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A G E N D A
CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA
Houston, TX
Saturday, February 23, 2019, 2:45 pm – 4:45 pm

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1. **Introduction**
   a. Minutes and overview plan from February 2018 meeting (Attachment 1)
   b. Introduction of incoming co-chair: **Ryotaro Nakamura, MD**; City of Hope; E-mail: rnakamura@coh.org
   c. Instructions for sign-in and voting
2. **Accrual summary** (Attachment 2)
3. **Presentations, Published or Submitted Papers**
   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 (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) **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. Introduction to TED (Transplant Essential Data) vs. CRF (Case Report Form) level databases (W Saber)

6. Future/Proposed Studies

a. **PROP 1810-12** Impact of conditioning regimen on outcomes for patients with previously treated CLL who underwent allogeneic hematopoietic transplantation. (H Kim) (Attachment 4)
b. **PROP 1811-27** Graft failure, donor lymphocyte infusion, and second transplant after allogeneic hematopoietic cell transplant for myelofibrosis. (S Kunte/A Gerds) (Attachment 5)
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) (Attachment 6), Outcomes of patients with T cell prolymphocytic leukemia undergoing allogeneic stem cell transplantation (S Bal/C Sauter) (Attachment 7), Allogeneic stem cell transplant for prolymphocytic leukemias (L Gowda/F Foss/M Kalaycio/H Alkhateeb) (Attachment 8)
d. **PROP 1811-51** Alternative donor vs HLA matched donor hematopoietic cell transplantation in patients with myelodysplastic syndrome (R Mehta) (Attachment 9)
e. **PROP 1811-72** Precision model to predict outcomes of myelofibrosis using artificial intelligence techniques. (S Hashmi/A Tefferi/N Gangat) (Attachment 10)
f. **PROP 1811-171** Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. (B Dholaria/B Savani/M Kharfan) (Attachment 11)

Dropped proposed studies

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.*

7. Study results presentations

a. **CK15-01** Comparison of transplant vs. non-transplant therapies for myelofibrosis. (K Ballen/RA Mesa/KL Gowin)
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).
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).
d. **CK18-01** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndrome. (A Nazha).

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA
Salt Lake City, UT
Wednesday, February 21, 2018, 12:15 p.m. – 2:15 p.m.

Co-Chair:	**Uday Popat, MD, MD Anderson Cancer Center**
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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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Statistical Director:	**Ying Liu, PhD, CIBMTR Statistical Center**
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1. Introduction

The Chronic Leukemia Working Committee (CKWC) met on Wednesday, February 21, 2018 at 12:15 p.m. The chairs, scientific director and statisticians were all presented at the meeting. Attendees were asked to have their name badges scanned at the front gate for attendance purpose and to maintain the committee membership roster.

As the scientific director of the CKWC, Dr. Wael Saber welcomed the attendees on behalf of the working committee leadership and 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. Saber welcomed the incoming chair, Dr. Bart Scott, from Fred Hutchinson Cancer Research Center, and thanked the departing chair, Dr. Edwin Alyea, for his leadership and guidance to the working committee in the past 5 years.

Dr. Saber 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 by the leadership. Minutes from the 2017 Tandem in Orlando were approved by the attendees.

2. Accrual summary

The accrual summary was reference by Dr. Alyea 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. Alyea went through the published or submitted papers in 2017, as well as abstracts that have been presented at various conferences, mentioning that it was a very productive year. Due to the full agenda, the papers were not presented. At the time, one study was published, and four abstracts were presented or accepted for presentation. These include:

a. **CK12-02b** Hill BT, Ahn KW, Hu Z-H, Aljurf M, Beitinjaneh A, Cahn JY, Cerny J, Kharfan-Dabaja MA, Ganguly S, Ghosh N, Grunwald MR, Inamoto Y, Kindwall-Keller T, Nishihori T, Olsson RF, Saad A, Seftel M, Seo S, Szer J, Tallman M, Ustun C, Wiernik PH, Maziarz RT, Kalaycio M, Alyea E, Popat U, Sobecks R, Saber W. Assessment of impact of human leukocyte antigen type on outcomes of allogeneic hematopoietic stem cell transplant for chronic lymphocytic leukemia. ***Biol Blood Marrow Transplant*. 2017 Oct. In Press.**
b. **CK12-01** Hu B, Lin X, Lee HC, Huang X, Slack R, Jabbour E, Verstovsek S, Ravandi F, Garcia-Manero G, Champlin R, Hu Z-H, Ahn KW, Lee Y, Popat U, Sobecks R, Alyea E, Kantarjian H, Cortes J, Saber W. Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era. ***59th ASH Annual Meeting and Exposition*. Poster.**
c. **CK14-02** Kim HT, Hu Z-H, Ahn KW, Davids MS, Volpe VO, Alyea E, Popat U, Sobecks R, Saber W, Brown JR. Prognostic score and cytogenetic risk classification for chronic lymphocytic leukemia patients who underwent reduced intensity conditioning allogeneic HCT: a CIBMTR report. ***59th ASH Annual Meeting and Exposition*. Oral.**
d. **CK15-02** Chhabra S, Ahn KW, Hu Z-H, Jain S, Stuart RK, Kalaycio M, Popat U, Sobecks R, Alyea E, Saber W. Comparison of outcomes after myeloablative versus reduced intensity conditioning allogeneic hematopoietic cell transplantation for chronic myeloid leukemia. ***59th ASH Annual Meeting and Exposition*. Oral.**
e. **CK16-02a** DeFilipp Z, Ancheta R, Liu Y, Ahn KW, Hu Z-H, Alyea E, Popat U, Sobecks R, Saber W. Contemporary role of maintenance tyrosine kinase inhibitors following allogeneic hematopoietic cell transplantation for chronic myeloid leukemia: a CIBMTR analysis. ***44th Annual Meeting of the EBMT*. Oral.**

4. Studies in Progress

Due to the full agenda, studies in progress were not presented at the meeting. Dr. Alyea 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. **CK14-02** Prognostic score and cytogenetic risk classification for chronic lymphocytic leukemia patients who underwent reduced intensity conditioning allogeneic HCT: a CIBMTR report. (H Kim/J Brown) **Manuscript Preparation**
c. **CK15-02** Comparison of outcomes after myeloablative versus reduced intensity conditioning allogeneic hematopoietic cell transplantation for chronic myeloid leukemia. (S Chhabra/S Jain/PK Stuart) **Manuscript Preparation**
d. **CK16-02a** Contemporary role of maintenance tyrosine kinase inhibitors following allogeneic hematopoietic cell transplantation for chronic myeloid leukemia: a CIBMTR analysis. (Z DeFilipp/R Ancheta) **Manuscript Preparation**
e. **CK16-02b** The benefit of donor lymphocyte infusion in the tyrosine kinase inhibitors era in chronic myeloid leukemia post allogeneic hematopoietic cell transplantation. (S Schmidt) **Analysis**
f. **CK15-01** Comparison of transplant vs. non-transplant therapies for myelofibrosis. (K Ballen/RA Mesa/KL Gowin) **Analysis**
g. **CK15-03** Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm. (V Gupta) **Data File Preparation**
h. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley) **Data File Preparation**

i. **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) **Protocol Development**
j. **CK17-02** Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. (B Oran) **Protocol Development**

5. Future/Proposed Studies

Dr. Saber gave a brief explanation of the difference between the TED data vs. CRF data; and asked the attendees to take that into account during the voting process. Dr. Alyea thanked the investigators whose proposals were submitted but not selected for presentation, emphasizing that the majority were dropped due to data availability issues. Dr. Alyea then announced the presenters for the first 3 proposals.

a. **PROP 1711-02** Impact of donor age on the outcomes of allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome. (G Murthy)

Dr. Guru Murthy presented the proposal. The goal of the proposal was to compare outcomes of MDS patients undergoing allo-HCT from older matched related vs. younger matched unrelated donors. Between 2002 and 2016, there were 906 MDS patients aged 50 years or older with HLA-id sibling donors vs. 1628 with well-matched unrelated donors. Dr. Murthy emphasized that donor age is an important factor for HCT outcomes and noted the larger sample size available for the study. During the discussion session, one attendee suggested also including T-cell depleted and CD34 selected cases in the study. Another comment was that it could be necessary to investigate the potential bias caused by the trend of choices of donors over the years.

b. **PROP 1711-30/PROP 1711-72** Clinical outcomes and prognostic factors in patients with Richter's syndrome treated with autologous or allogeneic hematopoietic stem-cell transplantation. (Y Sawalha/B Hill) Outcomes of allogeneic stem cell transplantation in patients with Richter's syndrome. (A Mukherjee/SR Pingali/NV Koshy)

Dr. Yazeed Sawalha presented the combined proposal. The goals of the proposal were to report the outcomes of auto- and allo-HCT for patients with Richter's syndrome, and to identify patient-, disease- and transplant-related factors that can predict post-HCT outcomes. There were 100 patients found in CRF undergoing allo-HCT for RS vs. 27 undergoing auto-HCT between 1994 and 2016, including 14 cases receiving novel agents. During the discussion session, one attendee asked whether information was available regarding whether the novel agents were given continually after HCT. It was suggested that it may require going back to the centers to get more information. Another attendee suggested excluding cases from the earlier years.

c. **PROP 1711-42** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes. (A Nazha/N Majhail)

Dr. Betty Hamilton presented the proposal. The goal of the proposal was to incorporate genomic-clinical data using machine learning algorithms to create a personalized prediction model for MDS HCT outcomes. There were 1,514 patients available from the previously published MDS study by Lindsley R using genomic/clinical data. Dr. Hamilton compared the difference between traditional vs. machine learning based prediction models and emphasized that machine learning model based on random survival forest and decision analysis is more personalized. Questions were raised by the attendees asking if there will be a training and a validation cohort and whether the number of available patients were sufficient for machine learning. Another question was regarding the type of genetic data available and Dr. Hamilton mentioned that data were available on a panel of 129 genes.

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

d. **PROP 1711-61** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/R Nakamura/R Pillai)

Dr. Ryotaro Nakamura presented the proposal. The goals of the proposal were to determine the impact of molecular genetics on the post-HCT outcomes in patients with CMML and to determine whether the CMML specific prognostic system (CPSS)-Mol score correlates with the post-HCT outcomes. Dr. Nakamura emphasized that there was no previous study investigating post-HCT outcomes for CMML based on molecular data. One question was raised asking the classification of the mutations in the analysis. Another question was regarding whether outcomes at 12 months post-HCT is sufficient and suggested to extend the time to 2-3 years.

e. **PROP 1711-75** Outcomes of patients with myelodysplastic syndrome who relapse post allogeneic hematopoietic stem cell transplantation. (R Tamari/B Gyurkocza/B Shaffer/SA Giralt)

Dr. Roni Tamari presented the proposal. The goal of the proposal was to identify patterns and characteristics of relapse post allo-HCT in patients with MDS. There were 1400 eligible MDS patients found between 2000 and 2016 who relapsed after undergoing initial allo-HCT. During the discussion session, one question was asked regarding whether genetic information will be available. Another attendee suggested also including T-cell depleted population in the study. The third suggestion was to also investigate GVHD and its grade prior to relapse.

f. **PROP 1711-111** Allogeneic stem cell transplantation for prolymphocytic leukemias. (L Gowda/F Foss/M Kalaycio/H Alkhateeb)

Dr. Lohith Gowda presented the proposal. The goal of the proposal was to evaluate outcomes of patients with PLL who underwent allo-HCT. There were 349 PLL patients identified in TED with 61 also in CRF who underwent allo-HCT between 1997 and 2016. Dr. Gowda emphasized that there were 50% patients in CR prior to HCT and it was a more updated population. During the discussion session, one attendee asked the validity of the disease status data. Another attendee suggested that there was no comparison to the non-HCT population and therefore it was more of a prognostic factor study.

Dr. Uday Popat announced the presenters for the next 3 proposals.

g. **PROP 1711-141** Allogeneic stem cell transplant outcomes in chronic myelogenous leukemia in the era of 2nd and 3rd generation TKIs for patients with recognized or unrecognized BCR ABL mutations. (LG Schachter/RT Maziarz/J Szer)

Dr. Levanto Schachter presented the proposal. The goals of the proposal were to determine outcomes after allo-HCT in patients with CML after treatments with second and/or third generation TKIs, as well as to investigate patient-, disease- and transplant-specific factors that may influence the outcomes. There were 1617 CML transplants found between 2004 and 2016, with in which 554 received second and/or third generation TKIs prior to conditioning. During the discussion session, one attendee commented on the potential bias caused by the peak number of cases between 2008 and 2009. Another attendee asked whether the information was available regarding the responses to TKIs. Another attendee suggested that third or fourth generation TKIs might also influence the outcomes.

h. **PROP 1711-147** Graft failure, donor lymphocyte infusion, and second transplant after allogenic hematopoietic cell transplant for myelofibrosis. (A Kishtagari/AT Gerds)

Dr. Ashwin Kishtagari presented the proposal. The goals of the proposal were to describe the rate of graft failure and associated risk factors in patients undergoing allo-HCT for myelofibrosis, and to describe the outcomes of DLI and second HCT as a salvage treatment for graft failure. Between 2000 and

2016, there were 128 patients with myelofibrosis in CRF who had graft failure vs. 746 who did not. During the discussion session, one attendee asked the distribution between primary and secondary graft failure. Another attendee asked the availability of the chimerism data. It was also suggested that with only 128 cases with graft failure, there might not be enough power to identify predictors without high hazard ratio.

i. **PROP 1711-85** Allogeneic stem cell transplant outcomes for patients with atypical chronic myeloid leukemia. (B Tomlinson/M Gallogly/M de Lima)

Dr. Benjamin Tomlinson presented the proposal. The goal of the proposal is to conduct a retrospective review of a cohort of aCML patients to define HCT outcomes and their potential prognostic factors for success of allo-HCT. There were 165 patients in TED undergoing allo-HCT for aCML between 2001 and 2016, including 49 cases also found in CRF. During the discussion session, questions were raised regarding the definition of aCML and its accurate diagnosis. It was suggested that controversies existed. One attendee also questioned the validity of conducting the study using the majority TED data.

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

a. **PROP 1709-03** JAK1/2 inhibitor prior to allogeneic stem cell transplantation in patients with myelofibrosis. *Dropped due to lack of long-term follow-up and few outcome events*.
b. **PROP 1710-03** Impact of post-transplant maintenance therapy with BCR-ABL tyrosine kinase inhibitors on outcomes of chronic myeloid leukemia accelerated phase or blast crisis in the era of reduced toxicity and non-myeloablative regimens. *Dropped due to overlapping with CK16-02a*.
c. **PROP 1711-77** To understand the outcomes and predictive factors of salvage DLI or a second hematopoietic cell transplant or both in patients with relapsed myelofibrosis after a first allo HCT. *Dropped due to insufficient number of eligible cases*.
d. **PROP 1711-98** Role of allogeneic stem cell transplant in ASXL1-mutated myeloid malignancies. *Dropped due to data not collected on the forms*.
e. **PROP 1711-120** Prognostic significance of response to pre-transplant therapy on outcomes after hematopoietic stem cell transplant in myelodysplastic syndromes. *Dropped due to overlapping with CK11-02*.

6. Other Business

The meeting was adjourned at 2:12 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, current scientific merit and impact of the studies on the field, the following studies were decided to move forward as the committee's research portfolio for the upcoming year:

a. **PROP 1711-02** Impact of donor age on the outcomes of allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome. (G Murthy) *This proposal is accepted as part of the CIBMTR Trainee-Fellow Research Program.*
b. **PROP 1711-42** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes. (A Nazha/N Majhail)
c. **PROP 1711-61** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/R Nakamura/R Pillai)

Working Committee Overview Plan for 2018-2019

a. **CK12-01** Optimal timing of allogeneic stem cell transplantation for chronic myeloid leukemia patients in the tyrosine kinase inhibitor era. (H Lee/J Cortes/M de Lima) We anticipate to having the manuscript submitted by July 2018. (Total hour: 30; Allocated for the fiscal year: 30)

b. **CK14-02** Validation of DFCI prognostic score for previously treated chronic lymphocytic leukemia patients who underwent reduced intensity conditioning allogeneic HSCT. (H Kim/J Brown) We anticipate to having the manuscript submitted by July 2018. (Total hour: 30; Allocated for the fiscal year: 30)

c. **CK15-01** Comparison of transplant vs. non-transplant therapies for myelofibrosis. (K Ballen/RA Mesa/KL Gowin) We anticipate to finalizing the analysis by July 2018 and having the manuscript submitted by July 2019. (Total hour: 100; Allocated for the fiscal year: 100)

d. **CK15-02** Comparison of outcomes after myeloablative and reduced intensity conditioning for allogeneic hematopoietic stem cell transplantation for chronic myeloid leukemia. (S Chhabra) We anticipate to having the manuscript published by July 2018. (Total hour: 10; Allocated for the fiscal year: 10)

e. **CK15-03** Outcome of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with antecedent history of Philadelphia-negative myeloproliferative neoplasm. (V Gupta) We plan to finalize the data file by July 2018 and finish the analysis by July 2019. (Total hour: 170; Allocated for the fiscal year: 100)

f. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients (L Godley) We anticipate to finalizing the analysis by July 2018 and having the manuscript submitted by July 2019. (Total hour: 130; Allocated for the fiscal year: 130)

g. **CK16-02a** Contemporary role of tyrosine kinase inhibitors post allogeneic hematopoietic stem cell transplantation for advanced phase chronic myeloid leukemia (R Ancheta/Z DeFilipp) We anticipate to having the final manuscript by July 2018 and have it submitted by the end of 2018. (Total hour: 70; Allocated for the fiscal year: 70)

h. **CK16-02b** Donor lymphocyte infusion vs. tyrosine kinase inhibitors in chronic myeloid leukemia post allogeneic hematopoietic cell transplantation (S Schmidt) We anticipate to having the final manuscript by July 2018 and have it submitted by the end of 2018. (Total hour: 70; Allocated for the fiscal year: 70)

i. **CK17-01** Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation. (T Roni/AG Sergio/P Jeanne) We anticipate to finalizing the protocol by July 2018 and completing the data file by July 2019. (Total hour: 280; Allocated for the fiscal year: 130)

j. **CK17-02** Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes. (B Oran/U Popat) We anticipate to finalizing the protocol by July 2018 and finishing the analysis by July 2019. (Total hour: 280; Allocated for the fiscal year: 210)

k. **CK18-01/PROP 1711-42** A personalized prediction model for outcomes after allogeneic stem cell transplant in patients with myelodysplastic syndromes. (A Nazha/N Majhail) This study will be analyzing a finalized data file from a previous study. We anticipate to finishing the analysis by July 2018 and having the manuscript submitted by July 2018. (Total hour: 170; Allocated for the fiscal year: 170)

l. **CK18-02/PROP 1711-61** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/R Nakamura/R Pillai) We anticipate to receiving the draft protocol by July 2018 and finalizing the protocol by July 2019. (Total hour: 310; Allocated for the fiscal year: 60)

Working Assignments for Working Committee Leadership (March 2018)

