Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA
San Antonio, TX
Thursday, February 22, 2024, 1:00 – 3:00 PM CST

Co-Chair:	**Ryotaro Nakamura, MD, City of Hope, Duarte, CA; Phone: 626-256-4673; Email: rnakamura@coh.org**
Co-Chair:	**Betul Oran, MD, MS, MD Anderson Cancer Center, Houston, TX; Phone: 713-145-3219; Email: boran@mdanderson.org**
Co-Chair:	**Mark Juckett, MD, University of Minnesota, Minneapolis, MN; E-mail: juck0001@umn.edu**
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Statistician:	**Charimar Santiago Parrilla, MPH, CIBMTR Statistical Center, Milwaukee, WI; E-mail: csantiago@mcw.edu**

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1. **Introduction**

   a. Minutes from February 2023 meeting (Attachment 1)

2. **Accrual summary** (Attachment 2)

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

   a. **CK17-01** Tamari R, McLornan DP, Ahn KW, Estrada-Merly N, Hernández-Boluda JC, Giralt S, Palmer J, Gale RP, DeFilipp Z, Marks DI, van der Poel M, Verdonck LF, Battiwalla M, Diaz MA, Gupta V, Ali H, Litzow MR, Lazarus HM, Gergis U, Bashey A, Liesveld J, Hashmi S, Pu JJ, Beitinjaneh A, Bredeson C, Rizzieri D, Savani BN, Abid MB, Ganguly S, Agrawal V, Ulrike Bacher V, Wirk B, Jain T, Cutler C, Aljurf M, Kindwall-Keller T, Kharfan-Dabaja MA, Hildebrandt GC, Pawarode A, Solh MM, Yared JA, Grunwald MR, Nathan S, Nishihori T, Seo S, Scott BL, Nakamura R, Oran B, Czerw T, Yakoub-Agha I, Saber W. A simple prognostic system in patients with myelofibrosis undergoing allogeneic stem cell transplantation: A CIBMTR/EBMT analysis***. Blood Advances. 2023 Aug 8; 7(15):3993-4002. doi:10.1182/bloodadvances.2023009886. Epub 2023 May 3. PMC10410129***.

   b. **CK20-01** Murthy GSG, Kim S, Estrada-Merly N, Abid MB, Aljurf M, Assal A, Badar T, Badawy SM, Ballen K, Beitinjaneh A, Cerny J, Chhabra S, DeFilipp Z, Dholaria B, Perez MAD, Farhan S, Freytes CO, Gale RP, Ganguly S, Gupta V, Grunwald MR, Hamad N, Hildebrandt GC, Inamoto Y, Jain T, Jamy O, Juckett M, Kalaycio M, Krem MM, Lazarus HM, Litzow M, Munker R, Murthy HS, Nathan S, Nishihori T, Ortí G, Patel SS, Van der Poel M, Rizzieri DA, Savani BN, Seo S, Solh M, Verdonck LF, Wirk B, Yared JA, Nakamura R, Oran B, Scott B, Saber W. Association between the choice of the conditioning regimen and outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis. ***Haematologica. 2023 Jul 1; 108(7):1900-1908. doi:10.3324/haematol.2022.281958. Epub 2023 Feb 14. PMC10316233.***

c. **CK21-01** Haploidentical Donor Transplantation versus Matched or Mismatched-unrelated Donor Allogeneic Blood or Bone Marrow Transplantation Outcomes in Patients with Myelofibrosis (T Jain/ Q Salas). ***Submitted.***

4. Studies in progress (Attachment 3)

a. **CK16-01b** Identification of germline predisposition mutations in young MDS patients (L Godley/ Q Salas). **Analysis**.
b. **CK22-01** Impact of somatic mutations on outcomes after allogeneic hematopoietic cell transplantation in patients with myelodysplastic syndrome with ring sideroblasts (MDS-RS) and MDS/myeloproliferative neoplasm with RS and thrombocytosis (MDS/MPN-RS-T) (S Arslan/ R Nakamura). **Protocol development**.
c. **CK22-02** Toxicity and survival of AML/MDS patients receiving allogeneic stem cell transplantation using reduced-intensity conditioning: A propensity score analysis (P Kongtim/ A Portuguese/ S Ciurea/ B Scott). **Protocol development**.
d. **CK23-01** Identifying the Optimal Graft-versus-Host Disease Regimen in Allogeneic Transplantation for Myelofibrosis (S Patel/ D Courier). **Protocol development**.
e. **CK23-02** The mutational landscape in Myelodysplastic Syndrome arising from Aplastic Anemia and its impact on Allogeneic Stem Cell Transplantation Outcomes (B Ball/ R Nakamura). **Protocol development**.
f. **GS19-02** Graft failure in MDS and acute leukemia patients after allogeneic stem cell transplantation receiving post-transplant cyclophosphamide (C Lynn Hickey/ R Romee/ C Cutler/ N Majhail). **Manuscript preparation**.

5. Future/proposed studies

a. **PROP 2310-19** Comparison of PTCY-Based Reduced Intensity Conditioning Regimens for Older Patients with AML and MDS (S Solomon/ L Bachier) (Attachment 4)
b. **PROP 2310-54; 2310-181; 2310-257** Outcomes of allogeneic hematopoietic stem cell transplantation in patients with DDX41-mutated myelodysplastic syndrome and acute myeloid leukemia (E Wong/ L Fox/ R Stubbins/ L Gowda/ S Seropian) (Attachment 5)
c. **PROP 2310-62** Revision of a Disease Risk Index in Patients with Hematologic Malignancies Undergoing Allogeneic Hematopoietic Cell Transplantation (H Kim/ V Ho) (Attachment 6)
d. **PROP 2310-66; 2310-150** Comparison of Reduced Intensity Conditioning Regimens for Haploidentical Donor Hematopoietic Cell Transplant with Post-Transplant Cyclophosphamide in patients with Acute Myeloid Leukemia or Myelodysplastic Syndromes (H Elmariah/ N Bejanyan/ S Arslan/ M Al Malki) (Attachment 7)
e. **PROP 2310-67; 2310-221** Identifying the Optimal Stem Cell Dosing for Peripheral Blood Stem Cell Transplantation with Post-Transplant Cyclophosphamide (H Elmariah/ N Bejanyan/ A Gandhi/ R Maziarz) (Attachment 8)
f. **PROP 2310-166** Predictive Factors and Outcomes of Patients who Experience Graft Failure After Allogeneic Stem Cell Transplant for Primary Myelofibrosis (A Law/ T Alfaro Moya) (Attachment 9)
g. **PROP 2310-183** Impact of Splenomegaly on Graft Failure in Chronic Leukemia Patients Using Post-Transplant Cyclophosphamide (K Minagawa/ S Mineishi) (Attachment 10)
h. **PROP 2310-180** Impact of Spleen Size Reduction Using JAK Inhibitors, Spleen Irradiation, or Splenectomy on Allogeneic Hematopoietic Cellular Transplantation Outcomes in Myelofibrosis (A Ali/ A Renteria) (Attachment 11)

Proposed studies; not accepted for consideration at this time

i. **PROP 2309-20** Outcomes of Allogeneic Stem Cell Transplant for Secondary Myeloid Malignancies in Aplastic Anemia Patients (N Hossain). *Dropped due to small sample size.*
j. **PROP 2310-110** Impact of Somatic Mutations on Outcomes of Allogeneic Blood or Marrow Transplantation in Atypical CML, Chronic Neutrophilic Leukemia, and MDS/MPN not Otherwise Specified (T Jain/ V Gupta). *Dropped due to small sample size.*
k. **PROP 2310-188** Outcomes of Haploidentical Allogeneic Hematopoietic Stem Cell Transplantation with Post-Transplant Cyclophosphamide for Myelofibrosis (X Bi/ U Gergis). *Dropped due to overlap with a current study.*

l. **PROP 2310-201** Effect of Different Condition Regimens on Disease Recurrence Following Allogenic Bone Marrow Transplant on Patients with Myelodysplastic Syndrome Based on Their Molecular International Prognostic Scoring System (Y Alnimer/ A Qasrawi) *Dropped due to supplemental/additional data needed.*
m. **PROP 2310-244** Post-Transplant Outcomes for Children, Adolescents and Young Adults with Advanced Phase Chronic Myeloid Leukemia (CML) (A Johnson/ T Lund). *Dropped due to small sample size.*
n. **PROP 2310-261** Outcomes of Allogeneic Stem Cell Transplant for Patients with High-Risk CLL (S Mirza/ T Nishihori). *Dropped due to small sample size.*

6. Other business

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

Co-Chair:	**Ryotaro Nakamura, MD, City of Hope**
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1. Introduction

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

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

2. Accrual summary

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

3. Presentations, Published or Submitted Papers

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

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

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

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

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

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

4. Studies in Progress

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

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

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

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

5. Future/Proposed Studies

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

6. Other Business

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

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

Working Assignments for Working Committee Leadership (March 2023)

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

Accrual Summary for the Chronic Leukemia Working Committee

Characteristics of recipients undergoing allogeneic HCT for MDS reported to the CIBMTR between 1995 and 2023

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	8844	1438	11111	7240
No. of centers	204	164	213	290
Age, median (range) - median (min-max)	61.7 (0.4-83.4)	44.6 (0.3-76.5)	58.6 (0.0-82.3)	53.3 (0.3-79.7)
Age, years - no. (%)				
< 10	272 (3.1)	125 (8.7)	327 (2.9)	310 (4.3)
10-19	309 (3.5)	124 (8.6)	449 (4.0)	414 (5.7)
20-29	250 (2.8)	150 (10.4)	380 (3.4)	477 (6.6)
30-39	387 (4.4)	204 (14.2)	643 (5.8)	700 (9.7)
40-49	777 (8.8)	275 (19.1)	1316 (11.8)	1217 (16.8)
50-59	1959 (22.2)	328 (22.8)	2972 (26.7)	1851 (25.6)
60-69	3704 (41.9)	208 (14.5)	3800 (34.2)	1995 (27.6)
>= 70	1186 (13.4)	24 (1.7)	1220 (11.0)	275 (3.8)
Not reported	0 (0.0)	0 (0.0)	4 (0.0)	1 (0.0)
Sex - no. (%)				
Male	5514 (62.3)	883 (61.4)	6699 (60.3)	4413 (61.0)
Female	3330 (37.7)	554 (38.5)	4412 (39.7)	2821 (39.0)
Not reported	0 (0.0)	1 (0.1)	0 (0.0)	6 (0.1)
Disease at diagnosis - no. (%)				
MDS unclassifiable, NOS	1452 (16.4)	167 (11.6)	2270 (20.4)	1435 (19.8)
Refractory anemia (RA)	810 (9.2)	300 (20.9)	793 (7.1)	733 (10.1)
Refractory anemia excess blasts (RAEB)	3849 (43.5)	613 (42.6)	4745 (42.7)	3037 (41.9)
Chronic myelomonocytic leukemia (CMML)	804 (9.1)	137 (9.5)	1193 (10.7)	618 (8.5)
Acquired idiopathic sideroblastic anemia (RARS)	331 (3.7)	40 (2.8)	248 (2.2)	144 (2.0)
Refactory anemia with multilineage dysplasia (RCMD)	1186 (13.4)	110 (7.6)	1513 (13.6)	962 (13.3)
Refactory anemia with dysplasia and ringed sideroblasts (RCMD/RS)	3 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
5q- syndrome	113 (1.3)	6 (0.4)	198 (1.8)	81 (1.1)
Other MDS, specified	275 (3.1)	59 (4.1)	91 (0.8)	168 (2.3)
Childhood myelodysplastic syndrome(Refractory cytopenia of childhood (RCC))	21 (0.2)	6 (0.4)	59 (0.5)	62 (0.9)
Graft source - no. (%)				
Bone marrow	1662 (18.8)	456 (31.7)	1771 (15.9)	1425 (19.7)
Peripheral blood	6589 (74.5)	894 (62.2)	8893 (80.0)	5556 (76.7)
Cord blood	569 (6.4)	88 (6.1)	336 (3.0)	157 (2.2)
Not reported	24 (0.3)	0 (0.0)	111 (1.0)	102 (1.4)
Donor type - no. (%)				
HLA-identical sibling	1956 (22.1)	586 (40.8)	3365 (30.3)	3010 (41.6)
Haplo	547 (6.2)	67 (4.7)	1095 (9.9)	265 (3.7)
Unrelated donor	5401 (61.1)	495 (34.4)	5755 (51.8)	3399 (46.9)
Cord blood	569 (6.4)	88 (6.1)	336 (3.0)	157 (2.2)
Other/missing	371 (4.2)	202 (14.0)	560 (5.0)	409 (5.6)
Year of transplant - no. (%)				
1995-1996	156 (1.8)	82 (5.7)	179 (1.6)	196 (2.7)
1997-1998	185 (2.1)	97 (6.7)	209 (1.9)	259 (3.6)
1999-2000	206 (2.3)	153 (10.6)	216 (1.9)	322 (4.4)
2001-2002	313 (3.5)	156 (10.8)	245 (2.2)	348 (4.8)
2003-2004	373 (4.2)	161 (11.2)	295 (2.7)	400 (5.5)
2005-2006	493 (5.6)	170 (11.8)	326 (2.9)	383 (5.3)
2007-2008	554 (6.3)	84 (5.8)	416 (3.7)	406 (5.6)
2009-2010	572 (6.5)	76 (5.3)	681 (6.1)	641 (8.9)
2011-2012	816 (9.2)	26 (1.8)	838 (7.5)	765 (10.6)
2013-2014	1273 (14.4)	124 (8.6)	789 (7.1)	644 (8.9)
2015-2016	1399 (15.8)	129 (9.0)	788 (7.1)	653 (9.0)
2017-2018	1332 (15.1)	100 (7.0)	1161 (10.4)	740 (10.2)
2019-2020	721 (8.2)	47 (3.3)	1835 (16.5)	605 (8.4)
2021-2022	355 (4.0)	16 (1.1)	2244 (20.2)	627 (8.7)
2023	96 (1.1)	17 (1.2)	889 (8.0)	251 (3.5)

