
Bone marrow	15 (17.9)	1 (2.4)	113 (41.4)	5 (2)
Peripheral blood	66 (78.6)	39 (95.1)	154 (56.4)	208 (85.2)
Missing	3 (3.6)	1 (2.4)	6 (2.2)	31 (12.7)
Year of transplant - no. (%)				
1995-1996	15 (17.9)	3 (7.3)	43 (15.8)	14 (5.7)
1997-1998	26 (31)	28 (68.3)	54 (19.8)	36 (14.8)
1999-2000	18 (21.4)	6 (14.6)	73 (26.7)	90 (36.9)
2001-2002	6 (7.1)	2 (4.9)	36 (13.2)	40 (16.4)
2003-2004	4 (4.8)	1 (2.4)	27 (9.9)	22 (9)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
2005-2006	9 (10.7)	0	7 (2.6)	23 (9.4)
2007-2008	3 (3.6)	0	6 (2.2)	4 (1.6)
2009-2010	2 (2.4)	0	5 (1.8)	8 (3.3)
2011-2012	0	0	9 (3.3)	5 (2)
2013-2014	1 (1.2)	0	5 (1.8)	1 (0.4)
2015-2016	0	1 (2.4)	2 (0.7)	0
2017-2018	0	0	4 (1.5)	1 (0.4)
2019	0	0	2 (0.7)	0

Unrelated Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	11197	3571	2013
Source of data			
CRF	7827 (70)	2361 (66)	1366 (68)
TED	3370 (30)	1210 (34)	647 (32)
Number of centers	228	190	259
Disease at transplant			
Other leukemia	1340 (12)	349 (10)	235 (12)
CML	3283 (29)	894 (25)	747 (37)
MDS	6574 (59)	2328 (65)	1031 (51)
MDS Disease status at transplant			
Early	1299 (20)	383 (17)	236 (23)
Advanced	4769 (73)	1811 (78)	644 (63)
Missing	465 (7)	121 (5)	140 (14)
Recipient age at transplant			
0-9 years	395 (4)	80 (2)	98 (5)
10-19 years	533 (5)	141 (4)	143 (7)
20-29 years	787 (7)	197 (6)	204 (10)
30-39 years	1336 (12)	342 (10)	277 (14)
40-49 years	1940 (17)	545 (15)	414 (21)
50-59 years	2729 (24)	858 (24)	449 (22)
60-69 years	2892 (26)	1127 (32)	374 (19)
70+ years	585 (5)	281 (8)	54 (3)
Median (Range)	53 (0-83)	56 (1-79)	47 (1-79)
Recipient race/ethnicity			
Caucasian, non-Hispanic	9728 (90)	3148 (90)	1580 (88)
African-American, non-Hispanic	494 (5)	119 (3)	87 (5)
Asian, non-Hispanic	182 (2)	92 (3)	60 (3)
Pacific islander, non-Hispanic	15 (<1)	6 (<1)	5 (<1)
Native American, non-Hispanic	34 (<1)	11 (<1)	6 (<1)
Hispanic	391 (4)	106 (3)	47 (3)
Other	19 (<1)	7 (<1)	5 (<1)
Unknown	334 (N/A)	82 (N/A)	223 (N/A)
Recipient sex			
Male	6866 (61)	2232 (63)	1207 (60)
Female	4331 (39)	1339 (37)	806 (40)
Karnofsky score			
10-80	3712 (33)	1283 (36)	577 (29)
90-100	7067 (63)	2142 (60)	1279 (64)
Missing	418 (4)	146 (4)	157 (8)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
HLA-A B DRB1 groups - low resolution			
<=3/6	5 (<1)	6 (<1)	1 (<1)
4/6	88 (1)	25 (1)	9 (<1)
5/6	1502 (14)	377 (12)	267 (15)
6/6	9459 (86)	2751 (87)	1532 (85)
Unknown	143 (N/A)	412 (N/A)	204 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	316 (3)	17 (1)	4 (<1)
6/8	514 (5)	20 (1)	33 (3)
7/8	2054 (19)	336 (15)	214 (20)
8/8	7988 (73)	1888 (84)	824 (77)
Unknown	325 (N/A)	1310 (N/A)	938 (N/A)
HLA-DPB1 Match			
Double allele mismatch	2798 (30)	202 (22)	94 (28)
Single allele mismatch	5057 (54)	489 (53)	169 (50)
Full allele matched	1476 (16)	239 (26)	76 (22)
Unknown	1866 (N/A)	2641 (N/A)	1674 (N/A)
High resolution release score			
No	2156 (19)	3510 (98)	1966 (98)
Yes	9041 (81)	61 (2)	47 (2)
KIR typing available			
No	7885 (70)	3538 (99)	2002 (99)
Yes	3312 (30)	33 (1)	11 (1)
Graft type			
Marrow	4203 (38)	1178 (33)	947 (47)
PBSC	6979 (62)	2362 (66)	1051 (52)
BM+PBSC	4 (<1)	0	1 (<1)
PBSC+UCB	3 (<1)	30 (1)	0
Others	8 (<1)	1 (<1)	14 (1)
Number of cord blood units			
1	3 (100)	0	0
Conditioning regimen			
Myeloablative	6946 (62)	1999 (56)	1341 (67)
RIC/Nonmyeloablative	4215 (38)	1562 (44)	641 (32)
TBD	36 (<1)	10 (<1)	31 (2)
Donor age at donation			
To Be Determined/NA	58 (1)	318 (9)	23 (1)
0-9 years	0	10 (<1)	0
10-19 years	285 (3)	111 (3)	35 (2)
20-29 years	4717 (42)	1496 (42)	683 (34)
30-39 years	3362 (30)	909 (25)	657 (33)
40-49 years	2109 (19)	544 (15)	466 (23)
50+ years	666 (6)	183 (5)	149 (7)
Median (Range)	32 (13-62)	30 (1-109)	34 (19-60)
Donor/Recipient CMV serostatus			
+/+	2561 (23)	913 (26)	493 (26)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
+/-	1425 (13)	503 (14)	227 (12)
-/+	3475 (31)	984 (28)	582 (31)
-/-	3613 (33)	1082 (31)	596 (31)
CB - recipient +	0	4 (<1)	0
Unknown	123 (N/A)	85 (N/A)	115 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	269 (2)	65 (2)	69 (3)
CD34 selection	155 (1)	76 (2)	23 (1)
Post-CY + other(s)	322 (3)	197 (6)	60 (3)
Post-CY alone	15 (<1)	6 (<1)	5 (<1)
Tacrolimus + MMF +- others	1388 (12)	359 (10)	174 (9)
Tacrolimus + MTX +- others (except MMF)	4703 (42)	1607 (45)	537 (27)
Tacrolimus + others (except MTX, MMF)	579 (5)	251 (7)	65 (3)
Tacrolimus alone	223 (2)	71 (2)	22 (1)
CSA + MMF +- others (except Tacrolimus)	664 (6)	164 (5)	152 (8)
CSA + MTX +- others (except Tacrolimus, MMF)	2221 (20)	587 (16)	706 (35)
CSA + others (except Tacrolimus, MTX, MMF)	241 (2)	66 (2)	73 (4)
CSA alone	110 (1)	25 (1)	66 (3)
Other GVHD prophylaxis	206 (2)	60 (2)	28 (1)
Missing	101 (1)	37 (1)	33 (2)
Donor/Recipient sex match			
Male-Male	4843 (43)	1538 (44)	824 (42)
Male-Female	2571 (23)	792 (23)	423 (21)
Female-Male	1984 (18)	644 (18)	368 (19)
Female-Female	1737 (16)	515 (15)	370 (19)
CB - recipient M	2 (<1)	22 (1)	0
CB - recipient F	3 (<1)	9 (<1)	0
Unknown	57 (N/A)	51 (N/A)	28 (N/A)
Year of transplant			
1986-1990	180 (2)	23 (1)	34 (2)
1991-1995	847 (8)	190 (5)	266 (13)
1996-2000	1286 (11)	488 (14)	315 (16)
2001-2005	1307 (12)	236 (7)	373 (19)
2006-2010	2221 (20)	450 (13)	315 (16)
2011-2015	3313 (30)	938 (26)	394 (20)
2016-2019	2043 (18)	1246 (35)	316 (16)
Follow-up among survivors, Months			
N Eval	4459	1675	756
Median (Range)	61 (0-362)	36 (0-336)	60 (3-337)

Unrelated Cord Blood Transplant Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired, recipient only and cord blood only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006-recipient only), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	728	202	161
Source of data			
CRF	573 (79)	155 (77)	105 (65)
TED	155 (21)	47 (23)	56 (35)
Number of centers	109	72	83
Disease at transplant			
Other leukemia	91 (13)	26 (13)	24 (15)
CML	117 (16)	33 (16)	31 (19)
MDS	520 (71)	143 (71)	106 (66)
MDS Disease status at transplant			
Early	163 (31)	36 (26)	48 (46)
Advanced	323 (62)	99 (70)	46 (44)
Missing	33 (6)	6 (4)	11 (10)
Recipient age at transplant			
0-9 years	104 (14)	28 (14)	36 (22)
10-19 years	70 (10)	13 (6)	19 (12)
20-29 years	53 (7)	9 (4)	12 (7)
30-39 years	67 (9)	21 (10)	14 (9)
40-49 years	104 (14)	25 (12)	18 (11)
50-59 years	155 (21)	45 (22)	36 (22)
60-69 years	144 (20)	50 (25)	24 (15)
70+ years	31 (4)	11 (5)	2 (1)
Median (Range)	47 (0-80)	51 (1-76)	40 (0-73)
Recipient race/ethnicity			
Caucasian, non-Hispanic	444 (63)	139 (70)	103 (70)
African-American, non-Hispanic	120 (17)	26 (13)	23 (16)
Asian, non-Hispanic	43 (6)	14 (7)	11 (7)
Pacific islander, non-Hispanic	6 (1)	0	2 (1)
Native American, non-Hispanic	3 (<1)	0	1 (1)
Hispanic	89 (13)	21 (11)	7 (5)
Other	0	0	1 (1)
Unknown	23 (N/A)	2 (N/A)	13 (N/A)
Recipient sex			
Male	430 (59)	124 (61)	92 (57)
Female	298 (41)	78 (39)	69 (43)
Karnofsky score			
10-80	183 (25)	59 (29)	42 (26)
90-100	530 (73)	129 (64)	105 (65)
Missing	15 (2)	14 (7)	14 (9)
HLA-A B DRB1 groups - low resolution			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
<=3/6	8 (1)	6 (4)	1 (1)
4/6	313 (45)	81 (53)	75 (50)
5/6	305 (44)	55 (36)	69 (46)
6/6	73 (10)	10 (7)	6 (4)
Unknown	29 (N/A)	50 (N/A)	10 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	377 (61)	74 (67)	78 (63)
6/8	147 (24)	19 (17)	33 (27)
7/8	64 (10)	16 (14)	10 (8)
8/8	27 (4)	2 (2)	3 (2)
Unknown	113 (N/A)	91 (N/A)	37 (N/A)
HLA-DPB1 Match			
Double allele mismatch	111 (47)	5 (38)	6 (46)
Single allele mismatch	113 (47)	6 (46)	5 (38)
Full allele matched	14 (6)	2 (15)	2 (15)
Unknown	490 (N/A)	189 (N/A)	148 (N/A)
High resolution release score			
No	538 (74)	199 (99)	160 (99)
Yes	190 (26)	3 (1)	1 (1)
KIR typing available			
No	570 (78)	202 (100)	160 (99)
Yes	158 (22)	0	1 (1)
Number of cord blood units			
1	587 (81)	0	132 (82)
2	141 (19)	0	29 (18)
Unknown	0 (N/A)	202 (N/A)	0 (N/A)
Graft type			
UCB	677 (93)	172 (85)	155 (96)
PBSC+UCB	51 (7)	30 (15)	6 (4)
Conditioning regimen			
Myeloablative	408 (56)	103 (51)	95 (59)
RIC/Nonmyeloablative	320 (44)	98 (49)	66 (41)
TBD	0	1 (<1)	0
Donor age at donation			
To Be Determined/NA	23 (3)	11 (5)	9 (6)
0-9 years	643 (88)	154 (76)	148 (92)
10-19 years	36 (5)	17 (8)	1 (1)
20-29 years	8 (1)	7 (3)	0
30-39 years	9 (1)	4 (2)	0
40-49 years	6 (1)	4 (2)	0
50+ years	3 (<1)	5 (2)	3 (2)
Median (Range)	3 (0-64)	4 (0-72)	3 (0-61)
Donor/Recipient CMV serostatus			
+/+	158 (22)	36 (18)	40 (25)
+/-	84 (12)	12 (6)	13 (8)
-/+	148 (20)	52 (26)	26 (16)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
-/-	94 (13)	26 (13)	20 (12)
CB - recipient +	132 (18)	42 (21)	27 (17)
CB - recipient -	106 (15)	27 (13)	27 (17)
CB - recipient CMV unknown	6 (1)	7 (3)	8 (5)
GvHD Prophylaxis			
Ex vivo T-cell depletion	1 (<1)	1 (<1)	0
CD34 selection	40 (5)	26 (13)	7 (4)
Post-CY to other(s)	0	1 (<1)	0
Tacrolimus + MMF +- others	215 (30)	57 (28)	25 (16)
Tacrolimus + MTX +- others (except MMF)	25 (3)	4 (2)	5 (3)
Tacrolimus + others (except MTX, MMF)	32 (4)	8 (4)	8 (5)
Tacrolimus alone	25 (3)	9 (4)	4 (2)
CSA + MMF +- others (except Tacrolimus)	314 (43)	77 (38)	81 (50)
CSA + MTX +- others (except Tacrolimus, MMF)	9 (1)	2 (1)	4 (2)
CSA + others (except Tacrolimus, MTX, MMF)	26 (4)	10 (5)	20 (12)
CSA alone	9 (1)	1 (<1)	3 (2)
Other GVHD prophylaxis	30 (4)	6 (3)	3 (2)
Missing	2 (<1)	0	1 (1)
Donor/Recipient sex match			
CB - recipient M	430 (59)	124 (61)	92 (57)
CB - recipient F	298 (41)	78 (39)	69 (43)
Year of transplant			
2001-2005	16 (2)	5 (2)	4 (2)
2006-2010	238 (33)	65 (32)	60 (37)
2011-2015	352 (48)	71 (35)	76 (47)
2016-2019	122 (17)	61 (30)	21 (13)
Follow-up among survivors, Months			
N Eval	290	97	79
Median (Range)	60 (3-159)	47 (3-149)	59 (1-164)

Related Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired, recipient only and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	1720	238	114
Source of data			
CRF	902 (52)	106 (45)	71 (62)
TED	818 (48)	132 (55)	43 (38)
Number of centers	69	39	25
Disease at transplant			
Other leukemia	170 (10)	30 (13)	18 (16)
CML	256 (15)	26 (11)	11 (10)
MDS	1294 (75)	182 (76)	85 (75)
MDS Disease status at transplant			
Early	203 (16)	21 (12)	16 (19)
Advanced	1051 (81)	151 (83)	67 (79)
Missing	40 (3)	10 (5)	2 (2)
Recipient age at transplant			
0-9 years	36 (2)	6 (3)	0
10-19 years	60 (3)	4 (2)	2 (2)
20-29 years	46 (3)	13 (5)	2 (2)
30-39 years	75 (4)	13 (5)	3 (3)
40-49 years	205 (12)	18 (8)	10 (9)
50-59 years	520 (30)	60 (25)	34 (30)
60-69 years	660 (38)	109 (46)	59 (52)
70+ years	118 (7)	15 (6)	4 (4)
Median (Range)	59 (1-78)	61 (2-76)	61 (17-74)
Recipient race/ethnicity			
Caucasian, non-Hispanic	1285 (77)	157 (68)	90 (82)
African-American, non-Hispanic	137 (8)	21 (9)	7 (6)
Asian, non-Hispanic	71 (4)	13 (6)	3 (3)
Pacific islander, non-Hispanic	8 (<1)	1 (<1)	0
Native American, non-Hispanic	5 (<1)	1 (<1)	1 (1)
Hispanic	172 (10)	38 (16)	9 (8)
Unknown	42 (N/A)	7 (N/A)	4 (N/A)
Recipient sex			
Male	1037 (60)	147 (62)	74 (65)
Female	683 (40)	91 (38)	40 (35)
Karnofsky score			
10-80	690 (40)	112 (47)	62 (54)
90-100	999 (58)	118 (50)	46 (40)
Missing	31 (2)	8 (3)	6 (5)
Graft type			
Marrow	276 (16)	31 (13)	22 (19)
PBSC	1433 (83)	205 (86)	92 (81)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
BM+PBSC	4 (<1)	0	0
BM+UCB	0	1 (<1)	0
Others	7 (<1)	1 (<1)	0
Conditioning regimen			
Myeloablative	846 (49)	117 (49)	48 (42)
RIC/Nonmyeloablative	872 (51)	120 (50)	66 (58)
TBD	2 (<1)	1 (<1)	0
Donor age at donation			
To Be Determined/NA	2 (<1)	1 (<1)	0
0-9 years	26 (2)	3 (1)	0
10-19 years	65 (4)	10 (4)	5 (4)
20-29 years	135 (8)	16 (7)	9 (8)
30-39 years	187 (11)	29 (12)	16 (14)
40-49 years	308 (18)	33 (14)	17 (15)
50+ years	997 (58)	146 (61)	67 (59)
Median (Range)	53 (0-80)	54 (1-75)	54 (17-73)
Donor/Recipient CMV serostatus			
+/+	674 (40)	97 (42)	42 (38)
+/-	220 (13)	14 (6)	17 (15)
-/+	396 (23)	57 (24)	23 (21)
-/-	407 (24)	65 (28)	30 (27)
Unknown	23 (N/A)	5 (N/A)	2 (N/A)
GvHD Prophylaxis			
Ex-vivo T-cell depletion	9 (1)	3 (1)	2 (2)
CD34 selection	11 (1)	8 (3)	0
Post-CY + other(s)	386 (22)	47 (20)	29 (25)
Post-CY alone	6 (<1)	0	0
TAC + MMF +- other(s) (except post-CY)	189 (11)	12 (5)	2 (2)
TAC + MTX +- other(s) (except MMF, post-CY)	753 (44)	113 (47)	64 (56)
TAC + other(s) (except MMF, MTX, post-CY)	160 (9)	36 (15)	13 (11)
TAC alone	14 (1)	3 (1)	0
CSA + MMF +- other(s) (except post-CY)	34 (2)	3 (1)	0
CSA + MTX +- other(s) (except MMF, post-CY)	94 (5)	12 (5)	1 (1)
CSA + other(s) (except MMF, MTX, post-CY)	1 (<1)	1 (<1)	0
CSA alone	9 (1)	0	0
Other(s)	26 (2)	0	2 (2)
Missing	28 (2)	0	1 (1)
Donor/Recipient sex match			
Male-Male	577 (34)	84 (35)	39 (34)
Male-Female	365 (21)	43 (18)	23 (20)
Female-Male	456 (27)	62 (26)	35 (31)
Female-Female	318 (19)	47 (20)	17 (15)
Unknown	4 (N/A)	2 (N/A)	0 (N/A)
Year of transplant			
2006-2010	143 (8)	20 (8)	10 (9)
2011-2015	793 (46)	90 (38)	42 (37)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
2016-2019	784 (46)	128 (54)	62 (54)
Follow-up among survivors, Months			
N Eval	976	130	66
Median (Range)	35 (1-123)	19 (2-124)	23 (2-123)

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Chronic Leukemia Working Committee Members

FROM: Wael Saber, MD, MS; Scientific Director for the Chronic Leukemia Working Committee

RE: 2019-2020 Studies in Progress Summary

CK12-01 Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era. (B Hu/H Lee) The objectives of the study are: 1) to estimate residual life expectancies for patients diagnosed with CML in CP based on the timing of various allo-HSCT strategies using data from both MD Anderson Cancer Center and the CIBMTR databases; 2) to calculate residual life expectancies for patients who did not undergo allo-HSCT and continued their TKI therapies. The manuscript is submitted. The goal of the study is to have the manuscript published by June 2020.

CK15-01 Comparison of transplant vs. non-transplant therapies for myelofibrosis. (KL Gowin/K Ballen/RA Mesa) The primary objectives of the study are: 1) to compare survivals after HCT vs. non-transplant therapies for myelofibrosis; 2) to determine patient-, disease-, and treatment-related prognostic factors that are associated with superior survival. The manuscript is submitted. The goal of the study is to have the manuscript published by June 2020.

CK15-03 Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm. (V Gupta) The primary aims of the study are: 1) to compare outcomes of HCT in patients with leukemic transformation from Philadelphia-negative MPN to those patients with de novo leukemia and to patients with leukemic transformation from MDS; 2) to identify patient, disease and transplant related factors associated with outcomes. The PI is working on the manuscript. The goal of the study is to have the manuscripts finalized and submitted by June 2020.

Companion study to CK15-03: Impact of genetic mutations on outcomes of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm. (V Gupta) The primary aims of the study are: 1) to evaluate the impact of genetic mutations on outcomes of AML with previous history of MPN, using targeted sequencing; 2) compare the mutation profile of patients whose disease was considered in remission at the time of transplant with those with active disease at the time of HCT. The abstract of this study will be presented at TCT. The PI is working on the manuscript. The goal of the study is to have the manuscript finalized and submitted by June 2020.

CK16-01 Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley) The primary aims of the study are: 1) to determine the frequency of germline variants in candidate genes in a cohort of paired samples derived from patients with myelodysplastic syndromes and their HLA-matched related donors; 2) to compare clinical/mobilization characteristics in related donors with a germline mutation versus related donors without germline mutations; 3) to compare engraftment parameters in MDS patients with germline deleterious mutations who underwent HCT from HLA-matched related donors who shared the germline variant versus those who do not share the variant. The protocol of the study has been presented and circulated among the working committee members. The PI is currently working on sequencing the DNA samples. The goal of this study is to finalize the analysis by June 2020.

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) The objective of the study is to compare differences in overall survival among CML patients who relapsed post HCT and went on to receive either: TKI alone or DLI (including DLI + TKI or DLI + others). The manuscript is submitted. The goal of this study is to have the manuscript published by June 2020.

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) The primary objective of the study is to identify patient-, disease-, and transplant-specific factors that positively associate with overall survival after allo-HCT for patients with myelofibrosis; the secondary objective is to develop a scoring system prognostic of OS post allo-HCT; the third objective is to validate the scoring system in an independent dataset. This study is in collaboration with the EBMT, currently pending resolution on data sharing agreement between CIBMTR and EBMT to validate score. The goal of this study is to complete the validation analysis by June 2020.

CK17-02 Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. (B Oran) The objective of the study is to compare the two most commonly utilized RIC regimens (Flu/mel vs. FB2) with respect to their impact on post HCT outcomes in older MDS patients undergoing RIC HCT. The PI is currently working on the draft manuscript. The study was presented orally at ASH 2019. The goal of this study is to have submitted the manuscript by June 2020.

CK18-01 A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome (A Nazha) The objectives of this study are: 1) build a personalized prediction model that can precisely predict outcomes after allogeneic stem cell transplant in MDS patients using state of the art multiple machine learning algorithms; 2) incorporate genomic and clinical data to develop the model; 3) evaluate the variable interactions between the genomic and clinical data that impact outcomes after transplant using variable interactions and variable dependence functions. The PI is currently working on the draft manuscript. The goal of this study is to have the manuscript submitted and published by June 2020.

CK18-02 The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/ R Nakamura/ R Pillai) The primary aims of this study are: 1) determine the impact of somatic mutations and copy numbers variants on outcomes after alloHCT in patients with CMML; 2) determine if the CPSS-Mol score correlates with outcomes after alloHCT in patients with CMML to improve the scoring system for alloHCT recipients with broader mutation analyses. The PI is currently working on sequencing the DNA samples. The goal of this study is to have completed the analysis by June 2020.

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) The primary objectives of this study are to describe clinical outcomes of patients with T-cell prolymphocytic leukemia undergoing allo-HCT which includes 1) calculate the overall survival 2) estimate Progression Free Survival 3) estimate the cumulative incidence of non-relapse mortality 4) calculate the cumulative incidence of acute graft versus host disease (aGVHD) 5) calculate the cumulative incidence of chronic graft versus host disease (aGVHD) and estimate the cumulative incidence of relapse. Also identify the impact of patient-, disease-, and transplant-related factors on the outcomes. The statistician is working on the protocol development. The goal of this study is to have the final protocol by June 2020.