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.
	CK17-01 Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation.
Uday Popat	**CK12-01** A decision analysis of the optimal timing of allogeneic hematopoietic stem cell transplantation in chronic myeloid leukemia in the era of Tyrosine Kinase Inhibitors.
	CK15-01 Comparison of transplant vs. non-transplant therapies for MPN.
	CK15-03 Outcome of allogeneic HCT in patients with AML with antecedent history of Philadelphia-negative myeloproliferative neoplasm.
	CK17-02 Reduced-intensity conditioning transplantation in older MDS: the effect of specific conditioning regimens on transplant outcomes.
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.
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 2018

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Number of patients	7207	1290	5163	4910
Number of centers	189	152	188	249
Age, median (range)	60 (<1-83)	44 (<1-77)	54 (<1-81)	50 (<1-80)
Age, years				
<10	241 (3)	113 (9)	193 (4)	229 (5)
10-19	275 (4)	107 (8)	268 (5)	298 (6)
20-29	220 (3)	138 (11)	242 (5)	384 (8)
30-39	353 (5)	187 (14)	406 (8)	558 (11)
40-49	710 (10)	254 (20)	862 (17)	946 (19)
50-59	1727 (24)	304 (24)	1759 (34)	1313 (27)
60-69	2907 (40)	167 (13)	1347 (26)	1082 (22)
≥ 70	774 (11)	20 (2)	82 (2)	99 (2)
Missing	0	0	4 (<1)	1 (<1)
Sex				
Male	4464 (62)	785 (61)	3006 (58)	2964 (60)
Female	2743 (38)	504 (39)	2157 (42)	1940 (40)
Missing	0	1 (<1)	0	6 (<1)
Disease at diagnosis				
MDS unclassifiable, NOS	1156 (16)	133 (10)	1284 (25)	861 (18)
RA	738 (10)	287 (22)	539 (10)	671 (14)
RAEB	3061 (42)	549 (43)	1995 (39)	2060 (42)
CMML	659 (9)	127 (10)	446 (9)	423 (9)
RARS	284 (4)	37 (3)	182 (4)	118 (2)
RCMD	912 (13)	94 (7)	534 (10)	545 (11)
RCMD/RS	55 (<1)	1 (<1)	33 (<1)	28 (<1)
5q- syndrome	79 (1)	4 (<1)	63 (1)	37 (<1)
Other MDS, specified	263 (4)	58 (4)	87 (2)	167 (3)
Graft source				
Bone marrow	1481 (21)	410 (32)	1144 (22)	1162 (24)
Peripheral blood	5188 (72)	793 (61)	3759 (73)	3538 (72)

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Cord blood	522 (7)	87 (7)	195 (4)	115 (2)
Missing	16 (<1)	0	65 (1)	95 (2)
Donor type				
HLA-identical sibling	1688 (23)	565 (44)	2229 (43)	2320 (47)
Haplo	290 (4)	30 (2)	166 (3)	24 (<1)
Unrelated donor	4395 (61)	439 (34)	2166 (42)	2147 (44)
Cord blood	522 (7)	87 (7)	195 (4)	115 (2)
Other/missing	312 (4)	169 (13)	407 (8)	304 (6)
Year of transplant				
1995-1996	153 (2)	82 (6)	176 (3)	196 (4)
1997-1998	181 (3)	93 (7)	202 (4)	259 (5)
1999-2000	195 (3)	147 (11)	203 (4)	322 (7)
2001-2002	289 (4)	145 (11)	226 (4)	348 (7)
2003-2004	353 (5)	149 (12)	278 (5)	399 (8)
2005-2006	471 (7)	169 (13)	307 (6)	382 (8)
2007-2008	563 (8)	86 (7)	334 (6)	353 (7)
2009-2010	573 (8)	78 (6)	609 (12)	546 (11)
2011-2012	807 (11)	27 (2)	747 (14)	655 (13)
2013-2014	1232 (17)	121 (9)	639 (12)	524 (11)
2015-2016	1361 (19)	126 (10)	677 (13)	475 (10)
2017-2018*	1029 (14)	67 (5)	765 (15)	451 (9)

* New cases are continually being reported during this period.

Characteristics of recipients undergoing allogeneic HCT for myelofibrosis reported to the CIBMTR between 1995 and 2018

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Number of patients	1469	358	1322	1176
Number of centers	127	86	128	157
Age, median (range)	59 (<1-79)	53 (2-74)	58 (<1-76)	55 (2-75)
Age, years				
<10	10 (<1)	3 (<1)	15 (1)	10 (<1)
10-19	10 (<1)	7 (2)	10 (<1)	22 (2)
20-29	12 (<1)	9 (3)	19 (1)	31 (3)
30-39	46 (3)	24 (7)	50 (4)	102 (9)
40-49	212 (14)	91 (25)	207 (16)	247 (21)
50-59	534 (36)	134 (37)	493 (37)	437 (37)
60-69	561 (38)	87 (24)	487 (37)	310 (26)
≥ 70	84 (6)	3 (<1)	41 (3)	17 (1)
Sex				
Male	846 (58)	234 (65)	794 (60)	735 (63)
Female	623 (42)	124 (35)	528 (40)	441 (38)
Disease at diagnosis				
PV	183 (12)	34 (9)	170 (13)	86 (7)
ET	223 (15)	45 (13)	192 (15)	137 (12)
Chronic myelofibrosis	1063 (72)	279 (78)	960 (73)	953 (81)
Graft source				
Bone marrow	171 (12)	79 (22)	127 (10)	186 (16)
Peripheral blood	1254 (85)	272 (76)	1169 (88)	970 (82)
Cord blood	43 (3)	7 (2)	17 (1)	9 (<1)
Missing	1 (<1)	0	9 (<1)	11 (<1)
Donor type				
HLA-identical sibling	397 (27)	143 (40)	599 (45)	546 (46)
Haplo	55 (4)	10 (3)	35 (3)	3 (<1)
Unrelated donor	904 (62)	174 (49)	597 (45)	562 (48)
Cord blood	43 (3)	7 (2)	17 (1)	9 (<1)
Other/missing	70 (5)	24 (7)	74 (6)	56 (5)
Year of transplant				
1995-1996	15 (1)	8 (2)	11 (<1)	19 (2)

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
1997-1998	22 (1)	11 (3)	13 (<1)	36 (3)
1999-2000	31 (2)	22 (6)	19 (1)	44 (4)
2001-2002	52 (4)	21 (6)	33 (2)	81 (7)
2003-2004	54 (4)	30 (8)	46 (3)	99 (8)
2005-2006	76 (5)	43 (12)	76 (6)	99 (8)
2007-2008	124 (8)	38 (11)	74 (6)	116 (10)
2009-2010	124 (8)	30 (8)	176 (13)	190 (16)
2011-2012	38 (3)	5 (1)	307 (23)	159 (14)
2013-2014	192 (13)	44 (12)	236 (18)	129 (11)
2015-2016	285 (19)	45 (13)	238 (18)	91 (8)
2017-2018*	456 (31)	61 (17)	93 (7)	113 (10)

* New cases are continually being reported during this period.

Characteristics of recipients undergoing allogeneic HCT for CML reported to the CIBMTR between 1995 and 2018

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Number of patients	4059	2928	4306	8336
Number of centers	176	192	200	272
Age, median (range)	40 (1-77)	36 (1-76)	43 (<1-76)	37 (<1-75)
Age, years				
<10	85 (2)	69 (2)	65 (2)	196 (2)
10-19	360 (9)	306 (10)	257 (6)	663 (8)
20-29	578 (14)	611 (21)	507 (12)	1661 (20)
30-39	1015 (25)	876 (30)	993 (23)	2479 (30)
40-49	1164 (29)	695 (24)	1286 (30)	2223 (27)
50-59	708 (17)	316 (11)	881 (20)	967 (12)
60-69	133 (3)	53 (2)	288 (7)	136 (2)
≥ 70	16 (<1)	1 (<1)	20 (<1)	4 (<1)
Missing	0	1 (<1)	9 (<1)	7 (<1)
Sex				
Male	2368 (58)	1790 (61)	2548 (59)	5002 (60)
Female	1691 (42)	1138 (39)	1751 (41)	3297 (40)
Missing	0	0	7 (<1)	37 (<1)
Graft source				
Bone marrow	2546 (63)	1700 (58)	1980 (46)	4626 (55)
Peripheral blood	1334 (33)	1149 (39)	2114 (49)	3307 (40)
Cord blood	178 (4)	74 (3)	135 (3)	102 (1)
Missing	1 (<1)	5 (<1)	77 (2)	301 (4)
Donor type				
HLA-identical sibling	871 (21)	1604 (55)	2596 (60)	5387 (65)
Haplo	44 (1)	9 (<1)	87 (2)	4 (<1)
Unrelated donor	2806 (69)	963 (33)	1012 (24)	2315 (28)
Cord blood	178 (4)	74 (3)	135 (3)	102 (1)
Other/missing	160 (4)	278 (9)	476 (11)	528 (6)
Year of transplant				
1995-1996	711 (18)	498 (17)	657 (15)	1344 (16)
1997-1998	754 (19)	547 (19)	723 (17)	1741 (21)

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
1999-2000	676 (17)	629 (21)	616 (14)	1775 (21)
2001-2002	357 (9)	391 (13)	277 (6)	1204 (14)
2003-2004	409 (10)	369 (13)	251 (6)	741 (9)
2005-2006	318 (8)	270 (9)	175 (4)	426 (5)
2007-2008	238 (6)	54 (2)	133 (3)	215 (3)
2009-2010	247 (6)	54 (2)	159 (4)	273 (3)
2011-2012	52 (1)	14 (<1)	389 (9)	258 (3)
2013-2014	125 (3)	44 (2)	329 (8)	159 (2)
2015-2016	114 (3)	41 (1)	324 (8)	110 (1)
2017-2018*	58 (1)	17 (<1)	273 (6)	90 (1)

* New cases are continually being reported during this period.

Characteristics of recipients undergoing autologous HCT for CLL reported to the CIBMTR between 1995 and 2018

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Number of patients	84	41	269	244
Number of centers	42	14	65	58
Age, median (range)	52 (33-73)	50 (38-67)	53 (19-81)	52 (27-72)
Age, years				
<10	0	0	1 (<1)	0
10-19	0	0	2 (<1)	4 (2)
20-29	12 (14)	3 (7)	14 (5)	12 (5)
30-39	25 (30)	18 (44)	81 (30)	76 (31)
40-49	26 (31)	18 (44)	111 (41)	114 (47)
50-59	19 (23)	2 (5)	55 (20)	37 (15)
60-69	2 (2)	0	5 (2)	1 (<1)
Sex				
Male	61 (73)	33 (80)	187 (70)	194 (80)
Female	23 (27)	8 (20)	82 (30)	49 (20)
Missing	0	0	0	1 (<1)
Disease at diagnosis				
CLL, NOS	21 (25)	24 (59)	85 (32)	48 (20)
CLL, B-cell	62 (74)	17 (41)	179 (67)	195 (80)
CLL, T-cell	1 (1)	0	5 (2)	1 (<1)
Graft source				
Bone marrow	15 (18)	1 (2)	113 (42)	5 (2)
Peripheral blood	66 (79)	39 (95)	150 (56)	208 (85)
Missing	3 (4)	1 (2)	6 (2)	31 (13)
Year of transplant				
1995-1996	15 (18)	3 (7)	43 (16)	14 (6)
1997-1998	26 (31)	28 (68)	54 (20)	36 (15)
1999-2000	18 (21)	6 (15)	73 (27)	90 (37)
2001-2002	6 (7)	2 (5)	36 (13)	40 (16)
2003-2004	4 (5)	1 (2)	27 (10)	22 (9)
2005-2006	9 (11)	0	7 (3)	23 (9)
2007-2008	3 (4)	0	6 (2)	4 (2)

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
2009-2010	2 (2)	0	5 (2)	8 (3)
2011-2012	0	0	9 (3)	5 (2)
2013-2014	1 (1)	0	5 (2)	1 (<1)
2015-2016	0	1 (2)	2 (<1)	0
2017-2018*	0	0	2 (<1)	1 (<1)

* New cases are continually being reported during this period.

Characteristics of recipients undergoing allogeneic HCT for CLL reported to the CIBMTR between 1995 and 2018

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Number of patients	1476	385	1891	1415
Number of centers	124	82	135	145
Age, median (range)	55 (12-75)	54 (2-71)	56 (7-80)	53 (4-74)
Age, years				
<10	0	1 (<1)	2 (<1)	3 (<1)
10-19	3 (<1)	1 (<1)	2 (<1)	0
20-29	12 (<1)	1 (<1)	15 (<1)	23 (2)
30-39	64 (4)	33 (9)	81 (4)	75 (5)
40-49	338 (23)	100 (26)	351 (19)	375 (27)
50-59	636 (43)	164 (43)	824 (44)	653 (46)
60-69	389 (26)	83 (22)	569 (30)	276 (20)
≥ 70	34 (2)	2 (<1)	47 (2)	10 (<1)
Sex				
Male	1097 (74)	283 (74)	1372 (73)	1026 (73)
Female	378 (26)	102 (26)	518 (27)	387 (27)
Missing	1 (<1)	0	1 (<1)	2 (<1)
Disease at diagnosis				
CLL, NOS	709 (48)	125 (32)	570 (30)	599 (42)
CLL, B-cell	763 (52)	260 (68)	1310 (69)	810 (57)
CLL, T-cell	4 (<1)	0	11 (<1)	6 (<1)
Graft source				
Bone marrow	297 (20)	61 (16)	249 (13)	160 (11)
Peripheral blood	1091 (74)	310 (81)	1602 (85)	1203 (85)
Cord blood	86 (6)	13 (3)	33 (2)	17 (1)
Missing	2 (<1)	1 (<1)	7 (<1)	35 (2)
Donor type				
HLA-identical sibling	409 (28)	223 (58)	963 (51)	774 (55)
Haplo	34 (2)	1 (<1)	53 (3)	1 (<1)
Unrelated donor	880 (60)	135 (35)	714 (38)	552 (39)
Cord blood	86 (6)	13 (3)	33 (2)	17 (1)
Other/missing	67 (5)	13 (3)	128 (7)	71 (5)

Variable	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Year of transplant				
1995-1996	61 (4)	29 (8)	46 (2)	34 (2)
1997-1998	57 (4)	22 (6)	63 (3)	41 (3)
1999-2000	85 (6)	36 (9)	87 (5)	101 (7)
2001-2002	108 (7)	44 (11)	125 (7)	163 (12)
2003-2004	179 (12)	49 (13)	121 (6)	164 (12)
2005-2006	210 (14)	55 (14)	165 (9)	183 (13)
2007-2008	258 (17)	33 (9)	182 (10)	146 (10)
2009-2010	115 (8)	24 (6)	392 (21)	186 (13)
2011-2012	56 (4)	14 (4)	426 (23)	233 (16)
2013-2014	175 (12)	48 (12)	156 (8)	101 (7)
2015-2016	96 (7)	20 (5)	56 (3)	41 (3)
2017-2018*	76 (5)	11 (3)	72 (4)	22 (2)

* New cases are continually being reported during this period.