Characteristics of recipients undergoing allogeneic HCT for myelofibrosis reported to the CIBMTR between 1995 and 2023

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	3362	432	1977	1859
No. of centers	145	96	149	188
Age, median (range) - median (min-max)	61.9 (0.6-80.8)	54.0 (1.7-73.5)	58.6 (0.5-79.2)	56.7 (1.5-75.5)
Age, years - no. (%)				
< 10	11 (0.3)	3 (0.7)	19 (1.0)	14 (0.8)
10-19	16 (0.5)	6 (1.4)	10 (0.5)	27 (1.5)
20-29	19 (0.6)	13 (3.0)	31 (1.6)	40 (2.2)
30-39	75 (2.2)	26 (6.0)	63 (3.2)	127 (6.8)
40-49	339 (10.1)	100 (23.1)	270 (13.7)	313 (16.8)
50-59	965 (28.7)	165 (38.2)	721 (36.5)	657 (35.3)
60-69	1521 (45.2)	115 (26.6)	759 (38.4)	635 (34.2)
>= 70	416 (12.4)	4 (0.9)	104 (5.3)	46 (2.5)
Sex - no. (%)				
Male	1971 (58.6)	276 (63.9)	1176 (59.5)	1153 (62.0)
Female	1391 (41.4)	156 (36.1)	801 (40.5)	706 (38.0)
Disease at diagnosis - no. (%)				
Polycythemia vera (PV)	445 (13.2)	45 (10.4)	246 (12.4)	170 (9.1)
Essential or primary thrombocythemia (ET)	560 (16.7)	45 (10.4)	293 (14.8)	222 (11.9)
Chronic myelofibrosis	2357 (70.1)	342 (79.2)	1438 (72.7)	1467 (78.9)
Graft source - no. (%)				
Bone marrow	231 (6.9)	80 (18.5)	166 (8.4)	224 (12.0)
Peripheral blood	3053 (90.8)	343 (79.4)	1774 (89.7)	1612 (86.7)
Cord blood	59 (1.8)	8 (1.9)	27 (1.4)	12 (0.6)
Not reported	19 (0.6)	1 (0.2)	10 (0.5)	11 (0.6)
Donor type - no. (%)				
HLA-identical sibling	736 (21.9)	169 (39.1)	810 (41.0)	774 (41.6)
Haplo	330 (9.8)	12 (2.8)	124 (6.3)	71 (3.8)
Unrelated donor	2129 (63.3)	213 (49.3)	926 (46.8)	913 (49.1)
Cord blood	59 (1.8)	8 (1.9)	27 (1.4)	12 (0.6)
Other/missing	108 (3.2)	30 (6.9)	90 (4.6)	89 (4.8)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Year of transplant - no. (%)				
1995-1996	16 (0.5)	8 (1.9)	12 (0.6)	19 (1.0)
1997-1998	24 (0.7)	11 (2.5)	15 (0.8)	36 (1.9)
1999-2000	31 (0.9)	22 (5.1)	21 (1.1)	44 (2.4)
2001-2002	53 (1.6)	21 (4.9)	35 (1.8)	82 (4.4)
2003-2004	56 (1.7)	32 (7.4)	51 (2.6)	100 (5.4)
2005-2006	83 (2.5)	43 (10.0)	81 (4.1)	102 (5.5)
2007-2008	154 (4.6)	41 (9.5)	112 (5.7)	120 (6.5)
2009-2010	153 (4.6)	33 (7.6)	221 (11.2)	192 (10.3)
2011-2012	37 (1.1)	5 (1.2)	336 (17.0)	176 (9.5)
2013-2014	187 (5.6)	44 (10.2)	258 (13.1)	155 (8.3)
2015-2016	276 (8.2)	44 (10.2)	276 (14.0)	118 (6.3)
2017-2018	555 (16.5)	79 (18.3)	160 (8.1)	187 (10.1)
2019-2020	724 (21.5)	35 (8.1)	138 (7.0)	181 (9.7)
2021-2022	685 (20.4)	9 (2.1)	169 (8.5)	240 (12.9)
2023	328 (9.8)	5 (1.2)	92 (4.7)	107 (5.8)

Characteristics of recipients undergoing allogeneic HCT for CML reported to the CIBMTR between 1995 and 2023

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	4374	3101	5650	8991
No. of centers	191	202	220	299
Age, median (range) - median (min-max)	40.0 (1.1-76.8)	35.6 (1.1-76.0)	43.0 (0.3-77.5)	37.1 (0.3-75.5)
Age, years - no. (%)				
< 10	92 (2.1)	71 (2.3)	81 (1.4)	214 (2.4)
10-19	390 (8.9)	326 (10.5)	345 (6.1)	716 (8.0)
20-29	630 (14.4)	650 (21.0)	658 (11.6)	1760 (19.6)
30-39	1075 (24.6)	927 (29.9)	1279 (22.6)	2628 (29.2)
40-49	1237 (28.3)	737 (23.8)	1579 (27.9)	2370 (26.4)
50-59	768 (17.6)	330 (10.6)	1181 (20.9)	1088 (12.1)
60-69	162 (3.7)	58 (1.9)	466 (8.2)	201 (2.2)
>= 70	20 (0.5)	1 (0.0)	52 (0.9)	7 (0.1)
Not reported	0 (0.0)	1 (0.0)	9 (0.2)	7 (0.1)
Sex - no. (%)				
Male	2548 (58.3)	1904 (61.4)	3361 (59.5)	5408 (60.1)
Female	1826 (41.7)	1197 (38.6)	2282 (40.4)	3546 (39.4)
Not reported	0 (0.0)	0 (0.0)	7 (0.1)	37 (0.4)
Graft source - no. (%)				
Bone marrow	2717 (62.1)	1822 (58.8)	2264 (40.1)	4777 (53.1)
Peripheral blood	1457 (33.3)	1200 (38.7)	3117 (55.2)	3800 (42.3)
Cord blood	196 (4.5)	74 (2.4)	179 (3.2)	112 (1.2)
Not reported	4 (0.1)	5 (0.2)	90 (1.6)	302 (3.4)
Donor type - no. (%)				
HLA-identical sibling	911 (20.8)	1622 (52.3)	3003 (53.2)	5645 (62.8)
Haplo	61 (1.4)	20 (0.6)	325 (5.8)	106 (1.2)
Unrelated donor	2951 (67.5)	997 (32.2)	1631 (28.9)	2557 (28.4)
Cord blood	196 (4.5)	74 (2.4)	179 (3.2)	112 (1.2)
Other/missing	255 (5.8)	388 (12.5)	512 (9.1)	571 (6.4)
Year of transplant - no. (%)				
1995-1996	736 (16.8)	516 (16.6)	682 (12.1)	1348 (15.0)
1997-1998	800 (18.3)	576 (18.6)	759 (13.4)	1744 (19.4)
1999-2000	723 (16.5)	667 (21.5)	644 (11.4)	1775 (19.7)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
2001-2002	394 (9.0)	419 (13.5)	298 (5.3)	1213 (13.5)
2003-2004	431 (9.9)	381 (12.3)	261 (4.6)	743 (8.3)
2005-2006	328 (7.5)	274 (8.8)	181 (3.2)	428 (4.8)
2007-2008	238 (5.4)	54 (1.7)	170 (3.0)	221 (2.5)
2009-2010	254 (5.8)	55 (1.8)	196 (3.5)	298 (3.3)
2011-2012	54 (1.2)	14 (0.5)	412 (7.3)	276 (3.1)
2013-2014	125 (2.9)	43 (1.4)	370 (6.5)	187 (2.1)
2015-2016	118 (2.7)	42 (1.4)	368 (6.5)	141 (1.6)
2017-2018	65 (1.5)	23 (0.7)	385 (6.8)	157 (1.7)
2019-2020	49 (1.1)	19 (0.6)	405 (7.2)	193 (2.1)
2021-2022	38 (0.9)	12 (0.4)	356 (6.3)	196 (2.2)
2023	21 (0.5)	6 (0.2)	163 (2.9)	71 (0.8)

Characteristics of recipients undergoing allogeneic HCT for CLL reported to the CIBMTR between 1995 and 2023