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) The primary objectives of this study are to describe clinical outcomes of patients with chronic neutrophilic leukemia undergoing first allo-HCT reported to the CIBMTR and EBMT. For this purpose of this study we'll calculate: the overall survival, leukemia free survival and relapse of the patients. This will may provide the largest experience of using allo-HCT in CNL and potentially define the curative role of allo-HCT for this disease. The statistician is working on the protocol development. This study is in collaboration with the EBMT, currently pending resolution on data sharing agreement between CIBMTR and EBMT. The goal of this study is to have the final protocol by June 2020.

Proposal: 1911-08

Title:
Myelodysplastic/ myeloproliferative neoplasms unclassifiable- Transplant outcomes and factors predicting survival- Retrospective analysis of chronic leukaemia working party of CIBMTR

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Scientific justification:
Myelodysplastic/myeloproliferative neoplasms, unclassifiable (MDS/MPN-U) represent a unique but poorly characterized subtype of MDS/MPN overlap syndrome without any effective disease modifying therapies and dismal outcomes, with a median overall survival of 2 years (Mangaonkar A et al. Leukemia 2019). Allogeneic hematopoietic stem cell transplantation (HCT) remains the only curative modality, but transplant-specific outcomes and prognosis (which patients benefit and whether pursuing an allogeneic HCT overcomes the adverse prognostic impact as predicted by the conventional prognostic scoring systems), among patients with MDS/MPN-U have not been addressed. Due to the relative rarity of this disease, conducting randomized prospective trials or large retrospective studies is not feasible. Therefore, we aim to utilize the unique resources of CIBMTR to answer these important clinical questions.

Scientific background:
Myelodysplastic/myeloproliferative neoplasm unclassifiable (MDS/MPN-U) has been categorized as a rare disorder within the subgroup of myelodysplastic/myeloproliferative neoplasms (MDS/MPN) [1], and is usually considered as a diagnosis of exclusion. Very similar to its closest counterpart chronic myelomonocytic leukaemia (CMML), it has features of myeloproliferation and dysplasia, however, its clinicopathological characteristics with genotypic correlation, prognosis and outcomes[2] have not been well-defined. [3 4 5 6] In addition, survival, outcomes and risk of evolution into acute myeloid leukaemia (AML) also vary across different studies [7 8].
It has been shown recently, and in the past, in studies involving various forms of treatment modalities, that survival correlates well with already defined prognostic classification based on IPSS/IPSS-R [9 10] as well as MD Anderson (MDA) [11] scoring system for MDS (myelodysplastic syndrome- incorporating hematologic indices, cytogenetic abnormalities, and transfusion dependency). [2,7] On the contrary, quiet surprisingly though, it bears no correlation with factors prognostic of myeloproliferative neoplasms [7]. Also, very similar to CMML [4] and unlike MDS/ myelofibrosis [10,12], it does not have a set of clearly defined recurrent cytogenetic abnormalities predicting prognosis[2,7]. Furthermore, more recently, using a comprehensive next generation-based sequencing platform it has been shown that MDS/MPN-U has a high frequency of recurring somatic mutations in epigenetic regulation (*ASXL1* -29%), DNA methylation (*TET2*-27%), signalling pathways (*JAK2* -25%), splicing mutations (*SRSF2* -25%) and transcription factors (*RUNX1*-13%). [13 14] As compared to CMML, wherein mutations in *RUNX1, NRAS, SETBP1, and ASXL1* appear to be associated with unfavourable survival, [15 16 5 17] CBL and p53 have been particularly predictive of worse prognosis for MDS/MPN-U [2].
Treatment of MDS/MPN-U with various treatment modalities only infrequently results in prolonged remission and overall outcomes remain quiet dismal [7 2]. Treatment with hypomethylating agents result in lesser toxicity than conventional chemotherapy; but again, remissions tend to be of short duration [2,18]. The main caveat in most of the studies related to this infrequent disorder has been that they include mixed bag of treatment with allogenic hematopoietic cell transplantation (HCT) comprising less than 10% of all the patients [2]. HCT, for long, has been a reasonably successful and only curative option for other similar disorders such as MDS[19], myelofibrosis [20 12] and CMML [21 22 17].
In view of lack of comprehensive data and conclusions on outcomes and factors predicting survival pertaining only to allogeneic stem cell transplant, we request the help of a large registry database

from CIBMTR, in order to address this important issue. We also wanted to evaluate whether previously defined prognostic systems like IPSS/IPSS-R for MDS/MPN-U, CPSS for CMML and disease risk index (DRI) (validated and standardised model predicting transplant outcomes across vast majority of diseases)[23] also correlate well and independently for post-transplant outcomes of MD/MPN-U.

Research hypothesis and study objectives/specific aims:
We propose to perform a retrospective analysis in all adult patients of MDS/MPN-U undergoing allogeneic transplant and reported to the CIBMTR. We aim at performing outcome analysis related to non-relapse mortality, relapse incidence, leukaemia-free survival and overall survival, engraftment and GVHD. We also wanted to analyse which factors were significant in predicting outcomes in univariate (UV) and multivariate (MV) analysis, and compare survival for 0-1 significant risk factor, 2 risk factors and >2 risk factors in MV analysis. We would further like to analyse outcomes (survival) as per IPSS/CPSS and DRI status (if classifiable as per database) and compare between the models. Given the scarcity of published data on this topic, we aim at identifying which categories of patients might benefit the most from allogeneic HCT. Of special interest might be looking at: cytogenetic and molecular abnormalities, percentage of bone marrow and peripheral blood blasts, depth of haematological abnormalities, response status prior to transplant, treatment prior to transplant and time interval from diagnosis to transplant.
Primary:

- To evaluate OS (overall survival), LFS (leukaemia free survival), and their prognostic factors in a UV and MV analysis.
- To assess if IPSS/IPSS-R, CPSS and DRI is prognostic for allograft and compare between the models

Secondary:

- NRM (Non-relapse mortality), RI (relapse incidence), GVHD free relapse free survival (GRFS), acute and chronic GVHD

Eligibility criteria: (patient inclusion/exclusion criteria)
Inclusion criteria:
All MDS/MPN-U above 18 years of age (excluding other defined MDS/MPN like CMML, JMML (juvenile myelomonocytic leukaemia), MDS/MPN-RS-T (ringed sideroblasts and thrombocytosis), allo-HSCT from HLA-identical sibling or unrelated (for URD: fully matched or 1 HLA mismatch), or haploidentical donors/cord transplant.

Exclusion criteria:
Previous auto or allo-HCT, Ex vivo T cell depletion.

Procedures, data requirements:
As per 2014 modification of data collection form MDS/MPN- attached

Factors for UV followed by MV analysis:
Date of birth (Age as continuous variable), date of diagnosis/ Date of transplant (time interval diagnosis to treatment as continuous variable), Hb/WBC and platelets at diagnosis and prior to transplant, HCT (as continuous variable, Blasts at diagnosis and prior to transplant (continuous), Chromosome analysis at diagnosis and prior to transplant, (CPSS classification, number of chromosomal abnormalities), Molecular analysis at diagnosis (especially *ASXL1, CBL and p53*, if information available), any primary tumour treated and diagnosed prior to diagnosis of MDS/MPN (details with dates), Treatment prior to transplant and number of lines (categorical variable), If transformed to leukaemia prior to transplant and details of treatment related to transformation, IPSS/IPSS-R, CPSS, DRI (disease risk index) at transplant, ECOG performance status, Date of allo-HSCT, Donor type (matched sibling or unrelated or haploidentical/cord), HLA match (for unrelated: 9/10 or

10/10), Donor age, Donor-recipient sex match, Donor/recipient CMV serostatus, Stem cell source (PBSCs or BM), Stem cell dose, Conditioning intensity (MAC or RIC), GVHD prophylaxis (CSA or CSA+MTX or CSA+MMF +- MTX, post Cy), ATG yes or no (in vivo T cell depletion)

Outcomes:
Engraftment and neutrophil and platelet recovery, Graft failure yes/no, Organ toxicity, VOD incidence and severity, 100-days chimerism (if available), aGvHD: yes/no; if yes onset date and maximum grade, cGvHD: yes/no; if yes onset date and maximum grade, Relapse yes/no, Date of relapse, DLI given yes/no and date, Further transplant yes/no and date (salvage treatment information after relapse), Secondary malignancy (yes/no) and date, Survival and disease status at last follow-up , cGvHD at last follow-up, Cause of death

Study design and scientific plan:
The Kruskal-Wallis test was used to assess continuous variables and $\chi 2$ was used for categorical variables. Univariate analyses were performed using Gray's test for cumulative incidence functions and the log rank test for OS and LFS. To study acute and chronic GVHD, we considered relapse and death to be competing events. Probabilities of OS, LFS, and GRFS were calculated using the Kaplan–Meier estimate. A Cox proportional hazards model was used for multivariate regression. All variables differing significantly between the three groups or factors associated with significant outcome in the univariate analysis were included in the cox model. Assessment of center effect was assessed by introducing a random effect or frailty for each center into the model. Results were expressed as the hazard ratio (HR) with the 95% confidence interval (95% CI). Proportional hazards assumptions were checked systematically for all proposed models using the Grambsch-Therneau residual-based test. C concordance test was used to compare across various prognostic models. All tests were 2-sided. Statistical analysis was performed using R 3.4.0 (R Core Team (2017).

No conflicts of interest to declare

References:
1. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20):2391-2405.
2. Mangaonkar AA, Swoboda DM, Coltro G, et al. Clinicopathologic characteristics, prognostication and treatment outcomes for myelodysplastic/myeloproliferative neoplasm, unclassifiable (MDS/MPN-U): Mayo Clinic-Moffitt Cancer Center study of 135 consecutive patients. *Leukemia*. 2019.
3. Itzykson R, Kosmider O, Renneville A, et al. Clonal architecture of chronic myelomonocytic leukemias. *Blood*. 2013;121(12):2186-2198.
4. Patnaik MM, Tefferi A. Chronic myelomonocytic leukemia: 2018 update on diagnosis, risk stratification and management. *Am J Hematol*. 2018;93(6):824-840.
5. Itzykson R, Kosmider O, Renneville A, et al. Prognostic score including gene mutations in chronic myelomonocytic leukemia. *J Clin Oncol*. 2013;31(19):2428-2436.
6. Malcovati L, Papaemmanuil E, Ambaglio I, et al. Driver somatic mutations identify distinct disease entities within myeloid neoplasms with myelodysplasia. *Blood*. 2014;124(9):1513-1521.
7. DiNardo CD, Daver N, Jain N, et al. Myelodysplastic/myeloproliferative neoplasms, unclassifiable (MDS/MPN, U): natural history and clinical outcome by treatment strategy. *Leukemia*. 2014;28(4):958-961.
8. Elena C, Galli A, Such E, et al. Integrating clinical features and genetic lesions in the risk assessment of patients with chronic myelomonocytic leukemia. *Blood*. 2016;128(10):1408-1417.
9. Greenberg P, Cox C, LeBeau MM, et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. *Blood*. 1997;89(6):2079-2088.

10. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. *Blood*. 2012;120(12):2454-2465.
11. Kantarjian H, O'Brien S, Ravandi F, et al. Proposal for a new risk model in myelodysplastic syndrome that accounts for events not considered in the original International Prognostic Scoring System. *Cancer*. 2008;113(6):1351-1361.
12. McLornan DP, Yakoub-Agha I, Robin M, Chalandon Y, Harrison CN, Kroger N. State-of-the-art review: allogeneic stem cell transplantation for myelofibrosis in 2019. *Haematologica*. 2019;104(4):659-668.
13. Meggendorfer M, Jeromin S, Haferlach C, Kern W, Haferlach T. The mutational landscape of 18 investigated genes clearly separates four subtypes of myelodysplastic/myeloproliferative neoplasms. *Haematologica*. 2018;103(5):e192-e195.
14. Bose P, Nazha A, Komrokji RS, et al. Mutational landscape of myelodysplastic/myeloproliferative neoplasm-unclassifiable. *Blood*. 2018;132(19):2100-2103.
15. Patnaik MM, Itzykson R, Lasho TL, et al. ASXL1 and SETBP1 mutations and their prognostic contribution in chronic myelomonocytic leukemia: a two-center study of 466 patients. *Leukemia*. 2014;28(11):2206-2212.
16. Laborde RR, Patnaik MM, Lasho TL, et al. SETBP1 mutations in 415 patients with primary myelofibrosis or chronic myelomonocytic leukemia: independent prognostic impact in CMML. *Leukemia*. 2013;27(10):2100-2102.
17. Woo J, Choi DR, Storer BE, et al. Impact of clinical, cytogenetic, and molecular profiles on long-term survival after transplantation in patients with chronic myelomonocytic leukemia. *Haematologica*. 2019.
18. Al-Kali A, Abou Hussein AK, Patnaik M, et al. Hypomethylating agents (HMAs) effect on myelodysplastic/myeloproliferative neoplasm unclassifiable (MDS/MPN-U): single institution experience. *Leuk Lymphoma*. 2018;59(11):2737-2739.
19. de Witte T, Bowen D, Robin M, et al. Allogeneic hematopoietic stem cell transplantation for MDS and CMML: recommendations from an international expert panel. *Blood*. 2017;129(13):1753-1762.
20. Robin M, de Wreede LC, Wolschke C, et al. Long-term outcome after allogeneic hematopoietic cell transplantation for myelofibrosis. *Haematologica*. 2019;104(9):1782-1788.
21. Liu HD, Ahn KW, Hu ZH, et al. Allogeneic Hematopoietic Cell Transplantation for Adult Chronic Myelomonocytic Leukemia. *Biol Blood Marrow Transplant*. 2017;23(5):767-775.
22. Kroger N, Zabelina T, Guardiola P, et al. Allogeneic stem cell transplantation of adult chronic myelomonocytic leukaemia. A report on behalf of the Chronic Leukaemia Working Party of the European Group for Blood and Marrow Transplantation (EBMT). *Br J Haematol*. 2002;118(1):67-73.
23. Armand P, Kim HT, Logan BR, et al. Validation and refinement of the Disease Risk Index for allogeneic stem cell transplantation. *Blood*. 2014;123(23):3664-3671.

Table 1. Characteristic of patients with Myelodysplastic/myeloproliferative neoplasms unclassifiable reported to the CIBMTR

Characteristic	N
No. of patients	281
No. of centers	97
track - no. (%)	
TED	202 (71.9)
CRF	79 (28.1)
Age - median (min-max)	60.68 (17.31-76.24)
Age - no. (%)	
<18	2 (0.7)
18-29	13 (4.6)
30-39	10 (3.6)
40-49	35 (12.5)
50-59	77 (27.4)
60-69	123 (43.8)
≥ 70	21 (7.5)
Sex - no. (%)	
Male	177 (63)
Female	104 (37)
Race - no. (%)	
Caucasian	220 (78.3)
African-American	20 (7.1)
Asian	6 (2.1)
Native American	2 (0.7)
More than one race	1 (0.4)
Missing	32 (11.4)
HCT-CI - no. (%)	
0	60 (21.4)
1	45 (16)
2	31 (11)
3+	145 (51.6)
Karnofsky score - no. (%)	
90-100	133 (47.3)
< 90	139 (49.5)
Missing	9 (3.2)
Time from diagnosis to HCT - no. (%)	
<6	62 (22.1)
6-11	74 (26.3)
≥12	117 (41.6)
Missing	28 (10)
Donor type - no. (%)	
HLA-identical sibling	88 (31.3)
Other related	32 (11.4)

Characteristic	N
Well-matched unrelated (8/8)	129 (45.9)
Partially-matched unrelated (7/8)	26 (9.3)
Cord blood	6 (2.1)
Donor/recipient sex match - no. (%)	
M-M	117 (41.6)
M-F	56 (19.9)
F-M	56 (19.9)
F-F	45 (16)
CB - recipient M	4 (1.4)
CB - recipient F	2 (0.7)
Missing	1 (0.4)
Graft type - no. (%)	
Bone marrow	36 (12.8)
Peripheral blood	239 (85.1)
Cord blood	6 (2.1)
Conditioning as reported by center - no. (%)	
MAC	113 (40.2)
RIC/NMA	167 (59.4)
Missing	1 (0.4)
Conditioning regimen - no. (%)	
TBI/Cy	5 (1.8)
TBI/Cy/Flu	27 (9.6)
TBI/Cy/Flu/TT	3 (1.1)
TBI/Mel	8 (2.8)
TBI/Flu	24 (8.5)
TBI/other(s)	1 (0.4)
Bu/Cy	26 (9.3)
Bu/Mel	4 (1.4)
Flu/Bu	110 (39.1)
Flu/Mel/TT	3 (1.1)
Flu/Mel	60 (21.4)
Cy/Flu	3 (1.1)
Mel/other(s)	1 (0.4)
Treosulfan	2 (0.7)
Carb/other(s)	1 (0.4)
Other(s)	2 (0.7)
None	1 (0.4)
GVHD prophylaxis - no. (%)	
CD34 selection	7 (2.5)
Post-CY	47 (16.7)
TAC based	178 (63.3)
CSA based	46 (16.4)
Other	3 (1.1)

Characteristic	N
TX year - no. (%)	
2012	1 (0.4)
2013	15 (5.3)
2014	40 (14.2)
2015	39 (13.9)
2016	63 (22.4)
2017	49 (17.4)
2018	63 (22.4)
2019	11 (3.9)
Follow-up - median (min-max)	24.08 (3.22-72.14)

Proposal: 1911-36

Title:
Clinical results of allogeneic hematopoietic stem cell transplantation for hairy cell leukemia

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Research hypothesis:
Hairy cell leukemia (HCL) is an indolent B-cell neoplasm comprising 2% of leukemias, estimated at around 1300-2000 new cases/year in the US.[1] There are two biologically distinct types of HCL including classic HCL that is CD25+ and usually BRAF V600E mutated, and HCL variant (HCLv) that is BRAF wild type. HCL responds well to purine analog treatment with CR rates of 75-90% and median response duration of 16 years.[2] However, there is no clear plateau in relapse-free survival and repeated treatments achieves shorter durations of response. Also, we reported patients with particularly high-risk HCL that have IGHV4-34 unmutated immunoglobulin rearrangement responding poorly to purine analog treatment.[3] HCLv often has a TP53 abnormality, such as deletion 17p,[4] responds very poorly to purine analog and has median overall survival (OS) less than 6-9 years. Those patients who progressed following purine analog combined immunochemotherapy have particularly poor OS with median OS following progression of less than three years. NCI/NIH hairy cell leukemia program has been a leader in clinical trial enrollment and drug development for HCL/HCLv, both in first line treatment with concurrent immunotherapy[5] and in relapsed disease by moxetumomab pasudotox [6] and dabrafenib-trametinib.[7] However, despite these improvements, their toxicity profile poses complex tolerance problems in these multi -treated patients and we have many patients desperate for alternative treatment options, and effective cellular therapy would be appropriate in many cases. Two factors supporting this need include the fact that the newer BRAF treatments for classic HCL are often only temporary and incomplete in efficacy, and patients which HCLv and/or BRAF WT HCL are not eligible for BRAF treatments.
Due to the rarity and usually indolent nature of the disease with modern treatments, allogeneic hematopoietic stem cell transplant (allo-HSCT) has been less incorporated to the treatment schema compared to other leukemic diseases. However, there remain a continuous unmet need for new treatment strategies particularly for relapsed/refractory high-risk HCL. Cellular immunotherapy such as allo-HSCT and chimeric antigen receptor T-cell (CAR-T) therapy are potential options needing evaluation. In a case report Zinzani et al. reported one case of refractory HCL who received allo-HSCT from matched related donor and achieved long-term remission. Interestingly, the case showed residual HCL(15%) in bone marrow four months after transplant which became negative at 12 months and 18 months following allo -HSCT suggesting graft versus leukemia (GVL) effect. [8] There has been a steady albeit limited influx of HCL patients who were reported to the CIBMTR over last three decades, reflecting an ongoing need for better therapies in patients who fail standard treatments.
Our primary objective of the study is to describe the outcome of allo-HSCT in patients with HCL. We hypothesize that allo-HSCT can achieve long-term remission and survival in a selected population of high-risk relapsed/refractory patients with HCL. We postulate that the benefit of allo-HSCT in HCLis largely due to a GVL effect. Due to expected limited number of cases, this study is going to be descriptive rather than analytical. However, if the number allows meaningful analysis, we would like to explore the differences in outcomes such as survival, NRM, incidence of GVHD by conditioning regimen,

reduced-intensity conditioning (RIC) vs myeloablative conditioning (MAC) and donor source.

Specific aims:

- 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.
    - Evaluate causes of death among allo-HCT recipients.
    - In an exploratory landmark analysis, evaluate the relationship between acute GVHD and relapse incidence among allo-HCT recipients.
- Possibly evaluate variables that may be associated with differences in HCT outcomes, including HCL classic vs HCL variant, prior lines of chemotherapy, duration of remission, time from diagnosis, disease status at transplant, pre-transplant performance status, patient age, conditioning intensity, HCT-CI score, and graft source(marrow vs peripheral blood), depending on number of patients.

Scientific impact:

This study will be one and only data of allo-HSCT for HCL and will be future reference of cellular therapy treatment of HCL.

Scientific justification:

Due to the rarity and limited indication, outcomes from allo-HSCT in HCL have never been systematically analyzed. Currently, ESMO guidelines from experts in this field states that allo-HSCT has a potential role in younger, heavily pretreated HCL patients who have had multiple relapses and are refractory to purine analogues and rituximab, although without body of evidence.[9] Since there is no prior data to report outcomes of allo-HSCT in patients with HCL other than case reports, we propose to conduct a study to evaluate the benefit of allo-HSCT in HCL.

We plan to evaluate long-term remission rates and morbidity/mortality with allo-HCT and this analysis would suggest the importance of a GVL effect and provide compelling data to support or against a consideration of allo-HSCT in patients with high-risk HCL who progressed following standard treatment options. Depending on the number of cases, we plan to explore and describe which disease (HCLor HCLv if possible), patient, what condition (disease status at transplant), and transplant factors are associated with better outcomes.

We previously proposed the study to evaluate the outcomes of allo-HSCT in HCL (CK08-02) and identified 17 patients who received allo-HSCT between 1983 and 2006. The OS after allo-HSCT at that time showed plateau after 4 years with 5-year OS of over 50% in median follow up duration of 78.5 months which is very promising in this multiply relapsed population (**Figure 1**). However, the study had challenges due to small number of cases and was never published as a result. Since 2006, there are considerable changes in

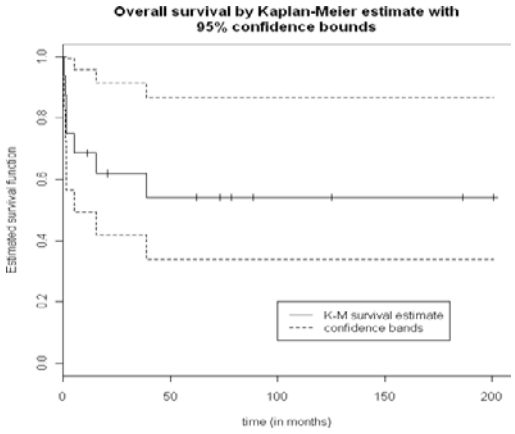
allo-HSCT such as expansion of donor source with significantly improved safety. Therefore, we will propose to update the data not only to have more patients but also to evaluate outcomes with more recent allo-HSCT.

Also, we will plan to collaborate with EBMT this time to have increased number of patients to perform more robust analysis allowing more comprehensive results of allo-HSCT, providing evidence to support patients and physicians making decisions. With a preliminary database search, we identified 26 cases from CIBMTR and 23 cases from EBMT. From CIBMTR, 15 and 7 cases are reported as TED and CRF for first transplant, 4 TED for second transplant (Appendix). Since 10 cases in CIBMTR are reported from Europe, research team will review the data to avoid duplication before the analysis.

Combining two largest transplant registry data in the world, this study is going to be one and only evidence of outcomes from allo-HSCT in HCL. Particularly since the field is moving rapidly with novel

cellular therapies such as CAR-T cells, this study will therefore be a reference and outcomes benchmark for all future trials evaluating cellular therapy in patients with HCL.