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	10592	3057	1857
Source of data			
CRF	7504 (71)	2079 (68)	1320 (71)
TED	3088 (29)	978 (32)	537 (29)
Number of centers	225	185	247
Disease at transplant			
Other leukemia	1312 (12)	328 (11)	227 (12)
CML	3217 (30)	856 (28)	715 (39)
MDS	6063 (57)	1873 (61)	915 (49)
MDS Disease status at transplant			
Early	1233 (20)	327 (18)	212 (23)
Advanced	4332 (72)	1419 (76)	568 (63)
Missing	457 (8)	114 (6)	124 (14)
Recipient age at transplant			
0-9 years	383 (4)	75 (2)	97 (5)
10-19 years	525 (5)	132 (4)	138 (7)
20-29 years	764 (7)	190 (6)	195 (11)
30-39 years	1315 (12)	326 (11)	262 (14)
40-49 years	1882 (18)	516 (17)	390 (21)
50-59 years	2602 (25)	740 (24)	408 (22)
60-69 years	2644 (25)	886 (29)	319 (17)
70+ years	477 (5)	192 (6)	48 (3)
Median (Range)	52 (0-81)	54 (1-79)	46 (1-79)
Recipient race/ethnicity			
Caucasian, non-Hispanic	9212 (88)	2682 (89)	1484 (87)
African-American, non-Hispanic	474 (5)	111 (4)	81 (5)
Asian, non-Hispanic	165 (2)	79 (3)	53 (3)
Pacific islander, non-Hispanic	13 (<1)	5 (<1)	2 (<1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Native American, non-Hispanic	34 (<1)	10 (<1)	6 (<1)
Hispanic	508 (5)	128 (4)	73 (4)
Other	19 (<1)	7 (<1)	5 (<1)
Unknown	167 (N/A)	35 (N/A)	153 (N/A)
Recipient sex			
Male	6508 (61)	1914 (63)	1121 (60)
Female	4084 (39)	1143 (37)	736 (40)
Karnofsky score			
10-80	3434 (32)	1027 (34)	521 (28)
90-100	6744 (64)	1898 (62)	1197 (64)
Missing	414 (4)	132 (4)	139 (7)
HLA-A B DRB1 groups - low resolution			
<=3/6	5 (<1)	6 (<1)	1 (<1)
4/6	86 (1)	21 (1)	9 (1)
5/6	1451 (14)	343 (13)	246 (15)
6/6	8941 (85)	2346 (86)	1411 (85)
Unknown	109 (N/A)	341 (N/A)	190 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	311 (3)	14 (1)	4 (<1)
6/8	507 (5)	18 (1)	31 (3)
7/8	1986 (19)	296 (16)	190 (20)
8/8	7516 (73)	1511 (82)	723 (76)
Unknown	272 (N/A)	1218 (N/A)	909 (N/A)
HLA-DPB1 Match			
Double allele mismatch	2683 (30)	131 (22)	68 (27)
Single allele mismatch	4804 (54)	324 (53)	134 (53)
Full allele matched	1371 (15)	152 (25)	53 (21)
Unknown	1734 (N/A)	2450 (N/A)	1602 (N/A)
High resolution release score			
No	103 (1)	58 (42)	94 (66)
Yes	8980 (99)	80 (58)	48 (34)
Unknown	1509 (N/A)	2919 (N/A)	1715 (N/A)
KIR typing available			
No	7284 (69)	3021 (99)	1846 (99)
Yes	3308 (31)	36 (1)	11 (1)
Graft type			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Marrow	4110 (39)	1115 (36)	927 (50)
PBSC	6477 (61)	1918 (63)	929 (50)
BM+PBSC	3 (<1)	0	1 (<1)
PBSC+UCB	2 (<1)	24 (1)	0
Number of cord units			
1	1 (100)	0	0
Conditioning regimen			
Myeloablative	6718 (63)	1819 (60)	1284 (69)
RIC/Nonmyeloablative	3838 (36)	1228 (40)	553 (30)
TBD	36 (<1)	10 (<1)	20 (1)
Donor age at donation			
To Be Determined/NA	40 (<1)	273 (9)	13 (1)
0-9 years	1 (<1)	5 (<1)	0
10-19 years	269 (3)	79 (3)	30 (2)
20-29 years	4326 (41)	1234 (40)	619 (33)
30-39 years	3229 (30)	794 (26)	611 (33)
40-49 years	2080 (20)	499 (16)	439 (24)
50+ years	647 (6)	173 (6)	145 (8)
Median (Range)	32 (3-62)	31 (1-109)	35 (19-64)
Donor/Recipient CMV serostatus			
+/+	2404 (23)	778 (26)	452 (26)
+/-	1370 (13)	415 (14)	210 (12)
-/+	3291 (31)	845 (28)	545 (31)
-/-	3408 (33)	931 (31)	548 (31)
CB - recipient +	0	1 (<1)	0
Unknown	119 (N/A)	87 (N/A)	102 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	268 (3)	63 (2)	68 (4)
CD34 selection	142 (1)	75 (2)	16 (1)
Tacrolimus + MMF +- others	1307 (12)	289 (9)	160 (9)
Tacrolimus + MTX +- others (except MMF)	4364 (41)	1363 (45)	489 (26)
Tacrolimus + others (except MTX, MMF)	546 (5)	207 (7)	63 (3)
Tacrolimus alone	211 (2)	57 (2)	20 (1)
CSA + MMF +- others (except Tacrolimus)	653 (6)	148 (5)	144 (8)
CSA + MTX +- others (except Tacrolimus, MMF)	2210 (21)	580 (19)	661 (36)
CSA + others (except Tacrolimus, MTX, MMF)	242 (2)	66 (2)	73 (4)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CSA alone	109 (1)	25 (1)	65 (4)
Other GVHD prophylaxis	204 (2)	55 (2)	27 (1)
Missing	336 (3)	129 (4)	71 (4)
Donor/Recipient sex match			
Male-Male	4590 (43)	1315 (43)	770 (42)
Male-Female	2411 (23)	678 (22)	396 (21)
Female-Male	1891 (18)	570 (19)	348 (19)
Female-Female	1661 (16)	445 (15)	336 (18)
CB - recipient M	1 (<1)	17 (1)	0
CB - recipient F	1 (<1)	7 (<1)	0
Unknown	37 (N/A)	25 (N/A)	7 (N/A)
Year of transplant			
1986-1990	180 (2)	23 (1)	34 (2)
1991-1995	847 (8)	190 (6)	260 (14)
1996-2000	1286 (12)	488 (16)	309 (17)
2001-2005	1307 (12)	236 (8)	374 (20)
2006-2010	2222 (21)	450 (15)	310 (17)
2011-2015	3296 (31)	948 (31)	376 (20)
2016-2019	1454 (14)	722 (24)	194 (10)
Follow-up among survivors, Months			
N Eval	4243	1339	663
Median (Range)	60 (0-344)	37 (0-313)	66 (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	705	177	151
Source of data			
CRF	563 (80)	137 (77)	98 (65)
TED	142 (20)	40 (23)	53 (35)
Number of centers	109	66	80
Disease at transplant			
Other leukemia	91 (13)	25 (14)	23 (15)
CML	112 (16)	29 (16)	28 (19)
MDS	502 (71)	123 (69)	100 (66)
MDS Disease status at transplant			
Early	161 (32)	30 (25)	46 (46)
Advanced	306 (61)	86 (71)	43 (43)
Missing	34 (7)	5 (4)	10 (10)
Recipient age at transplant			
0-9 years	104 (15)	24 (14)	35 (23)
10-19 years	68 (10)	13 (7)	16 (11)
20-29 years	51 (7)	9 (5)	10 (7)
30-39 years	64 (9)	16 (9)	14 (9)
40-49 years	101 (14)	23 (13)	18 (12)
50-59 years	150 (21)	40 (23)	34 (23)
60-69 years	139 (20)	44 (25)	22 (15)
70+ years	28 (4)	8 (5)	2 (1)
Median (Range)	47 (0-80)	50 (1-75)	41 (0-73)
Recipient race/ethnicity			
Caucasian, non-Hispanic	433 (63)	118 (67)	97 (70)
African-American, non-Hispanic	115 (17)	26 (15)	22 (16)
Asian, non-Hispanic	42 (6)	13 (7)	10 (7)
Pacific islander, non-Hispanic	6 (1)	0	1 (1)
Native American, non-Hispanic	3 (<1)	0	1 (1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Hispanic	87 (13)	19 (11)	6 (4)
Other	0	0	1 (1)
Unknown	19 (N/A)	1 (N/A)	13 (N/A)
Recipient sex			
Male	417 (59)	107 (60)	87 (58)
Female	288 (41)	70 (40)	64 (42)
Karnofsky score			
10-80	173 (25)	52 (29)	38 (25)
90-100	517 (73)	112 (63)	100 (66)
Missing	15 (2)	13 (7)	13 (9)
HLA-A B DRB1 groups - low resolution			
<=3/6	8 (1)	6 (5)	1 (1)
4/6	301 (44)	67 (51)	69 (50)
5/6	297 (44)	50 (38)	63 (45)
6/6	72 (11)	8 (6)	6 (4)
Unknown	27 (N/A)	46 (N/A)	12 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	367 (61)	64 (67)	72 (64)
6/8	140 (23)	15 (16)	28 (25)
7/8	64 (11)	14 (15)	9 (8)
8/8	28 (5)	2 (2)	3 (3)
Unknown	106 (N/A)	82 (N/A)	39 (N/A)
HLA-DPB1 Match			
Double allele mismatch	107 (48)	3 (33)	4 (57)
Single allele mismatch	104 (46)	4 (44)	1 (14)
Full allele matched	14 (6)	2 (22)	2 (29)
Unknown	480 (N/A)	168 (N/A)	144 (N/A)
High resolution release score			
No	18 (9)	1 (25)	3 (75)
Yes	189 (91)	3 (75)	1 (25)
Unknown	498 (N/A)	173 (N/A)	147 (N/A)
KIR typing available			
No	547 (78)	177 (100)	150 (99)
Yes	158 (22)	0	1 (1)
Cord blood number of units			
1	438 (62)	0	116 (77)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
2	267 (38)	0	35 (23)
Unknown	0 (N/A)	177 (N/A)	0 (N/A)
Graft type			
UCB	660 (94)	153 (86)	145 (96)
PBSC+UCB	45 (6)	24 (14)	6 (4)
Conditioning regimen			
Myeloablative	396 (56)	91 (51)	92 (61)
RIC/Nonmyeloablative	309 (44)	86 (49)	59 (39)
Donor age at donation			
To Be Determined/NA	12 (2)	11 (6)	9 (6)
0-9 years	628 (89)	133 (75)	136 (90)
10-19 years	44 (6)	15 (8)	3 (2)
20-29 years	8 (1)	6 (3)	0
30-39 years	7 (1)	2 (1)	0
40-49 years	3 (<1)	3 (2)	0
50+ years	3 (<1)	7 (4)	3 (2)
Median (Range)	4 (0-64)	4 (0-72)	3 (0-61)
Donor/Recipient CMV serostatus			
+/+	153 (22)	35 (20)	36 (24)
+/-	82 (12)	9 (5)	13 (9)
-/+	147 (21)	45 (25)	26 (17)
-/-	91 (13)	23 (13)	20 (13)
CB - recipient +	129 (18)	34 (19)	23 (15)
CB - recipient -	97 (14)	25 (14)	25 (17)
CB - recipient CMV unknown	6 (1)	6 (3)	8 (5)
GvHD Prophylaxis			
Ex vivo T-cell depletion	1 (<1)	1 (1)	0
CD34 selection	33 (5)	20 (11)	5 (3)
Tacrolimus + MMF +- others	205 (29)	49 (28)	24 (16)
Tacrolimus + MTX +- others (except MMF)	24 (3)	4 (2)	5 (3)
Tacrolimus + others (except MTX, MMF)	32 (5)	8 (5)	8 (5)
Tacrolimus alone	25 (4)	9 (5)	4 (3)
CSA + MMF +- others (except Tacrolimus)	308 (44)	68 (38)	75 (50)
CSA + MTX +- others (except Tacrolimus, MMF)	9 (1)	2 (1)	4 (3)
CSA + others (except Tacrolimus, MTX, MMF)	27 (4)	9 (5)	20 (13)
CSA alone	10 (1)	0	3 (2)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Other GVHD prophylaxis	30 (4)	6 (3)	2 (1)
Missing	1 (<1)	1 (1)	1 (1)
Donor/Recipient sex match			
CB - recipient M	417 (59)	107 (60)	87 (58)
CB - recipient F	288 (41)	70 (40)	64 (42)
Year of transplant			
2001-2005	16 (2)	5 (3)	4 (3)
2006-2010	243 (34)	63 (36)	58 (38)
2011-2015	355 (50)	68 (38)	76 (50)
2016-2019	91 (13)	41 (23)	13 (9)
Follow-up among survivors, Months			
N Eval	275	84	74
Median (Range)	56 (1-147)	40 (3-149)	53 (1-143)

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	1341	183	92
Source of data			
CRF	690 (51)	77 (42)	51 (55)
TED	651 (49)	106 (58)	41 (45)
Number of centers	66	35	26
Disease at transplant			
Other leukemia	141 (11)	26 (14)	19 (21)
CML	206 (15)	20 (11)	14 (15)
MDS	994 (74)	137 (75)	59 (64)
MDS Disease status at transplant			
Early	175 (18)	19 (14)	6 (10)
Advanced	789 (79)	114 (83)	51 (86)
Missing	30 (3)	4 (3)	2 (3)
Recipient age at transplant			
0-9 years	22 (2)	6 (3)	0
10-19 years	49 (4)	4 (2)	1 (1)
20-29 years	36 (3)	5 (3)	3 (3)
30-39 years	62 (5)	10 (5)	4 (4)
40-49 years	174 (13)	15 (8)	7 (8)
50-59 years	401 (30)	52 (28)	28 (30)
60-69 years	505 (38)	82 (45)	46 (50)
70+ years	92 (7)	9 (5)	3 (3)
Median (Range)	59 (1-78)	60 (2-76)	61 (18-74)
Recipient race/ethnicity			
Caucasian, non-Hispanic	1000 (76)	126 (70)	69 (78)
African-American, non-Hispanic	102 (8)	15 (8)	9 (10)
Asian, non-Hispanic	60 (5)	8 (4)	2 (2)
Pacific islander, non-Hispanic	7 (1)	1 (1)	0
Native American, non-Hispanic	5 (<1)	0	0
Hispanic	140 (11)	30 (17)	9 (10)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	27 (N/A)	3 (N/A)	3 (N/A)
Recipient sex			
Male	808 (60)	116 (63)	58 (63)
Female	533 (40)	67 (37)	34 (37)
Karnofsky score			
10-80	518 (39)	87 (48)	45 (49)
90-100	804 (60)	90 (49)	42 (46)
Missing	19 (1)	6 (3)	5 (5)
Graft type			
Marrow	206 (15)	28 (15)	18 (20)
PBSC	1131 (84)	155 (85)	74 (80)
BM+PBSC	4 (<1)	0	0
Conditioning regimen			
Myeloablative	685 (51)	86 (47)	41 (45)
RIC/Nonmyeloablative	654 (49)	96 (52)	51 (55)
TBD	2 (<1)	1 (1)	0
Donor age at donation			
To Be Determined/NA	4 (<1)	1 (1)	0
0-9 years	20 (1)	2 (1)	0
10-19 years	50 (4)	9 (5)	2 (2)
20-29 years	97 (7)	7 (4)	6 (7)
30-39 years	128 (10)	23 (13)	14 (15)
40-49 years	245 (18)	24 (13)	16 (17)
50+ years	797 (59)	117 (64)	54 (59)
Median (Range)	54 (0-80)	54 (3-74)	55 (17-73)
Donor/Recipient CMV serostatus			
+/+	526 (40)	77 (43)	36 (40)
+/-	172 (13)	10 (6)	16 (18)
-/+	301 (23)	40 (22)	17 (19)
-/-	321 (24)	53 (29)	21 (23)
Unknown	21 (N/A)	3 (N/A)	2 (N/A)
GvHD Prophylaxis			
Ex-vivo T-cell depletion	6 (<1)	2 (1)	1 (1)
CD34 selection	8 (1)	9 (5)	0
Post-CY + other(s)	254 (19)	34 (19)	20 (22)
Post-CY alone	5 (<1)	1 (1)	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
TAC + MMF +- other(s) (except post-CY)	169 (13)	8 (4)	3 (3)
TAC + MTX +- other(s) (except MMF, post-CY)	584 (44)	90 (49)	49 (53)
TAC + other(s) (except MMF, MTX, post-CY)	147 (11)	26 (14)	13 (14)
TAC alone	11 (1)	2 (1)	1 (1)
CSA + MMF +- other(s) (except post-CY)	30 (2)	1 (1)	0
CSA + MTX +- other(s) (except MMF, post-CY)	76 (6)	8 (4)	1 (1)
CSA + other(s) (except MMF, MTX, post-CY)	1 (<1)	1 (1)	0
CSA alone	8 (1)	0	0
Other(s)	17 (1)	1 (1)	3 (3)
Missing	25 (2)	0	1 (1)
Donor/Recipient sex match			
Male-Male	433 (32)	67 (37)	32 (35)
Male-Female	288 (21)	31 (17)	22 (24)
Female-Male	374 (28)	48 (26)	26 (28)
Female-Female	245 (18)	36 (20)	12 (13)
Unknown	1 (N/A)	1 (N/A)	0 (N/A)
Year of transplant			
2006-2010	125 (9)	13 (7)	7 (8)
2011-2015	714 (53)	88 (48)	49 (53)
2016-2019	502 (37)	82 (45)	36 (39)
Follow-up among survivors, Months			
N Eval	772	103	54
Median (Range)	26 (1-123)	24 (3-98)	24 (3-96)

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TO: Chronic Leukemia Working Committee Members

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

RE: 2018-2019 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 PI is currently working on finalizing the manuscript. The goal of the study is to have the manuscript published by June 2019.

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 study was presented at ASH. The first draft of the manuscript is circulated and reviewed by the writing committee. The goal of the study is to have the manuscript finalized and submitted by June 2019.

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 study will be presented at TCT. The first draft of the manuscript is circulated to the writing committee. The goal of the study is to have the manuscript finalized and submitted by June 2019.

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 data file by June 2019.

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 study was presented at ASH. The PI is currently working on finalizing the manuscript. The goal of this study is to have the manuscript submitted by June 2019.

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. The statistician is currently working on finalizing the data file for analysis. The goal of this study is to complete the initial analysis by June 2019.

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 statistician is currently working on finalizing the data file for analysis. The goal of this study is to complete the analysis by June 2019.

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 study was presented at ASH. The PI is currently working on the draft manuscript. The goal of this study is to have the manuscript submitted by June 2019.

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 statistician is working on the protocol development. The goal of this study is to have the final protocol by June 2019.

Proposal: 1810-12

Title:
Impact of conditioning regimen on outcomes for patients with previously treated CLL who underwent allogeneic hematopoietic transplantation

Haesook Teresa Kim, PhD, htkimc@jimmy.harvard.edu, Dana-Farber Cancer Institute, Harvard Chan School of Public Health

Hypothesis:
Conditioning regimen affects clinical outcome for patients with CLL after allogeneic transplantation

Specific aims:
- To investigate whether there is an optimal conditioning regimen for patients previously treated CLL who undergo allogeneic transplantation

Scientific impact:
Change of practice

Scientific justification:
There are two previous studies of CIBMTR that discussed the impact of conditioning intensity in previously treated CLL patients who underwent allogeneic transplant. In Sabloff et al (BBMT, 2014), MAC-TBI (N=126) was compared to MAC-CT (N=54) (mostly fludarabine based) and they found no difference in outcome between these two conditioning regimens. However, the sample size in the MAC-CT was small, the transplant period covered was from 1995 and 2007, and only HLA-identical sibling donor HCT were included. In Sobecks et al (BBMT, 2015) for the same patient population during the same transplant period (1995-2007), outcomes were compared between MAC (N=297) and RIC (N=134). The study found that for patients underwent HCT after 2000, RIC fared better in OS (p=0.02). However, the sample size was also small (N=38 vs N=107, respectively) and MAC regimen was primarily TBI based and detailed conditioning regimen was not assessed.

In modern era, the use of TBI based MAC has been limited due to toxicity and reduced toxicity myeloablative regimens, such as fludarabine/busulfan (FluBu) have emerged as alternatives to traditional TBI-based MAC. However, their impact on outcomes in the current era has not been fully investigated. Furthermore, reduced intensity (RIC) and/or non-myeloablative conditioning (NST) regimens cover a broad spectrum of various regimens and outcomes after these regimens have not been fully compared.

In the study #CK142-02, the data set we used to develop a CLL specific prognostic score (manuscript submitted), more than 25 different NST/RIC regimens were listed. Of these, the most frequently used NST/RIC conditioning regimens are NST-TBI/Flu (N=200), NST-Flu/Cy (N=189), RIC-Flu/Bu (N=93), and RIC-Flu/Mel (N=198). Taking advantage of the data we already have, we wish to compare outcomes after MAC-TBI (N=121) and MAC-Flu/Bu (N=93) to NST-TBI/Flu, NST-Flu/Cy, RIC-Flu/Bu, and RIC-Flu/Mel in previously treated CLL patients who underwent allogeneic transplantation.

Patient eligibility population:
1505 patients with a diagnosis of CLL underwent allogeneic HCT with 7/8 or 8/8 matched related or unrelated donors, peripheral blood or bone marrow transplants reported to CIBMTR between 2008 and 2014

Data requirements:
The CIBMTR data used for the study #CK142-02

Study design:
Retrospective data analysis

References:

1. Sabloff M, Sobecks RM, Ahn KW, et al. Does total body irradiation conditioning improve outcomes of myeloablative human leukocyte antigen-identical sibling transplantations for chronic lymphocytic leukemia? Biol Blood Marrow Transplant. 2014 Mar;20(3):421-4. doi: 10.1016/j.bbmt.2013.11.032. Epub 2013 Dec 7.
2. Sobecks RM, Leis JF, Gale RP, et al. Outcomes of human leukocyte antigen-matched sibling donor hematopoietic cell transplantation in chronic lymphocytic leukemia: myeloablative versus reduced-intensity conditioning regimens. Biol Blood Marrow Transplant. 2014 Sep;20(9):1390-8. doi: 10.1016/j.bbmt.2014.05.020. Epub 2014 May 28.
3. Kharfan-Dabaja MA, Kumar A, Hamadani M, et alClinical Practice Recommendations for Use of Allogeneic Hematopoietic Cell Transplantation in Chronic Lymphocytic Leukemia on Behalf of the Guidelines Committee of the American Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant. 2016 Dec;22(12):2117-2125. doi: 10.1016/j.bbmt.2016.09.013. Epub 2016 Sep 19. Review.