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	1538	410	2245	1579
No. of centers	129	89	146	153
Age, median (range) - median (min-max)	55.4 (11.7-75.2)	53.4 (1.7-71.0)	57.0 (7.3-80.4)	54.0 (3.9-75.1)
Age, years - no. (%)				
< 10	0 (0.0)	1 (0.2)	2 (0.1)	3 (0.2)
10-19	3 (0.2)	1 (0.2)	2 (0.1)	0 (0.0)
20-29	13 (0.8)	2 (0.5)	17 (0.8)	23 (1.5)
30-39	69 (4.5)	36 (8.8)	90 (4.0)	81 (5.1)
40-49	349 (22.7)	104 (25.4)	398 (17.7)	404 (25.6)
50-59	656 (42.7)	178 (43.4)	968 (43.1)	699 (44.3)
60-69	413 (26.9)	86 (21.0)	699 (31.1)	353 (22.4)
>= 70	35 (2.3)	2 (0.5)	69 (3.1)	16 (1.0)
Sex - no. (%)				
Male	1143 (74.3)	298 (72.7)	1621 (72.2)	1152 (73.0)
Female	394 (25.6)	112 (27.3)	623 (27.8)	425 (26.9)
Not reported	1 (0.1)	0 (0.0)	1 (0.0)	2 (0.1)
Disease at diagnosis - no. (%)				
Chronic lymphocytic leukemia, NOS	759 (49.3)	142 (34.6)	664 (29.6)	681 (43.1)
Chronic lymphocytic leukemia, B-cell	778 (50.6)	267 (65.1)	1574 (70.1)	892 (56.5)
Chronic lymphocytic leukemia, T-cell	1 (0.1)	1 (0.2)	7 (0.3)	6 (0.4)
Graft source - no. (%)				
Bone marrow	312 (20.3)	64 (15.6)	284 (12.7)	171 (10.8)
Peripheral blood	1138 (74.0)	327 (79.8)	1909 (85.0)	1355 (85.8)
Cord blood	86 (5.6)	18 (4.4)	45 (2.0)	18 (1.1)
Not reported	2 (0.1)	1 (0.2)	7 (0.3)	35 (2.2)
Donor type - no. (%)				
HLA-identical sibling	422 (27.4)	224 (54.6)	1097 (48.9)	822 (52.1)
Haplo	45 (2.9)	4 (1.0)	109 (4.9)	13 (0.8)
Unrelated donor	912 (59.3)	141 (34.4)	861 (38.4)	650 (41.2)
Cord blood	86 (5.6)	18 (4.4)	45 (2.0)	18 (1.1)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Other/missing	73 (4.7)	23 (5.6)	133 (5.9)	76 (4.8)
Year of transplant - no. (%)				
1995-1996	62 (4.0)	29 (7.1)	48 (2.1)	34 (2.2)
1997-1998	58 (3.8)	22 (5.4)	63 (2.8)	41 (2.6)
1999-2000	90 (5.9)	38 (9.3)	91 (4.1)	101 (6.4)
2001-2002	115 (7.5)	49 (12.0)	128 (5.7)	164 (10.4)
2003-2004	184 (12.0)	52 (12.7)	125 (5.6)	164 (10.4)
2005-2006	214 (13.9)	56 (13.7)	171 (7.6)	184 (11.7)
2007-2008	259 (16.8)	35 (8.5)	217 (9.7)	146 (9.2)
2009-2010	114 (7.4)	25 (6.1)	426 (19.0)	199 (12.6)
2011-2012	57 (3.7)	14 (3.4)	472 (21.0)	253 (16.0)
2013-2014	177 (11.5)	47 (11.5)	185 (8.2)	120 (7.6)
2015-2016	99 (6.4)	23 (5.6)	76 (3.4)	50 (3.2)
2017-2018	84 (5.5)	16 (3.9)	95 (4.2)	37 (2.3)
2019-2020	16 (1.0)	2 (0.5)	64 (2.9)	37 (2.3)
2021-2022	7 (0.5)	2 (0.5)	48 (2.1)	38 (2.4)
2023	2 (0.1)	0 (0.0)	36 (1.6)	11 (0.7)

Characteristics of recipients undergoing autologous HCT for CLL reported to the CIBMTR between 1995 and 2023

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	86	41	276	245
No. of centers	43	14	71	59
Age, median (range) - median (min-max)	51.9 (33.2-73.0)	49.8 (38.4-67.2)	53.2 (19.1-80.8)	52.1 (27.4-71.9)
Age, years - no. (%)				
10-19	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
20-29	0 (0.0)	0 (0.0)	2 (0.7)	4 (1.6)
30-39	12 (14.0)	3 (7.3)	14 (5.1)	12 (4.9)
40-49	26 (30.2)	18 (43.9)	81 (29.3)	77 (31.4)
50-59	26 (30.2)	18 (43.9)	115 (41.7)	114 (46.5)
60-69	20 (23.3)	2 (4.9)	56 (20.3)	37 (15.1)
>= 70	2 (2.3)	0 (0.0)	7 (2.5)	1 (0.4)
Sex - no. (%)				
Male	63 (73.3)	33 (80.5)	193 (69.9)	195 (79.6)
Female	23 (26.7)	8 (19.5)	83 (30.1)	49 (20.0)
Not reported	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Disease at diagnosis - no. (%)				
Chronic lymphocytic leukemia, NOS	23 (26.7)	24 (58.5)	87 (31.5)	48 (19.6)
Chronic lymphocytic leukemia, B-cell	62 (72.1)	17 (41.5)	184 (66.7)	196 (80.0)
Chronic lymphocytic leukemia, T-cell	1 (1.2)	0 (0.0)	5 (1.8)	1 (0.4)
Graft source - no. (%)				
Bone marrow	15 (17.4)	1 (2.4)	113 (40.9)	5 (2.0)
Peripheral blood	67 (77.9)	39 (95.1)	157 (56.9)	209 (85.3)
Not reported	4 (4.7)	1 (2.4)	6 (2.2)	31 (12.7)
Year of transplant - no. (%)				
1995-1996	15 (17.4)	3 (7.3)	43 (15.6)	14 (5.7)
1997-1998	27 (31.4)	28 (68.3)	54 (19.6)	36 (14.7)
1999-2000	18 (20.9)	6 (14.6)	73 (26.4)	90 (36.7)
2001-2002	6 (7.0)	2 (4.9)	36 (13.0)	40 (16.3)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
2003-2004	4 (4.7)	1 (2.4)	27 (9.8)	22 (9.0)
2005-2006	9 (10.5)	0 (0.0)	7 (2.5)	23 (9.4)
2007-2008	3 (3.5)	0 (0.0)	6 (2.2)	4 (1.6)
2009-2010	2 (2.3)	0 (0.0)	5 (1.8)	9 (3.7)
2011-2012	0 (0.0)	0 (0.0)	9 (3.3)	5 (2.0)
2013-2014	2 (2.3)	0 (0.0)	5 (1.8)	1 (0.4)
2015-2016	0 (0.0)	1 (2.4)	2 (0.7)	0 (0.0)
2017-2018	0 (0.0)	0 (0.0)	4 (1.4)	1 (0.4)
2019-2020	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
2021-2022	0 (0.0)	0 (0.0)	3 (1.1)	0 (0.0)
2023	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	13875	6701	3327
Source of data			
CRF	8696 (63)	3275 (49)	1825 (55)
TED	5179 (37)	3426 (51)	1502 (45)
Number of centers	241	214	303
Disease at transplant			
Other leukemia	1487 (11)	456 (7)	317 (10)
CML	3553 (26)	1171 (17)	1049 (32)
MDS	7232 (52)	3914 (58)	1638 (49)
MPN	1603 (12)	1160 (17)	323 (10)
MDS Disease status at transplant			
Early	1535 (21)	712 (18)	370 (23)
Advanced	4722 (65)	2956 (76)	921 (56)
Missing	975 (13)	246 (6)	347 (21)
Recipient age at transplant			
0-9 years	437 (3)	110 (2)	168 (5)
10-17 years	435 (3)	144 (2)	192 (6)
18-29 years	1001 (7)	304 (5)	324 (10)
30-39 years	1482 (11)	471 (7)	413 (12)
40-49 years	2178 (16)	764 (11)	578 (17)
50-59 years	3271 (24)	1408 (21)	688 (21)
60-69 years	3983 (29)	2518 (38)	755 (23)
70+ years	1088 (8)	982 (15)	209 (6)
Median (Range)	55 (0-83)	61 (1-82)	50 (1-81)
Recipient race			
White	12421 (92)	6044 (93)	2551 (89)
Black or African American	599 (4)	217 (3)	149 (5)
Asian	280 (2)	157 (2)	122 (4)
Native Hawaiian or other Pacific Islander	18 (<1)	12 (<1)	9 (<1)
American Indian or Alaska Native	42 (<1)	23 (<1)	15 (1)
Other	18 (<1)	7 (<1)	8 (<1)
More than one race	60 (<1)	27 (<1)	15 (1)
Unknown	437 (N/A)	214 (N/A)	458 (N/A)
Recipient ethnicity			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Hispanic or Latino	758 (7)	320 (5)	181 (7)
Non Hispanic or non-Latino	10176 (91)	5414 (93)	1684 (65)
Non-resident of the U.S.	275 (2)	87 (1)	718 (28)
Unknown	2666 (N/A)	880 (N/A)	744 (N/A)
Recipient sex			
Male	8422 (61)	4175 (62)	2047 (62)
Female	5453 (39)	2526 (38)	1280 (38)
Karnofsky score			
10-80	4973 (36)	2800 (42)	1013 (30)
90-100	8427 (61)	3747 (56)	2145 (64)
Missing	475 (3)	154 (2)	169 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	8 (<1)	29 (<1)	1 (<1)
4/6	104 (1)	33 (1)	16 (1)
5/6	1740 (13)	659 (11)	438 (14)
6/6	11731 (86)	5429 (88)	2581 (85)
Unknown	292 (N/A)	551 (N/A)	291 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	330 (2)	43 (1)	23 (1)
6/8	546 (4)	43 (1)	73 (3)
7/8	2386 (18)	711 (14)	402 (18)
8/8	10183 (76)	4419 (85)	1705 (77)
Unknown	430 (N/A)	1485 (N/A)	1124 (N/A)
HLA-DPB1 Match			
Double allele mismatch	3399 (28)	880 (22)	290 (24)
Single allele mismatch	6450 (54)	2072 (52)	609 (51)
Full allele matched	2161 (18)	1053 (26)	286 (24)
Unknown	1865 (N/A)	2696 (N/A)	2142 (N/A)
High resolution release score			
No	3588 (26)	6666 (99)	3146 (95)
Yes	10287 (74)	35 (1)	181 (5)
KIR typing available			
No	10528 (76)	6689 (>99)	3307 (99)
Yes	3347 (24)	12 (<1)	20 (1)
Graft type			
Marrow	4547 (33)	1391 (21)	1289 (39)
PBSC	9297 (67)	5259 (78)	2006 (60)
BM+PBSC	4 (<1)	4 (<1)	1 (<1)
PBSC+UCB	10 (<1)	44 (1)	2 (<1)
Others	17 (<1)	3 (<1)	29 (1)
Conditioning regimen			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Myeloablative	7947 (57)	2964 (44)	2018 (61)
RIC/Nonmyeloablative	5884 (42)	3717 (55)	1267 (38)
TBD	44 (<1)	20 (<1)	42 (1)
Donor age at donation			
To Be Determined/NA	217 (2)	262 (4)	77 (2)
0-9 years	0	9 (<1)	0
10-17 years	1 (<1)	5 (<1)	0
18-29 years	6623 (48)	3633 (54)	1337 (40)
30-39 years	3979 (29)	1716 (26)	1030 (31)
40-49 years	2328 (17)	812 (12)	673 (20)
50+ years	727 (5)	264 (4)	210 (6)
Median (Range)	30 (13-62)	29 (1-109)	33 (19-60)
Donor/Recipient CMV serostatus			
+/+	3240 (23)	1723 (26)	837 (25)
+/-	1729 (12)	960 (14)	375 (11)
-/+	4202 (30)	1786 (27)	957 (29)
-/-	4387 (32)	2028 (30)	961 (29)
CB - recipient +	7 (<1)	26 (<1)	2 (<1)
CB - recipient -	3 (<1)	19 (<1)	0
Missing	307 (2)	159 (2)	195 (6)
GvHD Prophylaxis			
No GvHD Prophylaxis	38 (<1)	23 (<1)	10 (<1)
TDEPLETION alone	23 (<1)	12 (<1)	5 (<1)
TDEPLETION +- other	260 (2)	64 (1)	81 (2)
CD34 select alone	61 (<1)	42 (1)	21 (1)
CD34 select +- other	110 (1)	62 (1)	17 (1)
Cyclophosphamide alone	60 (<1)	22 (<1)	13 (<1)
Cyclophosphamide +- others	1209 (9)	1372 (20)	251 (8)
FK506 + MMF +- others	1612 (12)	638 (10)	268 (8)
FK506 + MTX +- others(not MMF)	5795 (42)	2788 (42)	936 (28)
FK506 +- others(not MMF,MTX)	694 (5)	439 (7)	110 (3)
FK506 alone	289 (2)	130 (2)	54 (2)
CSA + MMF +- others(not FK506)	770 (6)	268 (4)	244 (7)
CSA + MTX +- others(not MMF,FK506)	2317 (17)	634 (9)	1041 (31)
CSA +- others(not FK506,MMF,MTX)	258 (2)	71 (1)	110 (3)
CSA alone	106 (1)	28 (<1)	90 (3)
Other GVHD Prophylaxis	224 (2)	82 (1)	41 (1)
Missing	49 (<1)	26 (<1)	35 (1)
Donor/Recipient sex match			
Male-Male	5925 (43)	2810 (42)	1369 (41)
Male-Female	3155 (23)	1467 (22)	682 (20)
Female-Male	2429 (18)	1228 (18)	650 (20)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Female-Female	2232 (16)	995 (15)	577 (17)
CB - recipient M	6 (<1)	32 (<1)	1 (<1)
CB - recipient F	4 (<1)	13 (<1)	1 (<1)
Missing	124 (1)	156 (2)	47 (1)
Year of transplant			
1986-1990	178 (1)	24 (<1)	40 (1)
1991-1995	863 (6)	185 (3)	313 (9)
1996-2000	1328 (10)	520 (8)	437 (13)
2001-2005	1376 (10)	265 (4)	496 (15)
2006-2010	2308 (17)	467 (7)	406 (12)
2011-2015	3411 (25)	933 (14)	570 (17)
2016-2020	2958 (21)	2183 (33)	707 (21)
2021-2023	1453 (10)	2124 (32)	358 (11)
Follow-up among survivors, Months			
N Eval	5871	3757	1511
Median (Range)	54 (0-384)	13 (0-334)	37 (0-385)