Figure 1. 1983-2006 CIBMTR database(N=17; unpublished data)



Patient eligibility population:

Patients (age>16) undergoing allo-HSCT for a diagnosis of hairy cell leukemia (classic and variant) HSCT between January 1983 and December 2018 (or available latest data)

Data requirements:

Variables – patient characteristics:

- Gender (male/female)
- Age at transplant
- Karnofsky Performance Status (80-100 vs 50-70 vs < 40)
- Lab data pre-HCT including CBC
- Sensitivity of disease to pre-HCT treatment (sensitive vs resistant vs untreated vs unknown)
- Disease remission status immediately prior to HCT, remission number (1 vs 2 vs 3 or higher)
- Time from HCL diagnosis to HCT
- Prior lines of chemotherapy including details of regimen and remission duration for each therapy
- Disease characteristics (HCLvs HCL variant: flow cytometry, immunohistochemistry, BRAF mutation status if possible)

Variables – graft characteristics:

- Donor age
- Donor-recipient gender (female into male vs other)
- Donor source (matched related, matched unrelated, haplo related) and degree of HLA matching
- Source of stem cells (bone marrow vs peripheral blood)

Variables – transplantation regimen:

- Year of transplant
- Non-myeloablative vs reduced intensity; radiation as part of prep (yes/no) Desired outcome variables:
- Response to the treatment including MRD status if available
- PFS: defined as the time to relapse/progression or death from any cause; patients without events will be censored at last follow-up
- OS: defined as the time to death; surviving patients censored at last follow-up
- NRM: defined as the time to death without evidence of disease presence
- Relapse incidence: defined as the time to onset of relapse; NRM will be a competing risk

- Grades II-IV aGVHD incidence, grades III-IV aGVHD incidence: competing risks include relapse/progression, death, graft failure: < 5% donor chimerism from any cause, or DLI
- cGVHD incidence (any, as well as limited vs. extensive, and mild vs. moderate vs. severe): competing risks include relapse/progression, death, graft failure defined as < 5% donor chimerism from any
- cause, or DLI
- Cause of death

Sample requirements:
None required

Study design:
Retrospective descriptive study

Non-CIBMTR data source:
We will collaborate with EBMT to describe outcome of allo-HSCT in larger number of patients. The variables we collect will be the same with CIBMTR and the way to merge data follows former collaboration. This PI and the study team will actively engage in facilitating any additional data collections from the transplant centers.

Conflicts of interest:
No

References:
1. Teras LR, DeSantis CE, Cerhan JR, Morton LM, Jemal A, Flowers CR. 2016 US lymphoid malignancy statistics by World Health Organization subtypes. *CA Cancer J Clin*. 2016.
2. Saven A, Burian C, Koziol JA, Piro LD. Long-term follow-up of patients with hairy cell leukemia after cladribine treatment. *Blood*. 1998;92(6):1918-1926.
3. Arons E, Suntum T, Stetler-Stevenson M, Kreitman RJ. VH4-34+ hairy cell leukemia, a new variant with poor prognosis despite standard therapy. *Blood*. 2009;114(21):4687-4695.
4. Hockley SL, Morgan GJ, Leone PE, et al. High-resolution genomic profiling in hairy cell leukemia- variant compared with typical hairy cell leukemia. *Leukemia*. 2011;25(7):1189-1192.
5. Chihara D, Arons E, Stetler-Stevenson M, et al. Randomized phase II study of cladribine with simultaneous or delayed rituximab in patients with untreated hairy cell leukemia. *Journal of Clinical Oncology*. 2019;37(15_suppl):7003-7003.
6. Kreitman RJ, Dearden C, Zinzani PL, et al. Moxetumomab pasudotox in relapsed/refractory hairy cell leukemia. *Leukemia*. 2018;32(8):1768-1777.
7. Kreitman RJ, Moreau P, Hutchings M, et al. Treatment with Combination of Dabrafenib and
8. Trametinib in Patients with Recurrent/Refractory BRAF V600E-Mutated Hairy Cell Leukemia (HCL). *Blood*. 2018;132(Supplement 1):391-391.
9. Zinzani PL, Bonifazi F, Pellegrini C, et al. Hairy cell leukemia: allogeneic transplantation could be an optimal option in selected patients. *Clin Lymphoma Myeloma Leuk*. 2012;12(4):287-289.
10. Robak T, Matutes E, Catovsky D, Zinzani PL, Buske C, Committee EG. Hairy cell leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2015;26 Suppl 5:v100-107.

Appendix

Table 1. Baseline characteristics of patients receiving first alloHCT for Hairy Cell Leukemia - CIBMTR

Characteristic	TED	CRF	Total
No. of patients	15	7	22
Age - no. (%)			
Median (min-max)	49.9 (20.52-61.89)	42.46 (21.42-51.83)	45.97 (20.52-61.89)
20-29 yrs	1 (6.7)	1 (14.3)	2 (9.1)
30-39 yrs	2 (13.3)	2 (28.6)	4 (18.2)
40-49 yrs	5 (33.3)	2 (28.6)	7 (31.8)
50-59 yrs	3 (20)	2 (28.6)	5 (22.7)
>= 60 yrs	4 (26.7)	0	4 (18.2)
Sex - no. (%)			
Male	12 (80)	6 (85.7)	18 (81.8)
Female	3 (20)	1 (14.3)	4 (18.2)
Race - no. (%)			
Caucasian	11 (73.3)	7	18 (81.8)
African-American	1 (6.7)	0	1 (4.5)
Missing	3 (20)	0	3 (13.6)
Graft type - no. (%)			
Bone marrow	6 (40)	3 (42.9)	9 (40.9)
Peripheral blood	8 (53.3)	3 (42.9)	11 (50)
Umbilical cord blood	0	1 (14.3)	1 (4.5)
Missing	1 (6.7)	0	1 (4.5)
Year of transplant - no. (%)			
1983	1 (6.7)	0	1 (4.5)
1984	1 (6.7)	0	1 (4.5)
1988	0	1 (14.3)	1 (4.5)
1989	0	1 (14.3)	1 (4.5)
1994	1 (6.7)	0	1 (4.5)
1995	1 (6.7)	1 (14.3)	2 (9.1)
1996	1 (6.7)	0	1 (4.5)
1997	0	1 (14.3)	1 (4.5)
1998	1 (6.7)	0	1 (4.5)
2002	2 (13.3)	0	2 (9.1)
2003	1 (6.7)	0	1 (4.5)
2004	1 (6.7)	0	1 (4.5)
2005	1 (6.7)	0	1 (4.5)
2006	1 (6.7)	0	1 (4.5)
2008	0	1 (14.3)	1 (4.5)
2010	0	1 (14.3)	1 (4.5)
2011	1 (6.7)	0	1 (4.5)
2012	1 (6.7)	0	1 (4.5)
2013	1 (6.7)	0	1 (4.5)
2015	0	1 (14.3)	1 (4.5)
Follow-up - median (min-max)	72.99 (0.89-243.98)	NE	72.99 (0.23-243.98)

Table 2. Baseline characteristics of patients receiving second or greater alloHCT for Hairy Cell Leukemia between 2000 -2017 CIBMTR

Characteristic	TED	CRF	Total
No. of patients	4	0	4
Age - no. (%)			
Median (min-max)	64.36 (59.48-64.68)	64.36 (59.48-64.68)	
50-59 yrs	1 (25)		1 (25)
>= 60 yrs	3 (75)		3 (75)
Gender: (2400 Q942) - no. (%)			
Male	3 (75)		3 (75)
Female	1 (25)		1 (25)
Race - no. (%)			
African-American	3 (75)		3 (75)
Missing	1 (25)		1 (25)
Graft type - no. (%)			
Peripheral blood	4		4
Year of transplant - no. (%)			
2006	3 (75)		3 (75)
2016	1 (25)		1 (25)
Follow-up - median (min-max)	72.99 (0.89-243.98)	72.99 (0.23-243.98)	

Table 3. Overall survival for all allo transplants (including 1st and 2nd or greater allo), N=26

Study population (N = 26) CIBMTR Outcomes	N Eval	Prob (95% CI)
dead	25	
1-year	12	55 (35-74)%
3-year	9	50 (31-70)%
5-year	6	38 (19-60)%

Table 4. Region and survival status for all transplants for Hairy Cell Leukemia (including 1st or 2nd or greater alloHCT) CIBMTR

Characteristic	N (%)
No. of patients	26
CCN region - no. (%)	
US	14 (53.8)
Canada	2 (7.7)
Europe	10 (38.5)
Overall survival - no. (%)	
No	10 (38.5)
Yes	15 (57.7)
Missing	1 (3.8)
Cause of death - no. (%)	
Alive	10 (38.5)
Primary disease	7 (26.9)
GVHD	2 (7.7)
Infection	2 (7.7)
Organ failure	2 (7.7)
Other cause	2 (7.7)
Unknown	1 (3.8)

Proposal: 1911-143

Title:
Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimens

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Hypothesis:
We postulate 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).

Specific aims:
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.

Scientific impact:
The proposed study would provide information about the differences in outcomes of allo-HCT for MF based on the individual conditioning regimen utilized. This information would be pivotal to choose the ideal conditioning regimen in the MAC or RIC setting for these patients and improve the transplant outcomes.

Scientific justification:
Myelofibrosis is a chronic myeloproliferative neoplasm that can arise either denovo (primary MF) or from antecedent essential thrombocytosis (post-ET MF) or polycythemia vera (post-PV MF). Allo-HCT remains the only potentially curative option for these patients. The availability of RIC in addition to MAC strategies have expanded the scope of allo-HCT for these patients who are often older adults. Several groups have studied the outcomes of MAC and RIC platforms for MF and demonstrated the feasibility and safety of these strategies [1, 2]. However, the optimal conditioning regimen either in the MAC or RIC setting is not well known. A few prior studies investigating the outcomes of MF based on different conditioning regimens have suggested varying results [2-5]. A retrospective study by EBMT reported that the OS is similar between MAC and RIC for MF, although MAC demonstrated a trend toward less relapse and significantly improved GVHD-free/relapse-free survival [2]. In the same study, no significant difference was noted between fludarabine/busulfan and fludarabine/melphalan in the RIC setting. A study from United States by Jain et al. compared the outcomes of three RIC regimens [fludarabine/busulfan, fludarabine/melphalan, fludarabine bis-chlorethyl-nitroso-urea/ carmustine melphalan (FBM)] and showed a similar OS, although the donor chimerism at day +30 and day +100 was better in patients who received FBM and fludarabine/melphalan [3]. The same study also noted a higher acute GVHD (all grades) in the FBM and fludarabine/melphalan groups. A study from CIBMTR by Gupta et al. evaluated the outcomes of RIC allo-HCT in MF and noted survival rates of 59% with fludarabine/melphan, 46% with fludarabine-total body irradiation, 41% with fludarabine/busulphan, and 28% in other heterogeneous conditioning regimens [4]. However, an advantage of the fludarabine/melphalan regimen was not confirmed on multivariate analysis. Fludarabine/melphalan

based regimen also showed a trend toward lower mortality compared with the fludarabine/busulfan-based regimen (RR, 0.63; P = .06) in this study. Another study by Robin et al. compared outcomes with fludarabine/busulfan and fludarabine/melphalan regimens for RIC in MF and noted similar OS and DFS although relapses were lower in fludarabine/melphalan group [5]. They also noted that the incidence of acute GVHD was lower in fludarabine/busulfan vs. fludarabine/melphalan group (31% vs 62%, P = .001) with a trend towards lower NRM in the fludarabine/busulfan group. In contrast to the few studies described above in the RIC setting, the outcomes of allo-HCT for MF based on various MAC regimens are largely unknown.
Hence, with the literature available currently, the optimal choice of conditioning regimen either in the MAC or RIC setting for MF is still unclear. This justifies the need for further research in this population as it would be an important factor in the clinical decision-making process.

Patient eligibility population:
Allo-HCT for primary MF or post ET MF or post PV MF between the period 2000 to 2018 and reported to CIBMTR will be included.

Data requirements:
This retrospective study requires analysis of CIBMTR collected data related to allo-HCT from 2000– 2018. This proposal does not require biologic samples

Outcomes:
Primary: OS, DFS

Secondary: time to engraftment, graft failure, NRM, relapse, incidence of acute GVHD, chronic GVHD

Variables to be analyzed:
Primary:
- Conditioning regimen - MAC: Fludarabine/Busulfan vs. Busulfan/Cytoxan (Bu/Cy) vs. others
- Conditioning regimen - RIC: Fludarabine/Busulfan vs. Fludarabine/Melphalan vs. others

Disease related:
- Type: primary MF vs post ET MF vs post PV MF
- Disease risk: DIPSS score

Patient related:
- Age
- Gender
- Race
- CMV status
- ABO status
- HCT-CI
- Performance status
- Interval between diagnosis and transplant

Donor related:
- HLA match: Matched sibling vs. 8/8 matched unrelated donors vs. mismatched unrelated (MMUD)
- Age

- Sex: male vs. female
- CMV status
- ABO status

Transplant related:
- Conditioning intensity: MAC vs RIC
- Source of stem cell: Bone marrow versus peripheral blood
- GVHD prophylaxis
- Year of transplant

Study design:
This is a retrospective analysis of the CIBMTR database. The study would include patients with a diagnosis of for primary MF or post ET MF or post PV MF who underwent allo-HCT and meet the above mentioned study criteria. Analysis of various conditioning regimens will be investigated separately in the MAC and RIC setting. The primary outcome will be OS and DFS. The secondary outcomes will be time to engraftment, graft failure, relapse rate, NRM, incidence of acute GVHD and chronic GVHD. Patient related, donor related and transplant related variables summarized above will be considered as prognostic factors which determine the outcomes. A multivariate logistic regression model will be built using these variables to identify independent prognostic factors associated with the outcomes.

Definitions of outcomes:
Overall survival:
Time from transplant to death. Death from any cause will be considered an event. Surviving patients will be censored at the time of last follow-up.

Disease free survival:
Time to treatment failure (relapse or death from any cause). Patients alive and in complete remission will be censored at last follow-up

Primary graft failure:
Alive on day 28 with ANC $<0.5\times10^9$/l. Death and progressive disease within 28 days will be treated as competing risks.

Time to neutrophil engraftment:
Time from transplant to ANC recovery $\geq 0.5 \times 10^9$/L as reported to CIBMTR

Time to platelet engraftment:
Time from transplant to platelet recovery $\geq 20 \times 10^9$/L as reported to CIBMTR

Acute and chronic GVHD:
Cumulative incidence of grade II-IV acute GVHD per consensus criteria and cumulative incidence of limited and extensive chronic GVHD [6, 7]. The outcomes will be evaluated by cumulative incidence estimates, with death without acute or chronic GVHD as competing risk. Patients will be censored at the date of last follow up.

Non-Relapse Mortality:
NRM will be defined as death from any cause in the first 28 days post allo-HCT or

death without evidence of disease recurrence beyond day 28. The outcome will be evaluated by the cumulative incidence estimate, with relapse as its competing risk.

Relapse:
Incidence of relapse. The outcome will be evaluated by the cumulative incidence estimate with non-relapse mortality as its competing risk. Patients are censored at the date of last follow up.

References:

1. Ballen KK, Shrestha S, Sobocinski KA et al. Outcome of transplantation for myelofibrosis. Biol Blood Marrow Transplant. 2010;16(3):358-67.
2. McLornan D, Szydlo R, Koster L et al. Myeloablative and Reduced-Intensity Conditioned Allogeneic Hematopoietic Stem Cell Transplantation in Myelofibrosis: A Retrospective Study by the Chronic Malignancies Working Party of the European Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant. 2019. pii: S1083-8791(19)30418-5.
3. Jain T, Kunze KL, Temkit M et al. Comparison of reduced intensity conditioning regimens used in patients undergoing hematopoietic stem cell transplantation for myelofibrosis. Bone Marrow Transplant. 2019;54(2):204-211
4. Gupta V, Malone AK, Hari PN et al. Reduced-intensity hematopoietic cell transplantation for patients with primary myelofibrosis: a cohort analysis from the center for international blood and marrow transplant research. Biol Blood Marrow Transplant. 2014;20(1):89-97
5. Robin M, Porcher R, Wolschke C et al. Outcome after Transplantation According to Reduced-Intensity Conditioning Regimen in Patients Undergoing Transplantation for Myelofibrosis. Biol Blood Marrow Transplant. 2016;22(7):1206-1211.
6. Rowlings PA, Przepiorka D, Klein JP et al. IBMTR Severity Index for grading acute graft-versus-host disease: retrospective comparison with Glucksberg grade. Br J Haematol 1997;97(4):855-864
7. Shulman HM, Sullivan KM, Weiden PL et al. Chronic graft-versus-host syndrome in man. A long-term clinicopathologic study of 20 Seattle patients. Am J Med 1980;69(2):204-217

Table 1. Characteristic of Allo-HCT for primary MF or post ET MF or post PV MF with MAC/RIC conditioning between the period 2000 to 2018 and reported to CIBMTR

Characteristic	N
No. of patients	1161
No. of centers	168
Patient age - median (min-max)	58.79 (18.98-78.91)
Age - no. (%)	
18-29	10 (0.9)
30-39	37 (3.2)
40-49	181 (15.6)
50-59	420 (36.2)
60-69	456 (39.3)
≥ 70	57 (4.9)
Sex - no. (%)	
Male	696 (59.9)
Female	465 (40.1)
Race - no. (%)	
Caucasian	1036 (89.2)
African-American	43 (3.7)
Asian	37 (3.2)
Pacific islander	11 (0.9)
Native American	3 (0.3)
Other	1 (0.1)
More than one race	1 (0.1)
Missing	29 (2.5)
HCT-CI - no. (%)	
0	232 (20)
1	131 (11.3)
2	142 (12.2)
3+	385 (33.2)
TBD, review needed for history of malignancies	1 (0.1)
NA, f2400 (pre-TED) not completed	263 (22.7)
Missing	7 (0.6)
Karnofsky score - no. (%)	
90-100	651 (56.1)
< 90	487 (41.9)
Missing	23 (2)
Subdisease - no. (%)	
Primary Myelofibrosis	915 (78.8)
Polycythemia vesa	107 (9.2)
Essential thrombocythemia	139 (12)

Characteristic	N
intdxtxgp - no. (%)	
<6	173 (14.9)
6-11	226 (19.5)
≥12	757 (65.2)
Missing	5 (0.4)
DIPSS prior to HCT - no. (%)	
Low	129 (11.1)
Intermediate-1	453 (39)
Intermediate-2	371 (32)
High	16 (1.4)
Missing	192 (16.5)
Donor type - no. (%)	
HLA-identical sibling	396 (34.1)
Well-matched unrelated (8/8)	619 (53.3)
Partially-matched unrelated (7/8)	124 (10.7)
Mis-matched unrelated (≤6/8)	22 (1.9)
Donor/recipient sex match - no. (%)	
M-M	456 (39.3)
M-F	271 (23.3)
F-M	236 (20.3)
F-F	192 (16.5)
Missing	6 (0.5)
Graft type - no. (%)	
Bone marrow	111 (9.6)
Peripheral blood	1050 (90.4)
Conditioning regimen: Main effect - no. (%)	
MAC: Fludarabine/Busulfan	296 (25.5)
MAC: Busulfan/Cytoxan (Bu/Cy)	196 (16.9)
MAC: Others	79 (6.8)
RIC: Fludarabine/Busulfan	183 (15.8)
RIC: Fludarabine/Melphalan	318 (27.4)
RIC: Others	89 (7.7)
Conditioning regimen intensity - no. (%)	
MAC	571 (49.2)
RIC	590 (50.8)
Conditioning regimen - no. (%)	
TBI/Cy	46 (4)
TBI/Cy/Flu	24 (2.1)
TBI/Cy/TT	1 (0.1)
TBI/Cy/VP	3 (0.3)
TBI/Mel	12 (1)

Characteristic	N
TBI/Flu	51 (4.4)
TBI/other(s)	8 (0.7)
Bu/Cy	196 (16.9)
Bu/Mel	4 (0.3)
Flu/Bu/TT	5 (0.4)
Flu/Bu	479 (41.3)
Flu/Mel/TT	5 (0.4)
Flu/Mel	324 (27.9)
Other(s)	3 (0.3)
GVHD prophylaxis - no. (%)	
No GVHD prophylaxis	7 (0.6)
Ex-vivo T-cell depletion	5 (0.4)
CD34 selection	17 (1.5)
Post-CY + other(s)	61 (5.3)
TAC + MMF ± other(s) (except post-CY)	135 (11.6)
TAC + MTX ± other(s) (except MMF, post-CY)	585 (50.4)
TAC + other(s) (except MMF, MTX, post-CY)	59 (5.1)
TAC alone	17 (1.5)
CSA + MMF ± other(s) (except post-CY)	52 (4.5)
CSA + MTX ± other(s) (except MMF, post-CY)	185 (15.9)
CSA + other(s) (except MMF, MTX, post-CY)	6 (0.5)
CSA alone	15 (1.3)
Other(s)	11 (0.9)
Missing	6 (0.5)
TX year - no. (%)	
2000	23 (2)
2001	22 (1.9)
2002	31 (2.7)
2003	30 (2.6)
2004	32 (2.8)
2005	53 (4.6)
2006	41 (3.5)
2007	37 (3.2)
2008	59 (5.1)
2009	64 (5.5)
2010	24 (2.1)
2011	10 (0.9)
2012	8 (0.7)
2013	30 (2.6)
2014	107 (9.2)
2015	90 (7.8)

Characteristic	N
2016	100 (8.6)
2017	198 (17.1)
2018	202 (17.4)
Follow-up - median (min-max)	24.08 (3.22-72.14)

Proposal: 1911-225

Title:
The Impact of Somatic Mutations on Allogeneic Hematopoietic Cell Transplant Outcomes in Patients with Low and Intermediate Risk Myelodysplastic Syndrome

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Research hypothesis:
We hypothesize that in patients with "lower-risk" (very low/low/intermediate risk by IPSS-R) myelodysplastic syndrome (MDS):

- Allogeneic hematopoietic cell transplantation (HCT) is a highly effective therapy with long-term survival, and
- Somatic mutations have prognostic relevance.

Specific aims:

- Evaluate HCT outcomes in patients with "lower-risk" MDS who underwent allogeneic HCT and were registered in the Center for International Blood and Marrow Transplant Research (CIBMTR).
- Identify clinical risk factors for HCT outcomes in patients with "lower-risk" MDS.
- Characterize the mutation profile in the "lower-risk" MDS who underwent HCT and determine the incidence of high-risk mutations in this population.
- Examine potential impact of somatic mutations in patients with "lower-risk" MDS on HCT outcomes.

Scientific impact:
While the benefit of allogeneic HCT in patients with high risk MDS has been widely accepted [1-3] the precise indication of HCT and optimal timing of the procedure for patients with "lower-risk" MDS have not been well studied or agreed by the transplant community. This is in part due to the heterogeneity in the clinical and prognostic conditions among patients with "lower-risk" MDS and relative lack of transplant data focused on this population. Our study would be one of the first to focus on patients with "lower-risk" MDS with regards to the patient demographics, transplant characteristics, and outcomes after allogeneic HCT. The descriptive outcome data from our analyses will inform physicians and patients in discussing about treatment options and approaches towards HCT. The proposed clinical risk factor analyses will also inform the researchers in the filed towards development of novel approaches for patients with identified risk factors.
Moreover, our proposed study will be the first to describe the landscape of somatic mutations in this specific patient population whose IPSS-R is not high, yet, clinically need allogeneic HCT. With the expected development of molecularly refined IPSS-R (IPSS-Mol) in the near future, our proposal 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. The proposed analyses would help us identifying MDS patients classified as "lower risk" by IPSS-R who could yet benefit from an early allogeneic HCT after diagnosis and help improve outcome. This analysis could also identify a subgroup of patients with "low-risk" MDS whose prognosis is poor despite of undergoing allogeneic HCT and thus require further modifications in conditioning regimen and/or GVHD prophylaxis and incorporation of novel therapeutic approaches such as mutation-specific kinase inhibitors.

Scientific justification:

MDS is a heterogeneous hematopoietic cell disorder driven by genetic alterations leading to ineffective hematopoiesis and cytopenia.[4] Clinical presentation of MDS ranges from mild asymptomatic cytopenia to severe symptomatic transfusion-dependent cytopenia, recurrent infections and rapid progression to acute leukemia. A Revised International Prognostic Scoring System (IPSS-R)[5] has been developed by the International Working Group for the Prognosis of MDS (IWG-PM) that utilizes clinical/hematologic prognostic features to risk stratify MDS. This risk stratification has been used to determine therapeutic interventions in patients with MDS, ranging from supportive care, hypomethylating agents (HMA), and allogeneic HCT.