Conflicts of interest:

□ Yes
x No

Table 1: Baseline characteristics for patients undergoing allo-HCT for CLL between 2008 and 2014

	RIC/NMA (N=606)		MAC (N=152)	
	N	%	N	%
Patient-related				
Age				
Median (range)	58 (26, 73)		56 (34, 72)	
< 40	12	2.0	3	2.0
40-49	71	11.7	34	22.4
50-59	272	44.9	74	48.7
60-69	233	38.5	38	25.0
≥ 70	18	3.0	3	2.0
Patient Sex				
Male	438	72.3	112	73.7
Female	168	27.7	40	26.3
Karnofsky Performance Score				
90-100%	415	68.5	81	53.3
< 90%	172	28.4	64	42.1
UNK	19	3.1	7	4.6
HCT Comorbidity Score				
0	242	39.9	54	35.5
1	109	18.0	23	15.1
2	77	12.7	23	15.1
3	86	14.2	28	18.4
≥4	91	15.0	24	15.8
UNK	1	0.2		
Disease-related				
LDH (U/L)				
Median (range)	214 (2.4, 2738)		260 (121, 1408)	
Normal	377	62.2	86	56.6
Elevated	208	34.3	61	40.1
UNK	21	3.5	5	3.3
Lymphocyte Count (/µL)				
Median (range)	0.8 (0, 177)		1.2 (0.02, 63)	
≤ 2000/µL	449	74.1	97	63.8
> 2000/µL	142	23.4	50	32.9
UNK	15	2.5	5	3.3
WBC Count (× 10^9/L)				
Median (range)	3.6 (0, 204)		4.4 (0.6, 108)	
< 2	84	13.9	25	16.4
2-10	448	73.9	99	65.1
> 10	71	11.7	25	16.4

	RIC/NMA (N=606)		MAC (N=152)	
	N	%	N	%
UNK	3	0.5	3	2
Disease Status				
CR	78	12.9	9	5.9
PR	308	50.8	63	41.5
Nodal PR	14	2.3	3	2.0
Stable	110	18.2	38	25.0
Progressive	75	12.4	34	22.4
Untreated	5	0.8	3	2.0
Not evaluable	7	1.2	1	0.7
UNK	9	1.5	1	0.7
Transplant-related				
Year of transplant				
2008-2009	197	33	54	36
2010-2011	153	25	29	19
2012-2013	195	32	45	30
2014	61	10	24	16
Time from Diagnosis to HSCT				
< 3 yrs	187	30.9	43	28.3
3-6 yrs	180	29.7	43	28.3
≥ 6 yrs	239	39.4	65	42.8
UNK			1	0.7
Donor Type				
HLA-identical sibling	225	37.1	57	37.5
Well-matched unrelated	319	52.6	76	50.0
Partially-matched unrelated	62	10.2	19	12.5
D-R Sex Match				
M-M	273	45.1	64	42.1
M-F	93	15.4	20	13.2
F-M	131	21.6	38	25.0
F-F	60	9.9	18	11.8
UNK	49	8.1	12	7.9
D-R CMV Sero Status				
+/+	147	24.3	42	27.6
+/-	66	10.9	17	11.2
-/+	173	28.6	43	28.3
-/-	168	27.7	36	23.7
UNK	52	8.6	14	9.2
HLA Type - Allele				
HLA-identical sibling	224	37.0	57	37.5

	RIC/NMA (N=606)		MAC (N=152)	
	N	%	N	%
URD 7/8	51	8.4	17	11.2
URD 8/8	294	48.5	72	47.4
UNK	37	6.1	6	4.0
HLA Type - Antigen				
HLA-identical sibling	224	37.0	57	37.5
URD 7/8	39	6.4	13	8.6
URD 8/8	338	55.8	82	54.0
UNK	5	0.8		
Graft Source				
BM	11	1.8	10	6.6
PBSC	594	98.0	142	93.4
UNK	1	0.2		
Conditioning regimen group				
MAC - TBI/cy			27	18
MAC - TBI/cy/others			3	2
MAC - TBI/others			21	14
MAC - TBI			1	< 1
MAC - bu/cy			5	3
MAC - bu/cy/others			2	1
MAC - bu/flud			38	25
MAC - bu/flud/others			1	< 1
MAC - flud/mel			4	3
MAC - others			50	33
RIC - TBI/cy/others	1	< 1		
RIC - TBI/flud	28	5		
RIC - TBI/flud/others	2	< 1		
RIC - TBI/others	3	< 1		
RIC - TBI	1	< 1		
RIC - bu/flud	185	31		
RIC - bu/flud/others	2	< 1		
RIC - flud/mel	85	14		
RIC - flud/mel/others	3	< 1		
NST - TBI/cy/others	22	4		
NST - TBI/flud	149	25		
NST - TBI/flud/others	1	< 1		
NST - TBI	2	< 1		
NST - flud/cy	50	8		
NST - flud	2	< 1		
NST - TLI	42	7		
RIC/NST - others	28	5		

	RIC/NMA (N=606)		MAC (N=152)	
	N	%	N	%
GVHD Prophylaxis				
Tacrolimus + MTX ± other(s)	251	41.4	65	42.8
Tacrolimus ± other(s)	149	24.6	64	42.1
Cyclosporine + MTX ± other(s)	29	4.8	10	6.6
Cyclosporine ± other(s)	164	27.1	10	6.6
Other	11	1.8	3	2.0
UNK	2	0.3		
Prior ATG/Campath				
ATG alone	118	19.5	36	23.7
Campath alone	20	3.3	4	2.6
No ATG or Campath	468	77.2	112	73.7
Median follow-up of survivors (range), months	49 (4-99)		60 (3-96)	

Proposal: 1811-27

Title:
Graft Failure, Donor Lymphocyte Infusion, and Second Transplant after Allogeneic Hematopoietic Cell Transplant for Myelofibrosis

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Specific aims:
Primary aim:

- Describe the rate, and risk factors associated with, graft failure after allogeneic hematopoietic cell transplantation for primary myelofibrosis and post-essential thrombocythemia/polycythemia vera myelofibrosis.

Secondary aims:

- Describe the outcomes of donor lymphocyte infusion as a salvage treatment for graft failure after allogeneic hematopoietic cell transplantation for primary myelofibrosis and post-essential thrombocythemia/polycythemia vera myelofibrosis.
- Describe outcomes of second transplant as a salvage treatment for graft failure after allogeneic hematopoietic cell transplantation for primary myelofibrosis and post-essential thrombocythemia/polycythemia vera myelofibrosis.

Scientific justification:
Myelofibrosis, a myeloproliferative neoplasm with cardinal features of cytopenias, hepatosplenomegaly, and constitutional symptoms, is associated with a decreased survival and risk of leukemic transformation [1]. Allogeneic hematopoietic cell transplantation (Allo-HCT) remains the only curative therapy for myelofibrosis. With the introduction of the reduced-intensity conditioning (RIC) regimen, Allo-HCT is feasible in patients not suitable for ablative conditioning [2]. The number of Allo-HCTs performed for myelofibrosis has steadily increased over the past years, even after the approval of the Janus Kinase (JAK) inhibitor, ruxolitinib. This increase may be attributed to improved patient selection based on the new prognostic molecular markers, more frequent use of matched unrelated donors, and improved supportive care. However, graft failure still remains an important contributor to morbidity and mortality in patients with myelofibrosis who undergo Allo-HCT and ranges from 2% to 24% [3]. Data on graft failure are not uniform and no definitive predictors for graft failure have yet been determined. The increasing use of RIC, and wider applications of alternative donors in recent years have the potential to turn graft failure into an increasing problem. Moreover, randomized prospective data comparing different intensity of conditioning regimens are lacking for myelofibrosis. A retrospective, small cohort study reported that the cumulative incidence of graft failure within 60 days after Allo-HCT was high (28%), and this was primarily associated with intensity of conditioning regimen [4]. In a large CIBMTR study published over a decade ago in the pre-ruxolitinib era, the rate of graft failure was higher in those with matched unrelated donors than in those with matched sibling donors (20% vs 9%) among 289 patients (median age 47 years) who underwent Allo-HCT for primary myelofibrosis [5]. Majority of the patients in the study received myeloablative conditioning regimen. It is important to identify patients who are at risk of graft failure to limit the number of risk factors to prevent this severe complication occurring after Allo-HCT.
The prognosis of patients with graft failure is poor [6], and there is no standard approach to the treatment of this dire complication; use of donor lymphocyte infusions (DLIs) and a second Allo-HCT have been suggested as therapeutic options to restore hematopoiesis. Robust data supporting either of these approaches are lacking. The use of DLI after Allo-HCT has been already suggested as safe and effective

approach in hematological malignancies. In patients with graft failure without autologous reconstitution, the only available treatment is a second transplant. Large series of graft failure after Allo-HCT for myelofibrosis and subsequent salvage treatment options are lacking.
Our hypothesis is that graft source, conditioning intensity, and degree of marrow fibrosis will be associated with graft failure. We also hypothesize that DLI and second transplant are feasible options for restoring hematopoiesis in patients who experience graft failure, leading to long-term survival. By identifying the risk factors that lead to graft failure after Allo-HCT for myelofibrosis, a high-risk population can be identified for intervention with the aim of improving post-transplant outcomes. Also, a descriptive study of patient who went on to DLI or second transplants can help inform treatment decisions in the case of graft failure. The rational of this study is that the results can inform the treatment decision making process for individual patients, and aid in and clinical trial design. Given the lower rates of graft failure, a large multicenter effort through the CIBMTR is needed.

Patient eligibility population:
Inclusion criteria:

- Diagnosis of primary myelofibrosis and post-essential thrombocythemia/polycythemia vera myelofibrosis.
- Age ≥ 18 years at the time of transplant
- Allogeneic stem cell transplant occurred between 2000 and 2017
- At least 1 year follow up forms completed

Data requirements:
Forms required:

- Myelodysplasia / Myeloproliferative Disorders Pre-HSCT Data (Form 2014 MDS)
- Pre-Transplant Essential Data (Form 2400 Pre-TED)
- Myelodysplasia / Myeloproliferative Disorders Post-HSCT Data (Form 2114 MDS)
- Post-Transplant Essential Data (Form 2450 Post-TED)

Patient-related:

- Age at HCT
- Sex
- Race
- Performance status
- HCT-CI (if available)
- CMV status

Disease-related:

- Date of diagnosis
- Subtype (PMF, Post-PV MF, vs. Post-ET MF)
- Degree of bone marrow fibrosis at HCT
- Cytogenetic results (if known)
- DIPSS risk score (if known)
- Pre-transplant therapy (if known)
- Mutation analysis (*JAK2*, *MPL*, *CALR*, if known)
- Spleen size at HCT
- Disease status prior to transplant

Transplant-related:

- Date of transplant
- Conditioning regimen
- Donor characteristics
- Donor-recipient HLA matching
- Cell dose
- Graft-versus-host disease (GVHD) prophylaxis

Post-transplant course:

- Date of relapse
- Post-transplant therapy - DLI and Second transplant
- Date of acute and chronic GVHD (if applicable)
- Date of death or last known contact
- Cause of death (if known)

Study design:

Patient, disease, and transplant-related variables for patients receiving allogeneic hematopoietic stem cell transplantation for primary myelofibrosis and post-essential thrombocythemia/polycythemia vera myelofibrosis will be described. Analyses will be stratified by conditioning regimen intensity, and reported separately for full-intensity (myeloablative) and reduced-intensity transplants. Univariate probabilities of overall and disease-free survival will be calculated using the Kaplan-Meier estimator; the log-rank test will be used for univariate comparisons. Probabilities of graft failure, acute and chronic GVHD, non-relapse mortality and relapse will be calculated using cumulative incidence curves accommodating competing risks. Assessment of potential risk factors for outcomes of interest will be evaluated in multivariate analyses using Cox proportional hazards regression. The proportional hazards assumption will be tested. If violated, it will be added as time-dependent covariate. Step-wise selection procedure will be used to select significant covariates.

References:

1. Mesa RA, Silverstein MN, Jacobsen SJ, Wollan PC, Tefferi A: Population-based incidence and survival figures in essential thrombocythemia and agnogenic myeloid metaplasia: An olmsted county study, 1976-1995. *Am J Hematol* 1999, 61:10–15.
2. 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*. 2013; 20(1):89-97.
3. Kröger NM, Deeg JH, Olavarria E, Niederwieser D, Bacigalupo A, Barbui T, Rambaldi A, Mesa R, Tefferi A, Griesshammer M, et al.: Indication and management of allogeneic stem cell transplantation in primary myelofibrosis: a consensus process by an EBMT/ELN international working group. *Leukemia* 2015, 29:2126–2133.
4. Slot S, Smits K, van de Donk NWCJ, Witte BI, Raymakers R, Janssen JJWM, Broers a EC, Te Boekhorst P a W, Zweegman S: Effect of conditioning regimens on graft failure in myelofibrosis: a retrospective analysis. *Bone Marrow Transplant* 2015, 50:1424–31.
5. Ballen KK, Shrestha S, Sobocinski KA, Zhang MJ, Bashey A, Bolwell BJ, Cervantes F, Devine SM, Gale RP, Gupta V, et al.: Outcome of Transplantation for Myelofibrosis. *Biol Blood Marrow Transplant* 2010, 16:358–367.
6. Olsson R, Remberger M, Schaffer M, Berggren DM, Svahn B-M, Mattsson J, Ringden O: Graft failure in the modern era of allogeneic hematopoietic SCT. *Bone Marrow Transplant* 2013, 48:537–543.

Baseline characteristics for patients >= 18 yrs of age receiving allo-HCT for MF between 2000 and 2017

Characteristic	Graft failure	No graft failure
Number of patients	169	1070
Number of centers	87	170
Age, median (range)	58 (20-74)	58 (19-79)
Age, yrs		
18-29	3 (2)	11 (1)
30-39	6 (4)	43 (4)
40-49	26 (15)	195 (18)
50-59	70 (41)	408 (38)
60-69	58 (34)	365 (34)
>= 70	6 (4)	48 (4)
Gender		
Male	98 (58)	631 (59)
Female	71 (42)	439 (41)
Karnofsky score		
90-100	90 (53)	614 (57)
< 90	78 (46)	421 (39)
Missing	1 (<1)	35 (3)
Disease at diagnosis		
Myelofibrosis	129 (76)	777 (73)
Polycythemia vesa	17 (10)	123 (11)
Essential thrombocythemia	23 (14)	170 (16)
DIPSS prior to HCT		
Low	14 (8)	149 (14)
Intermediate-1	64 (38)	447 (42)
Intermediate-2	78 (46)	403 (38)
High	3 (2)	23 (2)
Missing	10 (6)	48 (4)
Blast in peripheral blood at diagnosis, %	0 (0-10)	0 (0-18)
Blast in peripheral blood at diagnosis		
<= 1%	69 (41)	445 (42)
> 1%	23 (14)	125 (12)
Missing	77 (46)	500 (47)
Blast in peripheral blood prior to HCT, %	1 (0-17)	0 (0-19)
Blast in peripheral blood prior to HCT		
<= 1%	76 (45)	584 (55)
> 1%	61 (36)	316 (30)
Missing	32 (19)	170 (16)

Characteristic	Graft failure	No graft failure
Cytogenetics		
Favorable (normal)	65 (38)	431 (40)
Favorable (other)	15 (9)	115 (11)
Unfavorable	24 (14)	165 (15)
TBD	17 (10)	135 (13)
Not tested	12 (7)	49 (5)
Missing	36 (21)	175 (16)
Spleen status at diagnosis		
Normal	37 (22)	312 (29)
Splenomegaly	105 (62)	580 (54)
Missing	27 (16)	178 (17)
Spleen status prior transplant		
Normal	47 (28)	370 (35)
Splenomegaly	82 (49)	525 (49)
Splenectomy	10 (6)	31 (3)
Missing	30 (18)	144 (13)
Time from diagnosis to HCT	27 (3-485)	25 (1-522)
Time from diagnosis to HCT		
0-3 months	14 (8)	151 (14)
3-6 months	30 (18)	217 (20)
>= 6 months	125 (74)	696 (65)
Missing	0	6 (<1)
Year of transplant		
2000-2001	14 (8)	58 (5)
2002-2003	12 (7)	79 (7)
2004-2005	15 (9)	95 (9)
2006-2007	21 (12)	93 (9)
2008-2009	24 (14)	126 (12)
2010-2011	9 (5)	37 (3)
2012-2013	8 (5)	43 (4)
2014-2015	37 (22)	207 (19)
2016-2017	29 (17)	332 (31)
Donor type		
HLA-identical sibling	36 (21)	356 (33)
Twin	0	8 (<1)
Other related	12 (7)	57 (5)
Well-matched unrelated	79 (47)	473 (44)
Partially-matched unrelated	19 (11)	113 (11)
Mis-matched unrelated	4 (2)	18 (2)
Multi-donor	4 (2)	3 (<1)

Characteristic	Graft failure	No graft failure
Unrelated (matching TBD)	5 (3)	20 (2)
Cord blood	10 (6)	22 (2)
Donor-recipient sex match		
M-M	52 (31)	411 (38)
M-F	42 (25)	233 (22)
F-M	41 (24)	199 (19)
F-F	21 (12)	188 (18)
CB - recipient M	4 (2)	10 (<1)
CB - recipient F	6 (4)	12 (1)
Missing	3 (2)	17 (2)
Donor-recipient CMV status		
+/+	49 (29)	309 (29)
+/-	18 (11)	136 (13)
-/+	37 (22)	242 (23)
-/-	48 (28)	318 (30)
CB - recipient +	7 (4)	14 (1)
CB - recipient -	3 (2)	8 (<1)
Missing	7 (4)	43 (4)
Graft source		
Bone marrow	24 (14)	115 (11)
Peripheral blood	133 (79)	928 (87)
Cord blood	10 (6)	22 (2)
Missing	2 (1)	5 (<1)
Conditioning regimen intensity		
MAC	68 (40)	518 (48)
RIC	81 (48)	463 (43)
NMA	16 (9)	66 (6)
TBD	2 (1)	5 (<1)
Missing	2 (1)	18 (2)
ATG/Campath		
ATG + CAMPATH	1 (<1)	0
ATG alone	70 (41)	316 (30)
CAMPATH alone	5 (3)	27 (3)
No ATG or CAMPATH	91 (54)	711 (66)
Missing	2 (1)	16 (1)
GVHD prophylaxis		
Ex-vivo T-cell depletion	1 (<1)	8 (<1)
CD34 selection	5 (3)	17 (2)
Post-CY + other(s)	10 (6)	67 (6)
Post-CY alone	0	1 (<1)

Characteristic	Graft failure	No graft failure
TAC + MMF +- other(s) (except post-CY)	32 (19)	124 (12)
TAC + MTX +- other(s) (except MMF, post-CY)	54 (32)	469 (44)
TAC + other(s) (except MMF, MTX, post-CY)	8 (5)	46 (4)
TAC alone	2 (1)	18 (2)
CSA + MMF +- other(s) (except post-CY)	19 (11)	91 (9)
CSA + MTX +- other(s) (except MMF, post-CY)	26 (15)	168 (16)
CSA + other(s) (except MMF, MTX, post-CY)	2 (1)	13 (1)
CSA alone	3 (2)	19 (2)
Other(s)	1 (<1)	15 (1)
Missing	6 (4)	14 (1)
Receive subsequent HSCT		
No	100 (59)	1028 (96)
Yes	69 (41)	42 (4)
Received DCI?		
No	120 (71)	784 (73)
Yes	27 (16)	42 (4)
Missing	22 (13)	244 (23)
Received Ruxolitinib (Jakafi) as prior therapy		
No	117 (69)	715 (67)
Yes	50 (30)	345 (32)
Missing	2 (1)	10 (<1)

Proposal: 1811-47

Title:
Evaluating the efficacy of allogeneic hematopoietic cell transplantation for T-cell Prolymphocytic Leukemia (T-PLL)

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Hypothesis:
Allogeneic Hematopoietic Cell Transplantation (Allo-HCT) is an effective therapy for T cell prolymphocytic leukemia (T-PLL)

Specific aims:
- To describe clinical outcomes [progression-free survival (PFS), overall survival (OS), and non-relapse mortality (NRM)] following allo-HCT in patients with T-cell prolymphocytic leukemia
- To identify the impact of patient-, disease-, and transplant-related factors on the outcomes PFS, OS and NRM.