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	856	260	293
Source of data			
CRF	622 (73)	177 (68)	129 (44)
TED	234 (27)	83 (32)	164 (56)
Number of centers	123	80	112
Disease at transplant			
Other leukemia	98 (11)	30 (12)	37 (13)
CML	136 (16)	37 (14)	58 (20)
MDS	569 (66)	177 (68)	178 (61)
MPN	53 (6)	16 (6)	20 (7)
MDS Disease status at transplant			
Early	175 (31)	42 (24)	72 (40)
Advanced	341 (60)	120 (68)	84 (47)
Missing	53 (9)	15 (8)	22 (12)
Recipient age at transplant			
0-9 years	125 (15)	35 (13)	53 (18)
10-17 years	61 (7)	14 (5)	26 (9)
18-29 years	75 (9)	13 (5)	20 (7)
30-39 years	81 (9)	25 (10)	32 (11)
40-49 years	119 (14)	34 (13)	40 (14)
50-59 years	184 (21)	55 (21)	63 (22)
60-69 years	175 (20)	68 (26)	56 (19)
70+ years	36 (4)	16 (6)	3 (1)
Median (Range)	48 (0-80)	52 (1-76)	44 (0-73)
Recipient race			
White	600 (72)	194 (76)	187 (74)
Black or African American	148 (18)	37 (15)	35 (14)
Asian	55 (7)	20 (8)	19 (8)
Native Hawaiian or other Pacific Islander	9 (1)	0	2 (1)
American Indian or Alaska Native	4 (<1)	1 (<1)	2 (1)
Other	0	0	1 (<1)
More than one race	12 (1)	2 (1)	6 (2)
Unknown	28 (N/A)	6 (N/A)	41 (N/A)
Recipient ethnicity			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Hispanic or Latino	122 (15)	30 (12)	24 (8)
Non Hispanic or non-Latino	699 (85)	218 (87)	192 (67)
Non-resident of the U.S.	5 (1)	3 (1)	70 (24)
Unknown	30 (N/A)	9 (N/A)	7 (N/A)
Recipient sex			
Male	508 (59)	155 (60)	174 (59)
Female	348 (41)	105 (40)	119 (41)
Karnofsky score			
10-80	223 (26)	84 (32)	91 (31)
90-100	614 (72)	162 (62)	179 (61)
Missing	19 (2)	14 (5)	23 (8)
HLA-A B DRB1 groups - low resolution			
<=3/6	29 (4)	26 (13)	8 (3)
4/6	348 (45)	104 (51)	131 (53)
5/6	317 (41)	67 (33)	94 (38)
6/6	75 (10)	8 (4)	13 (5)
Unknown	87 (N/A)	55 (N/A)	47 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	432 (61)	123 (72)	129 (59)
6/8	166 (23)	28 (16)	60 (28)
7/8	78 (11)	18 (10)	22 (10)
8/8	38 (5)	3 (2)	7 (3)
Unknown	142 (N/A)	88 (N/A)	75 (N/A)
HLA-DPB1 Match			
Double allele mismatch	120 (40)	20 (35)	23 (37)
Single allele mismatch	150 (50)	31 (54)	32 (52)
Full allele matched	28 (9)	6 (11)	7 (11)
Unknown	558 (N/A)	203 (N/A)	231 (N/A)
High resolution release score			
No	679 (79)	256 (98)	291 (99)
Yes	177 (21)	4 (2)	2 (1)
KIR typing available			
No	697 (81)	260 (100)	292 (>99)
Yes	159 (19)	0	1 (<1)
Graft type			
UCB	784 (92)	215 (83)	270 (92)
PBSC+UCB	71 (8)	44 (17)	22 (8)
Others	1 (<1)	1 (<1)	1 (<1)
Number of cord units			
1	688 (80)	0	238 (82)
2	167 (20)	0	54 (18)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	1 (N/A)	260 (N/A)	1 (N/A)
Conditioning regimen			
Myeloablative	467 (55)	130 (50)	152 (52)
RIC/Nonmyeloablative	388 (45)	129 (50)	140 (48)
TBD	1 (<1)	1 (<1)	1 (<1)
Donor/Recipient CMV serostatus			
CB - recipient +	515 (60)	165 (63)	174 (59)
CB - recipient -	334 (39)	86 (33)	109 (37)
CB - recipient CMV unknown	7 (1)	9 (3)	10 (3)
GvHD Prophylaxis			
No GvHD Prophylaxis	2 (<1)	1 (<1)	1 (<1)
TDEPLETION +- other	1 (<1)	1 (<1)	0
CD34 select +- other	53 (6)	38 (15)	17 (6)
Cyclophosphamide +- others	1 (<1)	2 (1)	1 (<1)
FK506 + MMF +- others	281 (33)	85 (33)	56 (19)
FK506 + MTX +- others(not MMF)	26 (3)	5 (2)	10 (3)
FK506 +- others(not MMF,MTX)	34 (4)	11 (4)	14 (5)
FK506 alone	25 (3)	11 (4)	4 (1)
CSA + MMF +- others(not FK506)	357 (42)	87 (33)	143 (49)
CSA + MTX +- others(not MMF,FK506)	8 (1)	2 (1)	5 (2)
CSA +- others(not FK506,MMF,MTX)	26 (3)	10 (4)	27 (9)
CSA alone	9 (1)	1 (<1)	8 (3)
Other GVHD Prophylaxis	33 (4)	6 (2)	6 (2)
Missing	0	0	1 (<1)
Donor/Recipient sex match			
CB - recipient M	508 (59)	155 (60)	174 (59)
CB - recipient F	348 (41)	105 (40)	119 (41)
Year of transplant			
1996-2000	0	0	1 (<1)
2001-2005	16 (2)	7 (3)	4 (1)
2006-2010	249 (29)	70 (27)	77 (26)
2011-2015	363 (42)	74 (28)	117 (40)
2016-2020	178 (21)	81 (31)	65 (22)
2021-2023	50 (6)	28 (11)	29 (10)
Follow-up among survivors, Months			
N Eval	347	127	147
Median (Range)	60 (0-170)	45 (0-175)	37 (0-188)

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

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Number of patients	2681	423	209
Source of data			
CRF	1165 (43)	157 (37)	94 (45)
TED	1516 (57)	266 (63)	115 (55)
Number of centers	77	50	41
Disease at transplant			
Other leukemia	224 (8)	42 (10)	19 (9)
CML	359 (13)	50 (12)	26 (12)
MDS	1600 (60)	249 (59)	130 (62)
MPN	498 (19)	82 (19)	34 (16)
MDS Disease status at transplant			
Early	278 (17)	33 (13)	23 (18)
Advanced	1270 (79)	203 (82)	101 (78)
Missing	52 (3)	13 (5)	6 (5)
Recipient age at transplant			
0-9 years	59 (2)	13 (3)	3 (1)
10-17 years	76 (3)	6 (1)	6 (3)
18-29 years	108 (4)	17 (4)	6 (3)
30-39 years	126 (5)	23 (5)	12 (6)
40-49 years	278 (10)	37 (9)	20 (10)
50-59 years	725 (27)	112 (26)	56 (27)
60-69 years	1061 (40)	181 (43)	89 (43)
70+ years	248 (9)	34 (8)	17 (8)
Median (Range)	60 (1-78)	60 (1-77)	60 (6-75)
Recipient race			
White	2187 (84)	319 (79)	176 (87)
Black or African American	248 (10)	51 (13)	16 (8)
Asian	121 (5)	28 (7)	9 (4)
Native Hawaiian or other Pacific Islander	11 (<1)	3 (1)	0
American Indian or Alaska Native	11 (<1)	3 (1)	1 (<1)
More than one race	17 (1)	1 (<1)	0
Unknown	86 (N/A)	18 (N/A)	7 (N/A)
Recipient ethnicity			
Hispanic or Latino	313 (12)	66 (16)	26 (13)

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
Non Hispanic or non-Latino	2308 (88)	345 (84)	176 (86)
Non-resident of the U.S.	13 (<1)	1 (<1)	3 (1)
Unknown	47 (N/A)	11 (N/A)	4 (N/A)
Recipient sex			
Male	1632 (61)	264 (62)	136 (65)
Female	1049 (39)	159 (38)	73 (35)
Karnofsky score			
10-80	1142 (43)	205 (48)	104 (50)
90-100	1460 (54)	203 (48)	95 (45)
Missing	79 (3)	15 (4)	10 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	608 (25)	74 (20)	50 (31)
4/6	164 (7)	35 (9)	14 (9)
5/6	35 (1)	9 (2)	5 (3)
6/6	1649 (67)	252 (68)	94 (58)
Unknown	225 (N/A)	53 (N/A)	46 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	739 (31)	97 (28)	57 (40)
6/8	25 (1)	14 (4)	3 (2)
7/8	27 (1)	3 (1)	1 (1)
8/8	1600 (67)	231 (67)	82 (57)
Unknown	290 (N/A)	78 (N/A)	66 (N/A)
HLA-DPB1 Match			
Double allele mismatch	1 (<1)	0	0
Single allele mismatch	619 (28)	63 (29)	36 (40)
Full allele matched	1556 (72)	156 (71)	55 (60)
Unknown	505 (N/A)	204 (N/A)	118 (N/A)
High resolution release score			
No	1255 (47)	418 (99)	207 (99)
Yes	1426 (53)	5 (1)	2 (1)
Graft type			
Marrow	420 (16)	51 (12)	34 (16)
PBSC	2244 (84)	367 (87)	175 (84)
UCB	0	2 (<1)	0
BM+PBSC	5 (<1)	0	0
BM+UCB	0	1 (<1)	0
Others	12 (<1)	2 (<1)	0
Conditioning regimen			
Myeloablative	1245 (46)	184 (43)	85 (41)
RIC/Nonmyeloablative	1433 (53)	239 (57)	123 (59)
TBD	3 (<1)	0	1 (<1)
Donor age at donation			