Allogeneic HCT is the only curative therapy available for the patients with MDS. However, it is associated with significant risks of transplant-related mortality/morbidities due to graft-versus-host disease (GVHD), infections, and regimen-related toxicities. As a result, HCT has been generally offered to fit/younger patients with higher-risk disease, and such practice is supported by decision analysis studies in recipients of both myeloablative conditioning (MAC) and reduced intensity conditioning (RIC) HCT.[1,2]

While IPSS/IPSS-R are highly informative and predictive of MDS prognosis, the models do not consider somatic mutations as a prognostic variable. Several prognostic mutations have been identified in MDS and their role has been studied on survival after allogeneic HCT. A CIBMTR analysis of 1514 samples from the MDS patients who underwent HCT between 2005 and 2014 [6] included 746 patients who had lower-risk MDS (very low: 119, low: 287, and intermediate: 340). This analysis showed that TP53 mutations were present in 19% of the patients (13% of lower risk) and were associated with poor survival and increased risk of relapse with both RIC and MAC for HCT. Presence of RAS pathway mutations predicted poor survival and increased risk of relapse with RIC HCT and this poor risk feature was overcome by MAC HCT. JAK2 mutations predicted poor survival without an increased risk of relapse and this poor risk feature was not overcome by MAC HCT. However, no specific analyses were performed for a subgroup of patients with "lower-risk" MDS in this study.

A recent EBMT retrospective analysis on "lower-risk" (defined as low/intermediate-1 by IPSS) MDS patients showed that most of these patients (76%) were reclassified as intermediate or higher risk according to IPSS-R. The 3-year overall survival (OS) and PFS were 58% and 54%, respectively. [3] Although this report analyzed various factors that affected transplant outcome including IPSS-R, disease status at transplant, prior treatment, stem cell source, CMV serostatus, T-cell depletion, conditioning therapy, the role of somatic mutations was not evaluated.

Given the increasing knowledge and evidence of prognostic effect of somatic mutations, we propose a study to assess the outcome of allogeneic HCT in patients with "lower risk" MDS with the specific goal of determining the prognostic impact of somatic mutations in this understudied population.

Patient eligibility population:

Patients with very low, low, and intermediate risk MDS by IPSS-R, both at the time of diagnosis and at the time of HCT, aged 18 and above who underwent allogeneic HCT from 2001 through 2016 will be included in this study to allow at least a three-year follow-up period. All patients who progressed to high/very high risk by IPSS-R after initial diagnosis and before HCT would be excluded. Only patients who have available biologic samples in the NMDP repository will be included. To reduce the heterogeneity of the cohort, we plan to exclude those who received *ex-vivo* T cell depletion, haploidentical donor HCT, and umbilical cord blood as a stem cell source.

Data requirements:

Patient characteristics (age, gender, KPS, HCT-CI), disease-specific characteristics (prior treatment, blood and marrow blasts, HCT-specific IPSS), HCT-related variables (conditioning regimen, GVHD prophylaxis, donor type, graft source, donor-recipient sex match, donor-recipient CMV status).

Outcome measures will include GVHD (acute GVHD grade 2-4, chronic GVHD at 1, 3, and 5 years post-HCT), NRM, relapse, DFS, and OS (assessed at 100 days, six months, 1 year and 3-year time), and cause of death.

Sample requirements:
We propose to assay for recurrent somatic mutations using biologic samples from the NMDP repository, and our HopeSeq mutation assay. The feasibility of detecting genetic mutations using the archived CIBMTR sample repository has been previously demonstrated in a large successful MDS study by Lindsey et al,[6] We propose to include the data for "lower-risk" MDS patients from that study and include additional patients in the repository between 2001-2004 and 2015-2016. At City of Hope, We have collaborated Dr. Pillai on multiple successful projects in molecularly characterizing patients with MDS,[7] myelofibrosis,[8] and chronic myelomonocytic leukemia (CK18-02, PI: Mei) who underwent HCT, and the exact gene panels and methods have been described in detail. Depending on the final number of samples to be tested for somatic mutations, City of Hope's institutional fund would be available to support this project. Alternatively, to be consistent with the previous CIBMTR study,[6] we may consider another collaboration with Dr. Lindsley's team.

Study design:
The study will be a retrospective analysis of patients who underwent alloHCT for very low, low and intermediate risk MDS from 2001 through 2017. Descriptive analyses of patient-, disease- and donor-variables will be performed. Kaplan-Meier curves will be used for OS and DFS. Cumulative incidence curves will be used for NRM, relapse, and GVHD. Probabilities of OS, DFS, NRM, relapse, and GVHD at specified time points and 95%CIs will be estimated from these curves. Multivariate analyses for survival (OS, DFS), NRM, relapse, and GVHD will be performed using the Cox proportional hazards model and the proportional sub-distribution hazards model for competing risks adjusting for the effects of covariates whenever appropriate. The covariates to be evaluated will include patient-specific variables (age, gender, KPS, HCT-CI), disease-related variables (disease classification at the time of diagnosis, time from diagnosis to HCT, IPSS, and IPSS-R at diagnosis and pre-HCT, treatment before transplantation, diseases status at HCT, transfusion dependence, percentage of marrow blasts at transplant), and transplant-related variables (graft source, donor type, GVHD prophylaxis, conditioning regimen (RIC, MAC), donor-recipient sex match, donor-recipient CMV serostatus, donor-recipient ABO typing, year of transplantation). Both univariate and multivariate analyses will be conducted to examine the associations between single somatic mutations, composite mutations, and the IPSS-Mol (once published), and alloHCT outcomes.

Non-CIBMTR data source: None.

Conflicts of interest: None

References:
1. Cutler CS, Lee SJ, Greenberg P, et al. A decision analysis of allogeneic bone marrow transplantation for the myelodysplastic syndromes: delayed transplantation for low-risk myelodysplasia is associated with improved outcome. *Blood*. 2004;104(2):579-585.
2. Koreth J, Pidala J, Perez WS, et al. Role of reduced-intensity conditioning allogeneic hematopoietic stem-cell transplantation in older patients with de novo myelodysplastic syndromes: an international collaborative decision analysis. *J Clin Oncol*. 2013;31(21):2662-2670.
3. Robin M, Porcher R, Zinke-Cerwenka W, et al. Allogeneic haematopoietic stem cell transplant in patients with lower risk myelodysplastic syndrome: a retrospective analysis on behalf of the Chronic Malignancy Working Party of the EBMT. *Bone Marrow Transplant*. 2017;52(7):1081.

4. Steensma DP. Myelodysplastic syndromes current treatment algorithm 2018. *Blood Cancer J*. 2018;8(5):47.
5. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. *Blood*. 2012;120(12):2454-2465.
6. Lindsley RC, Saber W, Mar BG, et al. Prognostic Mutations in Myelodysplastic Syndrome after Stem-Cell Transplantation. *N Engl J Med*. 2017;376(6):536-547.
7. Aldoss I, Pham A, Li SM, et al. Favorable impact of allogeneic stem cell transplantation in patients with therapy-related myelodysplasia regardless of TP53 mutational status. *Haematologica*. 2017;102(12):2030-2038.
8. Ali H, Aldoss I, Yang D, et al. MIPSS70+ v2.0 predicts long-term survival in myelofibrosis after allogeneic HCT with the Flu/Mel conditioning regimen. *Blood Adv*. 2019;3(1):83-95.

Table 1. Characteristics of patients with very low, low, and intermediate risk MDS with biorepository samples from 2001 through 2016

Characteristic	N
No. of patients	621
No. of centers	107
Patient age - median (min-max)	59.58 (18.36-77.68)
Age - no. (%)	
18-29	28 (4.5)
30-39	32 (5.2)
40-49	66 (10.6)
50-59	197 (31.7)
60-69	264 (42.5)
≥ 70	34 (5.5)
Sex - no. (%)	
Male	401 (64.6)
Female	220 (35.4)
Race - no. (%)	
Caucasian	107 (73.8)
African-American	12 (8.3)
Asian	14 (9.7)
Pacific islander	1 (0.7)
Other	2 (1.4)
Missing	9 (6.2)
HCT-CI - no. (%)	
0	28 (19.3)
1	11 (7.6)
2	8 (5.5)
3+	38 (26.2)
NA, f2400 (pre-TED) not completed	57 (39.3)
Missing	3 (2.1)
Karnofsky score - no. (%)	
90-100	382 (61.5)
< 90	208 (33.5)
Missing	31 (5)
Time from diagnosis to HCT - no. (%)	
<6	167 (26.9)
6-11	215 (34.6)
≥12	239 (38.5)
Donor type - no. (%)	
HLA-identical sibling	164 (26.4)
Twin	4 (0.6)

Characteristic	N
Other related	7 (1.1)
Well-matched unrelated (8/8)	363 (58.5)
Partially-matched unrelated (7/8)	70 (11.3)
Mis-matched unrelated (≤6/8)	8 (1.3)
Multi-donor	3 (0.5)
Unrelated (matching TBD)	2 (0.3)
Donor/recipient sex match - no. (%)	
M-M	290 (46.7)
M-F	132 (21.3)
F-M	111 (17.9)
F-F	88 (14.2)
Donor/recipient CMV serostatus - no. (%)	
+/+	184 (29.6)
+/-	66 (10.6)
-/+	185 (29.8)
-/-	181 (29.1)
Missing	5 (0.8)
Graft type - no. (%)	
Bone marrow	95 (15.3)
Peripheral blood	526 (84.7)
Conditioning regimen intensity - no. (%)	
MAC	327 (52.7)
RIC	256 (41.2)
NMA	31 (5)
TBD	7 (1.1)
Conditioning regimen - no. (%)	
TBI/Cy	36 (5.8)
TBI/Cy/Flu	7 (1.1)
TBI/Cy/VP	2 (0.3)
TBI/Mel	4 (0.6)
TBI/Flu	45 (7.2)
TBI/other(s)	4 (0.6)
Bu/Cy	127 (20.5)
Bu/Mel	8 (1.3)
Flu/Bu	275 (44.3)
Flu/Mel/TT	1 (0.2)
Flu/Mel	87 (14)
Cy/Flu	5 (0.8)
Cy alone	1 (0.2)
Treosulfan	3 (0.5)
TLI	11 (1.8)

Characteristic	N
Other(s)	5 (0.8)
GVHD prophylaxis - no. (%)	
Ex-vivo T-cell depletion	7 (1.1)
CD34 selection	8 (1.3)
TAC + MMF ± other(s) (except post-CY)	84 (13.5)
TAC + MTX ± other(s) (except MMF, post-CY)	223 (35.9)
TAC + other(s) (except MMF, MTX, post-CY)	32 (5.2)
TAC alone	13 (2.1)
CSA + MMF ± other(s) (except post-CY)	37 (6)
CSA + MTX ± other(s) (except MMF, post-CY)	29 (4.7)
CSA + other(s) (except MMF, MTX, post-CY)	4 (0.6)
Other(s)	6 (1)
Missing	178 (28.7)
TX year - no. (%)	
2001	8 (1.3)
2002	8 (1.3)
2003	14 (2.3)
2004	17 (2.7)
2005	18 (2.9)
2006	21 (3.4)
2007	28 (4.5)
2008	54 (8.7)
2009	78 (12.6)
2010	52 (8.4)
2011	91 (14.7)
2012	93 (15)
2013	116 (18.7)
2014	11 (1.8)
2015	11 (1.8)
2016	1 (0.2)

Table 2a. Overlapped patients from Dr. Coleman's study:

Overlap	Frequency	Percent
No	367	59.1
Yes	254	40.9

Table 2b. Overlapped patients' distribution by years.

	Overlap			
	0 no		1 yes	
Year of HCT	N	%	N	%
2001	8	100	0	0
2002	8	100	0	0
2003	14	100	0	0
2004	17	100	0	0
2005	14	77.78	4	22.22
2006	6	28.57	15	71.43
2007	10	35.71	18	64.29
2008	34	62.96	20	37.04
2009	45	57.69	33	42.31
2010	26	50	26	50
2011	45	49.45	46	50.55
2012	53	56.99	40	43.01
2013	64	55.17	52	44.83
2014	11	100	0	0
2015	11	100	0	0
2016	1	100	0	0
Total	367	59.1	254	40.9

Proposal: 1911-245

Title:
Outcomes of allogenic hematopoietic stem cell transplantation for patients with B-cell prolymphocytic leukemia

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Research hypothesis:
- Allogenic hematopoietic stem cell transplantation (ASCT) for B-cell prolymphocytic leukemia (B-PLL) is associated with long term progression free survival and overall survival.
- Pre-transplant factors including age, disease duration, remission status, white count, HCT-CI and cytogenetics can help identify prognostic factors for patients with B-PLL undergoing ASCT.

Specific aims:
- To determine the outcomes of allogenic stem cell transplantation for B-PLL including progression free survival, overall survival, non-relapse and relapse mortality.
- To identify prognostic factors associated with outcomes for improved risk stratification.

Scientific impact:
- This study will help us determine the outcomes after ASCT for B-PLL and identify prognostic factors for risk stratification.

Scientific justification:
B-PLL is a rare disease, making up less than 1% of all mature B-cell malignancies.[1] It is a disease of elderly (median age of diagnosis 69 years), presenting with massive splenomegaly, marked lymphocytosis and prominent B-symptoms. However, some patients can be asymptomatic or have minimal symptoms. [2]The diagnosis of B-PLL requires the presence of more than 55% prolymphocytes in the peripheral blood. B PLL strongly expresses surface immunoglobulins along with various B-cell antigens (CD20, CD22, CD79a and FMC7). CD5 and CD23 are expressed in one third of the cases and are usually weak or absent.
The clinical course of B-PLL is highly variable and treatment strategies have not been defined. B-PLL is frequently described as having an aggressive course, poor prognosis and a median survival of 3 -5 years. However, there are reports of some patients having prolonged survival. [3]Definite prognostic factors have not been established and small case series have suggested advanced age, anemia, lymphocytosis, TP53 mutation and de novo PLL as indicators of poor outcomes. [4, 5]In the absence of robust data to guide treatment, B-PLL is most commonly treated with regimens similar to CLL. However the responses are often partial and short lived. Allogenic stem cell transplant has been suggested as a curative approach and durable responses have been reported in several case reports. [6, 7]We aim to study the outcomes after ASCT for B-PLL and determine risk factors which correlate with outcomes. This will help us determine the patient population that is most likely to benefit from transplant. The CIBMTR database is highly suitable for answering these questions. Kalaycio et al conducted a CIBMTR analysis evaluating the outcomes of all PLL patients (B-cell and T-cell PLL) with allotransplant, from 1995 to 2005. [8]However, the study was very limited in its scope due to the small numbers and heterogeneous population. We aim to carry out an updated analysis with recent data (1995 to 2017) in patients with B-PLL to better define the outcomes in this population.

Patient eligibility population:
All patients with B-PLL treated with allogenic stem cell transplant from 1995 to 2017

Data requirements:
All data is already available in the CIBMTR database using established forms.

Subject-related variables:
- Age at transplant
- KPS
- Gender
- Race
- HST-CI

Disease-related variables:
- Cytogenetics
- Disease duration
- Disease status at transplant

Transplant-related variables:
- Type of transplant
- Stem cell mobilization
- Conditioning regimen
- GVHD prophylaxis
- Stem cell dose
- Product manipulation

Disease–related variables/post-HSCT:
- Post-HCT treatment
- Chimerism
- Acute and Chronic GVHD
- Infections
- New malignancy

Complications:
- Early and late mortality

Outcomes considered at 100 days, 6 months, and annually throughout follow-up:
- PFS
- OS

Sample requirements:
None

Study design:
This is a retrospective cohort observational study. The OS and PFS will be estimated using Kaplan-Meier estimator. Multivariate cox regression analysis will be used to determine the variables affecting the PFS and OS

Non-CIBMTR data source:
None

Conflicts of interest:
No

References:
1. Dearden, Claire. "How I treat prolymphocytic leukemia." *Blood* 120.3 (2012): 538-551.
2. S. H. Swerdlow, E. Campo, and N. Harris, World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues, International Agency for Research on Cancer, Lyon, France, 2008
3. Van Der Velden, Vincent HJ, et al. "B-cell prolymphocytic leukemia: a specific subgroup of mantle cell lymphoma." *Blood* 124.3 (2014): 412-419.
4. Shvidel, Lev, et al. "B-cell prolymphocytic leukemia: a survey of 35 patients emphasizing heterogeneity, prognostic factors and evidence for a group with an indolent course." *Leukemia & lymphoma* 33.1-2 (1999): 169-179.
5. Hercher, Christel, et al. "A multicentric study of 41 cases of B-prolymphocytic leukemia: two evolutive forms: the Groupe Français d'Hématologie Cellulaire." *Leukemia & lymphoma* 42.5 (2001): 981-987.
6. Arima, Hiroshi, et al. "Successful allogeneic hematopoietic stem cell transplantation with reduced-intensity conditioning for B-cell prolymphocytic leukemia in partial remission." *International journal of hematology* 99.4 (2014): 519-522.
7. Castagna, L., et al. "Allogeneic peripheral stem-cell transplantation with reduced-intensity conditioning regimen in refractory primary B-cell prolymphocytic leukemia: a long-term follow-up." *Bone marrow transplantation* 35.12 (2005): 1225.
8. Kalaycio ME, Kukreja M, Woolfrey AE, et al. Allogeneic hematopoietic cell transplant for prolymphocytic leukemia. *Biol Blood Marrow Transplant*. 2010;16(4):543–547. doi:10.1016/j.bbmt.2009.11.021

Table 1. Characteristic of patients with B-Cell PLL from 2000-2018 reported to the CIBMTR

Characteristic	N
No. of patients	71
No. of centers	45
track - no. (%)	
TED	59 (83.1)
CRF	12 (16.9)
age - median (min-max)	59.26 (5.13-80.38)
Age - no. (%)	
<18	2 (2.8)
40-49	8 (11.3)
50-59	30 (42.3)
60-69	29 (40.8)
≥ 70	2 (2.8)
Sex - no. (%)	
Male	57 (80.3)
Female	14 (19.7)
Race - no. (%)	
Caucasian	61 (85.9)
African-American	2 (2.8)
Asian	2 (2.8)
Missing	6 (8.5)
HCT-CI - no. (%)	
0	18 (25.4)
1	3 (4.2)
2	10 (14.1)
3+	18 (25.4)
NA, f2400 (pre-TED) not completed	21 (29.6)
Missing	1 (1.4)
Karnofsky score - no. (%)	
90-100	34 (47.9)
< 90	33 (46.5)
Missing	4 (5.6)
Time from diagnosis to HCT - no. (%)	
<6	11 (15.5)
6-11	20 (28.2)
≥12	33 (46.5)
Missing	7 (9.9)
Donor type - no. (%)	
Autologous	4 (5.6)
HLA-identical sibling	31 (43.7)
Other related	4 (5.6)

Characteristic	N
Well-matched unrelated (8/8)	15 (21.1)
Partially-matched unrelated (7/8)	2 (2.8)
Unrelated (matching TBD)	10 (14.1)
Cord blood	5 (7)
Donor/recipient sex match - no. (%)	
M-M	32 (45.1)
M-F	8 (11.3)
F-M	17 (23.9)
F-F	5 (7)
CB - recipient M	5 (7)
Missing	4 (5.6)
Graft type - no. (%)	
Bone marrow	7 (9.9)
Peripheral blood	59 (83.1)
Cord blood	5 (7)
Conditioning as reported by center - no. (%)	
MAC	18 (25.4)
RIC/NMA	49 (69)
Missing	4 (5.6)
Conditioning regimen - no. (%)	
TBI/Cy	4 (5.6)
TBI/Cy/Flu	3 (4.2)
TBI/Cy/TT	1 (1.4)
TBI/Cy/VP	1 (1.4)
TBI/VP	1 (1.4)
TBI/Mel	1 (1.4)
TBI/Flu	14 (19.7)
TBI/other(s)	4 (5.6)
Bu/Cy	1 (1.4)
Flu/Bu	16 (22.5)
Flu/Mel	9 (12.7)
FCR	1 (1.4)
Cy/Flu	2 (2.8)
CBV	1 (1.4)
BEAM	1 (1.4)
BEAM like	2 (2.8)
Treosulfan	1 (1.4)
TLI	1 (1.4)
Other(s)	1 (1.4)
Missing	6 (8.5)
GVHD prophylaxis - no. (%)	

Characteristic	N
Ex-vivo T-cell depletion	1 (1.4)
CD34 selection	1 (1.4)
Post-CY	4 (5.6)
TAC based	31 (43.7)
CSA based	24 (33.8)
Other	1 (1.4)
Missing	9 (12.7)
TX year - no. (%)	
2000	3 (4.2)
2001	3 (4.2)
2002	2 (2.8)
2003	2 (2.8)
2004	4 (5.6)
2005	2 (2.8)
2006	4 (5.6)
2007	1 (1.4)
2008	5 (7)
2009	8 (11.3)
2010	9 (12.7)
2011	5 (7)
2012	3 (4.2)
2013	6 (8.5)
2014	2 (2.8)
2015	6 (8.5)
2017	3 (4.2)
2018	3 (4.2)
Follow-up - median (min-max)	72.99 (6.15-120.43)

Proposal: 1909-06/1911-04

Title:
Transplant outcomes for patients with large granular lymphocyte (LGL) leukemia

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Hypothesis:
Stem cell transplant is a safe and effective treatment modality for patients with T- and natural killer (NK)-cell large granular lymphocyte (LGL) leukemia.

Specific aims:
- To study the patient- and transplant related characteristics in LGL leukemia patients undergoing stem cell transplant.
- To analyze transplant outcomes including relapse-free (RFS), transplant-related mortality (TRM), overall survival (OS), and cumulative incidence of graft-*vs*-host disease (GVHD).

Scientific justification:
Large granular lymphocyte (LGL) leukemia is a rare lymphoproliferative disorder of T- (T-LGL leukemia) or natural killer (NK)-cells (NK-LGL leukemia). LGL leukemia is commonly associated with various autoimmune or hematological disorders with neutropenia and rheumatoid arthritis (RA) being the most common associations. While considered to be an indolent disorder, LGL leukemia imparts significant morbidity and mortality in patients (Zhang, Shah et al. 2010, Shah, Hook et al. 2016).
Most LGL leukemia patients will require treatment. The most common treatment options used are immunosuppressive agents such as steroids, methotrexate (MTX), cyclosporine A (CsA), and cyclophosphamide. Unfortunately, durable responses are a rarity, leaving a large proportion of patients without a reliable therapeutic options (Lamy and Loughran 2011, Shah, Hook et al. 2016). Thus, despite its rarity, LGL leukemia as an indication for transplant is not an infrequent dilemma in practice. Despite that, the safety and efficacy of transplant remain unanswered. Even the fundamental questions, such as whether autologous or allogeneic transplant should be performed are not known.
From stem cell transplant stand point, LGL leukemia presents some unique challenges including older population, associated autoimmune and/or hematological disorders, and pre-existing profound immunosuppression. Most literature available regarding transplant experience in LGL leukemia is in the form of case report or case series.(Seebach, Speich et al. 1995, La Nasa, Littera et al. 2004, Osuji, Matutes et al. 2005) The largest case series from the European Bone Marrow Transplant (EBMT) registry studying the experience of 16 heterogeneous transplants failed to provide any significant insights (Marchand, Lamy et al. 2016).
Given the rarity of the disease, no single center experience is likely to provide meaningful guidance, in turn proving a deterrent to making evidence-based decisions for future transplants. Preliminary analysis suggests that transplant data is available for **145 patients with T- or NK-LGL leukemia**. Given the robustness of the associated clinical information, CIBMTR study will, by far, be the largest study of transplant outcomes in LGL leukemia. Overall, the proposed study has a potential to advance the field and be the cornerstone in providing meaningful information to many patients and physicians.

Patient eligibility population:
The study will include all LGL leukemia patients undergoing HSCT between 2000 and 2018.