Scientific impact:
Results of this study have potential to significantly influence decision to proceed with consolidative allo-HCT after induction therapy for T-PLL. Due to larger patient cohort from CIBMTR, this study would potentially answer the impact of pre-HCT remission status and intensity of conditioning chemotherapy on allo-HCT outcomes.

Scientific justification:
T- cell prolymphocytic leukemia (T- PLL) is a rare aggressive malignancy, representing approximately 2% of mature lymphocytic leukemias in adults (1). Most patients with T-PLL have an aggressive clinical course with limited survival despite aggressive treatment. In a series of 119 patients from M. D. Anderson Cancer Center, the reported median survival was 19 months(2). Alemtuzumab, an anti-CD52 humanized monoclonal antibody, is the initial treatment of choice as CD52 is highly expressed in T-PLL. This treatment can yield complete remission (CR) rates of 60- 80%; however, relapses are commonly seen within a year(3,4) . Survival of patients with relapsed T-PLL is dismal and response rates to the second line therapy is limited and generally short lived (5,6).
Allo-HCT) represents a potential curative therapy for T-PLL and has been reported to yield durable remissions, notably in those in complete remission prior to transplantation. (7–11). Rates of survival and non-relapse mortality vary according to various small retrospective series, described in table 1. Factors associated with favorable relapse free survival include TBI based conditioning and short interval between diagnosis and allo-HCT. Although limited by the small number of patients and heterogeneous treatments received, all of these studies indicated that allo-HCT could provide effective disease control in selected patients. However these studies did highlight issues such as relatively high treatment-related mortality (approximately 40%) and with the majority of relapses occurring within 2 years(12).

Table 1: Selected studies of allo-sct in T-PLL

Author, year of publication [Ref]	Study	Number of patients	Remission status at time of allo-HCT (N)	Donor type	Regimen intensity (N)	Outcomes
Wiktor-Jedrzejczaet al.	EBMT	41	CR= 11 PR= 12 Other= 18	MRD= 21 MUD= 20	MAC= 26 NMA= 13	3 year OS: 21% 3 year NRM: 41%
*Kalaycio et al.	CIBMTR	47* (21 T-PLL	CR= 16 PR= 8 Other= 21	MRD= 11 MUD= 19 Other: 13	MAC= 19 NMA= 14	1 year OS: 48% 1 year NRM: 28%
Guillaume et al	French Society of stem cell transplantation	27	CR= 14 PR= 10 Other= 3	MRD= 10 MUD= 17	MAC= 10 NMA= 17	3 year OS: 36% 3 year NRM: 31%
Dholaria et al	Moffitt Cancer Center	11	CR=9 PR=1 Other=1	MRD = 5 MUD= 3 Other= 3	MAC= 8 RIC= 3	4 year OS: 56% 4 year NRM: 34%

** B-PLL and T-PLL*

There is a need for larger observational studies to help better inform clinical decision making regarding the role of allo-HCT in T-PLL. We propose to utilize the Center for International Blood and Marrow Transplantation Research (CIBMTR) database to evaluate and better define outcomes of allo-HCT in patients with T-PLL.

Patient eligibility population:

Adults ≥ 18 years of age with diagnosis of T-PLL who underwent their first allo-HCT between 2000-2016.

Data requirements:

We will utilize the following CIBMTR data forms:

- 2400: Pre-Transplant Essential Data
- 2013: Chronic Lymphocytic Leukemia Pre-HSCT Data
- 2113: Chronic Lymphocytic Leukemia Post-HSCT Data

Study outcomes:

Primary outcomes:

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

Secondary outcomes:

- Incidence of acute and chronic GVHD: Cumulative incidence of grade II-IV and grade III-IV acute GVHD per consensus criteria, with death as competing risk. Cumulative incidence of chronic GVHD, with death as competing risk.

- GVHD and relapse free survival (GRFS): Survival without grade 3-4 acute GVHD, systemic therapy-requiring chronic GVHD, relapse, or death in the first post-allo-HCT year.
- Progression-free survival: Survival following allogeneic HCT without relapse or progression. Relapse or progression of disease are considered events.
- Non-relapse mortality: Cumulative incidence of NRM. NRM is defined as death without preceding disease relapse/progression. Relapse and progression are competing events.
- Relapse/progression: Progressive disease or recurrences of disease would be counted as events. Treatment-related death, defined as death without relapse or progression, is the competing event. Those who survive without recurrence or progression would be censored at the time of last contact.
- Cause of death: Descriptive only.

Variables:

Patient-related:

- Age at transplant: continuous & by age group: decades
- Patient sex: male vs. female
- Karnofsky performance status at transplant: ≥ 90 vs. < 90 vs. missing
- HCT comorbidity index at transplant: 0 vs 1-2 vs ≥ 3 vs. missing
- Race: Caucasian vs. others vs. missing

Disease-related:

- Remission status at HCT: CR vs PR vs. resistant vs. untreated/unknown and CR1/PR1 vs beyod
- Number of lines of treatment prior to allo-HCT
- Alemtuzumab use in induction therapy: yes vs. no

Transplant-related:

- Graft source: peripheral blood vs bone marrow
- Cell source: matched-related, mismatched-related (Haplo), matched unrelated, mismatched unrelated, cord blood
- Conditioning intensity: myeloablative vs. reduced intensity conditioning.
- Total Body Irradiation: TBI vs non-TBI based conditioning regimen.
- GVHD prophylaxis: CNI based vs. non-CNI based GVHD
- ATG/alemtuzumab use in conditioning: no vs. yes
- Donor-recipient sex match: male-male vs. male-female vs. female-male vs. female-female vs. missing
- Donor-recipient CMV status: -/+ vs. others vs. missing
- Year of transplant: continuous

Study design:

This retrospective study will investigate the efficacy of HCT in patients with T-PLL who received an allogeneic HCT and were reported to Center for International Blood and Marrow Transplantation (CIBMTR).

Descriptive statistics of patients, disease and transplant-related factors will be reported as median (range) for continuous variables and percent of total for categorical variables. Overall survival and progression free survival probabilities will be estimated by Kaplan-Meier method. Survival probabilities will be calculated from transplant to date of death or last follow up. Cumulative incidence of

relapse/progression and NRM will be calculated using the Fine and Gray competing risk regression model

If sample size and number of events allow, a multivariate analysis will be performed using Cox proportional hazards models for various outcomes. A stepwise model building approach will then be used to identify the significant risk factors associated with the outcomes. Factors, which are significant at a 5% level, will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested.

Bibliography:

1. Jaffe ES. World Health Organization classification of tumours. ci.nii.ac.jp.
2. Jain P, Aoki E, Keating M, Wierda WG, O'Brien S, Gonzalez GN, et al. Characteristics, outcomes, prognostic factors and treatment of patients with T-cell prolymphocytic leukemia (T-PLL). Ann Oncol. 2017 Jul 1;28(7):1554–1559.
3. Dearden CE, Khot A, Else M, Hamblin M, Grand E, Roy A, et al. Alemtuzumab therapy in T-cell prolymphocytic leukemia: comparing efficacy in a series treated intravenously and a study piloting the subcutaneous route. Blood. 2011 Nov 24;118(22):5799–5802.
4. Dearden C. Management of prolymphocytic leukemia. Hematology Am Soc Hematol Educ Program. 2015;2015:361–367.
5. Sud A, Dearden C. T-cell Prolymphocytic Leukemia. Hematol Oncol Clin North Am. 2017;31(2):273–283.
6. Dearden C. How I treat prolymphocytic leukemia. Blood. 2012 Jul 19;120(3):538–551.
7. Wiktor-Jedrzejczak W, Dearden C, de Wreede L, van Biezen A, Brinch L, Leblond V, et al. Hematopoietic stem cell transplantation in T-prolymphocytic leukemia: a retrospective study from the European Group for Blood and Marrow Transplantation and the Royal Marsden Consortium. Leukemia. 2012 May 1;26(5):972–976.
8. Dholaria BR, Ayala E, Sokol L, Nishihori T, Chavez JC, Hussaini M, et al. Allogeneic hematopoietic cell transplantation in T-cell prolymphocytic leukemia: A single-center experience. Leuk Res. 2018 Jan 29;67:1–5.
9. Guillaume T, Beguin Y, Tabrizi R, Nguyen S, Blaise D, Deconinck E, et al. Allogeneic hematopoietic stem cell transplantation for T-prolymphocytic leukemia: a report from the French society for stem cell transplantation (SFGM-TC). Eur J Haematol. 2015 Mar;94(3):265–269.
10. Kalaycio ME, Kukreja M, Woolfrey AE, Szer J, Cortes J, Maziarz RT, et al. Allogeneic hematopoietic cell transplant for prolymphocytic leukemia. Biol Blood Marrow Transplant. 2010 Apr 1;16(4):543–547.
11. Krishnan B, Else M, Tjonnfjord GE. Stem cell transplantation after alemtuzumab in T-cell prolymphocytic leukaemia results in longer survival than after alemtuzumab alone: a multicentre retrospective …. Wiley Online Library.
12. Collignon A, Wanquet A, Maitre E, Cornet E. Prolymphocytic Leukemia: New Insights in Diagnosis and in Treatment. Springer.

Baseline characteristics of patients undergoing 1st allo-HCT for PLL, TED vs CRF, between 2000 and 2016

Variable	CRF only	TED only
Number of patients	55	234
Number of centers	36	86
Age, median (range), yrs	58 (34-72)	57 (25-76)
Age, yrs		
18-29	0	1 (<1)
30-39	2 (4)	11 (5)
40-49	12 (22)	41 (18)
50-59	18 (33)	101 (43)
60-69	22 (40)	64 (27)
>= 70	1 (2)	16 (7)
Gender		
Male	34 (62)	129 (55)
Female	21 (38)	105 (45)
Karnofsky score		
90-100	30 (55)	122 (52)
< 90	15 (27)	73 (31)
Missing	10 (18)	39 (17)
Disease status at HCT		
Complete Remission (CR)	27 (49)	111 (47)
Nodular Partial Remission (nPR)	0	1 (<1)
Partial Remission (PR)	15 (27)	75 (32)
No Response / Stable (NR/SD)	3 (5)	13 (6)
Progression	4 (7)	19 (8)
Relapse (untreated)	1 (2)	6 (3)
Missing	5 (9)	9 (4)
Time from diagnosis to transplant, median (range)	8 (3-193)	8 (2-100)
Time from diagnosis to transplant		
<6 months	2 (4)	7 (3)
6 - 12 months	12 (22)	66 (28)
>12 months	41 (75)	160 (68)
Missing	0	1 (<1)
Year of transplant		
2000-2001	0	2 (<1)
2002-2003	3 (5)	5 (2)
2004-2005	3 (5)	16 (7)
2006-2007	4 (7)	9 (4)

Variable	CRF only	TED only
2008-2009	19 (35)	18 (8)
2010-2011	1 (2)	48 (21)
2012-2013	2 (4)	59 (25)
2014-2015	16 (29)	44 (19)
2016	7 (13)	33 (14)
Graft source		
Bone marrow	10 (18)	19 (8)
Peripheral blood	37 (67)	209 (89)
Cord blood	8 (15)	6 (3)
Donor type		
HLA-identical sibling	14 (25)	86 (37)
Other related	6 (11)	20 (9)
Well-matched unrelated	20 (36)	70 (30)
Partially-matched unrelated	4 (7)	20 (9)
Multi-donor	1 (2)	0
Unrelated (matching TBD)	2 (4)	32 (14)
Cord blood	8 (15)	6 (3)
Conditioning regimen		
MAC	20 (36)	101 (43)
RIC	35 (64)	127 (54)
Missing	0	6 (3)

Proposal: 1811-54

Title:
Outcomes of patients with T-Cell prolymphocytic leukemia undergoing allogeneic stem cell transplantation

Susan Bal MD, bals@mskcc.org, Memorial Sloan-Kettering Cancer Center

Specific aims:

- To evaluate clinical outcomes of T-Cell prolymphocytic leukemia (T-PLL) patients undergoing allo- HCT stratified by the exposure to Alemtuzumab as it relates to the following:
  - Overall survival (OS)
  - Progression-free survival (PFS)
  - Cumulative incidence of treatment-related mortality (TRM)
  - Cumulative incidence of progression of disease (POD)
  - Cumulative incidence of acute GvHD
  - Cumulative incidence of chronic GvHD

Scientific justification:
T-Cell prolymphocytic leukemia (T-PLL) is a rare lymphoid malignancy with aggressive clinical course and poor outcomes[1,2]. Given the expression of CD52 on the malignant cells, alemtuzumab is a highly utilized primary induction strategy. However, while alemtuzumab results in an overall response rate (ORR) of 80%, patients ultimately progress and succumb to their diagnosis [3,4]. Median survival remains short (7·5–9 months) and is 15–16 months in patients achieving CR. Consolidation with allogeneic hematopoietic cell transplantation (allo-HCT) has been demonstrated by several European groups to improve OS while North American data is lacking. Concern remains regarding TRM as well as POD post-allo-HCT. Guillaume et al[5] retrospectively reported n=27 T- PLL cases proceeding to allo-HCT. With median follow-up of 33 months, 10 patients remain in continuous CR. At 3 years, OS was 36%, PFS was 26%, and TRM was 31%. The cumulative incidence of POD was 47%, with a median duration of 11.7 months and all relapses occurring within the first 2 years. Another series from Europe by Krishnan et al[6] looked at autologous as well as allogeneic hematopoietic cell transplantation. The allo-HCT patients (N=13) were significantly younger. At the time of transplantation, nine allo-HCT patients were in their first CR after alemtuzumab and four were in PR. Five allo-HCT patients remained alive and in CR at a follow-up of: 25, 28, 37, 43 and 110 months; all had MUD allografts, two with reduced-intensity conditioning (RIC). Four patients experienced POD, all after sibling allografts, two with full- intensity and two RIC. Szuszies et al[8] reported on n=3 T-PLL patients receiving RIC allo-HCT after induction of a CR with alemtuzumab, with loss of full-donor chimerism associated with POD.
To our knowledge, outcome of allogeneic stem cell transplant in T-Cell prolymphocytic leukemia has not been reported previously in the United States in a large multicenter analysis.

Patient eligibility population:

18 years of age undergoing allo-HCT from any donor source for T-PLL

Data Requirements:

Type of data	Data point	Specific data
Patient Specific	Patient specific characteristics	• Age at transplant (Date of birth) • Gender • Race • Disease risk (high risk or standard) • Prior autologous transplant • Remission status (CR1, CR2) • HCT-CI • HCT-CI/age
Transplant Specific	Transplant date	• Transplant date
	Preparative regimen used	• Myeloablative • RIC/ non-myeloablative
	GVHD prophylaxis	• Calcineurin inhibitor based (cyclosporine, tacrolimus) • Sirolimus • Corticosteroids • Other
	Graft characteristic	• Donor-recipient HLA match
Outcome Measures	Engraftment	• Time to absolute neutrophil count $\geq$500 cells/mm^3 for 3 consecutive laboratory readings • Time to unsupported platelets $\geq$20 x 10^9 cells/L and $\geq$50 x 10^9 cells/L • Donor-recipient chimerism • Graft failure (primary and secondary)
	GVHD	• Acute GVHD (aGVHD) o Incidence of grade II-IV acute GVHD (aGVHD) (subset evaluating grade III-IV aGVHD) o Time to aGVHD • GVHD after day 100 o Incidence of chronic GVHD (cGVHD) o Severity of GVHD after day 100
	Mortality	• Time to mortality • Day 100, 6 months and 1 year mortality • Treatment related mortality at 6 months and 1 year • Cause of mortality
	Disease relapse	• Incidence of POD • Time to POD

Study design:
The goal of this study is to evaluate the clinical outcomes of allo-HCT for adult patients with T- PLL according to clinical endpoints as listed above. The probabilities of PFS and OS will be calculated using the Kaplan Meier method. Values for other endpoints (TRM, POD, GVHD) will be generated using cumulative incidence estimates to account for competing risks. Full statistical analysis will be performed by members of the statistical team of the CIBMTR.

References:

1. Robak T, Robak P. Current treatment options in prolymphocytic leukemia. Med Sci Monit. 2007 Apr;13(4) RA69-80.
2. Dungarwalla, M & Matutes, Estela & Dearden, Claire. (2008). Prolymphocytic leukaemia of B- and T-cell subtype: A state-of-the-art paper. European journal of haematology. 80. 469-76. 10.1111/j.1600-0609.2008 01069.
3. Claire E. Dearden, Estella Matutes, Bruno Cazin, Geir E. Tjønnfjord, Antonio Parreira, Benet. Blood 2001 98:1721-1726;
4. Keating MJ, Cazin B, Coutre S,; et al ... J Clin Oncol 2002;20(1):205-213.
5. Guillaume T, Beguin Y, Tabrizi R, et al. (2015) Allogeneic hematopoietic stem cell transplantation for T-prolymphocytic leukemia: a report from the French society for stem cell transplantation (SFGM-TC). Eur J Haematol 94(3):265–269.
6. Krishnan B, Else M, Tjonnfjord GE et al. (2010) Stem cell transplantation after alemtuzumab in T- cell prolymphocytic leukaemia results in longer survival than after alemtuzumab alone: a multicentre retrospective study. Br J Haematol 149(6):907–910.
7. Szuszies CJ, Hasenkamp J, Jung W, et al. (2014) Loss of donor chimerism in remission after allogeneic stem cell transplantation of T-prolymphocytic leukemia patients following alemtuzumab induction therapy. Int J Hematol100(5):425–428.