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
To Be Determined/NA	1 (<1)	1 (<1)	0
0-9 years	37 (1)	10 (2)	3 (1)
10-17 years	69 (3)	11 (3)	4 (2)
18-29 years	318 (12)	43 (10)	32 (15)
30-39 years	375 (14)	69 (16)	31 (15)
40-49 years	469 (17)	63 (15)	35 (17)
50+ years	1412 (53)	226 (53)	104 (50)
Median (Range)	51 (0-82)	52 (0-76)	50 (3-73)
Donor/Recipient CMV serostatus			
+/+	1056 (39)	176 (42)	65 (31)
+/-	312 (12)	35 (8)	26 (12)
-/+	639 (24)	109 (26)	58 (28)
-/-	643 (24)	96 (23)	57 (27)
CB - recipient +	0	3 (1)	0
Missing	31 (1)	4 (1)	3 (1)
GvHD Prophylaxis			
No GvHD Prophylaxis	8 (<1)	1 (<1)	0
TDEPLETION alone	8 (<1)	4 (1)	2 (1)
TDEPLETION +- other	7 (<1)	0	2 (1)
CD34 select alone	6 (<1)	8 (2)	0
CD34 select +- other	9 (<1)	3 (1)	0
Cyclophosphamide alone	22 (1)	2 (<1)	2 (1)
Cyclophosphamide +- others	1019 (38)	134 (32)	85 (41)
FK506 + MMF +- others	195 (7)	23 (5)	6 (3)
FK506 + MTX +- others(not MMF)	985 (37)	160 (38)	87 (42)
FK506 +- others(not MMF,MTX)	207 (8)	61 (14)	18 (9)
FK506 alone	18 (1)	4 (1)	0
CSA + MMF +- others(not FK506)	36 (1)	5 (1)	2 (1)
CSA + MTX +- others(not MMF,FK506)	108 (4)	12 (3)	1 (<1)
CSA +- others(not FK506,MMF,MTX)	1 (<1)	1 (<1)	0
CSA alone	9 (<1)	0	1 (<1)
Other GVHD Prophylaxis	27 (1)	2 (<1)	3 (1)
Missing	16 (<1)	3 (<1)	0
Donor/Recipient sex match			
Male-Male	936 (35)	156 (37)	80 (38)
Male-Female	546 (20)	79 (19)	38 (18)
Female-Male	693 (26)	105 (25)	56 (27)
Female-Female	503 (19)	79 (19)	35 (17)
CB - recipient M	0	2 (<1)	0
CB - recipient F	0	1 (<1)	0
Missing	3 (<1)	1 (<1)	0
Year of transplant			
2006-2010	148 (6)	19 (4)	14 (7)

	Samples Available for Recipient and Donor	Samples Available for Recipient Only	Samples Available for Donor Only
2011-2015	816 (30)	97 (23)	41 (20)
2016-2020	1123 (42)	192 (45)	96 (46)
2021-2023	594 (22)	115 (27)	58 (28)
Follow-up among survivors, Months			
N Eval	1545	247	129
Median (Range)	25 (0-150)	24 (0-124)	23 (0-148)

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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Chronic Leukemia Working Committee Members

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

RE: 2024 Studies in Progress Summary

CK16-01b Identification of germline predisposition mutations in young myelodysplastic syndrome patients (L Godley). The primary aims of the study are 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. As secondary aims the study compares clinical/mobilization characteristics in related donors with a germline mutation versus related donors without germline mutations and 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. A secondary analysis is currently in progress. The goal is to have the manuscript submitted by June 2024.

CK21-01 Haploidentical Donor Transplantation versus Matched or Mismatched-unrelated Donor Allogeneic Blood or Bone Marrow Transplantation Outcomes in Patients with Myelofibrosis (T Jain/ M Queralt Sala/V Gupta/ T Nishikori). The objectives of this study are to explore the impact of donor type on overall survival of patient undergoing BMT for myelofibrosis. Also, we will compare clinical outcomes i.e. non-relapse mortality, cumulative incidence of relapse, acute GVHD, chronic GVHD, time to engraftment and primary graft failure between haploidentical donor, matched sibling donor (MSD), matched unrelated donor (MUD) and mismatched unrelated donors (MMUD). This study is currently in manuscript preparation. The goal is to have the manuscript submitted by January 2024.

CK22-01 Impact of somatic mutations on outcomes after allogeneic hematopoietic cell transplantation in patients with myelodysplastic syndrome with ring sideroblasts (MDS-RS) and MDS/myeloproliferative neoplasm with RS and thrombocytosis (MDS/MPN-RS-T) (Shukaib Arslan/ Ryotaro Nakamura). The objectives of this study are to evaluate the outcome of patients with MDS-RS or MDS/MPD-RS-T who underwent allo-HCT and were registered in the Center for International Blood and Marrow Transplant Research (CIBMTR). In addition, the study aims to characterize the mutation profile in the MDS-RS or MDS and MPD-RS-T in patients who underwent allo-HCT and determine the incidence of high-risk mutations in this population and examine potential impact of somatic mutations on HCT outcomes adjusted for other clinical risk factors. This study is currently on protocol development.

CK22-02 Toxicity and survival of AML/MDS patients receiving allogeneic stem cell transplantation using reduced-intensity conditioning: A propensity score analysis. (Piyanuch Kongtim/ Andrew Portuguese/ Stefan Ciurea/ Bart Scott). The primary objective of this study is to compare progression free survival (PFS) between the 5 commonly used RIC/NMA conditioning regimens: Fludarabine and melphalan 100 mg/m2 (FM100), Fludarabine and melphalan 140 mg/m2 (FM140), Fludarabine and 2 days of busulfan (4 mg/kg/day PO or 3.2 mg/kg/day) (FB), Fludarabine, cyclophosphamide (14.5 mg/kg/d x 2 days) and 2Gy TBI (FCT), Fludarabine and 2GyTBI (FT). The secondary objectives are to compare other clinical outcomes by the type of regimen. This study is currently on protocol development.

CK23-01 Identifying the Optimal Graft-versus-Host Disease Regimen in Allogeneic Transplantation for Myelofibrosis (Sagar Patel/ Daniel Courier*).* The objectives of this study are to identify the optimal GVHD prophylaxis strategy in allogeneic HCT for primary and secondary Myelofibrosis (MF) as assessed by graft-versus-host disease-free/relapse-free survival (GFRS), acute and chronic GVHD incidence, and severity. The secondary objectives are to evaluate risk factors for engraftment failure after alloHCT that received ATG vs PTCy, evaluate GFRS, acute and chronic GVHD incidence and severity in MF patients with impaired renal function, assess the impact of pre-transplant ruxolitinib use on engraftment and GFRS and the impact of GVHD prophylaxis in HCT outcomes. This study is currently on protocol development.

CK23-02 The mutational landscape in Myelodysplastic Syndrome arising from Aplastic Anemia and its impact on Allogeneic Stem Cell Transplantation Outcomes (Brian Ball/ Ryotaro Nakamura). The objectives of this study are to describe the mutational landscape including mutational burden (allele fraction) of sMDS arising from Aplastic Anemia (AA) in patients who underwent HCt and determine the impact of IPSS, IPSS-R and IPSS-M risk prior to conditioning on post-transplant outcomes (GVHD incidence, relapse, non-relapse mortality, relapse-free survival, overall survival) in patients with sMDS arising from AA. This study is currently on protocol development.

GS19-02 Graft Failure in MDS and Acute Leukemia Patients After Allogeneic Stem Cell Transplantation Receiving Post Transplant Cyclophosphamide (C Hickey et al). This study aims to examine graft failure and overall survival of haploidentical with PTCy, matched donors with PTCy in the reduced intensity conditioning setting. The study is in manuscript preparation.

Field	Response
Proposal Number	2310-19-SOLOMON
Proposal Title	Comparison of PTCY-Based Reduced Intensity Conditioning Regimens for Older Patients with AML and MDS.
Key Words	post-transplant cyclophosphamide, reduced intensity conditioning regimens, AML, MDS
Principal Investigator #1: - First and last name, degree(s)	Scott R. Solomon, MD
Principal Investigator #1: - Email address	ssolomon@bmtga.com
Principal Investigator #1: - Institution name	Northside Hospital Cancer Institute
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Lizamarie Bachier, MD
Principal Investigator #2 (If applicable): - Email address:)	lbachier@bmtga.com
Principal Investigator #2 (If applicable): - Institution name:	Northside Hospital Cancer Institute
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Scott Solomon
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Co-PI of a planned CIBMTR analysis, IB22-01. Impact of HLA-DPB1 matching on survival following unrelated donor transplantation with post transplant cyclophosphamide for adults with hematologic malignancies.
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Morbidity, Recovery and Survivorship
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No

Field	Response
RESEARCH QUESTION:	Post-transplant cyclophosphamide (PTCY) is being utilized more frequently as GVHD prophylaxis following reduced intensity conditioning (RIC) allogeneic transplant, regardless of transplant type. Given that PTCY involves the use of high doses of cyclophosphamide post-transplant (100mg/kg total dose), it can add substantially to regimen-related toxicity (RRT) of RIC regimens, particularly those that combine fludarabine with higher doses of an alkylating agent such as melphalan or busulfan. Therefore, it will be important clinically to understand the balance between RRT and relapse protection for an individual conditioning regimen, when treating older AML or MDS patients with PTCY-based RIC allogeneic transplant.
RESEARCH HYPOTHESIS:	1. In the context of PTCY-based RIC allogeneic transplant, there will be significant differences in RRT between individual RIC regimens that will alter the balance between non-relapse mortality (NRM) and relapse protection. 2. The efficacy and tolerability of individual RIC regimens will differ when comparing PTCY-based RIC allogeneic transplant to that historically reported in the context of conventional GVHD prophylaxis strategies. 3. In this analysis, we aim to identify RIC regimens with the best RFS in the context of PTCY-based RIC allogeneic transplant for AML or MDS.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary endpoint: Relapse-free survival (RFS) – whole cohort and subgroup analysis in HLA-mismatched related and unrelated donor (HAPLO/MMUD) and HLA-matched sibling and unrelated donor (MSD/MUD) subsets. Other endpoints: (whole cohort and subgroup analysis in HAPLO/MMUD and MRD/MUD) - NRM - Relapse/progression - Overall survival (OS) - Current RFS (multi-state model). - GVHD-free, relapse-free survival (GRFS) - Acute GVHD - Chronic GVHD
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Given the rapid expansion of PTCY-based GVHD prophylaxis in both HLA-mismatched and HLA-matched transplants from related and unrelated donors, it is critical to understand the safety and efficacy of various non-myeoablative and reduced intensity conditioning regimens utilized in the context of PTCY-based allogeneic transplant for older AML and MDS patients. The goal will be to identify an optimal regimen in these patients.

SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Allogeneic hematopoietic cell transplantation (HCT) is a potentially curative therapy for patients with AML and MDS. An essential component of HCT is the pre-transplant conditioning regimen, which should facilitate engraftment and reduce or eliminate tumor cells. An understanding of the significant contribution of the graft-versus-leukemia effect and the high RRT of the commonly used conditioning regimens, led to the introduction of RIC strategies, with the aim of making HCT less toxic and more applicable to broader populations such as older or less fit patients. In general, studies suggest a correlation between increasing intensity and NRM and an inverse correlation with relapse incidence (RI). In general, lower intensity regimens have been classified as nonmyeloablative (NMAC) when they are felt to have minimal hematopoietic toxicity and do not require stem cell support. In contrast, RIC regimens, typically consisting of higher doses of alkylators or total body irradiation (TBI), lead to prolonged cytopenias and require stem cell support.(1) Although this distinction between NMAC and RIC has been a useful tool to analyze retrospective studies, it has significant limitations as regimens classified as RIC can vary widely in in the risks of RRT (e.g. mucosal toxicity), GVHD and NRM. Studies analyzing RIC regimens in more granular detail are clearly needed, in order to identify optimal regimens for disease-specific and patient-specific populations. A prior CIBMTR analysis by Eapen at al. examined the efficacy of specific high- and low-intensity conditioning regimens for AML and MDS patients.(2) This study analyzed 2,209 AML/MDS patients reported to CIBMTR from 2009-2014, of which 1,271 (58%) received myeloablative conditioning (Bu/Cy or Flu/Bu4). In this analysis, there was no differences in the risk of NRM and RI between Flu/Mel (RIC) and the myeloablative regimens, Bu/Cy or Flu/Bu4. Three-year RFS was identical with Flu/Mel (52%), Bu/Cy (44%) and Flu/Bu4 (44%). In contrast, RFS was significantly lower with Flu/Bu2 compared with Flu/Mel due to higher RI, with only a modest reduction in NRM. Of note, patients in this study represented a younger population with only 42% of transplants done for patients 60yrs or older, and no patients in this analysis received HIDT or PTCY. In the context of conventional GVHD prophylaxis, multiple publications have compared Flu/Mel vs. Flu/Bu2 for RIC MSD/MUD and have shown significantly higher NRM and lower RI with the use of Flu/Mel, leading to similar overall survival.(3-6) In contrast, there is much less published data analyzing the safety and efficacy of RIC regimens in the context of PTCY-based GVHD prophylaxis. PTCY has been the standard-of-care

Field	Response
	approach for GVHD prophylaxis for HID transplantation worldwide for over a decade, due to its ability to achieve reliable engraftment with acceptable rates of GVHD and NRM, which has led to a rapid expansion in the use of HIDs for HCT.(7,8) More recently, PTCY has been established as the preferred GVHD prophylaxis strategy for RIC allogeneic transplant from MSD and 7/8 or 8/8 MUD based on the recently published phase III randomized controlled trial, BMT-CTN 1703.(9) Therefore, studies evaluating safety and efficacy of various RIC regimens in the context of PTCY are clearly needed. Investigators from MD Anderson recently analyzed the impact of donor type and melphalan dose on RIC allogeneic transplant for lymphoma.(10) Of the 25 HID transplants, all received PTCY and 2/3 received Flu/Mel100 (the rest Flu/Mel140). In the MSD [63] and MUD [98], none received PTCy and 90% received Flu/Mel140. Three-year NRM was 31% for HID, 32% for MUD, 10% for MRD. Interestingly, the higher rate of NRM in HIDT-PTCY vs. MRD was despite the lower dose of melphalan and lower rates of acute and chronic GVHD, suggesting that optimal conditioning intensity needs to be considered in the context of donor type and GVHD prophylaxis strategy. In a letter to editor, Eastburg et al. analyzed 38 patients at 2 centers (median age 60, 29% prior allo) receiving PTCY-based HID transplant with PBSC grafts and Flu/Mel conditioning (95% Flu/Mel140). NRM was 21.1% at day +100 and 34.4% at one-year. In this analysis, high early NRM was highly correlated with CRS.(11) Our group has prospectively analyzed Flu/Mel140 RIC for PTCY-based HID transplantation in 25 patients with a median age of 57 years. In this study, overall NRM was 20% but was significantly higher for patients ≥ 65 years or those with a comorbidity index of ≥3.(12) We intend to study the following RIC regimen classes (Flu/Bu low and moderate dose regimens, Flu/Mel low and moderate dose regimens, and Flu/TBI low and moderate dose regimens): 1. Flu/Bu-low ≤6.4 mg/kg IV or ≤8 mg/kg PO (± TBI 200-300 cGy or Cy <50mg/kg) 2. Flu/Bu-mod >6.4 ≤9.6 mg/kg IV or >8 ≤12 mg/kg PO (± TBI 200-300 cGy or Cy <50mg/kg) 3. Flu/Mel-low <140mg/m2 (± TBI 200-300 cGy or Cy <50mg/kg) 4. Flu/Mel-mod 140mg/m2 (± TBI 200-300 cGy or Cy <50mg/kg) 5. Flu/TBI-low 200-300 cGy (± Cy <50mg/kg) 6. Flu/TBI-mod >300 - ≤800 cGy (± Cy <50mg/kg)

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion 1. Age ≥50 years 2. Diagnosis of either AML or MDS 3. Receiving a RIC or non-myeloablative allogeneic transplant from a matched sibling donor (MSD, 9/10 -10/10 HLA match), matched unrelated donor (MUD, 9/10 -10/10 HLA match) OR haploidentical donor (HID, 6/10 – 8/10 HLA match). 4. BM or PBSC graft source 5. Use of PTCY 6. Use of a calcineurin inhibitor (CNI) or sirolimus post-transplant 7. 2001-2023 Exclusion 1. In vivo T cell depletion with ATG or Campath 2. Ex vivo T cell depletion 3. Use of thiotepa 4. AML with ≥5% marrow blasts pre-transplant 5. MDS with ≥10% marrow blasts pre-transplant 6. Diagnosis of myelofibrosis.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Aim of study is to evaluate optimal RIC regimens for older patients with AML and MDS
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Variables analyzed: Patient-related - Age - Sex - KPS - HCT -CI - CMV status Disease-related - Disease - Pre-BMT status (CR, CRp/CRi, advanced) - DRI - Presence of measurable residual disease (MRD) Transplant-related - Donor type (MSD, MUD, MMUD, HAPLO) -Graft source (BM, PBSC) - Conditioning intensity (RIC vs. NMA) - Donor age - Sex match (F-to-M vs. other) - CMV serostatus donor-recipient (matched, mismatched) - GVHD prophylaxis (CNI vs. sirolimus) - Planned post-transplant maintenance
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A desc	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary o	N/A

Field	Response
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A

REFERENCES:	1. Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant. 2009;15(12):1628-1633. 2. Eapen M, Brazauskas R, Hemmer M, et al. Hematopoietic cell transplant for acute myeloid leukemia and myelodysplastic syndrome: conditioning regimen intensity. Blood Adv. 2018;2(16):2095-2103. 3. Baron F, Labopin M, Peniket A, et al. Reduced-intensity conditioning with fludarabine and busulfan versus fludarabine and melphalan for patients with acute myeloid leukemia: a report from the Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation. Cancer. 2015;121(7):1048-1055. 4. Kawamura K, Kako S, Mizuta S, et al. Comparison of Conditioning with Fludarabine/Busulfan and Fludarabine/Melphalan in Allogeneic Transplantation Recipients 50 Years or Older. Biol Blood Marrow Transplant. 2017;23(12):2079-2087. 5. Jain T, Alahdab F, Firwana B, Sonbol MB, Almader-Douglas D, Palmer J. Choosing a Reduced-Intensity Conditioning Regimen for Allogeneic Stem Cell Transplantation, Fludarabine/Busulfan versus Fludarabine Melphalan: A Systematic Review and Meta-Analysis. Biol Blood Marrow Transplant. 2019;25(4):728-733. 6. Yamashita T, Takami A, Uchida N, et al. Reduced-intensity stem cell transplantation for acute myeloid leukemia with fludarabine-based conditioning with intravenous busulfan versus melphalan. Bone Marrow Transplant. 2020;55(10):1955-1965. 7. D'Souza A, Lee S, Zhu X, Pasquini M. Current Use and Trends in Hematopoietic Cell Transplantation in the United States. Biol Blood Marrow Transplant. 2017;23(9):1417-1421. 8. Passweg JR, Baldomero H, Bader P, et al. Use of haploidentical stem cell transplantation continues to increase: the 2015 European Society for Blood and Marrow Transplant activity survey report. Bone Marrow Transplant. 2017;52(6):811-817. 9. Bolaños-Meade J, Hamadani M, Wu J, et al. Post-Transplantation Cyclophosphamide-Based Graft-versus-Host Disease Prophylaxis. New England Journal of Medicine. 2023;388(25):2338-2348. 10. Saini NY, Saliba RM, Rondon G, et al. Impact of Donor Type and Melphalan Dose on Allogeneic Transplantation Outcomes for Patients with Lymphoma. Biol Blood Marrow Transplant. 2019;25(7):1340-1346. 11. Eastburg L, Russler-Germain DA, DiPersio JF, et al. Increased early mortality after

Field	Response
	fludarabine and melphalan conditioning with peripheral blood grafts in haploidentical hematopoietic cell transplantation with post-transplant cyclophosphamide. Leuk Lymphoma. 2022;63(1):222-226. 12. Solh MM, Hinojosa G, Laporte J, et al. A Phase II Trial of Melphalan Based Reduced-Intensity Conditioning for Transplantation of T-Replete HLA-Haploidentical Peripheral Blood Stem Cells with Posttransplant Cyclophosphamide in Patients with Hematologic Malignancies. Adv Hematol. 2021;2021:8868142.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Table 1. Characteristics of patients who underwent a first allo-HCT for AML or MDS with PTCy-based GVHD prophylaxis, 2008-2022

Characteristic	Flu/Mel100	Flu/Mel140	Flu/TBI	Flu/Bu2	Flu/Bu4	Total
No. of patients	118	109	826	107	188	1348
No. of centers	30	39	101	29	39	116
Recipient age - no. (%)						
Median (min-max)	67.0 (53.6-78.4)	65.3 (50.9-73.3)	66.3 (50.0-78.6)	67.0 (50.4-77.3)	61.2 (50.1-75.3)	65.7 (50.0-78.6)
50-54	2 (1.7)	8 (7.3)	56 (6.8)	4 (3.7)	39 (20.7)	109 (8.1)
55-59	9 (7.6)	10 (9.2)	85 (10.3)	12 (11.2)	41 (21.8)	157 (11.6)
>=60	107 (90.7)	91 (83.5)	685 (82.9)	91 (85.0)	108 (57.4)	1082 (80.3)
Track - no. (%)						
CRF	118 (100)	109 (100)	826 (100)	107 (100)	188 (100)	1348 (100)
CCN region at transplant - no. (%)						
US	118 (100)	107 (98.2)	799 (96.7)	97 (90.7)	157 (83.5)	1278 (94.8)
Canada	0 (0.0)	0 (0.0)	0 (0.0)	5 (4.7)	9 (4.8)	14 (1.0)
Europe	0 (0.0)	0 (0.0)	5 (0.6)	0 (0.0)	10 (5.3)	15 (1.1)
Asia	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.9)	0 (0.0)	3 (0.2)
Australia/New Zealand	0 (0.0)	2 (1.8)	12 (1.5)	4 (3.7)	11 (5.9)	29 (2.2)
Central/South America	0 (0.0)	0 (0.0)	8 (1.0)	0 (0.0)	1 (0.5)	9 (0.7)
Sex - no. (%)						
Male	56 (47.5)	67 (61.5)	498 (60.3)	71 (66.4)	125 (66.5)	817 (60.6)
Female	62 (52.5)	42 (38.5)	328 (39.7)	36 (33.6)	63 (33.5)	531 (39.4)
Race - no. (%)						
White	97 (82.2)	93 (85.3)	647 (78.3)	96 (89.7)	162 (86.2)	1095 (81.2)
Black or African American	12 (10.2)	9 (8.3)	100 (12.1)	4 (3.7)	8 (4.3)	133 (9.9)
Asian	7 (5.9)	6 (5.5)	48 (5.8)	3 (2.8)	7 (3.7)	71 (5.3)