Data requirements:
Recipient baseline data (2000), Infectious disease markers (2004), CLL pre-HCT data (2013); Post-HCT data (2100); and CLL post-HCT data (2113)

Variables to be analyzed:
Patient related variables:

- Age at diagnosis
- Sex: Female vs. male
- Age at the time of transplantation
- History of autoimmune diseases
- Associated hematological malignancies
- History of smoking
- Interval between time of diagnosis and transplant
- Karnofsky performance score (< 70 vs. ≥ 70)
- Hematopoietic stem cell transplant comorbidity index (HCT-CI)

Disease related variables at diagnosis and pre-transplant treatment:

- Histological subtype (T- vs. NK-cell) of LGL leukemia
- Complete blood count (hemoglobin, absolute neutrophil count, and platelet) at diagnosis
- Systemic therapies given prior to transplant (corticosteroids, cyclophosphamide, Campath, and other)
- Best response to systemic therapy prior to transplant

Disease related variables prior to transplant (before initiation of conditioning regimen):

- Complete blood count (hemoglobin, absolute neutrophil count, platelet, and absolute lymphocyte count) at the time of transplant
- Percentage bone marrow involvement with lymphocytes
- Pre-transplant serum creatinine
- Pre-transplant liver function (AST and bilirubin)
- Pre-transplant infections (CRF patients, n=41)
- Time from diagnosis to transplant (<6 months, 6-11 months, ≥12 months)
- T-cell gene rearrangement (positive vs. negative, when available)

Transplant related variables:

- Type of transplant – autologous vs. allogeneic
- For allogeneic transplant, donor type – HLA-matched sibling, HLA-matched unrelated, cord blood unit, or haploidentical donor.
- Conditioning regimen using the standard CIBMTR definition (RIC vs. MAC)
- Graft source – bone marrow (BM) vs. peripheral blood stem cell (PBSC)
- CD34 cell dose infusion
- Graft manipulation, if any
- Donor and recipient CMV serologic status
- GVHD prophylaxis – cyclosporine-based, calcineurin inhibitor-based, methotrexate, post-transplant cyclophosphamide,

- Alemtuzumab (yes vs. no) and ATG (yes vs. no)
- TBI based regimen (yes vs. no)
- GVHD prophylaxis (Tac vs. CSA based regimen)
- Year of transplant (2000-2004, 2005-2010, 2010-2014, 2015-now)

Study variables post-transplant:
- Time to neutrophil recovery
- Time to platelet recovery
- Acute GVHD – grade 0-I vs. grade II-IV
- Chronic GVHD – yes vs. no
- Lymphocyte subset analysis (CD3, CD8, and CD56 when available)

Response criteria:
Standard response criteria will be used (Lamy and Loughran 2011). Briefly, hematologic complete response (**CR**) is defined as the complete normalization of blood counts (i.e. hemoglobin>12g/dL, platelets>150x10^9/L, ANC>1.5x10^9/L, and lymphocytosis<4x10^9/L), and circulating LGL in the normal range using flow cytometry. Hematologic partial response (**PR**) is defined as an improvement in blood counts that do not meet criteria for complete remission (*e.g*. sustained absolute neutrophil count>500 without growth factor support or decreasing transfusion requirements over 8 weeks duration). Treatment failure is defined as any response not meeting these criteria within 4 months after the transplant. Progressive disease is the worsening of cytopenia or organomegaly.

Study end points and definitions:
Primary study end-points are:
- 5-year relapse-free (RFS) and overall survival (OS).
- Secondary study-endpoints are-
- Transplant related mortality (TRM) at day 100, 1-year and 5-years post-transplant
- Time to neutrophil recovery
- Cumulative incidence of acute GVHD grades 2-4
- Cumulative incidence of chronic GVHD
- Relapse: Relapsed LGL leukemia as defined by the WHO. This event will be summarized by cumulative incidence estimate with TRM as the competing risk.
- RFS: Survival without disease progression or relapse; patients alive without disease progression or relapse will be censored at the time of last follow-up.
- TRM: Time to death without the evidence of disease relapse. This event will be summarized as cumulative incidence estimate with relapse as competing risk.
- OS: Time to death, patients censored at last follow-up.
- Time to neutrophil recovery: Frist of the 3 consecutive days with absolute neutrophil count of ≥ 500 neutrophils/mL post-transplant
- GVHD: Grades 2- 4 acute GVHD and chronic GVHD as defined.(Shulman, Sullivan et al. 1980, Przepiorka, Weisdorf et al. 1995)

Sample requirements:
All requested data is available from existing data collection forms.

Study design:

This is a retrospective cohort analysis to study the transplant outcomes for LGL leukemia patients. The patient and disease characteristics will be studied. The differences between categorical covariates will be tested using Fisher's exact test, and the differences between continuous covariates will be compared using Wilcoxon's rank-sum test.

Next, transplant outcomes will be studied. The incidence rates of neutrophil engraftment, TRM, disease progression, and GVHD will be estimated using the cumulative incidence method to account for competing risks as described above. Disease progression or death attributable to the 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 RFS and OS will be estimated using the Kaplan-Meier method.

References:

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3. Marchand, T., T. Lamy, H. Finel, W. Arcese, S. Choquet, J. Finke, A. Huynh, G. Irrera, D. Karakasis, J. Konopacki, J. Lambert, M. Michieli, H. C. Schouten, W. Schroyens, G. Sucak, J. Tischer, E. Vandenberghe and P. Dreger (2016). "Hematopoietic stem cell transplantation for T-cell large granular lymphocyte leukemia: a retrospective study of the European Society for Blood and Marrow Transplantation." Leukemia **30**(5): 1201-1204.
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Table 1. Characteristic of patients with large granular lymphocyte (LGL) leukemia

Characteristic	N
No. of patients	145
No. of centers	90
track - no. (%)	
TED	104 (71.7)
CRF	41 (28.3)
age - median (min-max)	39.8 (1.49-73.12)
Age - no. (%)	
<18	26 (17.9)
18-29	26 (17.9)
30-39	22 (15.2)
40-49	25 (17.2)
50-59	30 (20.7)
60-69	14 (9.7)
≥ 70	2 (1.4)
Sex - no. (%)	
Male	100 (69)
Female	45 (31)
Race - no. (%)	
Caucasian	107 (73.8)
African-American	12 (8.3)
Asian	14 (9.7)
Pacific islander	1 (0.7)
Other	2 (1.4)
Missing	9 (6.2)
HCT-CI - no. (%)	
0	28 (19.3)
1	11 (7.6)
2	8 (5.5)
3+	38 (26.2)
NA, f2400 (pre-TED) not completed	57 (39.3)
Missing	3 (2.1)
Karnofsky score - no. (%)	
90-100	56 (38.6)
< 90	75 (51.7)
Missing	14 (9.7)
Time from diagnosis to HCT - no. (%)	
<6	35 (24.1)
6-11	27 (18.6)
≥12	73 (50.3)

Characteristic	N
Missing	10 (6.9)
Donor type - no. (%)	
Autologous	10 (6.9)
HLA-identical sibling	60 (41.4)
Other related	7 (4.8)
Well-matched unrelated (8/8)	27 (18.6)
Partially-matched unrelated (7/8)	7 (4.8)
Mis-matched unrelated (≤6/8)	1 (0.7)
Unrelated (matching TBD)	16 (11)
Cord blood	15 (10.3)
Missing	2 (1.4)
Donor/recipient sex match - no. (%)	
M-M	52 (35.9)
M-F	20 (13.8)
F-M	29 (20)
F-F	17 (11.7)
CB - recipient M	9 (6.2)
CB - recipient F	6 (4.1)
Missing	12 (8.3)
Graft type - no. (%)	
Bone marrow	32 (22.1)
Peripheral blood	98 (67.6)
Cord blood	15 (10.3)
Conditioning as reported by center - no. (%)	
MAC	82 (56.6)
RIC/NMA	41 (28.3)
Missing	22 (15.2)
Conditioning regimen - no. (%)	
TBI/Cy	27 (18.6)
TBI/Cy/Flu	12 (8.3)
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TBI/VP	13 (9)
TBI/Mel	4 (2.8)
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TBI/other(s)	8 (5.5)
Bu/Cy	10 (6.9)
Bu/Mel	1 (0.7)
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Flu/Bu	17 (11.7)

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Flu/Mel/TT	1 (0.7)
Flu/Mel	14 (9.7)
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BEAM	7 (4.8)
TLI	1 (0.7)
Other(s)	3 (2.1)
None	1 (0.7)
Missing	5 (3.4)
GVHD prophylaxis - no. (%)	
Ex-vivo T-cell depletion	1 (0.7)
CD34 selection	2 (1.4)
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TAC based	60 (41.4)
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2003	11 (7.6)
2004	5 (3.4)
2005	11 (7.6)
2006	5 (3.4)
2007	5 (3.4)
2008	2 (1.4)
2009	10 (6.9)
2010	6 (4.1)
2011	5 (3.4)
2012	14 (9.7)
2013	10 (6.9)
2014	12 (8.3)
2015	5 (3.4)
2016	10 (6.9)
2017	4 (2.8)
2018	8 (5.5)
Follow-up - median (min-max)	60.56 (3.32-192.96)

Proposal: 1909-06

Title:
Transplant outcomes for patients with T- and Natural Killer (NK)-cell large granular lymphocyte (LGL) leukemia

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Ronald S Go, MD, Mayo Clinic
Hassan Alkhateeb, MD, Mayo Clinic

Hypothesis:
Stem cell transplant is a safe and effective treatment modality for patients with T- and natural killer (NK)-cell large granular lymphocyte (LGL) leukemia.

Specific aims:
- To study the patient- and transplant related characteristics in LGL leukemia patients undergoing stem cell transplant.
- To analyze transplant outcomes including relapse-free (RFS), transplant-related mortality (TRM), overall survival (OS), and cumulative incidence of graft-*vs*-host disease (GVHD).

Scientific justification:
Large granular lymphocyte (LGL) leukemia is a rare lymphoproliferative disorder of T- (T-LGL leukemia) or natural killer (NK)-cells (NK-LGL leukemia). LGL leukemia is commonly associated with various autoimmune or hematological disorders with neutropenia and rheumatoid arthritis (RA) being the most common associations. While considered to be an indolent disorder, LGL leukemia imparts significant morbidity and mortality in patients (Zhang, Shah et al. 2010, Shah, Hook et al. 2016).
Most LGL leukemia patients will require treatment. The most common treatment options used are immunosuppressive agents such as steroids, methotrexate (MTX), cyclosporine A (CsA), and cyclophosphamide. Unfortunately, durable responses are a rarity, leaving a large proportion of patients without a reliable therapeutic options (Lamy and Loughran 2011, Shah, Hook et al. 2016). Thus, despite its rarity, LGL leukemia as an indication for transplant is not an infrequent dilemma in practice. Despite that, the safety and efficacy of transplant remain unanswered. Even the fundamental questions, such as whether autologous or allogeneic transplant should be performed are not known.
From stem cell transplant stand point, LGL leukemia presents some unique challenges including older population, associated autoimmune and/or hematological disorders, and pre-existing profound immunosuppression. Most literature available regarding transplant experience in LGL leukemia is in the form of case report or case series.(Seebach, Speich et al. 1995, La Nasa, Littera et al. 2004, Osuji, Matutes et al. 2005) The largest case series from the European Bone Marrow Transplant (EBMT) registry studying the experience of 16 heterogeneous transplants failed to provide any significant insights (Marchand, Lamy et al. 2016).
Given the rarity of the disease, no single center experience is likely to provide meaningful guidance, in turn proving a deterrent to making evidence-based decisions for future transplants. Preliminary analysis suggests that transplant data is available for **79 patients with T- or NK-LGL leukemia** (Kenny Hu, CIBMTR, *personal communication*). Given the robustness of the associated clinical information, CIBMTR study will, by far, be the largest study of transplant outcomes in LGL leukemia. Overall, the proposed study has a potential to advance the field and be the cornerstone in providing meaningful information to many patients and physicians.

Patient eligibility population:
The study will include all LGL leukemia patients undergoing HSCT between July 2000 and January 2016.

Data requirements:
Form 2014, Form 2114, Pre-TED (2400) and Comprehensive Baseline (2000)

Variables to be analyzed:
Patient related variables:

- Age at diagnosis
- Sex: Female *vs*. male
- Age at the time of transplantation
- History of autoimmune diseases
- Associated hematological malignancies
- History of smoking
- Interval between time of diagnosis and transplant
- Karnofsky performance score (< 70 *vs*. ≥ 70)
- Hematopoietic stem cell transplant comorbidity index (HCT-CI)

Disease related variables at diagnosis and pre-transplant treatment:

- Histological subtype (T- vs. NK-cell) of LGL leukemia
- Complete blood count (hemoglobin, absolute neutrophil count, and platelet) at diagnosis
- Immunophenotype (flow cytometry) of T- and NK-cell at diagnosis in the peripheral blood including peripheral absolute LGL count
- Percentage bone marrow involvement by LGL leukemia at diagnosis
- T-cell receptor gene rearrangement (positive vs. negative) for T-cell LGL leukemia patients
- Killer immunoglobulin-like receptor (KIR) expression pattern (monotypic vs. not, representative gene when available) for NK-LGL leukemia patients
- Systemic therapies given prior to transplant
- Best response to systemic therapy prior to transplant

Disease related variables prior to transplant (before initiation of conditioning regimen):

- Complete blood count (hemoglobin, absolute neutrophil count, and platelet) at the time of transplant
- Immunophenotype (flow cytometry) of T- and NK-cell in the peripheral blood including peripheral absolute LGL count at the time of transplant
- Percentage bone marrow involvement by LGL leukemia at the time of transplant
- T-cell receptor gene rearrangement (positive vs. negative) for T-cell LGL leukemia patients
- Killer immunoglobulin-like receptor (KIR) expression pattern (monotypic vs. not, representative gene when available) for NK-LGL leukemia patients
- Pre-transplant serum creatinine
- Pre-transplant liver function (AST and bilirubin)
- Pre-transplant infections

Transplant related variables:

- Type of transplant – autologous vs. allogeneic
- For allogeneic transplant, donor type – HLA-matched sibling, HLA-matched unrelated, cord blood unit, or haploidentical donor.
- Conditioning regimen using the standard CIBMTR definition
- Graft source – bone marrow (BM) vs. peripheral blood stem cell (PBSC)
- Graft manipulation, if any

- Donor and recipient CMV serologic status
- GVHD prophylaxis – cyclosporine-based, calcineurin inhibitor-based, methotrexate, post-transplant cyclophosphamide,
- Alemtuzumab (yes vs. no) and ATG (yes vs. no)

Study variables post-transplant:
- Time to neutrophil recovery
- Time to platelet recovery
- Acute GVHD – grade 0-I vs. grade II-IV
- Chronic GVHD – yes vs. no

Response criteria:
Standard response criteria will be used (Lamy and Loughran 2011). Briefly, hematologic complete response (**CR**) is defined as the complete normalization of blood counts (i.e. hemoglobin>12g/dL, platelets>150x10^9/L, ANC>1.5x10^9/L, and lymphocytosis<4x10^9/L), and circulating LGL in the normal range using flow cytometry. Hematologic partial response (**PR**) is defined as an improvement in blood counts that do not meet criteria for complete remission (*e.g*. sustained absolute neutrophil count>500 without growth factor support or decreasing transfusion requirements over 8 weeks duration). Treatment failure is defined as any response not meeting these criteria within 4 months after the transplant. Progressive disease is the worsening of cytopenia or organomegaly.

Study end points and definitions:
Primary study end-points are:
- 3-year relapse-free (RFS) and overall survival (OS).
- Secondary study-endpoints are-
- Transplant related mortality (TRM) at day 100, 1-year and 3-years post-transplant
- 3-year incidence of disease progression
- Time to neutrophil recovery
- Cumulative incidence of acute GVHD grades 2-4
- Cumulative incidence of chronic GVHD
- **Relapse:** Relapsed LGL leukemia as defined by the WHO. This event will be summarized by cumulative incidence estimate with TRM as the competing risk.
- **RFS:** Survival without disease progression or relapse; patients alive without disease progression or relapse will be censored at the time of last follow-up.
- **TRM:** Time to death without the evidence of disease relapse. This event will be summarized as cumulative incidence estimate with relapse as competing risk.
- **OS:** Time to death, patients censored at last follow-up.
- Time to neutrophil recovery: Frist of the 3 consecutive days with absolute neutrophil count of ≥ 500 neutrophils/mL post-transplant
- **GVHD:** Grades 2- 4 acute GVHD and chronic GVHD as defined.(Shulman, Sullivan et al. 1980, Przepiorka, Weisdorf et al. 1995)

Sample requirements:
All requested data is available from existing data collection forms.

Study design:

This is a retrospective cohort analysis to study the transplant outcomes for LGL leukemia patients. The patient and disease characteristics will be studied. The differences between categorical covariates will be tested using Fisher's exact test, and the differences between continuous covariates will be compared using Wilcoxon's rank-sum test.

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References:

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Pacific islander	1 (0.7)
Other	2 (1.4)
Missing	9 (6.2)
HCT-CI - no. (%)	
0	28 (19.3)
1	11 (7.6)
2	8 (5.5)
3+	38 (26.2)
NA, f2400 (pre-TED) not completed	57 (39.3)
Missing	3 (2.1)
Karnofsky score - no. (%)	
90-100	56 (38.6)
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Missing	14 (9.7)
Time from diagnosis to HCT - no. (%)	
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Donor type - no. (%)	
Autologous	10 (6.9)
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Other related	7 (4.8)
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Donor/recipient sex match - no. (%)	
M-M	52 (35.9)
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Characteristic	N
Flu/Mel/TT	1 (0.7)
Flu/Mel	14 (9.7)
Cy/Flu	3 (2.1)
Cy alone	1 (0.7)
BEAM	7 (4.8)
TLI	1 (0.7)
Other(s)	3 (2.1)
None	1 (0.7)
Missing	5 (3.4)
GVHD prophylaxis - no. (%)	
Ex-vivo T-cell depletion	1 (0.7)
CD34 selection	2 (1.4)
Post-CY	5 (3.4)
TAC based	60 (41.4)
CSA based	50 (34.5)
Missing	27 (18.6)
TX year - no. (%)	
2000	3 (2.1)
2001	8 (5.5)
2002	11 (7.6)
2003	11 (7.6)
2004	5 (3.4)
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2006	5 (3.4)
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2012	14 (9.7)
2013	10 (6.9)
2014	12 (8.3)
2015	5 (3.4)
2016	10 (6.9)
2017	4 (2.8)
2018	8 (5.5)
Follow-up - median (min-max)	60.56 (3.32-192.96)

Proposal: 1911-04

Title:
Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Large Granular Lymphocytic Leukemia

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Ahmad Samer Al-Homsi, MD, Samer.Al-Homsi@nyulangone.org, NYU SOM
Mohamed Kharfan-Dabaja, MD, KharfanDabaja.Mohamed@mayo.edu, Mayo Clinic

Research hypothesis:
Allogeneic hematopoietic stem cell transplantation (HSCT) is a successful treatment option in refractory large granular lymphocytic leukemia (LGL) patients with severe neutropenia.

Specific aims:
Report the outcomes of allogeneic HSCT in patients with LGL with a focus on overall survival (OS), disease-free survival (DFS), treatment-related mortality (TRM) and graft-versus-host disease (GvHD).

Scientific impact:
Establish with evidence the safety of allogeneic HSCT in patients with LGL.

Scientific justification:
No treatment guidelines are available for LGL patients with severe cytopenias after failure of multiple treatment options. Accordingly, there is need to demonstrate the efficacy of allogeneic HSCT in LGL.
Only case reports found in literature review on allogeneic HSCT in patients with LGL. One case report had a patient with LGL and multiple sclerosis (La Nasa et al. Annals of Hematology 2004) and another had 2 patients with LGL (Donato et al. Blood 2007). We recently successfully performed allogeneic HSCT in a patient with LGL and severe neutropenia that was resistant to all therapies.

Patient eligibility population:
All patients with a previous history of LGL who underwent the first allogeneic HSCT will be eligible.

Data requirements:
FormNet3 and AGNIS data will be needed. No supplemental data will be required.
The variables will include age, sex, donor type, conditioning intensity, performance, status, HCT-CI, and CMV serology.

Study design:
All patients with prior history of LGL that received allogeneic HSCT will be accounted for in the CIBMTR registry.
We will report descriptive statistics and Kaplan-Meier curves.
Primary endpoint:

- The primary end-point of this study is LGL-free survival (LFS) (1-year, 2-year, and 5-year)

Secondary endpoints:

- Overall survival (OS) at (1-year, 2-year, and 5-year)
- Cumulative incidence of relapse (CIR) at (1-year, 2-year, and 5-year)
- Cumulative incidence of non-relapse mortality (NRM) at 100-days, 1-year, 2-year, and 5-year)

Inclusion criteria:

- Age ≥ 18 years of age
- Diagnosis of LGL
- First allogeneic-HSCT
- Preparative regimen could be RIC (which includes non-myeloablative (NMA)) or MAC regimens

Variables to be analyzed:

Recipient specific variables:

- Age
- Gender
- CMV serologic status
- Karnofsky performance score
- HCT-CI score

Donor specific variables: (Includes information for both first HCT and DLI/second HCT)

- Age
- Gender
- CMV serologic status

Transplant specific variables:

- Stem cell source (BM, PBSC)
- Donor source (HLA identical sibling donor, unrelated Donor (HLA-matched or mismatched), cord blood, haploidentical)
- Degree of HLA matching
- Conditioning regimens (RIC vs. MAC)- and specify regimens
- GVHD prophylaxis regimens
- CD34 cell dose
- Use of ATG or Alemtuzumab or ex vivo T cell depletion
- Year of allo-HCT (From 2000 to 2017)

Disease specific variables:

- Prior lines of therapy

Data source:

CIBMTR research database will be used.

Conflict of interest:

None

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≥12	73 (50.3)

Characteristic	N
Missing	10 (6.9)
Donor type - no. (%)	
Autologous	10 (6.9)
HLA-identical sibling	60 (41.4)
Other related	7 (4.8)
Well-matched unrelated (8/8)	27 (18.6)
Partially-matched unrelated (7/8)	7 (4.8)
Mis-matched unrelated (≤6/8)	1 (0.7)
Unrelated (matching TBD)	16 (11)
Cord blood	15 (10.3)
Missing	2 (1.4)
Donor/recipient sex match - no. (%)	
M-M	52 (35.9)
M-F	20 (13.8)
F-M	29 (20)
F-F	17 (11.7)
CB - recipient M	9 (6.2)
CB - recipient F	6 (4.1)
Missing	12 (8.3)
Graft type - no. (%)	
Bone marrow	32 (22.1)
Peripheral blood	98 (67.6)
Cord blood	15 (10.3)
Conditioning as reported by center - no. (%)	
MAC	82 (56.6)
RIC/NMA	41 (28.3)
Missing	22 (15.2)
Conditioning regimen - no. (%)	
TBI/Cy	27 (18.6)
TBI/Cy/Flu	12 (8.3)
TBI/Cy/TT	3 (2.1)
TBI/Cy/VP	5 (3.4)
TBI/VP	13 (9)
TBI/Mel	4 (2.8)
TBI/Flu	8 (5.5)
TBI/other(s)	8 (5.5)
Bu/Cy	10 (6.9)
Bu/Mel	1 (0.7)
Flu/Bu/TT	1 (0.7)
Flu/Bu	17 (11.7)

Characteristic	N
Flu/Mel/TT	1 (0.7)
Flu/Mel	14 (9.7)
Cy/Flu	3 (2.1)
Cy alone	1 (0.7)
BEAM	7 (4.8)
TLI	1 (0.7)
Other(s)	3 (2.1)
None	1 (0.7)
Missing	5 (3.4)
GVHD prophylaxis - no. (%)	
Ex-vivo T-cell depletion	1 (0.7)
CD34 selection	2 (1.4)
Post-CY	5 (3.4)
TAC based	60 (41.4)
CSA based	50 (34.5)
Missing	27 (18.6)
TX year - no. (%)	
2000	3 (2.1)
2001	8 (5.5)
2002	11 (7.6)
2003	11 (7.6)
2004	5 (3.4)
2005	11 (7.6)
2006	5 (3.4)
2007	5 (3.4)
2008	2 (1.4)
2009	10 (6.9)
2010	6 (4.1)
2011	5 (3.4)
2012	14 (9.7)
2013	10 (6.9)
2014	12 (8.3)
2015	5 (3.4)
2016	10 (6.9)
2017	4 (2.8)
2018	8 (5.5)
Follow-up - median (min-max)	60.56 (3.32-192.96)

Combined Proposal: 1911-129, 1911-173, 1911-66, 1811-28, 1811-123

Title:
Haploidentical Allogeneic Stem Cell Transplantation In Patients With Myelofibrosis and it's Comparison to Full-Matched Donor Allogeneic Stem Cell Transplantation

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Hypothesis:
Allogeneic stem cell transplantation (HCT) using a haploidentical related donor and post-HCT cyclophosphamide based graft versus host disease (GVHD) prophylaxis results in long-term remission and are comparable to matched related or matched unrelated donor HCT.