Baseline characteristics of patients undergoing 1st allo-HCT for PLL, TED vs CRF, between 2000 and 2016

Variable	CRF only	TED only
Number of patients	55	234
Number of centers	36	86
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40-49	12 (22)	41 (18)
50-59	18 (33)	101 (43)
60-69	22 (40)	64 (27)
>= 70	1 (2)	16 (7)
Gender		
Male	34 (62)	129 (55)
Female	21 (38)	105 (45)
Disease status at HCT		
Complete Remission (CR)	27 (49)	111 (47)
Nodular Partial Remission (nPR)	0	1 (<1)
Partial Remission (PR)	15 (27)	75 (32)
No Response / Stable (NR/SD)	3 (5)	13 (6)
Progression	4 (7)	19 (8)
Relapse (untreated)	1 (2)	6 (3)
Missing	5 (9)	9 (4)
Time from diagnosis to transplant, median (range)	8 (3-193)	8 (2-100)
Time from diagnosis to transplant		
<6 months	2 (4)	7 (3)
6 - 12 months	12 (22)	66 (28)
>12 months	41 (75)	160 (68)
Missing	0	1 (<1)
Year of transplant		
2000-2001	0	2 (<1)
2002-2003	3 (5)	5 (2)
2004-2005	3 (5)	16 (7)
2006-2007	4 (7)	9 (4)
2008-2009	19 (35)	18 (8)
2010-2011	1 (2)	48 (21)
2012-2013	2 (4)	59 (25)
2014-2015	16 (29)	44 (19)
2016	7 (13)	33 (14)
Graft source		

Variable	CRF only	TED only
Bone marrow	10 (18)	19 (8)
Peripheral blood	37 (67)	209 (89)
Cord blood	8 (15)	6 (3)
Donor type		
HLA-identical sibling	14 (25)	86 (37)
Other related	6 (11)	20 (9)
Well-matched unrelated	20 (36)	70 (30)
Partially-matched unrelated	4 (7)	20 (9)
Multi-donor	1 (2)	0
Unrelated (matching TBD)	2 (4)	32 (14)
Cord blood	8 (15)	6 (3)
Conditioning regimen		
MAC	20 (36)	101 (43)
RIC	35 (64)	127 (54)
Missing	0	6 (3)

Proposal 1711-111

Title:
Allogeneic stem cell transplant for prolymphocytic leukemias

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Hypothesis:
We hypothesize that hematopoietic cell transplant is an effective consolidative strategy for patients with prolymphocytic leukemia (PLL).

Objectives:
This study will evaluate transplant outcomes of patients with PLL who underwent allogeneic HCT (allo-HCT). Our specific aims are:

Primary aim:

- To determine the overall survival (OS) and progression free survival (PFS) in patients with PLL after allo-HCT.

Secondary aims:

- To determine the incidence and severity of acute and chronic graft-versus-host disease (GVHD) after allo-HCT
- To determine the incidence and frequency of non-relapsed mortality (NRM) and cumulative incidence of relapse following transplant
- To determine causes of death post-transplant
- To determine engraftment outcomes

Study justification:
Pro lymphocytic leukemias, both, B and T cell lineage (B-PLL and T-PLL) are a rare group of lymphoid leukemias (<2%) that affect individuals in their 60's and generally presents with either symptomatic splenomegaly or lymphocytosis (1). Skin lesions, pleural/peritoneal effusions and high LDH are a few other hallmark manifestations that frequently manifests in patients with PLL. Historically, survival for patients with T- PLL was low with a median OS of 7 months while using CHOP like regimens and about 30-50 months for B-PLL (1, 2). Monoclonal antibodies like Alemtuzumab, either alone or in combination with chemotherapy has shown enhanced overall response rates (ORR) compared to CHOP like chemotherapy(3). Apart from alemtuzumab, other T cell targeting agents like nelarabine, pentostatin and bendamustine are also increasingly used in management of T-PLL with encouraging response rates (ORR- 30%- 50%) (4, 5). Similarly, in B-PLL, B cell receptor inhibitors like Ibrutinib are making foray in to clinical practice and offer an effective alternative to conventional multiagent chemo-immunotherapy options used for several decades(6, 7). Collectively, these measures in small series appear to impart improved response rates to induction therapy. Despite this progress, disease relapse post induction remains the commonest cause of treatment failure in PLL. Hence, allogeneic stem cell transplant is used an effective consolidation strategy. However, to date no large study has evaluated the role of allo-SCT in modern era with better supportive care options. In addition, a recent study has questioned the conventional wisdom of performing allo-SCT for PLL patients achieving complete remission (CR) with induction (8, 9)). A prior study from CIBMTR showed the utility of HCT in select patients in CR, but was limited in numbers (10). Due to the rarity of this disorder and continued paucity of prospective data, a

revised large registry study may be our only option to identify predictors of survival in PLL patients opting to proceed for allo-HCT.

Study population:
Inclusion Criteria:

- Patients with a diagnosis of PLL undergoing first allo-HCT between 1995-2016
- Myeloablative and reduced-intensity conditioning (MC or RIC) transplants
- Bone marrow (BM), peripheral blood (PB) and umbilical cord (UC) graft sources

Data requirements:
Data will be analyzed from the CIBMTR Report forms. Supplemental data if made available will be utilized.

Outcomes:

- Neutrophil engraftment: Time to neutrophils (ANC) > 0.5 x10^9/L sustained for 3 consecutive days.
- Platelet engraftment: Time to achieve a platelet count >20 x 10^9/L independent of platelet transfusions for 7 consecutive days.
- Acute Graft-versus-host disease (aGVHD) severity: cumulative incidence of grades II-IV; time from transplant to first grade 2-4 and 3-4 aGVHD.
- Chronic Graft-versus-host disease (cGVHD) severity: Limited and extensive; time from transplant to first limited chronic GVHD and time from transplant to first extensive cGVHD.
- Non-relapse mortality (NRM): Cumulative incidence of NRM at day 100 and 1, 3, and 5 years. Defined as death without preceding disease relapse/progression. Relapse/progression are competing events.
- Relapse/Progression: Cumulative incidence of disease relapse/progression at 1 and 3 years, with NRM as competing event.
- Progression-free survival (PFS): Survival without relapse/progression or death. Relapse or progression of disease and death are competing events. Those who survive without relapse/progression are censored at last follow-up.
- Overall survival (OS): Time to death. Death from any cause will be considered an event. Surviving patients will be censored at the time of last follow-up.

Variables to be studied: (Highlighted will be included in multi variate models):
Patient-related:

- Gender: Male vs. Female
- Age at HCT
- Karnofsky performance score: ≥90 vs. <90
- Race: White vs. Black vs. Hispanic vs. others
- Hematopoietic cell transplantation co-morbidity index (HCT-CI) (≥3 vs. <3)
- CMV serostatus matching (+/-, +/+, -/-, -/+) between donor and recipient

Disease-related:

- Disease status pre-transplant (CR1 or > CR1 or primary induction failure)
- Time from diagnosis to transplant
- Time to achieve first complete remission
- Relapse post SCT (yes vs. no)
- Time to relapse post SCT
- Cytogenetics at Diagnosis and pre- SCT

- Causes of Death

Treatment-related:

- Conditioning intensity (myeloablative vs. reduced intensity vs. nonmyeloablative)
- GVHD prophylaxis for allo-HCT
- Donor Type: HLA-identical sibling vs unrelated donor vs haplo-identical
- Graft Source: BM vs PB vs UCB
- HLA matching Status

CRF data (if available):

- Creatinine at diagnosis: <2 mg/dL vs. ≥2 mg/dL
- LDH at diagnosis: Continuous
- Beta-2-microglobulin at diagnosis: mcg/mL: continuous
- Hemoglobin at diagnosis: g/dL, continuous
- WBC at diagnosis: k/l, continuous
- Pleuro-peritoneal effusion: yes vs. no

Study design:

This is a retrospective study examining HCT outcomes for those with PLL. The analysis will be restricted to transplants performed from 1996 to 2016. Patient, disease and transplant-related factors will be compared between groups (those in CR vs not in CR) using the Chi-square test for categorical variables and the Wilcoxon two sample test for continuous variables. Kaplan-Meier product limit estimates will be used to calculate the probabilities of OS and PFS. The cumulative incidence of NRM, disease progression, and acute and chronic GVHD will be estimated accounting for competing risks. Cox proportional hazards regression will be used to compare the two groups (in CR vs not in CR at the time of transplant): NRM, relapse/progression, PFS, OS, neutrophil and platelet engraftment.

References:

1. Graham RL, Cooper B, Krause JR. T-cell prolymphocytic leukemia. Proceedings. 2013 Jan;26(1):19-21. PubMed PMID: 23382603. Pubmed Central PMCID: 3523759.
2. Matutes E, Brito-Babapulle V, Swansbury J, Ellis J, Morilla R, Dearden C, et al. Clinical and laboratory features of 78 cases of T-prolymphocytic leukemia. Blood. 1991 Dec 15;78(12):3269-74. PubMed PMID: 1742486.
3. Hopfinger G, Busch R, Pflug N, Weit N, Westermann A, Fink AM, et al. Sequential chemoimmunotherapy of fludarabine, mitoxantrone, and cyclophosphamide induction followed by alemtuzumab consolidation is effective in T-cell prolymphocytic leukemia. Cancer. 2013 Jun 15;119(12):2258-67. PubMed PMID: 23512246.
4. Gandhi V, Tam C, O'Brien S, Jewell RC, Rodriguez CO, Jr., Lerner S, et al. Phase I trial of nelarabine in indolent leukemias. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2008 Mar 01;26(7):1098-105. PubMed PMID: 18309944.
5. Ravandi F, Aribi A, O'Brien S, Faderl S, Jones D, Ferrajoli A, et al. Phase II study of alemtuzumab in combination with pentostatin in patients with T-cell neoplasms. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2009 Nov 10;27(32):5425-30. PubMed PMID: 19805674. Pubmed Central PMCID: 4881363.
6. Gordon MJ, Raess PW, Young K, Spurgeon SEF, Danilov AV. Ibrutinib is an effective treatment for B-cell prolymphocytic leukaemia. British journal of haematology. 2017 Nov;179(3):501-3. PubMed PMID: 27391978.
7. Dearden C. B- and T-cell prolymphocytic leukemia: antibody approaches. Hematology / the Education Program of the American Society of Hematology American Society of Hematology Education Program. 2012;2012:645-51. PubMed PMID: 23233647.

8. Jain P, Aoki E, Keating M, Wierda WG, O'Brien S, Gonzalez GN, et al. Characteristics, outcomes, prognostic factors and treatment of patients with T-cell prolymphocytic leukemia (T-PLL). Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2017 Jul 01;28(7):1554-9. PubMed PMID: 28379307.
9. Guillaume T, Beguin Y, Tabrizi R, Nguyen S, Blaise D, Deconinck E, et al. Allogeneic hematopoietic stem cell transplantation for T-prolymphocytic leukemia: a report from the French society for stem cell transplantation (SFGM-TC). European journal of haematology. 2015 Mar;94(3):265-9. PubMed PMID: 25130897.
10. Kalaycio ME, Kukreja M, Woolfrey AE, Szer J, Cortes J, Maziarz RT, et al. Allogeneic hematopoietic cell transplant for prolymphocytic leukemia. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation. 2010 Apr;16(4):543-7. PubMed PMID: 19961946. Pubmed Central PMCID: 2839005.

Baseline characteristics of patients undergoing 1st allo-HCT for PLL, TED vs CRF

Variable	Ted only	CRF
Number of patients	288	61
Age, median (range), yrs	58 (24-76)	57 (34-80)
Age, yrs		
20-29	2 (<1)	0
30-39	11 (4)	2 (3)
40-49	49 (17)	11 (18)
50-59	125 (43)	23 (38)
60-69	83 (29)	22 (36)
≥ 70	18 (6)	3 (5)
Gender		
Male	171 (59)	40 (66)
Female	117 (41)	21 (34)
Disease status at HCT		
CR	132 (46)	25 (41)
Nodular PR	2 (<1)	0
PR	85 (30)	15 (25)
No response/stable	17 (6)	3 (5)
Progression	23 (8)	7 (11)
Relapse	5 (2)	2 (3)
Missing	24 (8)	9 (15)
Time from diagnosis to transplant, median (range)	8 (<1-115)	8 (2-193)
Time from diagnosis to transplant		
0-3 months	10 (3)	3 (5)
3-6 months	76 (26)	15 (25)
≥ 6 months	201 (70)	43 (70)
Missing	1 (<1)	0
Year of transplant		
1997-1998	2 (<1)	0
1999-2000	3 (1)	1 (2)
2001-2002	4 (1)	2 (3)
2003-2004	21 (7)	4 (7)
2005-2006	19 (7)	3 (5)
2007-2008	13 (5)	15 (25)
2009-2010	51 (18)	14 (23)
2011-2012	66 (23)	0
2013-2014	56 (19)	8 (13)
2015-2016	53 (18)	14 (23)
Graft source		
Bone marrow	24 (8)	10 (16)

Variable	Ted only	CRF
Peripheral blood	257 (89)	41 (67)
Cord blood	6 (2)	10 (16)
Missing	1 (<1)	0
Donor type		
HLA-identical sibling	117 (41)	15 (25)
Twin	0	1 (2)
Other related	26 (9)	8 (13)
Well-matched unrelated	76 (26)	19 (31)
Partially-matched unrelated	22 (8)	5 (8)
Unrelated (matching TBD)	40 (14)	3 (5)
Cord blood	6 (2)	10 (16)
Missing	1 (<1)	0
Conditioning regimen		
MAC	110 (38)	24 (39)
RIC/NST	170 (59)	37 (61)
Missing	8 (3)	0

Proposal: 1811-51

Title:
Alternative donor versus HLA-matched donor hematopoietic cell transplantation in patients with myelodysplastic syndrome

Rohtesh S. Mehta, MD, rmehta1@mdanderson.org, The University of Texas MD Anderson Cancer Center

Hypothesis
We hypothesize that the survival of adult patients (age ≥ 18 years) with de novo or secondary myelodysplastic syndrome (MDS) who underwent haploidentical HCT with post transplantation cyclophosphamide (PTCy) would be similar to those with HLA-matched sibling (MSD) or unrelated donor (MUD) HCT, and better than HLA-mismatched unrelated donor (7/8-MMUD) or umbilical cord blood (UCB) HCT.

Specific aims:
The goal of the proposed study is to compare the outcomes of patients with MDS after (a) MSD, (b) MUD, (c) haploidentical donor, (d) one-antigen mismatched unrelated donor (7/8-MMUD) or (e) umbilical cord blood (UCB) hematopoietic cell transplantation (HCT).

- The primary outcomes of interest are:
  - overall survival (OS)
  - relapse
  - non-relapse mortality (NRM)
  - grade III-IV acute GVHD
  - systemic therapy-requiring chronic GVHD

- The secondary outcomes of interest are:
  - grade II-IV acute GVHD
  - chronic GVHD
  - Neutrophil engraftment
  - Graft failure
  - Donor chimerism
  - disease free survival (DFS)
  - GVHD-free relapse free survival (GRFS)
  - Chronic GVHD-free relapse-free survival (CRFS)
  - Cumulative incidence of viral infections (reactivation of CMV, HHV-6, EBV, or adenovirus and BK cystitis)

Scientific impact:
Multiple studies reported outcomes of HCT using a variety of donors, and compared one donor type to another. However, data on contemporaneous comparison of various donor types, especially haploidentical with PTCy, are lacking.

Scientific justification:
A collaborative from Eurocord and Chronic Malignancies Working Party showed better outcomes with 10/10-PB MUD (lower NRM, better DFS and OS) than with UCB or 9/10-PB MUD.[1] A study by the CIBMTR compared 7/8-MMUD, 8/8-MUD and MSD and showed significantly poorer outcomes with the worst

DSF and OS in the 7/8-MMUD group than MUD or MSD.[2] Haploidentical HCT (using non-PTCy based GVHD prophylaxis regimens) have also been compared with MUD or MSD in patients with MDS,[3] including those with transformation to AML (tAML)[3] and MDS combined with a variety of other hematologic malignancies.[4,5] Haploidentical group had lower risk of relapse than MSD or MUD but high NRM, resulting in similar DFS.[4] Outcomes of haploidentical with PTCy have also been contrasted to those without post-Cy.[6] However, data on contemporaneous comparison of various donor types, especially haploidentical with PTCy, are lacking. Conclusions about haploidentical HCT from previous studies that used non-PTCy regimens are obsolete in the current era where PTCy is routinely incorporated as the standard GVHD prophylaxis.

Patient eligibility population:

Inclusion criteria:

- Adults, ages ≥ 18 years
- De novo or secondary myelodysplastic syndrome (MDS)
- Donor type:
    - MSD (PB or BM graft)
    - MUD (PB or BM graft)
    - Haploidentical HCT (PB or BM graft) with PTCy
    - UCB HCT only with TCF conditioning (total body irradiation, cyclophosphamide and fludarabine), ≥4/6 HLA match (HLA-A and –B at antigen level and –DRB1 at allele level) and TNC dose ≥2.5 $X10^7$/kg
    - 7/8-MMUD (PB or BM graft); mismatch at any one of the loci - HLA-A, -B, -C, or -DRB1
- HCT year 01/2000- 12/2015
- Any conditioning intensity – myeloablative or RIC
- With or without in-vivo T-cell depletion using ATG/ALG/ Campath
- Any GVHD prophylaxis, but haploidentical HCT must have PTCy.

Exclusion criteria:

- Prior allogeneic HSCT
- Solid organ malignancies
- Recipients of HSCT with ex vivo graft manipulations - such as CD34+ selected or T-cell depleted grafts
- UCB with <4/6 HLA match unit, or TNC dose <2.5 $X10^7$/kg

Primary outcomes:

- Overall survival: Time to death from any cause. The event will be summarized by a Kaplan-Meier survival curve. Patients are censored at the date of last follow-up. There are no competing risks.
- Relapse/Progression: Time to the recurrence of the underlying malignancy for which the allogeneic HCT was performed. The event will be summarized by the cumulative incidence estimate with NRM treated as a competing risk. Patients will be censored at second transplant or date of last follow-up.
- Non relapse mortality (NRM): Time to death without relapse/progression. The event will be summarized by the cumulative incidence estimate with relapse/progression treated as a competing risk. Patients will be censored at second transplant or date of last follow-up.
- Acute GVHD III-IV: Time to the development of Grade III-IV acute GVHD using the Glucksberg grading system. The event will be summarized by the cumulative incidence estimate, where death without Grade III-IV acute GVHD will be treated as a competing risk. Patients will be censored at second transplant or date of last follow-up.

- Chronic GVHD requiring systemic IST: Time to the development of limited or extensive chronic GVHD. The event will be summarized by the cumulative incidence estimate, where death without chronic GVHD will be treated as a competing risk. Patients will be censored at second transplant or date of last follow-up.

Secondary outcomes:

- Acute GVHD II-IV: Time to the development of Grade II-IV acute GVHD using the Glucksberg grading system. The event will be summarized by the cumulative incidence estimate, where death without Grade III-IV acute GVHD will be treated as a competing risk. Patients will be censored at second transplant or date of last follow-up.
- Chronic GVHD: Time to the development of any (limited or extensive) chronic GVHD. The event will be summarized by the cumulative incidence estimate, where death without chronic GVHD will be treated as a competing risk. Patients will be censored at second transplant or date of last follow-up.
- Engraftment: Time to achieving an absolute neutrophil count $\geq$ 500/mm^3 for 3 consecutive days, in patients surviving a minimum of 14 days post-transplant. Patients will be censored at second transplant or date of last follow-up.
- Graft failure: Failure to attain ANC $\geq$ 500/mm^3 for 3 consecutive days prior to subsequent HCT or death, in patients surviving a minimum of 14 days post-transplant.
- Donor Chimerism at day 30, day 100, day 180 and 1 year
- Disease-free survival (DFS): Time to treatment failure (death or relapse/progression). This event will be summarized by a Kaplan-Meier survival curve. Patients will be censored at second transplant or date of last follow-up. There are no competing risks.
- GVHD-free, relapse-free survival (GRFS): Grade III-IV acute GVHD, chronic GVHD, disease relapse/progression and death are treated as events. There will be no competing risks. This event will be summarized by a survival curve. Patients will be censored at second transplant or date of last follow-up.
- Chronic GVHD-free relapse-free survival (CRFS): chronic GVHD, disease relapse/progression and death are treated as events. There will be no competing risks. This event will be summarized by a survival curve. Patients will be censored at second transplant or date of last follow-up.
- Cumulative incidence of viral reactivations, including CMV, HHV-6, EBV, or adenovirus and BK cystitis at any time after HCT.