Characteristic	Flu/Mel100	Flu/Mel140	Flu/TBI	Flu/Bu2	Flu/Bu4	Total
Native Hawaiian or other Pacific Islander	1 (0.8)	0 (0.0)	7 (0.8)	1 (0.9)	2 (1.1)	11 (0.8)
American Indian or Alaska Native	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.5)	2 (0.1)
More than one race	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)
Not reported	1 (0.8)	1 (0.9)	21 (2.5)	3 (2.8)	8 (4.3)	34 (2.5)
Karnofsky score prior to HCT - no. (%)						
90-100%	65 (55.1)	64 (58.7)	359 (43.5)	52 (48.6)	113 (60.1)	653 (48.4)
< 90%	52 (44.1)	45 (41.3)	457 (55.3)	52 (48.6)	73 (38.8)	679 (50.4)
Not reported	1 (0.8)	0 (0.0)	10 (1.2)	3 (2.8)	2 (1.1)	16 (1.2)
HCT-CI - no. (%)						
0	9 (7.6)	11 (10.1)	131 (15.9)	18 (16.8)	37 (19.7)	206 (15.3)
1	20 (16.9)	25 (22.9)	127 (15.4)	10 (9.3)	30 (16.0)	212 (15.7)
2	20 (16.9)	8 (7.3)	128 (15.5)	18 (16.8)	27 (14.4)	201 (14.9)
3	24 (20.3)	26 (23.9)	132 (16.0)	22 (20.6)	36 (19.1)	240 (17.8)
4	12 (10.2)	13 (11.9)	102 (12.3)	7 (6.5)	20 (10.6)	154 (11.4)
5	12 (10.2)	10 (9.2)	83 (10.0)	11 (10.3)	19 (10.1)	135 (10.0)
6	8 (6.8)	7 (6.4)	49 (5.9)	10 (9.3)	11 (5.9)	85 (6.3)
7+	12 (10.2)	8 (7.3)	66 (8.0)	10 (9.3)	6 (3.2)	102 (7.6)
Missing/TBD	1 (0.8)	1 (0.9)	8 (1.0)	1 (0.9)	2 (1.1)	13 (1.0)
Primary disease - no. (%)						
Acute myelogenous leukemia or ANLL	67 (56.8)	63 (57.8)	530 (64.2)	72 (67.3)	128 (68.1)	860 (63.8)
Myelodysplastic/myeloprolifterative disorders (please classify all preleukemias)	51 (43.2)	46 (42.2)	296 (35.8)	35 (32.7)	60 (31.9)	488 (36.2)
Graft source - no. (%)						
Bone marrow	6 (5.1)	8 (7.3)	246 (29.8)	3 (2.8)	41 (21.8)	304 (22.6)
Peripheral blood	112 (94.9)	101 (92.7)	580 (70.2)	104 (97.2)	147 (78.2)	1044 (77.4)
Donor type - no. (%)						

Characteristic	Flu/Mel100	Flu/Mel140	Flu/TBI	Flu/Bu2	Flu/Bu4	Total
HLA-identical sibling	17 (14.4)	19 (17.4)	26 (3.1)	13 (12.1)	24 (12.8)	99 (7.3)
Haploidentical	14 (11.9)	22 (20.2)	675 (81.7)	26 (24.3)	91 (48.4)	828 (61.4)
Well-matched unrelated (8/8)	62 (52.5)	55 (50.5)	78 (9.4)	54 (50.5)	48 (25.5)	297 (22.0)
Partially-matched unrelated (7/8)	25 (21.2)	13 (11.9)	47 (5.7)	14 (13.1)	25 (13.3)	124 (9.2)
Conditioning regimen intensity - no. (%)						
MAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	188 (100)	188 (13.9)
RIC	118 (100)	109 (100)	109 (13.2)	106 (99.1)	0 (0.0)	442 (32.8)
NMA	0 (0.0)	0 (0.0)	717 (86.8)	1 (0.9)	0 (0.0)	718 (53.3)
Conditioning regimen - no. (%)						
MAC						
Flu/Bu/TT	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	32 (17.0)	32 (2.4)
Flu/Bu	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	156 (83.0)	156 (11.6)
RIC						
TBI/Cy/Flu	0 (0.0)	0 (0.0)	60 (7.3)	0 (0.0)	0 (0.0)	60 (4.5)
TBI/Flu	0 (0.0)	0 (0.0)	49 (5.9)	0 (0.0)	0 (0.0)	49 (3.6)
Flu/Bu	0 (0.0)	0 (0.0)	0 (0.0)	106 (99.1)	0 (0.0)	106 (7.9)
Flu/Mel	118 (100)	109 (100)	0 (0.0)	0 (0.0)	0 (0.0)	227 (16.8)
NMA						
TBI/Cy/Flu	0 (0.0)	0 (0.0)	706 (85.5)	0 (0.0)	0 (0.0)	706 (52.4)
TBI/Flu	0 (0.0)	0 (0.0)	11 (1.3)	0 (0.0)	0 (0.0)	11 (0.8)
Flu/Bu	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	1 (0.1)
Melphalan Dose - median	97.8	134.3	NE	NE	NE	
GVHD prophylaxis - no. (%)						
PTCy + Siro	17 (14.4)	10 (9.2)	81 (9.8)	1 (0.9)	16 (8.5)	125 (9.3)
PTCy + CNI (TAC or CSA)	101 (85.6)	99 (90.8)	745 (90.2)	106 (99.1)	172 (91.5)	1223 (90.7)
Year of current transplant - no. (%)						

Characteristic	Flu/Mel100	Flu/Mel140	Flu/TBI	Flu/Bu2	Flu/Bu4	Total
2008	0 (0.0)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.3)
2009	0 (0.0)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.3)
2010	0 (0.0)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	6 (0.4)
2011	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
2012	0 (0.0)	1 (0.9)	12 (1.5)	0 (0.0)	1 (0.5)	14 (1.0)
2013	0 (0.0)	1 (0.9)	37 (4.5)	0 (0.0)	2 (1.1)	40 (3.0)
2014	0 (0.0)	6 (5.5)	47 (5.7)	1 (0.9)	2 (1.1)	56 (4.2)
2015	8 (6.8)	16 (14.7)	68 (8.2)	17 (15.9)	13 (6.9)	122 (9.1)
2016	5 (4.2)	9 (8.3)	93 (11.3)	5 (4.7)	20 (10.6)	132 (9.8)
2017	8 (6.8)	8 (7.3)	93 (11.3)	4 (3.7)	29 (15.4)	142 (10.5)
2018	10 (8.5)	8 (7.3)	137 (16.6)	16 (15.0)	32 (17.0)	203 (15.1)
2019	11 (9.3)	19 (17.4)	126 (15.3)	10 (9.3)	36 (19.1)	202 (15.0)
2020	20 (16.9)	26 (23.9)	86 (10.4)	21 (19.6)	18 (9.6)	171 (12.7)
2021	28 (23.7)	9 (8.3)	77 (9.3)	20 (18.7)	20 (10.6)	154 (11.4)
2022	27 (22.9)	6 (5.5)	36 (4.4)	13 (12.1)	15 (8.0)	97 (7.2)
Median follow-up of survivors (range), months - median (range)	24.1 (3.7-140.4)	36.4 (3.6-97.1)	47.9 (0.0-154.7)	36.0 (3.0-99.7)	47.2 (0.0-98.1)	45.5 (0.0-154.7)

Study Title: Outcomes of allogeneic hematopoietic stem cell transplantation in patients with *DDX41*-mutated myelodysplastic syndrome and acute myeloid leukemia

Keywords: Germline mutations, inherited predispositions, myelodysplastic syndrome, acute myeloid leukemia, myeloid malignancy, transplantation, graft-versus-host disease

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Junior Investigator Status: RJS [Yes], EW and LF [No], LG and SS [No]

Underrepresented minority: No

Would you like assistance in identifying a senior mentor? No

Current ongoing work with CIBMTR: Multiple CIBMTR projects as co-PI

PI(s) with a CIBMTR WC study in manuscript preparation >6 months? No

Proposed working committee: Chronic leukemia

Please indicate if you have spoken with a scientific director or chair: No

Research Questions:

Patients with *DDX41*-mutated (*DDX41*-mt) myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) have unique biology and treatment responses as compared to *DDX41*-wild type (*DDX41*-wt) MDS/AML patients. Many patients with *DDX41*-mt MDS/AML require allogeneic hematopoietic stem cell transplantation (allo-HSCT) as part of their therapy. We will define predictors of efficacy and toxicity for patients with *DDX41*-mt MDS/AML undergoing allo-HSCT.

Research Hypothesis:

We hypothesize that patients with MDS/AML undergoing allo-HSCT who are *DDX41*-mt will have higher rates of non-relapse mortality (NRM) with standard transplantation approaches as compared to *DDX41*-wt MDS/AML patients.

Specific Objectives/Outcomes to be Investigated:

Primary outcome:

- Rate and predictors† of NRM for MDS/AML patients undergoing allo-HSCT who are *DDX41*-mt versus *DDX41*-wt‡

Secondary outcomes:

- Cumulative incidence and predictors† of severe acute or chronic graft-versus-host disease (GVHD) for *DDX41*-mt versus *DDX41*-wt patients
- Cumulative incidence and predictors† of relapse for *DDX41*-mt versus *DDX41*-wt patients
- All cause mortality for *DDX41*-mt versus *DDX41*-wt patients
- GVHD-free relapse-free survival (GRFS), relapse-free survival (RFS), and overall survival (OS) for *DDX41*-mt versus *DDX41*-wt patients

Exploratory outcomes‡:

- Genomic and transcriptional‖ correlates of NRM, RFS, and OS in *DDX41*-mt patients
- NRM, RFS, and OS in *DDX41*-mt patients with missense versus non-missense (truncating or start-loss) mutations
- For *DDX41*-mt patients with NRM or relapse and a related donor, *DDX41* and testing status of the related donor

† - Stratifications include: GVHD prophylaxis, conditioning intensity, and donor type.
‡ - If the *DDX41*-wt group is confounded by the presence of patients not tested for *DDX41*, we will use alternate control groups (*e.g.,* intermediate-risk MDS/AML).
ǂ - If sufficient data and/or samples available. We will not ask sites for additional data, though they may voluntarily update prior to analysis.
‖ - Whole-genome sequencing (WGS) and bulk RNA-sequencing on marrow aspirate.

Scientific Impact:

Previous small studies have suggested that *DDX41*-mt MDS/AML patients undergoing allo-HSCT have a higher risk of NRM with standard transplant approaches. Specifically, these smaller cohorts have suggested not using post-transplant cyclophosphamide (PTCy) based GVHD prophylaxis may lead to higher NRM in patients

with *DDX41*-mt MDS/AML. Validation of these findings in a large, real-world cohort has the potential to be practice changing, and these findings will establish the standard of care for *DDX41*-mt MDS/AML patients undergoing allo-HSCT.

Scientific Justification:

MDS and AML associated with germline *DDX41* mutations are a recently described subgroup of myeloid neoplasms recognized within the new International Consensus Classification (ICC) and World Health Organization (WHO) 2022 classification schemes.[1,2] Recent data suggests that approximately 5% of newly diagnosed MDS/AML patients can be found to have a germline *DDX41* mutation, and that the biology of *DDX41* mutated MDS/AML is unique, resulting in treatment responses that are not well characterized by current clinical prognostic models.[3] A loss of *DDX41* protein function within hematopoietic cells impairs RNA splicing, and may also result in aberrant inflammatory signalling through the STING pathway.[4-6] This results in an approximately 40% lifetime risk of development MDS or AML, with a median age at onset of 68 years.[3] Germline *DDX41* mutations are most commonly truncating or start-loss mutations and, upon progression to MDS/AML, acquisition of a second somatic mutation on the other *DDX41* allele is common, usually the recurrent R525H single-nucleotide variant.[3] Truncating and start-loss mutations identified by somatic tumor tissue testing have a high pre-test probability of being germline, likely in excess of 95%, and comprise approximately two-thirds of pathogenic *DDX41* variants.[3] Pathogenic *DDX41* single-nucleotide variants occurring in the germline context comprise about one-third of pathogenic *DDX41* variants, but may represent a weaker predisposing factor for the development of MDS/AML *vs.* truncating and start-loss variants, and the biology may vary between mutation type.[7]

Patients with *DDX41*-associated MDS/AML have specific pathologic and molecular features in comparison to other forms of *de novo* MDS/AML. Those with AML typically have lower blast counts with less proliferative disease, they usually have a normal karyotype, and also demonstrate lower mutational burden, often only having one or two pathogenic *DDX41* mutations alone.[3] Interestingly, prognosis in *DDX41*-mutated MDS/AML seems to be independent of described markers for other forms of *de novo* MDS/AML, with studies demonstrating that the International Prognostic Scoring System and *TP53*-mutational status do not correlate with outcomes.[3] Collectively, these features suggest that *DDX41*-mutated MDS/AML is a biologically and clinically unique subgroup, and that clinical findings from other genetic subgroups of MDS/AML cannot necessarily be generalized to patients with *DDX41*-mutated MDS/AML.