Specific aims:
- AIM 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 outcomes thereof
- AIM 2: To identify preferred donor types for HCT in patients with myelofibrosis by comparing overall survival, relapse free survival, acute and chronic GVHD, GVHD-free and relapse-free survival (GRFS) and treatment related mortality in patients with myelofibrosis who undergo haploidentical donor HCT to other donor types i.e. matched sibling, matched unrelated and cord blood transplantation

Scientific impact/ justification:
Myelofibrosis is clonal hematopoietic disorder that is seen in patients typically of older age with a median age at diagnosis over 65 years [1]. Allogeneic stem cell transplantation remains the only curative therapy although limited by treatment related morbidity and mortality. Identification of the suitable donor remains a challenge, as these patients are likely to have older sibling who may not be preferred candidates, as older age of the donor is known to have inferior outcomes [2]. Unrelated donors are likely to be found in around 75% patients with Caucasian ethnicity but less likely in other ethnic groups. Nevertheless, costs and logistics of the process can sometimes be challenging. Haploidentical donor transplants, with post-transplantation cyclophosphamide platform, have gained popularity given the ease of donor pursuit, lower cost and potentially younger age of donors. However, data on outcomes using haploidentical donors in patients with myelofibrosis is sparse. A recent retrospective analysis by the European Society for Blood and Marrow Transplantation (EBMT) of 56 MF patients who underwent HLA-haploidentical transplantation demonstrated a 1-year and 2-year survival rates of 61% and 56% and

a 2-year cumulative incidence of relapse of 19% [3]. Of note, 70% of patients underwent myeloablative conditioning. How these outcomes fair in North America has never been reported.
It also remains unknown how these outcomes compare to other donor types. Historically, superior outcomes have been seen with full matched donors compared with partially mismatched donors for HCTs done between 1997 and 2010 [4,5]. Since then however, the use of haploidentical donor HCT using post-transplantation cyclophosphamide has been described and been increasingly used especially as an alternate donor option [6]. While various studies have compared outcomes with haploidentical donor HCTs with matched sibling donors for acute myeloid leukemia and lymphomas, such data is not available for patients who undergo HCT for myelofibrosis and hence, leaves a no-evidence zone while making clinical decisions [7,8].
Hence, we propose this study to understand the outcomes of HCT using haploidentical donors in myelofibrosis to gain evidence to guide clinical practice.

Reason to do this study via CIBMTR data:
Allogeneic stem cell transplantation for myelofibrosis is less common, due to various reasons including less common prevalence, older age at diagnosis or inability of patients to undergo transplantation due to disease or patient related factors. Of these, haploidentical donor transplants likely constitute an even smaller fraction. Hence, using data reported to the CIBMTR registry from many centers across the globe is the sole means to study this in a meaningful way with a high enough sample size.

Patient eligibility population:
- Adult patients (age > 18 years)
- First HCT using haploidentical related donor HCT for myelofibrosis using post transplantation cyclophosphamide for graft versus host disease
- First HCT using matched sibling, matched unrelated donors
- Years 2013 -2018 (due to more uniform practices in recent years and increase in haploidentical HCT since 2013)
- Diagnosis of primary myelofibrosis, post-polycythemia myelofibrosis, post-essential thrombocythemia myelofibrosis
- There will be no restrictions on risk score, transplant regimen, prior treatments, or other factors.

Data requirements:
Patient factors:
- Age at diagnosis and HCT
- Gender
- Karnofsky performance score
- HCT CI

Disease factors:
- Time from diagnosis to HCT
- Type of myelofibrosis: primary or post-polycythemia vera or post-essential thrombocythemia
- Driver mutation: JAK2 vs MPL vs CALR vs triple negative
- Non-driver molecular mutations, if available
- DIPSS risk score at HCT
- DIPSS Plus risk score at HCT
- Spleen size at HCT
- Cytogenetics at diagnosis

- Treatment prior to HCT (or JAK inhibitors prior to HCT: yes vs no)
- Best response to the systemic therapy prior to allogeneic stem cell transplant

Transplant factors:
- Date of HCT
- Conditioning regimen intensity (myeloablative vs reduced intensity)
- Graft type: bone marrow or peripheral blood stem cell
- Donor age
- Donor gender
- Donor-recipient (D-R) gender mismatch
- D-R CMV status
- D-R ABO incompatibility
- Graft versus host disease prophylaxis (Post-HCT cyclophosphamide vs calcineurin based)
- Donor specific HLA antibodies
- Cell dose
- ATG vs no ATG, dose of ATG

Outcomes:
- Overall survival (date of death or last contact)
- Time to engraftment for neutrophils and platelets
- Relapse/ Progression (yes vs no) and date of relapse/ progression
- Non relapse mortality at day +100 and 1 year
- Acute graft versus host disease, grade 2-4 and grade 3-4
- Chronic graft versus host disease, extensive chronic graft versus host disease
- Primary graft failure and secondary graft failure
- Poor graft function (as defined by cytopenia in at least two lineages and/or with transfusion requirements beyond day + 28)
- Graft versus host disease-free and relapse-free survival (GRFS)
- DLI used – yes vs no
- Second allogeneic stem cell infusion following primary graft failure or relapse
- Cause of death

No supplemental data is required.

Sample requirements:
Not applicable

Study design:
Adult patients (age > 18 years) who underwent their first HCT using haploidentical related donor for the diagnosis of myelofibrosis after 2013 would be included in this analysis. Patient who had transformed to acute myeloid leukemia at the time of HCT would not be included. Univariate probabilities of overall survival and relapse free survival can be generated using Kaplan-Meier estimates and compared using log rank tests. The incidence rates of neutrophil engraftment, TRM, disease relapse/progression, graft failures and GVHD will be estimated using the cumulative incidence method to account for competing risks. Disease progression or death attributable to the 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 RFS and OS will be estimated using the Kaplan-Meier method
Additional multivariate analysis using Cox proportional hazards model would be conducted to study potential factors that potentially affect HCT outcomes in other settings, that is, patient age, HCT CI, donor age, DIPSS score at HCT, DIPSS Plus score at HCT, conditioning intensity and type of graft versus host disease prophylaxis.

Non-CIBMTR Data Source:
Not applicable

References:
1. Mesa RA, Li CY, Ketterling RP, Schroeder GS, Knudson RA, Tefferi A. Leukemic transformation in myelofibrosis with myeloid metaplasia: a single-institution experience with 91 cases. *Blood.* 2005;105(3):973-977.
2. Shaw BE, Logan BR, Spellman SR, et al. Development of an Unrelated Donor Selection Score Predictive of Survival after HCT: Donor Age Matters Most. *Biol Blood Marrow Transplant.* 2018;24(5):1049-1056.
3. Raj K, Eikema DJ, McLornan DP, et al. Family Mismatched Allogeneic Stem Cell Transplantation for Myelofibrosis: Report from the Chronic Malignancies Working Party of European Society for Blood and Marrow Transplantation. *Biol Blood Marrow Transplant.* 2019;25(3):522-528.
4. Gupta V, Malone AK, Hari PN, et al. Reduced-intensity hematopoietic cell transplantation for patients with primary myelofibrosis: a cohort analysis from the center for international blood and marrow transplant research. *Biol Blood Marrow Transplant.* 2014;20(1):89-97.
5. Rondelli D, Goldberg JD, Isola L, et al. MPD-RC 101 prospective study of reduced-intensity allogeneic hematopoietic stem cell transplantation in patients with myelofibrosis. *Blood.* 2014;124(7):1183-1191.
6. Luznik L, O'Donnell PV, Symons HJ, et al. HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, posttransplantation cyclophosphamide. *Biol Blood Marrow Transplant.* 2008;14(6):641-650.
7. Rashidi A, Hamadani M, Zhang MJ, et al. Outcomes of haploidentical vs matched sibling transplantation for acute myeloid leukemia in first complete remission. *Blood Adv.* 2019;3(12):1826-1836.
8. Salvatore D, Labopin M, Ruggeri A, et al. Outcomes of hematopoietic stem cell transplantation from unmanipulated haploidentical versus matched sibling donor in patients with acute myeloid leukemia in first complete remission with intermediate or high-risk cytogenetics: a study from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. *Haematologica.* 2018;103(8):1317-1328.

Table 1a. Characteristics of patients Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation in Patients with Myelofibrosis, TED vs. CRF

Characteristic	TED	CRF
No. of patients	489	939
No. of centers	136	133
Patients age - median (min-max)	59.15 (3.8-75.99)	61.54 (2.89-77.9)
Age - no. (%)		
<18	4 (0.8)	5 (0.5)
18-29	3 (0.6)	1 (0.1)
30-39	18 (3.7)	15 (1.6)
40-49	59 (12.1)	94 (10)
50-59	176 (36)	280 (29.8)
60-69	209 (42.7)	471 (50.2)
≥ 70	20 (4.1)	73 (7.8)
Sex - no. (%)		
Male	277 (56.6)	552 (58.8)
Female	212 (43.4)	387 (41.2)
Race - no. (%)		
Caucasian	376 (76.9)	803 (85.5)
African-American	16 (3.3)	44 (4.7)
Asian	20 (4.1)	43 (4.6)
Pacific islander	1 (0.2)	11 (1.2)
Native American	1 (0.2)	5 (0.5)
More than one race	1 (0.2)	2 (0.2)
Missing	74 (15.1)	31 (3.3)
HCT-CI - no. (%)		
0	139 (28.4)	209 (22.3)
1	64 (13.1)	151 (16.1)
2	76 (15.5)	145 (15.4)
3+	206 (42.1)	432 (46)
TBD, review needed for history of malignancies	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.1)
Missing	4 (0.8)	0
Karnofsky score - no. (%)		
90-100	270 (55.2)	493 (52.5)
< 90	211 (43.1)	432 (46)
Missing	8 (1.6)	14 (1.5)
Subdisease - no. (%)		
Primary Myelofibrosis	313 (64)	630 (67.1)
Polycythemia vesa	86 (17.6)	140 (14.9)
Essential thrombocythemia	90 (18.4)	169 (18)

Characteristic	TED	CRF
Graft type - no. (%)		
Bone marrow	30 (6.1)	63 (6.7)
Peripheral blood	459 (93.9)	876 (93.3)
Time from diagnosis to HCT - no. (%)		
<6	45 (9.2)	80 (8.5)
6-11	69 (14.1)	144 (15.3)
≥12	341 (69.7)	669 (71.2)
Missing	34 (7)	46 (4.9)
Donor type - no. (%)		
HLA-identical sibling	222 (45.4)	293 (31.2)
Haplo	28 (5.7)	92 (9.8)
URD 8/8	239 (48.9)	554 (59)
Donor/recipient sex match - no. (%)		
M-M	174 (35.6)	369 (39.3)
M-F	124 (25.4)	228 (24.3)
F-M	103 (21.1)	183 (19.5)
F-F	87 (17.8)	158 (16.8)
Missing	1 (0.2)	1 (0.1)
Conditioning as reported by center - no. (%)		
MAC	183 (37.4)	365 (38.9)
RIC/NMA	301 (61.6)	573 (61)
Missing	5 (1)	1 (0.1)
Conditioning regimen - no. (%)		
TBI/Cy	2 (0.4)	7 (0.7)
TBI/Cy/Flu	22 (4.5)	44 (4.7)
TBI/Mel	7 (1.4)	25 (2.7)
TBI/Flu	35 (7.2)	63 (6.7)
TBI/other(s)	0	1 (0.1)
Bu/Cy/Mel	1 (0.2)	0
Bu/Cy	58 (11.9)	93 (9.9)
Bu/Mel	0	2 (0.2)
Flu/Bu/TT	2 (0.4)	20 (2.1)
Flu/Bu	206 (42.1)	386 (41.1)
Flu/Mel/TT	2 (0.4)	6 (0.6)
Flu/Mel	140 (28.6)	273 (29.1)
Cy/Flu	6 (1.2)	10 (1.1)
Treosulfan	1 (0.2)	1 (0.1)
TLI	3 (0.6)	1 (0.1)
Other(s)	4 (0.8)	6 (0.6)
None	0	1 (0.1)
GHVD-prophylaxis - no. (%)		

Characteristic	TED	CRF
PTcy + CNIs + MMF	34 (7)	117 (12.5)
PTcy + CNIs + MTX	0	2 (0.2)
PT-Cy + others	11 (2.2)	42 (4.5)
PT-Cy alone	1 (0.2)	1 (0.1)
CNI + MMF	78 (16)	117 (12.5)
CNI + MTX	299 (61.1)	578 (61.6)
CNI + others	57 (11.7)	63 (6.7)
CNI alone	9 (1.8)	19 (2)
TX year - no. (%)		
2013	119 (24.3)	36 (3.8)
2014	73 (14.9)	134 (14.3)
2015	96 (19.6)	123 (13.1)
2016	104 (21.3)	137 (14.6)
2017	53 (10.8)	247 (26.3)
2018	44 (9)	262 (27.9)
Follow-up - median (min-max)	36.05 (3.26-73.42)	23.52 (3.16-73.95)

Table 1b. Characteristics of patients Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation in Patients with Myelofibrosis

Characteristic	HLA-identical sibling	Haplo	URD 8/8
No. of patients	515	120	793
No. of centers	142	58	131
track - no. (%)			
TED	222 (43.1)	28 (23.3)	239 (30.1)
CRF	293 (56.9)	92 (76.7)	554 (69.9)
Patients age - median (min-max)	59.13 (3.8-74.52)	61 (2.89-74.78)	61.99 (3.99-77.9)
Age - no. (%)			
<18	5 (1)	1 (0.8)	3 (0.4)
18-29	2 (0.4)	1 (0.8)	1 (0.1)
30-39	10 (1.9)	4 (3.3)	19 (2.4)
40-49	62 (12)	18 (15)	73 (9.2)
50-59	196 (38.1)	32 (26.7)	228 (28.8)
60-69	227 (44.1)	53 (44.2)	400 (50.4)
≥ 70	13 (2.5)	11 (9.2)	69 (8.7)
Sex - no. (%)			
Male	296 (57.5)	68 (56.7)	465 (58.6)
Female	219 (42.5)	52 (43.3)	328 (41.4)
Race - no. (%)			
Caucasian	394 (76.5)	80 (66.7)	705 (88.9)
African-American	23 (4.5)	16 (13.3)	21 (2.6)
Asian	34 (6.6)	10 (8.3)	19 (2.4)
Pacific islander	5 (1)	2 (1.7)	5 (0.6)
Native American	2 (0.4)	1 (0.8)	3 (0.4)
More than one race	1 (0.2)	1 (0.8)	1 (0.1)
Missing	56 (10.9)	10 (8.3)	39 (4.9)
HCT-CI - no. (%)			
0	147 (28.5)	28 (23.3)	173 (21.8)
1	68 (13.2)	23 (19.2)	124 (15.6)
2	80 (15.5)	17 (14.2)	124 (15.6)
3+	218 (42.3)	51 (42.5)	369 (46.5)
TBD, review needed for history of malignancies	0	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.8)	0
Missing	2 (0.4)	0	2 (0.3)
Karnofsky score - no. (%)			
90-100	290 (56.3)	68 (56.7)	405 (51.1)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
< 90	215 (41.7)	51 (42.5)	377 (47.5)
Missing	10 (1.9)	1 (0.8)	11 (1.4)
Subdisease - no. (%)			
Primary Myelofibrosis	334 (64.9)	74 (61.7)	535 (67.5)
Polycythemia vesa	81 (15.7)	22 (18.3)	123 (15.5)
Essential thrombocythemia	100 (19.4)	24 (20)	135 (17)
Graft type - no. (%)			
Bone marrow	25 (4.9)	22 (18.3)	46 (5.8)
Peripheral blood	490 (95.1)	98 (81.7)	747 (94.2)
Time from diagnosis to HCT - no. (%)			
<6	56 (10.9)	7 (5.8)	62 (7.8)
6-11	70 (13.6)	19 (15.8)	124 (15.6)
≥12	356 (69.1)	94 (78.3)	560 (70.6)
Missing	33 (6.4)	0	47 (5.9)
Donor/recipient sex match - no. (%)			
M-M	163 (31.7)	46 (38.3)	334 (42.1)
M-F	99 (19.2)	24 (20)	229 (28.9)
F-M	133 (25.8)	22 (18.3)	131 (16.5)
F-F	119 (23.1)	28 (23.3)	98 (12.4)
Missing	1 (0.2)	0	1 (0.1)
Donor age at donation - no. (%)			
0-17	6 (1.2)	5 (4.2)	0
18-29	3 (0.6)	38 (31.7)	474 (59.8)
30-39	15 (2.9)	42 (35)	192 (24.2)
40-49	77 (15)	23 (19.2)	83 (10.5)
50-59	212 (41.2)	10 (8.3)	37 (4.7)
60-69	163 (31.7)	2 (1.7)	1 (0.1)
70-79	15 (2.9)	0	0
Missing	24 (4.7)	0	6 (0.8)
Donor age at donation, median (range), yr - median (min-max)	56.8 (0-75.8)	34.7 (15-63)	27.91 (18.58-68.1)
Conditioning as reported by center - no. (%)			
MAC	205 (39.8)	42 (35)	301 (38)
RIC/NMA	304 (59)	78 (65)	492 (62)
Missing	6 (1.2)	0	0
Conditioning regimen - no. (%)			
TBI/Cy	1 (0.2)	0	8 (1)
TBI/Cy/Flu	15 (2.9)	45 (37.5)	6 (0.8)
TBI/Mel	6 (1.2)	13 (10.8)	13 (1.6)
TBI/Flu	15 (2.9)	16 (13.3)	67 (8.4)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
TBI/other(s)	0	0	1 (0.1)
Bu/Cy/Mel	1 (0.2)	0	0
Bu/Cy	70 (13.6)	12 (10)	69 (8.7)
Bu/Mel	0	2 (1.7)	0
Flu/Bu/TT	2 (0.4)	16 (13.3)	4 (0.5)
Flu/Bu	229 (44.5)	7 (5.8)	356 (44.9)
Flu/Mel/TT	1 (0.2)	3 (2.5)	4 (0.5)
Flu/Mel	160 (31.1)	4 (3.3)	249 (31.4)
Cy/Flu	8 (1.6)	2 (1.7)	6 (0.8)
Treosulfan	0	0	2 (0.3)
TLI	1 (0.2)	0	3 (0.4)
Other(s)	5 (1)	0	5 (0.6)
None	1 (0.2)	0	0
GHVD-prophylaxis - no. (%)			
PTcy + CNIs + MMF	15 (2.9)	110 (91.7)	26 (3.3)
PTcy + CNIs + MTX	0	1 (0.8)	1 (0.1)
PT-Cy + others	17 (3.3)	9 (7.5)	27 (3.4)
PT-Cy alone	1 (0.2)	0	1 (0.1)
CNI + MMF	78 (15.1)	0	117 (14.8)
CNI + MTX	345 (67)	0	532 (67.1)
CNI + others	48 (9.3)	0	72 (9.1)
CNI alone	11 (2.1)	0	17 (2.1)
TX year - no. (%)			
2013	60 (11.7)	4 (3.3)	91 (11.5)
2014	77 (15)	10 (8.3)	120 (15.1)
2015	94 (18.3)	10 (8.3)	115 (14.5)
2016	91 (17.7)	19 (15.8)	131 (16.5)
2017	101 (19.6)	38 (31.7)	161 (20.3)
2018	92 (17.9)	39 (32.5)	175 (22.1)
Follow-up - median (min-max)	24.57 (3.26-73.95)	12.96 (3.22-73.88)	24.41 (3.16-73.42)

Proposal: 1911-129

Title:
Outcomes With Haploidentical Allogeneic Stem Cell Transplantation In Patients With Myelofibrosis

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Hypothesis:
Allogeneic stem cell transplantation (HCT) using a haploidentical related donor results in long-term remission and survival in patients with myelofibrosis.

Primary aim:
- To determine clinical outcomes of patients who undergo HCT using a haploidentical related donor

Secondary aims:
- To determine the influence of patient, donor and transplant related factors in outcomes of haploidentical donor HCT in myelofibrosis

Scientific impact/ justification:
Myelofibrosis is clonal hematopoietic disorder that is seen in patients typically of older age with a median age at diagnosis over 65 years [1]. Allogeneic stem cell transplantation remains the only curative therapy although limited by treatment related morbidity and mortality. Identification of the suitable donor remains a challenge, as these patients are likely to have older sibling who may not be preferred candidates, as older age of the donor is known to have inferior outcomes [2]. Unrelated donors are likely to be found in around 75% patients with Caucasian ethnicity but less likely in other ethnic groups. Nevertheless, costs and logistics of the process can sometimes be challenging. Haploidentical donor transplants, with post-transplantation cyclophosphamide platform, have gained popularity given the ease of donor pursuit, lower cost and potentially younger age of donors. Some of the concerns in the earlier studies included possibility of higher relapses, which has not been shown in subsequent studies for allogeneic HCT in patients with various hematological malignancies [3-5]
However, no data on outcomes is available for HCT using haploidentical donors in patients with myelofibrosis to guide clinical practice and inform patients in this context. Hence, we propose this study to study the outcomes of HCT using haploidentical donors in myelofibrosis to gain evidence to guide clinical practice.

Reason to do this study via CIBMTR data:
Allogeneic stem cell transplantation for myelofibrosis is less common, due to various reasons including less common prevalence, older age at diagnosis or inability of patients to undergo transplantation due to disease or patient related factors. Of these, haploidentical donor transplants likely constitute an even smaller fraction. Hence, using data reported to the registry from many centers across the globe is the sole means to study this in a meaningful way with a high enough sample size.

Patient eligibility population:
Patients who underwent first HCT using haploidentical related donor HCT for myelofibrosis using post transplantation cyclophosphamide for graft versus host disease, since it's first description in 2008 [3].

Data requirements:

Patient factors:

- Age at diagnosis and HCT
- Gender
- Karnofsky performance score
- HCT CI

Disease factors:

- Time from diagnosis to HCT
- Type of myelofibrosis: primary or post-polycythemia vera or post-essential thrombocythemia
- Driver mutation: JAK2 vs MPL vs CALR vs triple negative
- DIPSS risk score at HCT
- DIPSS Plus risk score at HCT
- Spleen status at HCT
- Cytogenetics
- Treatment prior to HCT (or JAK inhibitors prior to HCT: yes vs no)

Transplant factors:

- Conditioning regimen intensity
- Graft type: bone marrow or peripheral blood stem cell
- Donor age
- Donor gender
- Donor-recipient (D-R) gender mismatch
- D-R CMV status
- D-R ABO incompatibility
- Graft versus host disease prophylaxis

Outcomes:

- Overall survival
- Time to engraftment for neutrophils and platelets
- Relapse
- Non relapse mortality at day +100
- Acute graft versus host disease, grade 2-4 and grade 3-4
- Chronic graft versus host disease, extensive chronic graft versus host disease
- Primary graft failure

No supplemental data is required.

Sample requirements:

Not applicable

Study design:

Adult patients (age > 18 years) who underwent their first HCT using haploidentical related donor for the diagnosis of myelofibrosis after 2008 would be included in this analysis. Patient who had transformed to acute myeloid leukemia at the time of HCT would not be included. Univariate probabilities of overall survival and relapse free survival can be generated using Kaplan-Meier estimates and compared using

log rank tests. Cumulative incidence can be used to calculate probabilities of relapse, non relapse mortality, acute of chronic graft versus host disease and graft failure.
Additional multivariate analysis using Cox proportional hazards model would be conducted to study potential factors that potentially affect HCT outcomes in other settings, that is, patient age, HCT CI, donor age, DIPSS score at HCT, DIPSS Plus score at HCT, conditioning intensity and type of graft versus host disease prophylaxis.

Non-CIBMTR data source:
Not applicable

References:
1. Mesa RA, Li CY, Ketterling RP, Schroeder GS, Knudson RA, Tefferi A. Leukemic transformation in myelofibrosis with myeloid metaplasia: a single-institution experience with 91 cases. *Blood.* 2005;105(3):973-977.
2. Shaw BE, Logan BR, Spellman SR, et al. Development of an Unrelated Donor Selection Score Predictive of Survival after HCT: Donor Age Matters Most. *Biol Blood Marrow Transplant.* 2018;24(5):1049-1056.
3. Luznik L, O'Donnell PV, Symons HJ, et al. HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, posttransplantation cyclophosphamide. *Biol Blood Marrow Transplant.* 2008;14(6):641-650.
4. Rashidi A, Hamadani M, Zhang MJ, et al. Outcomes of haploidentical vs matched sibling transplantation for acute myeloid leukemia in first complete remission. *Blood Adv.* 2019;3(12):1826-1836.
5. Salvatore D, Labopin M, Ruggeri A, et al. Outcomes of hematopoietic stem cell transplantation from unmanipulated haploidentical versus matched sibling donor in patients with acute myeloid leukemia in first complete remission with intermediate or high-risk cytogenetics: a study from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. *Haematologica.* 2018;103(8):1317-1328.