Baseline characteristics:

- Patient Age $\geq$18
- Patient Gender
- Patient Race/ethnicity
- Disease (de novo MDS vs secondary MDS)
- IPSS and R-IPSS
- Performance status (<90 vs $\geq$90)
- Disease status at HCT- CR1, CR2, relapsed, PIF
- Revised disease risk index (rDRI): low/intermediate vs high/very high
- HCT-CI (0-2 vs $\geq$3)
- HLA match
- Major ABO mismatch (yes/no)
- Donor-recipient gender (female-donor-to-male vs. all others)
- Donor-recipient CMV status

- Donor age
- Conditioning regimen – (a) myeloablative vs (b) reduced intensity/non-myeloablative
- GVHD prophylaxis regimen
- In vivo T cell depletion (ATG/ALG or alemtuzumab) – yes/no
- TNC dose $x10^7$/kg: <2.5, 2.5-<5, ≥5
- CD34 dose $x10^6$/kg: <2.5, 2.5-<5, ≥5
- CD3 dose $x10^6$/kg: <0.2, 0.2-<2, ≥2
- Year of HCT
- Follow-up period

Other data needed for outcome analysis:

- Graft failure (yes/no)
- Relapse/Progression (Yes/No)
- Acute GVHD grade II-IV (Yes/No)
- Acute GVHD grade III-IV (Yes/No),
- Chronic GVHD (Yes/No)
- Systemic-therapy requiring chronic GVHD (Yes/No),
- Death (yes/no),
- Cause of death
- Viral infections – CMV reactivation, EBV, adenovirus, BK cystitis. (cumulative incidence and time from HCT)

Study design:

We will analyze patients with MDS who received HCT with MSD, MUD, 7/8-MMUD, haploidentical donor or UCB. We will use the Wilcoxon sign-rank test to compare characteristics across donor sources for continuous variables and the Chi-square test for categorical variables. The rates of relapse and NRM will be estimated in a competing risks framework—with NRM and relapse, respectively, as the competing risks—using the cumulative incidence method of Gooley et al.[29] The association between NRM and relapse and variables of interest will be assessed using the method of Fine and Gray.[30] The median time to engraftment was compared using the Wilcoxon rank sum test. Acute and chronic GVHD will be assessed with competing risks of relapse and death, again using the methods of Gooley et al. and Fine and Gray.[7,8] The Kaplan-Meier curves will be used to estimate OS, DFS, GRFS and CRFS for all donor types, and the log-rank test will be used to test differences between groups based on variables of interest. Proportional hazards will be checked using martingale residuals. Multivariate analyses will be performed using Cox regression model to examine the independent impact of variables on OS, relapse, NRM, DFS, GRFS and CRFS. If the adjusted factors violate the proportional hazards assumption, they will be adjusted through stratification. If the main testing variable (donor type) violates the proportional hazards assumption, the optimal cut point will be determined based on the maximum likelihood method with different hazard ratios (HR) within each time interval.

Data source: CIBMTR Research Database.

R**eferences:**

1. Robin M, Ruggeri A, Labopin M, et al. Comparison of unrelated cord blood and peripheral blood stem cell transplantation in adults with myelodysplastic syndrome after reduced-intensity conditioning regimen: a collaborative study from Eurocord (Cord blood Committee of Cellular

Therapy & Immunobiology Working Party of EBMT) and Chronic Malignancies Working Party. *Biol Blood Marrow Transplant.* 2015;21(3):489-495.
2. Saber W, Cutler CS, Nakamura R, et al. Impact of donor source on hematopoietic cell transplantation outcomes for patients with myelodysplastic syndromes (MDS). *Blood.* 2013;122(11):1974-1982.
3. Wang Y, Wang HX, Lai YR, et al. Haploidentical transplant for myelodysplastic syndrome: registry-based comparison with identical sibling transplant. *Leukemia.* 2016;30(10):2055-2063.
4. Luo Y, Xiao H, Lai X, et al. T-cell-replete haploidentical HSCT with low-dose anti-T-lymphocyte globulin compared with matched sibling HSCT and unrelated HSCT. *Blood.* 2014;124(17):2735-2743.
5. Chen D, Zhou D, Guo D, Xu P, Chen B. Comparison of outcomes in hematological malignancies treated with haploidentical or HLA-identical sibling hematopoietic stem cell transplantation following myeloablative conditioning: A meta-analysis. *PLoS One.* 2018;13(1):e0191955.
6. Robin M, Porcher R, Ciceri F, et al. Haploidentical transplant in patients with myelodysplastic syndrome. *Blood Adv.* 2017;1(22):1876-1883.
7. Gooley TA, Leisenring W, Crowley J, Storer BE. Estimation of failure probabilities in the presence of competing risks: new representations of old estimators. *Stat Med.* 1999;18(6):695-706.
8. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *Journal of the American Statistical Association.* 1999;94:496-509.

Baseline characteristics for patients undergoing allo-HCT for MDS between 2000 and 2016

Characteristic	HLA-id sibling	Haplo	URD 8/8	URD 7/8	Cord blood
Number of patients	1310	131	2242	291	267
Number of centers	163	47	135	86	76
Age, median (range)	59 (18-78)	66 (20-78)	62 (18-83)	59 (18-81)	59 (18-75)
Age					
18-29	58 (4)	4 (3)	85 (4)	17 (6)	27 (10)
30-39	81 (6)	5 (4)	100 (4)	18 (6)	26 (10)
40-49	158 (12)	5 (4)	195 (9)	33 (11)	33 (12)
50-59	423 (32)	25 (19)	542 (24)	85 (29)	65 (24)
60-69	515 (39)	64 (49)	1029 (46)	110 (38)	95 (36)
>= 70	75 (6)	28 (21)	291 (13)	28 (10)	21 (8)
Gender					
Male	812 (62)	94 (72)	1384 (62)	191 (66)	145 (54)
Female	498 (38)	37 (28)	858 (38)	100 (34)	122 (46)
Karnofsky score					
90-100	775 (59)	62 (47)	1225 (55)	174 (60)	182 (68)
< 90	498 (38)	65 (50)	938 (42)	109 (37)	75 (28)
Missing	37 (3)	4 (3)	79 (4)	8 (3)	10 (4)
Secondary disorder					
No	977 (75)	100 (76)	1629 (73)	220 (76)	204 (76)
Yes	269 (21)	29 (22)	560 (25)	66 (23)	57 (21)
Missing	64 (5)	2 (2)	53 (2)	5 (2)	6 (2)
HCT-CI					
0	224 (17)	22 (17)	317 (14)	50 (17)	49 (18)
1	100 (8)	17 (13)	202 (9)	24 (8)	34 (13)
2	105 (8)	11 (8)	239 (11)	26 (9)	27 (10)

Characteristic	HLA-id sibling	Haplo	URD 8/8	URD 7/8	Cord blood
3+	518 (40)	81 (62)	1052 (47)	112 (38)	128 (48)
NA, pre-TED not completed	351 (27)	0	407 (18)	73 (25)	28 (10)
Missing	12 (<1)	0	25 (<1)	6 (2)	1 (<1)
Disease status at transplant					
CR1	467 (36)	40 (31)	767 (34)	107 (37)	85 (32)
CR2	748 (57)	75 (57)	1296 (58)	158 (54)	162 (61)
>CR2	95 (7)	16 (12)	179 (8)	26 (9)	20 (7)
IPSS prior to transplant					
Low	154 (12)	15 (11)	256 (11)	28 (10)	41 (15)
Intermediate-1	621 (47)	59 (45)	1013 (45)	114 (39)	105 (39)
Intermediate-2	289 (22)	41 (31)	595 (27)	82 (28)	76 (28)
High	16 (1)	2 (2)	58 (3)	12 (4)	9 (3)
Missing	230 (18)	14 (11)	320 (14)	55 (19)	36 (13)
IPSS karyotype category					
Favorable	476 (36)	37 (28)	812 (36)	88 (30)	87 (33)
Intermediate	263 (20)	21 (16)	399 (18)	53 (18)	35 (13)
Poor	467 (36)	66 (50)	879 (39)	118 (41)	127 (48)
TBD (needs rev.)	35 (3)	2 (2)	56 (2)	14 (5)	10 (4)
Not tested	13 (<1)	0	41 (2)	10 (3)	1 (<1)
Missing	56 (4)	5 (4)	55 (2)	8 (3)	7 (3)
Treatment prior to condtioning					
No	359 (27)	15 (11)	402 (18)	56 (19)	38 (14)
Yes	932 (71)	116 (89)	1823 (81)	233 (80)	227 (85)
Missing	19 (1)	0	17 (<1)	2 (<1)	2 (<1)
Time from diagnosis to transplant, median (range)	7 (<1-497)	10 (1-165)	8 (<1-370)	10 (1-237)	8 (<1-207)
Time from diagnosis to transplant					
< 6 months	558 (43)	31 (24)	730 (33)	74 (25)	85 (32)

Characteristic	HLA-id sibling	Haplo	URD 8/8	URD 7/8	Cord blood
6-12 months	346 (26)	45 (34)	774 (35)	95 (33)	86 (32)
>= 12 months	403 (31)	53 (40)	725 (32)	121 (42)	95 (36)
Missing	3 (<1)	2 (2)	13 (<1)	1 (<1)	1 (<1)
Year of transplant					
2000-2001	93 (7)	0	48 (2)	19 (7)	4 (1)
2002-2003	93 (7)	0	72 (3)	16 (5)	1 (<1)
2004-2005	103 (8)	0	121 (5)	21 (7)	7 (3)
2006-2007	67 (5)	0	181 (8)	18 (6)	18 (7)
2008-2009	146 (11)	1 (<1)	229 (10)	43 (15)	54 (20)
2010-2011	149 (11)	5 (4)	242 (11)	29 (10)	47 (18)
2012-2013	241 (18)	29 (22)	480 (21)	56 (19)	53 (20)
2014-2015	296 (23)	54 (41)	567 (25)	64 (22)	60 (22)
2016	122 (9)	42 (32)	302 (13)	25 (9)	23 (9)
Donor age at donation, median (range), yr	56 (18-82)	39 (18-69)	29 (18-62)	33 (19-58)	Not applicable
Donor age at donation					
10-19	8 (<1)	3 (2)	84 (4)	3 (1)	0
20-29	37 (3)	21 (16)	1093 (49)	109 (37)	0
30-39	114 (9)	49 (37)	560 (25)	88 (30)	0
40-49	199 (15)	35 (27)	338 (15)	55 (19)	0
50-59	483 (37)	12 (9)	106 (5)	21 (7)	0
60-69	394 (30)	9 (7)	6 (<1)	0	0
70-79	58 (4)	0	0	0	0
>= 80	1 (<1)	0	0	0	0
Missing	16 (1)	2 (2)	55 (2)	15 (5)	267
Donor/recipient CMV serostatus					
+/+	523 (40)	41 (31)	580 (26)	76 (26)	0
+/-	157 (12)	6 (5)	220 (10)	33 (11)	0

Characteristic	HLA-id sibling	Haplo	URD 8/8	URD 7/8	Cord blood
-/+	310 (24)	44 (34)	707 (32)	99 (34)	0
-/-	291 (22)	35 (27)	687 (31)	79 (27)	0
CB - recipient +	0	0	0	0	174 (65)
CB - recipient F	0	0	0	0	91 (34)
CB - recipient sex unknown	0	0	0	0	2 (<1)
Missing	29 (2)	5 (4)	48 (2)	4 (1)	0
Donor/recipient sex match					
M-M	423 (32)	59 (45)	1064 (47)	128 (44)	0
M-F	236 (18)	30 (23)	553 (25)	52 (18)	0
F-M	364 (28)	35 (27)	316 (14)	63 (22)	0
F-F	241 (18)	7 (5)	301 (13)	48 (16)	0
CB - recipient M	0	0	0	0	145 (54)
CB - recipient F	0	0	0	0	122 (46)
Missing	46 (4)	0	8 (<1)	0	0
Donor/recipient ABO match					
Matched	854 (65)	82 (63)	1055 (47)	125 (43)	0
Minor mismatch	189 (14)	26 (20)	564 (25)	72 (25)	0
Major mismatch	202 (15)	20 (15)	438 (20)	68 (23)	0
Bi-directional	54 (4)	2 (2)	161 (7)	23 (8)	0
CB - recipient A	0	0	0	0	91 (34)
CB - recipient B	0	0	0	0	35 (13)
CB - recipient AB	0	0	0	0	12 (4)
CB - recipient O	0	0	0	0	129 (48)
Missing	11 (<1)	1 (<1)	24 (1)	3 (1)	0
Graft type					
Bone marrow	111 (8)	63 (48)	355 (16)	48 (16)	0
Peripheral blood	1198 (91)	68 (52)	1887 (84)	243 (84)	0

Characteristic	HLA-id sibling	Haplo	URD 8/8	URD 7/8	Cord blood
Cord blood	0	0	0	0	267
Missing	1 (<1)	0	0	0	0
Conditioning regimen intensity					
MAC	627 (48)	28 (21)	904 (40)	125 (43)	95 (36)
RIC	493 (38)	23 (18)	1117 (50)	139 (48)	61 (23)
NMA	111 (8)	76 (58)	161 (7)	21 (7)	101 (38)
TBD	52 (4)	4 (3)	56 (2)	6 (2)	9 (3)
Missing	27 (2)	0	4 (<1)	0	1 (<1)
ATG/Campath					
ATG alone	169 (13)	2 (2)	750 (33)	116 (40)	112 (42)
CAMPATH alone	45 (3)	0	82 (4)	14 (5)	1 (<1)
No ATG or CAMPATH	1070 (82)	129 (98)	1408 (63)	161 (55)	154 (58)
Missing	26 (2)	0	2 (<1)	0	0
GVHD prophylaxis					
Post-CY + other(s)	20 (2)	117 (89)	49 (2)	8 (3)	0
TAC + MMF +- other(s) (except post-CY)	190 (15)	14 (11)	469 (21)	55 (19)	99 (37)
TAC + MTX +- other(s) (except MMF, post-CY)	488 (37)	0	1119 (50)	133 (46)	6 (2)
TAC + other(s) (except MMF, MTX, post-CY)	87 (7)	0	169 (8)	21 (7)	14 (5)
TAC alone	33 (3)	0	56 (2)	7 (2)	10 (4)
CSA + MMF +- other(s) (except post-CY)	160 (12)	0	165 (7)	24 (8)	110 (41)
CSA + MTX +- other(s) (except MMF, post-CY)	230 (18)	0	128 (6)	27 (9)	1 (<1)
CSA + other(s) (except MMF, MTX, post-CY)	28 (2)	0	10 (<1)	0	3 (1)
CSA alone	38 (3)	0	11 (<1)	3 (1)	3 (1)
Other(s)	15 (1)	0	29 (1)	5 (2)	17 (6)
Missing	21 (2)	0	37 (2)	8 (3)	4 (1)

Proposal: 1811-72

Title:
Precision model to predict outcomes of myelofibrosis using artificial intelligence techniques

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Primary aim:
To develop a precision medicine model for prediction of clinical outcomes post-allogeneic transplantation for primary myelofibrosis (PMF) using multiple machine learning algorithms.

Secondary aims:

- To evaluate multiple variables (both traditional transplant related, genomic and patient related) for multiple interactions between them via deep learning methods
- To evaluate multiple interactions within mutations via neural networks in predicting survival and mortality in PMF.

Hypothesis and scientific justification:
Significant advances in myelofibrosis drug development have led to the availability of efficacious drugs which include (both FDA approved and on trials) hydroxyurea, ruxolitinib, pomalidomide, IMiDs (thalidomide, lenalidomide, pomalidomide), imetelstat, anabolic steroids (danazol, flouxymesterone), momelotinib, pacritinib and many others besides localized treatments (e.g. splenectomy). However, in 2019, allogeneic hematopoietic cell transplantation (HCT) remains the only potentially curative modality for its treatment. Though many risk models to predict outcomes of PMF exist, none of the models currently being used routinely is specific to predict post-HCT outcomes.
When it comes to establishing prediction models, over time, almost all of the models lose their validity as new information gathers. In the field of oncology, particularly in hematologic malignancies, information on the genomics has revolutionized the current diagnostic and prognostic paradigm and continues to refine it as more data on driver versus downstream mutations gathers. In 1988, Barosi et al. presented a prognostic model of PMF based on the variables which were considered important at that time for PMF; in 1997, Reilly et al. published a prognostic schema for PMF based on traditional variables, but also incorporating karyotypic information. In 2009, Cervantes et al. published a highly discriminative model based on 5 variables for predicting prognosis of PMF called IPSS. In 2010, Passamonti et al. developed the IPSS into DIPSS by incorporating the risk of acquisition of risk factors and age. In 2011, Gangat et al. further developed the model by further incorporating unfavorable karyotype, thrombocytopenia and transfusion needs; which became the gold standard for prognosis (DIPSS plus). Most of the predictive modeling above was done via statistical techniques in which weights (e.g. hazard ratio or relative risk based) are assigned to each variable and are given points on the training set which is then applied to a validation set.
Fast forward 8 years from the publication of the DIPPS plus scoring system, a lot more data has gathered regarding the mutations in calreticulin & MPL, and their interplays with JAK2 mutation. To make the data interpretation by clinicians even more complicated, many more mutations have been independently associated by different groups with survival and include IDH1, IDH2, ASXL1, SRSF2, ASXL1, EZH2, and SRSF1, TET2, DNMT3A, and others. Many more mutations are being discovered in the current

era of next generation sequencing (some of which carry a high allele burden and are independently associated with inferior survival). Equally important to the genomic and traditional disease risk factors of PMF are significant amount of variables within the transplant arena which are well-known to effect the transplant outcomes. These include (but are not limited to) GVHD prophylaxis regimens, use of radiation (TBI) or not, pre-HCT splenectomy status, conditioning regimen intensity (RIC vs MAC vs NMA), donor type, stem cell source (CBT vs PBSC vs BM), donor/recipient gender mismatch, donor/recipient age difference, recipient health indicator (HCT-CI), progenitor cell acquisition method (bone marrow vs peripheral blood stem cells), development of acute or chronic GVHD, and many others.
The essential question in transplant arena, on which patient to transplant and what would be the prognosis AFTER transplant, thus becomes even perplexing in the current era of genomics for a practicing clinician.
Machine learning (ML) is a branch of artificial intelligence (AI) which has been used for decades for inference of complex data however its application in healthcare sector is relatively recent. Currently, most of the ML techniques used in preparing cancer prediction models, use either known or unknown dependencies (or both) and come up with outputs using one of many known techniques (decision trees, bayesian networks, artificial neural networks etc.) where the performance analysis of each proposed model is measured in terms of sensitivity, specificity, accuracy and the area under the curve (AUC). Predictive models using ML techniques have widely been published and changing the current practice paradigm in medicine including the field of oncology. Within cancers, in 2005, Delen et al. published a survival prediction model using cross validation from 200,000 breast cancer patients (From SEER database) which had an accuracy of 93%. For prediction of relapsed ALL in children, Pan et al. recently published a prediction model using the ML method of random forest which achieved an AUC of >0.9. Nazha et al. recently analyzed the MDS data to evaluate the currently used models for prognosis and devised model using ML utilizing random survival forest which yielded a C-index of 0.71 for overall survival and 0.76 for MDS→AML transformation. The new model outperformed all commonly used models for OS and AML transformation including IPSS (c-index 0.65, 0.72), IPSS-R (0.67, 0.73), WHO prognostic scoring system (WPSS) (0.65, 0.73) and MD Anderson prognostic model (MDAPSS) (0.65, 0.7), respectively. Currently a CIBMTR project utilizing ML is ongoing to devise prediction models of MDS utilizing CIBMTR MDS data (CK 18-01). For MF, CIBMTR contains extensive data on both disease and transplant related factors which are important to predict outcomes and additionally, to evaluate the genomic findings, extensive data on mutations which have already been sequenced are available at the institutions of PI's of the current project. Thereby we propose to integrate the clinical data with the genomic data to establish a precision medicine model for predicting post-transplant outcomes.