Table 1. Characteristics of patients Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation in Patients with Myelofibrosis, TED vs. CRF

Characteristic	TED	CRF
No. of patients	954	1172
No. of centers	168	143
age - median (min-max)	58.28 (3.8-75.99)	60.51 (1.12-77.9)
Age - no. (%)		
<18	6 (0.6)	9 (0.8)
18-29	8 (0.8)	6 (0.5)
30-39	40 (4.2)	23 (2)
40-49	138 (14.5)	143 (12.2)
50-59	354 (37.1)	381 (32.5)
60-69	378 (39.6)	531 (45.3)
≥ 70	30 (3.1)	79 (6.7)
Gender: (2400 Q942) - no. (%)		
Male	567 (59.4)	685 (58.4)
Female	387 (40.6)	487 (41.6)
Race - no. (%)		
Caucasian	731 (76.6)	1010 (86.2)
African-American	35 (3.7)	51 (4.4)
Asian	41 (4.3)	51 (4.4)
Pacific islander	3 (0.3)	13 (1.1)
Native American	1 (0.1)	4 (0.3)
More than one race	1 (0.1)	3 (0.3)
Missing	142 (14.9)	40 (3.4)
HCT-CI - no. (%)		
0	295 (30.9)	307 (26.2)
1	121 (12.7)	171 (14.6)
2	127 (13.3)	176 (15)
3+	362 (37.9)	504 (43)
TBD, review needed for history of malignancies	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.1)
Missing	49 (5.1)	12 (1)
Karnofsky score - no. (%)		
90-100	540 (56.6)	641 (54.7)
< 90	400 (41.9)	509 (43.4)
Missing	14 (1.5)	22 (1.9)
Subdisease - no. (%)		
Primary Myelofibrosis	629 (65.9)	800 (68.3)
Polycythemia vesa	147 (15.4)	172 (14.7)
Essential thrombocythemia	178 (18.7)	200 (17.1)

Characteristic	TED	CRF
Graft type - no. (%)		
Bone marrow	64 (6.7)	88 (7.5)
Peripheral blood	890 (93.3)	1084 (92.5)
Time from diagnosis to HCT - no. (%)		
<6	105 (11)	103 (8.8)
6-11	147 (15.4)	186 (15.9)
≥12	642 (67.3)	825 (70.4)
Missing	60 (6.3)	58 (4.9)
Donor type - no. (%)		
HLA-identical sibling	513 (53.8)	390 (33.3)
Haplo	31 (3.2)	95 (8.1)
URD 8/8	410 (43)	687 (58.6)
Donor/recipient sex match - no. (%)		
M-M	349 (36.6)	452 (38.6)
M-F	211 (22.1)	286 (24.4)
F-M	218 (22.9)	233 (19.9)
F-F	175 (18.3)	200 (17.1)
Missing	1 (0.1)	1 (0.1)
Conditioning as reported by center - no. (%)		
MAC	383 (40.1)	494 (42.2)
RIC/NMA	563 (59)	676 (57.7)
Missing	8 (0.8)	2 (0.2)
Conditioning regimen - no. (%)		
TBI/Cy	15 (1.6)	19 (1.6)
TBI/Cy/Flu	32 (3.4)	45 (3.8)
TBI/Cy/Flu/TT	1 (0.1)	1 (0.1)
TBI/Mel	10 (1)	25 (2.1)
TBI/Flu	66 (6.9)	76 (6.5)
TBI/other(s)	4 (0.4)	6 (0.5)
Bu/Cy/Mel	1 (0.1)	0
Bu/Cy	124 (13)	156 (13.3)
Bu/Mel	11 (1.2)	7 (0.6)
Flu/Bu/TT	2 (0.2)	20 (1.7)
Flu/Bu	388 (40.7)	467 (39.8)
Flu/Mel/TT	3 (0.3)	6 (0.5)
Flu/Mel	267 (28)	321 (27.4)
Cy/Flu	14 (1.5)	10 (0.9)
Treosulfan	3 (0.3)	1 (0.1)
TLI	4 (0.4)	2 (0.2)
Other(s)	9 (0.9)	9 (0.8)
None	0	1 (0.1)

Characteristic	TED	CRF
GHVD-prophylaxis - no. (%)		
No prophylaxis	3 (0.3)	6 (0.5)
CD34 selection/TCD	16 (1.7)	10 (0.9)
PTcy + CNIs + MMF	35 (3.7)	113 (9.6)
PTcy + CNIs + MTX	0	2 (0.2)
PT-Cy + others	12 (1.3)	42 (3.6)
PT-Cy alone	1 (0.1)	1 (0.1)
CNI + MMF	188 (19.7)	153 (13.1)
CNI + MTX	535 (56.1)	740 (63.1)
CNI + others	105 (11)	68 (5.8)
CNI alone	40 (4.2)	25 (2.1)
Other prophylaxis	19 (2)	12 (1)
TX year - no. (%)		
2008	29 (3)	77 (6.6)
2009	68 (7.1)	77 (6.6)
2010	98 (10.3)	36 (3.1)
2011	110 (11.5)	14 (1.2)
2012	144 (15.1)	11 (0.9)
2013	124 (13)	39 (3.3)
2014	75 (7.9)	137 (11.7)
2015	99 (10.4)	125 (10.7)
2016	111 (11.6)	141 (12)
2017	54 (5.7)	250 (21.3)
2018	42 (4.4)	265 (22.6)
Follow-up - median (min-max)	49.28 (3.26-128.13)	24.57 (3.06-131.05)

Table 1b. Characteristics of patients Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation in Patients with Myelofibrosis

Characteristic	HLA-identical sibling	Haplo	URD 8/8
No. of patients	903	126	1097
No. of centers	175	59	141
track - no. (%)			
TED	513 (56.8)	31 (24.6)	410 (37.4)
CRF	390 (43.2)	95 (75.4)	687 (62.6)
age - median (min-max)	57.92 (3.8-74.52)	60.97 (2.89-74.78)	60.66 (1.12-77.9)
Age - no. (%)			
<18	8 (0.9)	1 (0.8)	6 (0.5)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
18-29	5 (0.6)	1 (0.8)	8 (0.7)
30-39	30 (3.3)	4 (3.2)	29 (2.6)
40-49	135 (15)	18 (14.3)	128 (11.7)
50-59	352 (39)	35 (27.8)	348 (31.7)
60-69	351 (38.9)	56 (44.4)	502 (45.8)
≥ 70	22 (2.4)	11 (8.7)	76 (6.9)
Gender: (2400 Q942) - no. (%)			
Male	548 (60.7)	72 (57.1)	632 (57.6)
Female	355 (39.3)	54 (42.9)	465 (42.4)
Race - no. (%)			
Caucasian	673 (74.5)	85 (67.5)	983 (89.6)
African-American	40 (4.4)	19 (15.1)	27 (2.5)
Asian	54 (6)	11 (8.7)	27 (2.5)
Pacific islander	9 (1)	1 (0.8)	6 (0.5)
Native American	2 (0.2)	0	3 (0.3)
More than one race	1 (0.1)	1 (0.8)	2 (0.2)
Missing	124 (13.7)	9 (7.1)	49 (4.5)
HCT-CI - no. (%)			
0	292 (32.3)	28 (22.2)	282 (25.7)
1	116 (12.8)	23 (18.3)	153 (13.9)
2	121 (13.4)	20 (15.9)	162 (14.8)
3+	325 (36)	54 (42.9)	487 (44.4)
TBD, review needed for history of malignancies	0	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.8)	0
Missing	49 (5.4)	0	12 (1.1)
Karnofsky score - no. (%)			
90-100	518 (57.4)	69 (54.8)	594 (54.1)
< 90	366 (40.5)	56 (44.4)	487 (44.4)
Missing	19 (2.1)	1 (0.8)	16 (1.5)
Subdisease - no. (%)			
Primary Myelofibrosis	607 (67.2)	77 (61.1)	745 (67.9)
Polycythemia vesa	127 (14.1)	24 (19)	168 (15.3)
Essential thrombocythemia	169 (18.7)	25 (19.8)	184 (16.8)
Graft type - no. (%)			
Bone marrow	49 (5.4)	28 (22.2)	75 (6.8)
Peripheral blood	854 (94.6)	98 (77.8)	1022 (93.2)
Time from diagnosis to HCT - no. (%)			
<6	113 (12.5)	8 (6.3)	87 (7.9)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
6-11	133 (14.7)	20 (15.9)	180 (16.4)
≥12	602 (66.7)	97 (77)	768 (70)
Missing	55 (6.1)	1 (0.8)	62 (5.7)
Donor/recipient sex match - no. (%)			
M-M	295 (32.7)	50 (39.7)	456 (41.6)
M-F	162 (17.9)	24 (19)	311 (28.4)
F-M	253 (28)	22 (17.5)	176 (16)
F-F	192 (21.3)	30 (23.8)	153 (13.9)
Missing	1 (0.1)	0	1 (0.1)
Conditioning as reported by center - no. (%)			
MAC	373 (41.3)	42 (33.3)	462 (42.1)
RIC/NMA	521 (57.7)	84 (66.7)	634 (57.8)
Missing	9 (1)	0	1 (0.1)
Conditioning regimen - no. (%)			
TBI/Cy	12 (1.3)	2 (1.6)	20 (1.8)
TBI/Cy/Flu	21 (2.3)	47 (37.3)	9 (0.8)
TBI/Cy/Flu/TT	0	2 (1.6)	0
TBI/Mel	8 (0.9)	13 (10.3)	14 (1.3)
TBI/Flu	40 (4.4)	15 (11.9)	87 (7.9)
TBI/other(s)	4 (0.4)	0	6 (0.5)
Bu/Cy/Mel	1 (0.1)	0	0
Bu/Cy	146 (16.2)	11 (8.7)	123 (11.2)
Bu/Mel	4 (0.4)	2 (1.6)	12 (1.1)
Flu/Bu/TT	2 (0.2)	16 (12.7)	4 (0.4)
Flu/Bu	370 (41)	6 (4.8)	479 (43.7)
Flu/Mel/TT	1 (0.1)	4 (3.2)	4 (0.4)
Flu/Mel	267 (29.6)	6 (4.8)	315 (28.7)
Cy/Flu	14 (1.6)	2 (1.6)	8 (0.7)
Treosulfan	1 (0.1)	0	3 (0.3)
TLI	3 (0.3)	0	3 (0.3)
Other(s)	8 (0.9)	0	10 (0.9)
None	1 (0.1)	0	0
GHVD-prophylaxis - no. (%)			
No prophylaxis	2 (0.2)	2 (1.6)	5 (0.5)
CD34 selection/TCD	8 (0.9)	5 (4)	13 (1.2)
PTcy + CNIs + MMF	15 (1.7)	108 (85.7)	25 (2.3)
PTcy + CNIs + MTX	0	1 (0.8)	1 (0.1)
PT-Cy + others	19 (2.1)	7 (5.6)	28 (2.6)
PT-Cy alone	1 (0.1)	0	1 (0.1)
CNI + MMF	166 (18.4)	3 (2.4)	172 (15.7)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
CNI + MTX	556 (61.6)	0	719 (65.5)
CNI + others	81 (9)	0	92 (8.4)
CNI alone	37 (4.1)	0	28 (2.6)
Other prophylaxis	18 (2)	0	13 (1.2)
TX year - no. (%)			
2008	59 (6.5)	1 (0.8)	46 (4.2)
2009	73 (8.1)	2 (1.6)	70 (6.4)
2010	79 (8.7)	1 (0.8)	54 (4.9)
2011	79 (8.7)	1 (0.8)	44 (4)
2012	82 (9.1)	1 (0.8)	72 (6.6)
2013	64 (7.1)	5 (4)	94 (8.6)
2014	77 (8.5)	11 (8.7)	124 (11.3)
2015	97 (10.7)	11 (8.7)	116 (10.6)
2016	94 (10.4)	20 (15.9)	138 (12.6)
2017	105 (11.6)	34 (27)	165 (15)
2018	94 (10.4)	39 (31)	174 (15.9)
Follow-up - median (min-max)	37.6 (3.06-131.05)	18.45 (3.22-74.31)	36.61 (3.16-128.13)

Table. Median follow-up for Haploidentical donors

Characteristic	N
Follow-up - median (min-max)	18.45 (3.22-74.31)

Proposal: 1911-173

Title:
Comparison of Outcomes With Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation In Patients With Myelofibrosis

Tania Jain, tjain2@jhmi.edu, Johns Hopkins University
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Hypothesis:
Allogeneic stem cell transplantation (HCT) using a haploidentical related donor and post-HCT cyclophosphamide based graft versus host disease (GVHD) prophylaxis results in similar overall survival compared to matched related or unrelated donor HCT using calcineurin based GVHD prophylaxis.

Primary aim:
- To compare overall survival in patients with myelofibrosis undergoing haploidentical donor HCT and fully matched donor HCT.

Secondary aim:
- To determine differences in clinical outcomes i.e. relapse, non relapse mortality, acute and chronic GVHD in these patients

Scientific impact/ justification:
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. Historically, superior outcomes have been seen with full matched donors compared with partially mismatched donors for HCTs done between 1997 and 2010 [1]. Since then however, the use of haploidentical donor HCT using post-transplantation cyclophosphamide has been described and been increasingly used especially as an alternate donor option [2]. While various studies have compared outcomes with haploidentical donor HCTs with matched sibling donors for acute myeloid leukemia and lymphomas, such data is not available for patients who undergo HCT for myelofibrosis and hence, leaves a no-evidence zone while making clinical decisions [3,4]. In clinical practice, identification of donor for patients with myelofibrosis remains challenging, as the patients are often older and have likely older siblings.
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 single institution studies are limited by low numbers. A data registry such Center for International Blood and Marrow Transplant Research (CIBMTR) registry is the most suitable way to conduct this study.

Patient eligibility population:
Patients who underwent first HCT for myelofibrosis using haploidentical donor/ post transplantation cyclophosphamide based GVHD prophylaxis and matched donor/ calcineurin based for GVHD prophylaxis in the recent years i.e. 2008 through 2017.

Data requirements:
<u>Patient factors:</u>
- Age at diagnosis and HCT
- Gender

- Karnofsky performance score
- HCT CI

Disease factors:
- Time from diagnosis to HCT
- Type of myelofibrosis: primary or post-polycythemia vera or post-essential thrombocythemia
- Driver mutation: JAK2 vs MPL vs CALR vs triple negative
- DIPSS risk score at HCT
- DIPSS Plus risk score at HCT
- Spleen status at HCT
- Cytogenetics
- Treatment prior to HCT (or JAK inhibitors prior to HCT: yes vs no)

Transplant factors:
- Conditioning regimen intensity
- Graft type: bone marrow or peripheral blood stem cell
- Donor age
- Donor gender
- Degree of match
- Donor related or unrelated
- Donor-recipient (D-R) gender mismatch
- D-R CMV status
- D-R ABO incompatibility
- Graft versus host disease prophylaxis
- Year of HCT

Outcomes:
- Overall survival
- Relapse/ progression
- Non relapse mortality at day +100, 1 yr
- Acute graft versus host disease: all grade, grade 2-4 and grade 3-4
- Chronic graft versus host disease: all grade, extensive
- Graft failure

No supplemental data is required.

Sample requirements:
Not applicable

Study design:
This would be 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). Kaplan Meier curve estimates would be used to generate probability of overall survival and progression-free survival. Cumulative incidence can be used to calculate probabilities of relapse, non relapse mortality, acute of chronic graft versus host disease and graft failure. Univariate analysis can be used to identify differences in outcomes using donor type while

multivariate Cox Proportional Hazard model can be constructed to estimate the effect of other selected potential predictors of outcomes.

Non-CIBMTR Data Source:
Not applicable

References:
1. Gupta V, Malone AK, Hari PN, et al. Reduced-intensity hematopoietic cell transplantation for patients with primary myelofibrosis: a cohort analysis from the center for international blood and marrow transplant research. Biol Blood Marrow Transplant. 2014;20(1):89-97.
2. Luznik L, O'Donnell PV, Symons HJ, et al. HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, posttransplantation cyclophosphamide. Biol Blood Marrow Transplant. 2008;14(6):641-650.
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4. Rashidi A, Hamadani M, Zhang MJ, et al. Outcomes of haploidentical vs matched sibling transplantation for acute myeloid leukemia in first complete remission. Blood Adv. 2019;3(12):1826-1836.

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18-29	8 (0.8)	6 (0.5)
30-39	40 (4.2)	23 (2)
40-49	138 (14.5)	143 (12.2)
50-59	354 (37.1)	381 (32.5)
60-69	378 (39.6)	531 (45.3)
≥ 70	30 (3.1)	79 (6.7)
Gender: (2400 Q942) - no. (%)		
Male	567 (59.4)	685 (58.4)
Female	387 (40.6)	487 (41.6)
Race - no. (%)		
Caucasian	731 (76.6)	1010 (86.2)
African-American	35 (3.7)	51 (4.4)
Asian	41 (4.3)	51 (4.4)
Pacific islander	3 (0.3)	13 (1.1)
Native American	1 (0.1)	4 (0.3)
More than one race	1 (0.1)	3 (0.3)
Missing	142 (14.9)	40 (3.4)
HCT-CI - no. (%)		
0	295 (30.9)	307 (26.2)
1	121 (12.7)	171 (14.6)
2	127 (13.3)	176 (15)
3+	362 (37.9)	504 (43)
TBD, review needed for history of malignancies	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.1)
Missing	49 (5.1)	12 (1)
Karnofsky score - no. (%)		
90-100	540 (56.6)	641 (54.7)
< 90	400 (41.9)	509 (43.4)
Missing	14 (1.5)	22 (1.9)
Subdisease - no. (%)		
Primary Myelofibrosis	629 (65.9)	800 (68.3)
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Characteristic	TED	CRF
Graft type - no. (%)		
Bone marrow	64 (6.7)	88 (7.5)
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<6	105 (11)	103 (8.8)
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MAC	383 (40.1)	494 (42.2)
RIC/NMA	563 (59)	676 (57.7)
Missing	8 (0.8)	2 (0.2)
Conditioning regimen - no. (%)		
TBI/Cy	15 (1.6)	19 (1.6)
TBI/Cy/Flu	32 (3.4)	45 (3.8)
TBI/Cy/Flu/TT	1 (0.1)	1 (0.1)
TBI/Mel	10 (1)	25 (2.1)
TBI/Flu	66 (6.9)	76 (6.5)
TBI/other(s)	4 (0.4)	6 (0.5)
Bu/Cy/Mel	1 (0.1)	0
Bu/Cy	124 (13)	156 (13.3)
Bu/Mel	11 (1.2)	7 (0.6)
Flu/Bu/TT	2 (0.2)	20 (1.7)
Flu/Bu	388 (40.7)	467 (39.8)
Flu/Mel/TT	3 (0.3)	6 (0.5)
Flu/Mel	267 (28)	321 (27.4)
Cy/Flu	14 (1.5)	10 (0.9)
Treosulfan	3 (0.3)	1 (0.1)
TLI	4 (0.4)	2 (0.2)
Other(s)	9 (0.9)	9 (0.8)
None	0	1 (0.1)

Characteristic	TED	CRF
GHVD-prophylaxis - no. (%)		
No prophylaxis	3 (0.3)	6 (0.5)
CD34 selection/TCD	16 (1.7)	10 (0.9)
PTcy + CNIs + MMF	35 (3.7)	113 (9.6)
PTcy + CNIs + MTX	0	2 (0.2)
PT-Cy + others	12 (1.3)	42 (3.6)
PT-Cy alone	1 (0.1)	1 (0.1)
CNI + MMF	188 (19.7)	153 (13.1)
CNI + MTX	535 (56.1)	740 (63.1)
CNI + others	105 (11)	68 (5.8)
CNI alone	40 (4.2)	25 (2.1)
Other prophylaxis	19 (2)	12 (1)
TX year - no. (%)		
2008	29 (3)	77 (6.6)
2009	68 (7.1)	77 (6.6)
2010	98 (10.3)	36 (3.1)
2011	110 (11.5)	14 (1.2)
2012	144 (15.1)	11 (0.9)
2013	124 (13)	39 (3.3)
2014	75 (7.9)	137 (11.7)
2015	99 (10.4)	125 (10.7)
2016	111 (11.6)	141 (12)
2017	54 (5.7)	250 (21.3)
2018	42 (4.4)	265 (22.6)
Follow-up - median (min-max)	49.28 (3.26-128.13)	24.57 (3.06-131.05)

Table 1b. Characteristics of patients Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation in Patients with Myelofibrosis

Characteristic	HLA-identical sibling	Haplo	URD 8/8
No. of patients	903	126	1097
No. of centers	175	59	141
track - no. (%)			
TED	513 (56.8)	31 (24.6)	410 (37.4)
CRF	390 (43.2)	95 (75.4)	687 (62.6)
Patient Age - median (min-max)	57.92 (3.8-74.52)	60.97 (2.89-74.78)	60.66 (1.12-77.9)
Age - no. (%)			
<18	8 (0.9)	1 (0.8)	6 (0.5)
18-29	5 (0.6)	1 (0.8)	8 (0.7)
30-39	30 (3.3)	4 (3.2)	29 (2.6)
40-49	135 (15)	18 (14.3)	128 (11.7)
50-59	352 (39)	35 (27.8)	348 (31.7)
60-69	351 (38.9)	56 (44.4)	502 (45.8)
≥ 70	22 (2.4)	11 (8.7)	76 (6.9)
Gender: (2400 Q942) - no. (%)			
Male	548 (60.7)	72 (57.1)	632 (57.6)
Female	355 (39.3)	54 (42.9)	465 (42.4)
Race - no. (%)			
Caucasian	673 (74.5)	85 (67.5)	983 (89.6)
African-American	40 (4.4)	19 (15.1)	27 (2.5)
Asian	54 (6)	11 (8.7)	27 (2.5)
Pacific islander	9 (1)	1 (0.8)	6 (0.5)
Native American	2 (0.2)	0	3 (0.3)
More than one race	1 (0.1)	1 (0.8)	2 (0.2)
Missing	124 (13.7)	9 (7.1)	49 (4.5)
HCT-CI - no. (%)			
0	292 (32.3)	28 (22.2)	282 (25.7)
1	116 (12.8)	23 (18.3)	153 (13.9)
2	121 (13.4)	20 (15.9)	162 (14.8)
3+	325 (36)	54 (42.9)	487 (44.4)
TBD, review needed for history of malignancies	0	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.8)	0
Missing	49 (5.4)	0	12 (1.1)
Karnofsky score - no. (%)			

Characteristic	HLA-identical sibling	Haplo	URD 8/8
90-100	518 (57.4)	69 (54.8)	594 (54.1)
< 90	366 (40.5)	56 (44.4)	487 (44.4)
Missing	19 (2.1)	1 (0.8)	16 (1.5)
Subdisease - no. (%)			
Primary Myelofibrosis	607 (67.2)	77 (61.1)	745 (67.9)
Polycythemia vesa	127 (14.1)	24 (19)	168 (15.3)
Essential thrombocythemia	169 (18.7)	25 (19.8)	184 (16.8)
Graft type - no. (%)			
Bone marrow	49 (5.4)	28 (22.2)	75 (6.8)
Peripheral blood	854 (94.6)	98 (77.8)	1022 (93.2)
Time from diagnosis to HCT - no. (%)			
<6	113 (12.5)	8 (6.3)	87 (7.9)
6-11	133 (14.7)	20 (15.9)	180 (16.4)
≥12	602 (66.7)	97 (77)	768 (70)
Missing	55 (6.1)	1 (0.8)	62 (5.7)
Donor/recipient sex match - no. (%)			
M-M	295 (32.7)	50 (39.7)	456 (41.6)
M-F	162 (17.9)	24 (19)	311 (28.4)
F-M	253 (28)	22 (17.5)	176 (16)
F-F	192 (21.3)	30 (23.8)	153 (13.9)
Missing	1 (0.1)	0	1 (0.1)
Conditioning as reported by center - no. (%)			
MAC	373 (41.3)	42 (33.3)	462 (42.1)
RIC/NMA	521 (57.7)	84 (66.7)	634 (57.8)
Missing	9 (1)	0	1 (0.1)
Conditioning regimen - no. (%)			
TBI/Cy	12 (1.3)	2 (1.6)	20 (1.8)
TBI/Cy/Flu	21 (2.3)	47 (37.3)	9 (0.8)
TBI/Cy/Flu/TT	0	2 (1.6)	0
TBI/Mel	8 (0.9)	13 (10.3)	14 (1.3)
TBI/Flu	40 (4.4)	15 (11.9)	87 (7.9)
TBI/other(s)	4 (0.4)	0	6 (0.5)
Bu/Cy/Mel	1 (0.1)	0	0
Bu/Cy	146 (16.2)	11 (8.7)	123 (11.2)
Bu/Mel	4 (0.4)	2 (1.6)	12 (1.1)
Flu/Bu/TT	2 (0.2)	16 (12.7)	4 (0.4)
Flu/Bu	370 (41)	6 (4.8)	479 (43.7)
Flu/Mel/TT	1 (0.1)	4 (3.2)	4 (0.4)
Flu/Mel	267 (29.6)	6 (4.8)	315 (28.7)
Cy/Flu	14 (1.6)	2 (1.6)	8 (0.7)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
Treosulfan	1 (0.1)	0	3 (0.3)
TLI	3 (0.3)	0	3 (0.3)
Other(s)	8 (0.9)	0	10 (0.9)
None	1 (0.1)	0	0
GHVD-prophylaxis - no. (%)			
No prophylaxis	2 (0.2)	2 (1.6)	5 (0.5)
CD34 selection/TCD	8 (0.9)	5 (4)	13 (1.2)
PTcy + CNIs + MMF	15 (1.7)	108 (85.7)	25 (2.3)
PTcy + CNIs + MTX	0	1 (0.8)	1 (0.1)
PT-Cy + others	19 (2.1)	7 (5.6)	28 (2.6)
PT-Cy alone	1 (0.1)	0	1 (0.1)
CNI + MMF	166 (18.4)	3 (2.4)	172 (15.7)
CNI + MTX	556 (61.6)	0	719 (65.5)
CNI + others	81 (9)	0	92 (8.4)
CNI alone	37 (4.1)	0	28 (2.6)
Other prophylaxis	18 (2)	0	13 (1.2)
TX year - no. (%)			
2008	59 (6.5)	1 (0.8)	46 (4.2)
2009	73 (8.1)	2 (1.6)	70 (6.4)
2010	79 (8.7)	1 (0.8)	54 (4.9)
2011	79 (8.7)	1 (0.8)	44 (4)
2012	82 (9.1)	1 (0.8)	72 (6.6)
2013	64 (7.1)	5 (4)	94 (8.6)
2014	77 (8.5)	11 (8.7)	124 (11.3)
2015	97 (10.7)	11 (8.7)	116 (10.6)
2016	94 (10.4)	20 (15.9)	138 (12.6)
2017	105 (11.6)	34 (27)	165 (15)
2018	94 (10.4)	39 (31)	174 (15.9)
Follow-up - median (min-max)	37.6 (3.06-131.05)	18.45 (3.22-74.31)	36.61 (3.16-128.13)

Proposal: 1911-66

Title:
Comparison of outcomes following allogeneic stem cell transplantation for myelofibrosis with HLA-haploidentical versus matched donors

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Research hypothesis:
Our research hypothesis is that HLA-haploidentical transplantation is associated with a comparable median overall survival in patients with myelofibrosis (MF) as compared to matched donors

Specific aims:
- AIM 1: To compare overall survival in patients with MF who have received an allogeneic stem cell transplantation from an HLA-haploidentical donor as compared to other donor types.
- AIM 2: To determine patient, disease, and treatment related factors associated with survival in HLA-haploidentical donor transplantations for MF, in particular pre-transplantation JAK inhibition.
- AIM 3: To define preferred donor types for allogeneic stem cell transplantation in patients with MF and provide basis for prospective clinical trials.

Scientific impact:
Donor selection in patients with MF can often be challenging given the advanced age of patients and their siblings. Multiple retrospective and prospective trials have shown that donor type is one of the major variables that impacts transplant outcomes with mismatched unrelated donors demonstrating the worst outcomes. Use of matched unrelated donors has been associated with worse outcomes as compared to matched related donors in some studies,[1,2] but not others.[3]
Over the past decade, HLA-haploidentical transplantation has become a compelling option in patients without matched donors. Moreover, recent reports demonstrate comparable outcomes using HLA-haploidentical transplantation as compared to matched sibling and unrelated donors in patients with acute myeloid leukemia.[4] Data on transplant outcomes using HLA-haploidentical as compared to matched donors in patients with myelofibrosis is lacking. The impact of this study would inform the use of HLA-haploidentical transplantation in the treatment of MF and help guide decision as it related to donor selection.

Scientific justification:
Allogeneic stem cell transplantation is the only curative option for patients with MF. Recent advances have been made that have led to the improved survival in this population, particularly reduced intensity condition regimen. The Myeloproliferative Disorder Research Consortium (MPD-RC) 101 trial included 66 patients with MF receiving fludarabine/melphalan condition. This study, which our center led, demonstrated excellent overall survival (OS) in patients receiving a matched-related donor (median not reached after 25 months follow up) but a poor median OS of only 6 months in patients who received an allogeneic transplantation from an unrelated donor.[2] This finding has been confirmed by multiple retrospective studies, including CIBMTR analysis and a recent study from our group.[1,5-7]
The use of a HLA-haploidentical donor has become an attractive option in allogeneic transplantation in a number of hematologic malignancies. Based on data from the CIBMTR, the use of HLA-haploidentical donor source has steadily increased in the last several years.[8] Compared with other hematologic

malignancies, there is a relative paucity of information on HLA-haploidentical transplantation in MF. In addition, HLA-haploidentical transplantation is challenging in patients with MF given the already higher rates of graft failure and poor graft function that is seen with matched donors.[3,6,9]
An Italian study of 95 MF patients who underwent allogeneic transplantation over a period of 14 years included 23 patients who received an HLA-haploidentical transplantation. As compared to patients transplanted before 2010, patients who were transplanted between 2010-2014 had improved overall survival, which was attributed to multiple factors including increasing use of HLA-haploidentical donors.[10] However, this study did not account for baseline differences in the study groups and may therefore be subject to bias. In addition, there was no comparison of outcomes between patients receiving unrelated donors and HLA-haploidentical donors. Finally, many of these patients receiving a myeloablative conditioning strategy which has fallen out of favor in MF. A recent retrospective analysis by the European Society for Blood and Marrow Transplantation (EBMT) of 56 MF patients who underwent HLA-haploidentical transplantation demonstrated a 1-year and 2-year survival rates of 61% and 56% and a 2-year cumulative incidence of relapse of 19%. Of note, 70% of patients underwent myeloablative conditioning.[11] What remains unknown is how these outcomes compared to transplantation with matched donors.
Our proposed study would be of significant importance to both clinicians and patients in understanding transplant outcomes in patients with MF using HLA-haploidentical donor as well as guide decision making when multiple donors are available. The results of this study would provide rational for future prospective clinical trials.

Patient eligibility population:
The patient requirements are as follows:

- At least 18 years of age
- Received allogeneic stem cell transplantation between 2005-2018.
- Diagnosis of primary myelofibrosis, post-polycythemia myelofibrosis, post-essential thrombocythemia myelofibrosis, or myeloproliferative-neoplasm blast phase.

There will be no restrictions on risk score, transplant regimen, prior treatments, or other factors.

Data requirements:
The following CIBMTR data collection forms will be needed

- 2000: Recipient Baseline Data
- HLA: Confirmation of HLA Typing
- Hematopoietic Stem Cell Transplantation Infusion
- 2008: HCT Canceled or Delayed
- 2100: Post-HSCT Data
- 2400: Pre-transplant Essential Data
- 2402: Pre-Transplant Essential Data: Disease Classification
- 2450: Post-Transplant Essential Data
- 2500: Recipient Eligibility Form
- 2532: BMT CTN 1702 Enrollment Form 2532
- 2533: BMT CTN 1702 Donor Testing Form 2533
- 2534: BMT CTN 1702 Monthly Update Form 2534
- 2535: BMT CTN 1702 Adverse Event Form 2535
- 2536: BMT CTN 1702 Off Study Form 2536
- 2537: BMT CTN 1702 Protocol Deviation / Violation Form 2537

- 2556: Myelofibrosis CMS Study Pre-HCT Supplemental Form
- 2557: Myelofibrosis CMS Study Post-HCT Supplemental Form
- 2900: Recipient Death Data

Sample requirements:
At this time, we are not planning correlative lab studies necessitating access to the NMDP Research Sample Repository in this study.

Study design:
This will be a retrospective cohort study of patients with myelofibrosis who have undergone allogeneic stem cell transplantation. The primary end point will be OS. Secondary endpoints include NRM, time to progression (TTP), time to neutrophil and platelet engraftment, rates of primary and secondary graft failure, poor graft function (as defined by cytopenia in at least two lineages and/or with transfusion requirements beyond day + 28), re-transplantation, stem cell boost or donor lymphocyte infusion. In addition, we will examine rates of infection, incidence of vaso-occlusive disease, rates of acute and chronic graft-versus-host disease (GVHD), and GVHD-free, relapse free survival.
A cohort of patients who have received a matched donor will be compared with a separate cohort who have received an HLA-haploidentical transplantation for outcomes as listed above. We will also perform a separate comparison of matched unrelated donors versus HLA-haploidentical transplantation. Moreover, we will include patients who have received umbilical cord donation and describe their outcomes.
To adjust for baseline differences between these two groups, we will employ propensity score adjustment matching if numbers allow this statistical adjustment. Otherwise, we will perform univariable and multivariable analysis.

Non-CIBMTR data source:
We will use data from the CIBMTR Research Database. We will not link to any external data.

Conflicts of interest:
- Dr. Mascarenhas received clinical research funding paid to the institution from Incyte, Novartis, Roche, Promedior, Merck, CTI Biopharma, Janssen, PharmaEssentia, Celgene, Merus, and Arog. Clinical trial steering committee member for Roche, Incyte, Celgene, and CTI Biopharma.
- Drs. Keyzner and Tremblay have no financial conflicts of interest to report.

References:
1. Gupta V, Malone AK, Hari PN, et al. Reduced-intensity hematopoietic cell transplantation for patients with primary myelofibrosis: a cohort analysis from the center for international blood and marrow transplant research. Biol Blood Marrow Transplant. 2014;20(1):89-97.
2. Rondelli D, Goldberg JD, Isola L, et al. MPD-RC 101 prospective study of reduced-intensity allogeneic hematopoietic stem cell transplantation in patients with myelofibrosis. Blood. 2014;124(7):1183-1191.
3. Kroger N, Holler E, Kobbe G, et al. Allogeneic stem cell transplantation after reduced-intensity conditioning in patients with myelofibrosis: a prospective, multicenter study of the Chronic Leukemia Working Party of the European Group for Blood and Marrow Transplantation. Blood. 2009;114(26):5264-5270.
4. Devillier R, Legrand F, Rey J, et al. HLA-Matched Sibling versus Unrelated versus Haploidentical Related Donor Allogeneic Hematopoietic Stem Cell Transplantation for Patients Aged Over 60 Years

with Acute Myeloid Leukemia: A Single-Center Donor Comparison. Biol Blood Marrow Transplant. 2018;24(7):1449-1454.
5. Ballen KK, Shrestha S, Sobocinski KA, et al. Outcome of transplantation for myelofibrosis. Biol Blood Marrow Transplant. 2010;16(3):358-367.
6. Keyzner A, Han S, Shapiro S, et al. Outcome of Allogeneic Hematopoietic Stem Cell Transplantation for Patients with Chronic and Advanced Phase Myelofibrosis. Biol Blood Marrow Transplant. 2016;22(12):2180-2186.
7. Deeg HJ, Bredeson C, Farnia S, et al. Hematopoietic Cell Transplantation as Curative Therapy for Patients with Myelofibrosis: Long-Term Success in all Age Groups. Biol Blood Marrow Transplant. 2015;21(11):1883-1887.
8. D'Souza A, C F. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides. https://www.cibmtr.org. Published 2018. Accessed.
9. Alchalby H, Yunus DR, Zabelina T, Ayuk F, Kroger N. Incidence and risk factors of poor graft function after allogeneic stem cell transplantation for myelofibrosis. Bone Marrow Transplant. 2016;51(9):1223-1227.
10. Bregante S, Dominietto A, Ghiso A, et al. Improved Outcome of Alternative Donor Transplantations in Patients with Myelofibrosis: From Unrelated to Haploidentical Family Donors. Biol Blood Marrow Transplant. 2016;22(2):324-329.
11. Raj K, Eikema DJ, McLornan DP, et al. Family Mismatched Allogeneic Stem Cell Transplantation for Myelofibrosis: Report from the Chronic Malignancies Working Party of European Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant. 2019;25(3):522-528.

Table 1. Characteristics of patients Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation in Patients with Myelofibrosis, TED vs. CRF

Characteristic	TED	CRF
No. of patients	954	1172
No. of centers	168	143
age - median (min-max)	58.28 (3.8-75.99)	60.51 (1.12-77.9)
Age - no. (%)		
<18	6 (0.6)	9 (0.8)
18-29	8 (0.8)	6 (0.5)
30-39	40 (4.2)	23 (2)
40-49	138 (14.5)	143 (12.2)
50-59	354 (37.1)	381 (32.5)
60-69	378 (39.6)	531 (45.3)
≥ 70	30 (3.1)	79 (6.7)
Gender: (2400 Q942) - no. (%)		
Male	567 (59.4)	685 (58.4)
Female	387 (40.6)	487 (41.6)
Race - no. (%)		
Caucasian	731 (76.6)	1010 (86.2)
African-American	35 (3.7)	51 (4.4)
Asian	41 (4.3)	51 (4.4)
Pacific islander	3 (0.3)	13 (1.1)
Native American	1 (0.1)	4 (0.3)
More than one race	1 (0.1)	3 (0.3)
Missing	142 (14.9)	40 (3.4)
HCT-CI - no. (%)		
0	295 (30.9)	307 (26.2)
1	121 (12.7)	171 (14.6)
2	127 (13.3)	176 (15)
3+	362 (37.9)	504 (43)
TBD, review needed for history of malignancies	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.1)
Missing	49 (5.1)	12 (1)
Karnofsky score - no. (%)		
90-100	540 (56.6)	641 (54.7)
< 90	400 (41.9)	509 (43.4)
Missing	14 (1.5)	22 (1.9)
Subdisease - no. (%)		
Primary Myelofibrosis	629 (65.9)	800 (68.3)
Polycythemia vesa	147 (15.4)	172 (14.7)
Essential thrombocythemia	178 (18.7)	200 (17.1)
Graft type - no. (%)		

Characteristic	TED	CRF
Bone marrow	64 (6.7)	88 (7.5)
Peripheral blood	890 (93.3)	1084 (92.5)
Time from diagnosis to HCT - no. (%)		
<6	105 (11)	103 (8.8)
6-11	147 (15.4)	186 (15.9)
≥12	642 (67.3)	825 (70.4)
Missing	60 (6.3)	58 (4.9)
Donor type - no. (%)		
HLA-identical sibling	513 (53.8)	390 (33.3)
Haplo	31 (3.2)	95 (8.1)
URD 8/8	410 (43)	687 (58.6)
Donor/recipient sex match - no. (%)		
M-M	349 (36.6)	452 (38.6)
M-F	211 (22.1)	286 (24.4)
F-M	218 (22.9)	233 (19.9)
F-F	175 (18.3)	200 (17.1)
Missing	1 (0.1)	1 (0.1)
Conditioning as reported by center - no. (%)		
MAC	383 (40.1)	494 (42.2)
RIC/NMA	563 (59)	676 (57.7)
Missing	8 (0.8)	2 (0.2)
Conditioning regimen - no. (%)		
TBI/Cy	15 (1.6)	19 (1.6)
TBI/Cy/Flu	32 (3.4)	45 (3.8)
TBI/Cy/Flu/TT	1 (0.1)	1 (0.1)
TBI/Mel	10 (1)	25 (2.1)
TBI/Flu	66 (6.9)	76 (6.5)
TBI/other(s)	4 (0.4)	6 (0.5)
Bu/Cy/Mel	1 (0.1)	0
Bu/Cy	124 (13)	156 (13.3)
Bu/Mel	11 (1.2)	7 (0.6)
Flu/Bu/TT	2 (0.2)	20 (1.7)
Flu/Bu	388 (40.7)	467 (39.8)
Flu/Mel/TT	3 (0.3)	6 (0.5)
Flu/Mel	267 (28)	321 (27.4)
Cy/Flu	14 (1.5)	10 (0.9)
Treosulfan	3 (0.3)	1 (0.1)
TLI	4 (0.4)	2 (0.2)
Other(s)	9 (0.9)	9 (0.8)
None	0	1 (0.1)
GHVD-prophylaxis - no. (%)		

Characteristic	TED	CRF
No prophylaxis	3 (0.3)	6 (0.5)
CD34 selection/TCD	16 (1.7)	10 (0.9)
PTcy + CNIs + MMF	35 (3.7)	113 (9.6)
PTcy + CNIs + MTX	0	2 (0.2)
PT-Cy + others	12 (1.3)	42 (3.6)
PT-Cy alone	1 (0.1)	1 (0.1)
CNI + MMF	188 (19.7)	153 (13.1)
CNI + MTX	535 (56.1)	740 (63.1)
CNI + others	105 (11)	68 (5.8)
CNI alone	40 (4.2)	25 (2.1)
Other prophylaxis	19 (2)	12 (1)
TX year - no. (%)		
2008	29 (3)	77 (6.6)
2009	68 (7.1)	77 (6.6)
2010	98 (10.3)	36 (3.1)
2011	110 (11.5)	14 (1.2)
2012	144 (15.1)	11 (0.9)
2013	124 (13)	39 (3.3)
2014	75 (7.9)	137 (11.7)
2015	99 (10.4)	125 (10.7)
2016	111 (11.6)	141 (12)
2017	54 (5.7)	250 (21.3)
2018	42 (4.4)	265 (22.6)
Follow-up - median (min-max)	49.28 (3.26-128.13)	24.57 (3.06-131.05)

Table 1b. Characteristics of patients Haploidentical Donor versus Full-Matched Donor Allogeneic Stem Cell Transplantation in Patients with Myelofibrosis

Characteristic	HLA-identical sibling	Haplo	URD 8/8
No. of patients	903	126	1097
No. of centers	175	59	141
track - no. (%)			
TED	513 (56.8)	31 (24.6)	410 (37.4)
CRF	390 (43.2)	95 (75.4)	687 (62.6)
age - median (min-max)	57.92 (3.8-74.52)	60.97 (2.89-74.78)	60.66 (1.12-77.9)
Age - no. (%)			
<18	8 (0.9)	1 (0.8)	6 (0.5)
18-29	5 (0.6)	1 (0.8)	8 (0.7)
30-39	30 (3.3)	4 (3.2)	29 (2.6)
40-49	135 (15)	18 (14.3)	128 (11.7)
50-59	352 (39)	35 (27.8)	348 (31.7)
60-69	351 (38.9)	56 (44.4)	502 (45.8)
≥ 70	22 (2.4)	11 (8.7)	76 (6.9)
Gender: (2400 Q942) - no. (%)			
Male	548 (60.7)	72 (57.1)	632 (57.6)
Female	355 (39.3)	54 (42.9)	465 (42.4)
Race - no. (%)			
Caucasian	673 (74.5)	85 (67.5)	983 (89.6)
African-American	40 (4.4)	19 (15.1)	27 (2.5)
Asian	54 (6)	11 (8.7)	27 (2.5)
Pacific islander	9 (1)	1 (0.8)	6 (0.5)
Native American	2 (0.2)	0	3 (0.3)
More than one race	1 (0.1)	1 (0.8)	2 (0.2)
Missing	124 (13.7)	9 (7.1)	49 (4.5)
HCT-CI - no. (%)			
0	292 (32.3)	28 (22.2)	282 (25.7)
1	116 (12.8)	23 (18.3)	153 (13.9)
2	121 (13.4)	20 (15.9)	162 (14.8)
3+	325 (36)	54 (42.9)	487 (44.4)
TBD, review needed for history of malignancies	0	0	1 (0.1)
TBD, inconsistencies between parent and sub-questions	0	1 (0.8)	0
Missing	49 (5.4)	0	12 (1.1)
Karnofsky score - no. (%)			
90-100	518 (57.4)	69 (54.8)	594 (54.1)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
< 90	366 (40.5)	56 (44.4)	487 (44.4)
Missing	19 (2.1)	1 (0.8)	16 (1.5)
Subdisease - no. (%)			
Primary Myelofibrosis	607 (67.2)	77 (61.1)	745 (67.9)
Polycythemia vesa	127 (14.1)	24 (19)	168 (15.3)
Essential thrombocythemia	169 (18.7)	25 (19.8)	184 (16.8)
Graft type - no. (%)			
Bone marrow	49 (5.4)	28 (22.2)	75 (6.8)
Peripheral blood	854 (94.6)	98 (77.8)	1022 (93.2)
Time from diagnosis to HCT - no. (%)			
<6	113 (12.5)	8 (6.3)	87 (7.9)
6-11	133 (14.7)	20 (15.9)	180 (16.4)
≥12	602 (66.7)	97 (77)	768 (70)
Missing	55 (6.1)	1 (0.8)	62 (5.7)
Donor/recipient sex match - no. (%)			
M-M	295 (32.7)	50 (39.7)	456 (41.6)
M-F	162 (17.9)	24 (19)	311 (28.4)
F-M	253 (28)	22 (17.5)	176 (16)
F-F	192 (21.3)	30 (23.8)	153 (13.9)
Missing	1 (0.1)	0	1 (0.1)
Conditioning as reported by center - no. (%)			
MAC	373 (41.3)	42 (33.3)	462 (42.1)
RIC/NMA	521 (57.7)	84 (66.7)	634 (57.8)
Missing	9 (1)	0	1 (0.1)
Conditioning regimen - no. (%)			
TBI/Cy	12 (1.3)	2 (1.6)	20 (1.8)
TBI/Cy/Flu	21 (2.3)	47 (37.3)	9 (0.8)
TBI/Cy/Flu/TT	0	2 (1.6)	0
TBI/Mel	8 (0.9)	13 (10.3)	14 (1.3)
TBI/Flu	40 (4.4)	15 (11.9)	87 (7.9)
TBI/other(s)	4 (0.4)	0	6 (0.5)
Bu/Cy/Mel	1 (0.1)	0	0
Bu/Cy	146 (16.2)	11 (8.7)	123 (11.2)
Bu/Mel	4 (0.4)	2 (1.6)	12 (1.1)
Flu/Bu/TT	2 (0.2)	16 (12.7)	4 (0.4)
Flu/Bu	370 (41)	6 (4.8)	479 (43.7)
Flu/Mel/TT	1 (0.1)	4 (3.2)	4 (0.4)
Flu/Mel	267 (29.6)	6 (4.8)	315 (28.7)
Cy/Flu	14 (1.6)	2 (1.6)	8 (0.7)
Treosulfan	1 (0.1)	0	3 (0.3)

Characteristic	HLA-identical sibling	Haplo	URD 8/8
TLI	3 (0.3)	0	3 (0.3)
Other(s)	8 (0.9)	0	10 (0.9)
None	1 (0.1)	0	0
GHVD-prophylaxis - no. (%)			
No prophylaxis	2 (0.2)	2 (1.6)	5 (0.5)
CD34 selection/TCD	8 (0.9)	5 (4)	13 (1.2)
PTcy + CNIs + MMF	15 (1.7)	108 (85.7)	25 (2.3)
PTcy + CNIs + MTX	0	1 (0.8)	1 (0.1)
PT-Cy + others	19 (2.1)	7 (5.6)	28 (2.6)
PT-Cy alone	1 (0.1)	0	1 (0.1)
CNI + MMF	166 (18.4)	3 (2.4)	172 (15.7)
CNI + MTX	556 (61.6)	0	719 (65.5)
CNI + others	81 (9)	0	92 (8.4)
CNI alone	37 (4.1)	0	28 (2.6)
Other prophylaxis	18 (2)	0	13 (1.2)
TX year - no. (%)			
2008	59 (6.5)	1 (0.8)	46 (4.2)
2009	73 (8.1)	2 (1.6)	70 (6.4)
2010	79 (8.7)	1 (0.8)	54 (4.9)
2011	79 (8.7)	1 (0.8)	44 (4)
2012	82 (9.1)	1 (0.8)	72 (6.6)
2013	64 (7.1)	5 (4)	94 (8.6)
2014	77 (8.5)	11 (8.7)	124 (11.3)
2015	97 (10.7)	11 (8.7)	116 (10.6)
2016	94 (10.4)	20 (15.9)	138 (12.6)
2017	105 (11.6)	34 (27)	165 (15)
2018	94 (10.4)	39 (31)	174 (15.9)
Follow-up - median (min-max)	37.6 (3.06-131.05)	18.45 (3.22-74.31)	36.61 (3.16-128.13)

Table. Median follow-up for Haploidentical donors

Characteristic	N
Follow-up - median (min-max)	18.45 (3.22-74.31)