Patient eligibility population (ALLOGENEIC ONLY):
Selection criteria (both TED level and *available CRF* in CIBTMR database):

- All adult patients who underwent allogeneic HCT between 01/01/2000 and 12/31/2016 for primary myelofibrosis, and survived for 2 years after transplant.
- All donor sources will be included (related (matched, Haploidentical), unrelated (matched, mismatched)
- All stem cell source will be included (bone marrow, peripheral blood, cord blood)
- All conditioning types will be included (reduced intensity [RIC], myeloablative [MA], non-myeloablative [NMA])

Variables:
<u>Patient-related:</u>

- Age: person years at risk: continuous variable

- Age: age at HCT: continuous variable
- Age at diagnosis: continuous and by decades
- Gender: male or female
- Smoking status prior to HSCT: Y/N
- Karnovsky performance score at the time of transplant
- Race of the patient: nominal variable

Disease related:

- Time from date of MF diagnosis to HCT: continuous and 6 month intervals
- Disease: PMF versus post-PV versus post-ET versus post-prefibrosis (pre-fibrotic phase)
- DIPSS plus risk group at the time of HCT: low versus Int-1 versus Int-2 versus high
- Hb at diagnosis: < 10 g/L versus ≥ 10 g/L
- Hb prior to HCT: < 10 g/L versus ≥ 10 g/L
- WBC at diagnosis: ≤ 25 × 10(9) / L versus > 25 × 10(9) / L
- WBC prior to HCT: ≤ 25 × 10(9) / L vs. > 25 × 10(9) / L
- Constitutional symptoms at diagnosis: presence or absence
- Constitutional symptoms prior to HCT: presence or absence
- Circulating blasts percentage at diagnosis: ≤ 1% versus > 1%
- Circulating blasts percentage prior to HCT: ≤ 1% versus > 1%
- Platelet count at diagnosis: ≥ 100 × 10(9) / L versus 50-100 × 10(9) / L vs. < 50 × 10(9) / L
- Platelet count at HCT: ≥ 100 × 10(9) / L versus 50-100 × 10 (9) / L versus < 50 × 10 (9) / L
- Cytogenetics: unfavorable (complex [≥ 3], +8, -7, -5, i(17)q, 12p-, inv(3), 11q23 abnormal) versus all others
- JAK2 mutation status: negative versus positive versus unknown
- MPL mutation status: negative versus positive versus unknown
- CALR mutation status: negative versus positive versus unknown
- Spleen status at HCT: normal versus splenomegaly versus splenectomy
- Treatment with hydrea: Yes versus No versus Unknown
- Treatment with ruxolitinib: Yes versus No versus Unknown

Transplant-related:

- Graft sources: PBSC vs CBU vs BM
- Graft sources for haplos: Haplo PBSC vs haplo marrow
- Recipient CMV status: positive/negative
- Donor CMV status: positive/negative
- Acute GVHD: yes/no
- Acute GVHD grade: continuos
- Chronic GVHD: yes/no
- Chronic GVHD grade (NIH grade, or extensive/limited classification): continuos
- Preparative Regimen: NMA vs RIC vs MA
- Preparative regimen: TBI yes/no
- T cell depleted graft: yes/no
- Matching: degree of HLA match: Donor/Recipient
- Matching: degree of HLA match: Donor/Donor CBU (if double cord transplant)
- Donor sex: male versus female (for both units in double CBT)

- Transplant related mortality at 1 year, 2 years, and 5 years
- TBI dose ≤800 cGy: yes/no
- Platelet engraftment: days as continuous variable
- Neutrophil engraftment: Days as continuous variable

Methods:

Data extraction will be done from the CIBMTR database for all groups (graft sources) to produce descriptive tables of patient, disease, and transplant related factors. Chi-square tests for categorical and Kruskal-Wallis tests for continuous variables will be utilized. Kaplan Meier estimates will be used for generating OS and TRM probabilities. Variance will be estimated by Greenwood's formula. Type I error of 0.05 significance will be set. The log rank test will be used to compare survival curves. Time from day 0 of HCT to death will be done once data is available to generate incident rates. Patients will be censored at the time of last follow up

For the machine learning algorithms, the CIBMTR data will be supplemented by the data on MF patients from institutional database from the Mayo Clinic and the Cleveland Clinic given comprehensive sequencing data which would be available in the institutional databases. The clinical data will be combined with the genomic data and multiple ML techniques will be used to provide predictive models. This part of ML which requires institutional database will occur locally and would not happen at CIBMTR. The ML algorithms will be tested based on the C-statistic values and AUCs will be generated.

Random forest algorithms would generate algorithms via log-rank testing for censored data. For dichotomous outcomes, multiple ML algorithms will be used which will include bagging, decision tree, Bayesian networks, random forest, and K-nearest neighbor. The entire data generated for this study will be randomly divided into training and validation cohorts.

Above mentioned study by CIBMTR chronic leukemia working party (CK 18-01) by Nazha et al. utilized multiple ML algorithms to evaluate the MDS prognosis and is being presented at the Annual ASH meeting in San Diego in December 2018, and vouches for utility of CIBMTR database for developing models based on ML modeling.

Baseline characteristics of patients undergoing allo-HCT for MF, 2000-2016

Variable	N (%)
Number of patients	887
Number of centers	164
Patient-related	
Age, median (range)	56 (19-79)
Age, yrs	
18-29	10 (1)
30-39	36 (4)
40-49	169 (19)
50-59	377 (43)
60-69	265 (30)
>= 70	30 (3)
Gender	
Male	534 (60)
Female	353 (40)
Karnofsky score	
90-100	516 (58)
< 90	341 (38)
Missing	30 (3)
Disease-related	
Time from diagnosis to HCT	23 (1-522)
Time from diagnosis to HCT	
<6 months	125 (14)
6 - 12 months	190 (21)
>12 months	567 (64)
Missing	5 (<1)
Disease at diagnosis	
Myelofibrosis	737 (83)
Polycythemia vesa	57 (6)
Essential thrombocythemia	93 (10)
DIPSS prior to HCT	
Low	117 (13)
Intermediate-1	381 (43)
Intermediate-2	334 (38)
High	16 (2)
Missing	39 (4)
JAK2 mutation	
No	89 (10)
Yes	248 (28)
No tested	25 (3)

Variable	N (%)
Not available before 2007	326 (37)
Missing	199 (22)
Spleen status	
Normal	197 (22)
Splenomegaly	658 (74)
Unknown	32 (4)
Prior therapy	
No	210 (24)
Yes	667 (75)
Missing	10 (1)
Number of lines of pre-treatments	
0	210 (24)
1	339 (38)
2	166 (19)
3+	154 (17)
Missing	18 (2)
Transplant-related	
Year of transplant	
2000-2001	63 (7)
2002-2003	79 (9)
2004-2005	94 (11)
2006-2007	96 (11)
2008-2009	139 (16)
2010-2011	36 (4)
2012-2013	49 (6)
2014-2015	216 (24)
2016	115 (13)
Use of TBI	
No	704 (79)
Yes	177 (20)
Missing	6 (<1)
Conditioning regimen intensity	
MAC	434 (49)
RIC	378 (43)
NMA	60 (7)
TBD	6 (<1)
Missing	9 (1)
Donor type	
HLA-identical sibling	282 (32)
Twin	8 (<1)

Variable	N (%)
Other related	38 (4)
Well-matched unrelated	388 (44)
Partially-matched unrelated	106 (12)
Mis-matched unrelated	22 (2)
Multi-donor	3 (<1)
Unrelated (matching TBD)	15 (2)
Cord blood	25 (3)
Graft source	
Bone marrow	111 (13)
Peripheral blood	747 (84)
Cord blood	25 (3)
Missing	4 (<1)
GVHD prophylaxis	
Ex-vivo T-cell depletion	7 (<1)
CD34 selection	18 (2)
Post-CY + other(s)	27 (3)
TAC + MMF +- other(s) (except post-CY)	117 (13)
TAC + MTX +- other(s) (except MMF, post-CY)	354 (40)
TAC + other(s) (except MMF, MTX, post-CY)	38 (4)
TAC alone	14 (2)
CSA + MMF +- other(s) (except post-CY)	93 (10)
CSA + MTX +- other(s) (except MMF, post-CY)	168 (19)
CSA + other(s) (except MMF, MTX, post-CY)	11 (1)
CSA alone	18 (2)
Other(s)	10 (1)
Missing	12 (1)

Proposal: 1811-171

Title:
Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation

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Hypothesis:
Allogeneic hematopoietic cell transplantation (allo-HCT) improves survival of patients with chronic neutrophilic leukemia (CNL).

Specific aims:
Analyze outcomes of CNL patients who underwent allo-HCT.

Scientific impact:
CNL is a rare but aggressive myeloproliferative neoplasm (MPN) with no standard treatment options. Allo-HCT has been shown to be the only potentially curative treatment for CNL. This study will provide new information on outcomes of allo-HCT in CNL, when prospective studies are unlikely to happen due to rarity of this diagnosis. Results of this study will help establish a reference point for other systemic treatment options.

Scientific justification:
CNL is a rare disorder characterized by mature granulocytic proliferation in the blood and marrow, and infiltration into the organs resulting in hepatosplenomegaly. The Ph chromosome and its products are not detected in patients with chronic neutrophilic leukemia. Although these patients do not usually progress to AML, their survival is short and usually less than two years(1, 2). There is no standard treatment of CNL due to rarity of this diagnosis and most studies are limited to single case reports or series. Interferon-alfa and hydroxyurea have been tried with limited success with cytoreduction and improvement in splenomegaly(3, 4). However, these treatments are non-specific and most patient eventually progress with no good savage therapy options. Identification of pathognomic CSF3R mutations in CNL has led to development of molecularly targeted therapies like ruxolitinib(5). Ruxolitinib has been show to reduce neutrophilia, splenomegaly and CSF3R allele burden and durable responses lasting up to 11 months have been reported(1, 6). Progress in defining the role of ruxolitinib is now under-way through a multicenter Phase II trial evaluating its use in the treatment of CNL and aCML (clinicaltrials.gov ID: 02092324).
Given potential progressive neutrophilia and progressive blast phase, Allo-HCT has been attempted with variable success and currently the only potentially curative therapy for this CNL. Only single case reports available in literature with variable success. Teferri et al. reviewed 9 published cases of allo-HCT in CNL. Most cases were using myeloablative conditioning and matched sibling donor, resulting relapse free survival ranging 1 to 78 months(2). There is no published data on using cord or haploidentical donors for allo-HCT in this disease.
This study may provide largest experience of using allo-HCT in CNL and potentially define curative role of allo-HCT for this disease. It may also help optimize transplant strategy (conditioning regimen, donor type etc.) and estimate transplant related complications in CNL.

Patient eligibility population:
Inclusion:

- Adult patients (ages ≥18 years) who underwent first allo-HCT through 2017.
- Diagnosis of CNL

Exclusion:

- Patients with diagnosis of atypical chronic myeloid leukemia

Data requirements:
We will utilize the following CIBMTR data forms:

- 2400: Pre-Transplant Essential Data
- 2450: Post-Transplant Essential Data
- 2014: Myelodysplasia / Myeloproliferative Disorders Pre-HCT Data
- 2114: Myelodysplasia / Myeloproliferative Disorders Post-HCT Data

Outcomes:

- **Relapse/progression**: Progressive disease or recurrence of disease would be counted as an event. Treatment related death, defined as death without relapse or progression, is the competing event. Those who survive without recurrence or progression would be censored at the time of last contact.
- **Progression-free survival (PFS)**: Survival without recurrence or tumor progression starting following allo-HCT. Recurrence of progression of disease and death would be counted as events. Those who survive without recurrence or progression would be censored at the time of last contact.
- **Overall survival (OS)**: Time to death following allo-HCT. Death from any cause will be considered an event. Surviving patients will be censored at the time of last follow up.
- **Chronic GVHD**: Occurrence of limited and extensive chronic GVHD.
- **Non-relapse mortality (NRM)**: Death without relapse or progression, where relapse or progression would be competing risks. Those who survive without recurrence or progression would be censored at the time of last contact.
- **Neutrophil and platelet engraftment**: Neutrophil recovery defined as the first of 3 successive days with absolute neutrophil count (ANC) ≥500/μL after post-transplantation nadir. Platelet recovery defined as achieving platelet counts ≥20,000/μL for at least 7 days, unsupported by transfusion. For neutrophil and platelet recovery, death without the event is considered a competing risk.

Variables to be analyzed:

Patient-related:

- Age at transplant
- Gender: male or female
- Karnofsky performance status at transplant: < 90% vs. ≥ 90%
- HCT comorbidity index at transplant 0, 1, 2, and ≥ 3
- Cytomegalovirus (CMV) status
- ABO blood group

Donor-related:

- Degree of HLA match per Weisdorf criteria
- Graft source: Bone marrow vs PBSC
- Gender: male or female
- Cytomegalovirus (CMV) status
- ABO blood group
- Female parity: nulliparous vs ≥1 parity

Disease-related:

- Molecular makers
- Disease risk index
- Number of prior therapy (before transplant): 1 vs. 2 vs. ≥ 3
- Disease status at the time of transplant: complete remission vs stable disease vs progressive disease

Transplant-related:

- Year of transplant
- Conditioning regimen: MAC vs RIC
- Time from diagnosis to transplantation: months
- Graft versus host disease prophylaxis
- Graft type: bone marrow vs peripheral blood
- Cell dose (bone marrow, total nucleated cells or peripheral blood, CD34 cell dose)
- Donor-recipient CMV status: +/+ vs. +/- vs. -/+ vs. -/-
- Donor-recipient gender match: male-male vs. male-female vs. female-male vs. female-female
- Duration of follow up

Study Design:

This will be a retrospective analysis of the CIBMTR database. The goal of this study is to analyze clinical of CNL patients following their first allo-HCT. Descriptive tables of patient, disease-, and transplant-related factors will be created. The tables will list median and range for continuous variables and percent of total for categorical variables. Probabilities of relapse/progression, OS and PFS will be calculated using the Kaplan-Meier estimator, with the variance estimated by Greenwood's formula. Values for other endpoints will be generated using cumulative incidence estimates to account for competing risks. Multivariate analysis will be performed using Cox proportional hazards models for various outcomes. A stepwise model building approach will then be used to identify the significant risk factors associated with the outcomes. A backward stepwise model selection approach will be used to identify all significant risk factors. Factors which are significant at a 5% level will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested.

Non-CIBMTR Data Source:

For this study, we will utilize the CIBMTR Research Database. If there are insufficient number of CNL patients, we plan to apply for EBMT database access.

Conflicts of Interest:

□ Yes

✓ No

References:

1. Gotlib J, Maxson JE, George TI, Tyner JW. The new genetics of chronic neutrophilic leukemia and atypical CML: implications for diagnosis and treatment. Blood. 2013;122(10):1707-11.
2. Elliott MA, Tefferi A. Chronic neutrophilic leukemia: 2018 update on diagnosis, molecular genetics and management. Am J Hematol. 2018;93(4):578-87.
3. Kurzrock R, Bueso-Ramos CE, Kantarjian H, Freireich E, Tucker SL, Siciliano M, et al. BCR rearrangement-negative chronic myelogenous leukemia revisited. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2001;19(11):2915-26.
4. Elliott MA, Hanson CA, Dewald GW, Smoley SA, Lasho TL, Tefferi A. WHO-defined chronic neutrophilic leukemia: a long-term analysis of 12 cases and a critical review of the literature. Leukemia. 19. England2005. p. 313-7.
5. Maxson JE, Gotlib J, Pollyea DA, Fleischman AG, Agarwal A, Eide CA, et al. Oncogenic CSF3R mutations in chronic neutrophilic leukemia and atypical CML. The New England journal of medicine. 2013;368(19):1781-90.
6. Nooruddin Z, Miltgen N, Wei Q, Schowinsky J, Pan Z, Tobin J, et al. Changes in allele frequencies of CSF3R and SETBP1 mutations and evidence of clonal evolution in a chronic neutrophilic leukemia patient treated with ruxolitinib. Haematologica. 102. Italy2017. p. e207-e9.

Baseline characteristics of patients undergoing 1st allo-HCT for CNL, TED vs CRF, between 2000 and 2017

Characteristic	CRF only	TED only
Number of patients	10	20
Number of centers	10	19
Age, median (range), yrs	52 (42-72)	58 (33-72)
Age		
30-39	0	3 (15)
40-49	4 (40)	2 (10)
50-59	4 (40)	6 (30)
60-69	1 (10)	8 (40)
>= 70	1 (10)	1 (5)
Gender		
Male	5 (50)	10 (50)
Female	5 (50)	10 (50)
Karnofsky score		
90-100	5 (50)	15 (75)
< 90	4 (40)	5 (25)
Missing	1 (10)	0
Year of HCT		
2002-2003	2 (20)	0
2004-2005	1 (10)	0
2010-2011	2 (20)	4 (20)
2012-2013	1 (10)	6 (30)
2014-2015	0	3 (15)
2016-2017	4 (40)	7 (35)
Graft source		
Bone marrow	3 (30)	2 (10)
Peripheral blood	6 (60)	18 (90)
Cord blood	1 (10)	0
Donor type		
HLA-identical sibling	3 (30)	5 (25)
Other related	0	1 (5)
Well-matched unrelated	4 (40)	7 (35)
Partially-matched unrelated	1 (10)	2 (10)
Unrelated (matching TBD)	1 (10)	5 (25)
Cord blood	1 (10)	0
Conditioning regimen		

Characteristic	CRF only	TED only
MAC	7 (70)	11 (55)
RIC	3 (30)	9 (45)