Treatment responses for patients with *DDX41*-mutated MDS/AML have been described in several single and multi-center cohort studies.[3,8-12] These have generally demonstrated that patients with *DDX41*-mutated MDS/AML have high rates of complete remission (CR) in response to standard MDS/AML therapies, including induction chemotherapy as well as hypomethylating agents with or without venetoclax. Despite these high upfront CR rates, durable remissions do not seem to be achieved with chemotherapy alone, and a consolidative allo-HSCT is generally considered the standard of care for eligible *DDX41*-mutated patients with MDS/AML.[3,8-12] While several of these

cohorts have described small subgroups of *DDX41*-mutated patients who received allo-HSCT, they were unable to comprehensively examine transplant outcomes for these patients. One study by Saygin *et al* did describe the outcomes of allo-HSCT in a small number (N=21) of *DDX41*-mutated patients.[12] Interestingly, they observed high rates of stage 3-4 acute GVHD (38%) in *DDX41*-mutated patients undergoing allo-HSCT, and this effect appeared to be ameliorated with the use of PTCy.[12] There is also a plausible biological rationale for the presence of higher rates of acute GVHD in *DDX41*-mutated patients, as the presence of a mutated germline *DDX41* allele in non-hematopoietic tissues could result in inflammatory dysregulation, which is a factor that can contribute to the development of GVHD.[13] While compelling, it is difficult to draw definitive conclusions from this relatively small study. A comprehensive description of the clinical outcomes of allo-HSCT in patients with *DDX41*-mutated MDS/AML is desperately needed to establish the standard of care for transplantation in this distinct genetic subgroup of MDS/AML.

Participant Selection Criteria:

Inclusion criteria:

- Presence of either a known pathogenic *DDX41* mutation or *DDX41*-wt status
- Pathologic diagnosis of MDS or AML of any subtype
- Adult patients (≥18 years old)
- Receipt of an allo-HSCT including any type of conditioning, donor, and GVHD prophylaxis

Exclusion criteria:

- Unavailable molecular data
- Presence of a *DDX41* variant of unclear significance (VUS), curated per the provisional Myeloid Malignancy Variant Curation Expert Committee guidelines, without an additional pathogenic mutation
- Lack of available data on conditioning regimen, GVHD prophylaxis, or follow-up

For this study, patients will not need to have proven germline status of the identified *DDX41* mutation. Proving germline status in this context would be prohibitive, and somatic *DDX41* mutations occurring in absence of a germline *DDX41* mutation on the other allele are relatively rare.

Does this study include pediatric patients? No

Data Requirements:

- Recipient baseline data: Age, gender, ethnicity, conditioning regimen, use of in-vivo T-cell depletion
- Hematopoietic cellular transplant infusion: Product type, CD34 cell count, produce processing/manipulation, date of product infusion
- AML pre-infusion data: Disease assessment at diagnosis, response to therapy prior to allo-HSCT, minimal residual disease status prior to HCT
- MDS pre-infusion data: Disease assessment at diagnosis, diagnostic studies including molecular markers performed, IPSS-R prognosis score, cytogenetics, receipt of therapy prior to allo-HSCT (Y/N) and response

- Post HSCT status: Hematopoietic recovery, chimerism, acute GVHD (onset, severity), chronic GVHD (onset, severity), subsequent cellular infusions (donor lymphocyte infusion or second transplant)
- AML post infusion: Best response to allo-HSCT, post-transplant therapy, current disease status (relapse)
- MDS post infusion: Best response to allo-HSCT, post-transplant therapy, current disease status (relapse)
- Pre-transplant essential data: Recipient information (age, sex), receipt of prior allo-HSCT, donor information, product type, related donor type, unrelated donor type, degree of match, donor age and sex, donor cytomegalovirus antibodies, clinical status of recipient prior to conditioning (functional status, recipient cytomegalovirus antibodies), pre-HSCT preparative regimen – intensity, use of radiation, drugs used, use of T-cell depleting agents or alemtuzumab, GVHD prophylaxis regimen
- Pre-TED disease classification: Primary diagnosis, AML classification, transformation from prior MDS/MPN, therapy related, predisposing conditions, cytogenetics, molecular features (including whether *DDX41* is mentioned and specifics of *DDX41* mutation/s present), status at transplantation including minimal residual disease, MDS subtype, predisposing condition (specifically *DDX41* associated familial MDS including the specifics of the *DDX41* mutation/s present), cytogenetics, transformation to AML, status at transplantation
- Post-transplant essential data: Alive/dead, subsequent allo-HSCT, donor lymphocyte infusion, hematopoietic recovery, acute GVHD onset and severity, veno-occlusive disease incidence, chimerism, disease response, relapse or progression post infusion
- Recipient death data: Date of death, primary cause of death, contributing cause of death
- Subsequent neoplasms: Hematologic malignancy, solid tumors, date of diagnosis, donor derived

Patient reported outcome requirements:
Not required

Machine learning:
Not applicable

Sample requirements:
If available, diagnostic bone marrow aspirate from *DDX41*-mt patients with ≥10% blast cells will be obtained and used to perform WGS and bulk RNA-seq.

Non-CIBMTR Data Source:
Not applicable

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Conflicts of Interest:
No COI relevant to this study

Other COI for RJS:
Honoraria: AbbVie, Jazz Pharmaceuticals, Pfizer, Takeda
Advisory Board: AbbVie
Research Funding: Jazz Pharmaceuticals

Table 1. Characteristics of patients undergoing a 1st allo HCT for AML with a known pathogenic DDX41 mutation or DDX41-wt status, 2008-2022

Characteristic	DDX41 not detected	DDX41 detected	Total
No. of patients	48099	218	48317
No. of centers	391	67	391
Recipient age - no. (%)			
Median (min-max)	55.1 (18.0-87.8)	64.1 (26.4-76.6)	55.1 (18.0-87.8)
18-29	4983 (10.4)	1 (0.5)	4984 (10.3)
30-39	5472 (11.4)	4 (1.8)	5476 (11.3)
40-49	7813 (16.2)	15 (6.9)	7828 (16.2)
50-59	12472 (25.9)	50 (22.9)	12522 (25.9)
60-69	14050 (29.2)	107 (49.1)	14157 (29.3)
>=70	3309 (6.9)	41 (18.8)	3350 (6.9)
Track - no. (%)			
TED	37193 (77.3)	176 (80.7)	37369 (77.3)
CRF	10586 (22.0)	42 (19.3)	10628 (22.0)
Not reported	320 (0.7)	0 (0.0)	320 (0.7)
CCN region at transplant - no. (%)			
US	33483 (69.6)	197 (90.4)	33680 (69.7)
Canada	2688 (5.6)	6 (2.8)	2694 (5.6)
Europe	5313 (11.0)	1 (0.5)	5314 (11.0)
Asia	1960 (4.1)	0 (0.0)	1960 (4.1)
Australia/New Zealand	2091 (4.3)	14 (6.4)	2105 (4.4)
Mideast/Africa	1034 (2.1)	0 (0.0)	1034 (2.1)
Central/South America	1530 (3.2)	0 (0.0)	1530 (3.2)
Sex - no. (%)			
Male	25732 (53.5)	162 (74.3)	25894 (53.6)
Female	22367 (46.5)	56 (25.7)	22423 (46.4)
Race - no. (%)			
White	34653 (72.0)	180 (82.6)	34833 (72.1)
Black or African American	2246 (4.7)	13 (6.0)	2259 (4.7)
Asian	3321 (6.9)	5 (2.3)	3326 (6.9)
Native Hawaiian or other Pacific Islander	158 (0.3)	1 (0.5)	159 (0.3)
American Indian or Alaska Native	146 (0.3)	0 (0.0)	146 (0.3)
More than one race	241 (0.5)	0 (0.0)	241 (0.5)
Not reported	7334 (15.2)	19 (8.7)	7353 (15.2)
Karnofsky score prior to HCT - no. (%)			
90-100%	29024 (60.3)	118 (54.1)	29142 (60.3)

Characteristic	DDX41 not detected	DDX41 detected	Total
< 90%	18089 (37.6)	94 (43.1)	18183 (37.6)
Not reported	986 (2.0)	6 (2.8)	992 (2.1)
HCT-CI - no. (%)			
0	13791 (28.7)	49 (22.5)	13840 (28.6)
1	7104 (14.8)	41 (18.8)	7145 (14.8)
2	6502 (13.5)	26 (11.9)	6528 (13.5)
3	7342 (15.3)	46 (21.1)	7388 (15.3)
4	4843 (10.1)	28 (12.8)	4871 (10.1)
5	2796 (5.8)	12 (5.5)	2808 (5.8)
6	1642 (3.4)	4 (1.8)	1646 (3.4)
7+	1603 (3.3)	12 (5.5)	1615 (3.3)
Missing/TBD	2476 (5.1)	0 (0.0)	2476 (5.1)
Specify ALL classification - no. (%)			
AML with BCR-ABL1	112 (0.2)	0 (0.0)	112 (0.2)
AML with mutated NPM1	2520 (5.2)	5 (2.3)	2525 (5.2)
AML with t(9;11) (p22;q23);MLLT 3-MLL:	410 (0.9)	1 (0.5)	411 (0.9)
AML with t(6;9) (p23;q24); DEK-NUP214:	208 (0.4)	0 (0.0)	208 (0.4)
AML with inv(3) (q21;q26.2) or t(3;3) (q21;q26.2);RPN1-EVI1:	210 (0.4)	0 (0.0)	210 (0.4)
AML (megakaryoblastic) with t(1;22) (p13;q13);RBM15-MKL1:	2 (0.0)	0 (0.0)	2 (0.0)
Therapy related AML (t-AML):	1449 (3.0)	8 (3.7)	1457 (3.0)
AML or ANLL	133 (0.3)	0 (0.0)	133 (0.3)
MDS	9 (0.0)	0 (0.0)	9 (0.0)
Myelodysplastic syndrome with single lineage dysplasia (MDS-SLD) (RA, RCUD_RA)	2 (0.0)	0 (0.0)	2 (0.0)
CMMoL Chronic myelomonocytic leukemia:	6 (0.0)	0 (0.0)	6 (0.0)
RARS Acquired idiopathic sideroblastic anemia:	3 (0.0)	0 (0.0)	3 (0.0)
MDS with excess blasts-1 (MDS-EB-1) (RAEB-1)	5 (0.0)	0 (0.0)	5 (0.0)
MDS with excess blasts-2 (MDS-EB-2 (RAEB-2)	38 (0.1)	0 (0.0)	38 (0.1)
Myelodysplastic syndrome with multilineage dysplasia (MDS-MLD) (RCMD)	6 (0.0)	0 (0.0)	6 (0.0)
AML/ANLL, not otherwise specified:	14258 (29.6)	114 (52.3)	14372 (29.7)
AML with t(8;21)(q22;q22)(AML1/ETO):	1158 (2.4)	0 (0.0)	1158 (2.4)
AML with abnormal BM eosinophils (CBFb/MYH11):	1332 (2.8)	5 (2.3)	1337 (2.8)
AML with 11q23 (MLL) abnormalities:	1518 (3.2)	1 (0.5)	1519 (3.1)
AML with multi-lineage dysplasia:	6365 (13.2)	49 (22.5)	6414 (13.3)
AML minimally differentiated (M0):	1391 (2.9)	6 (2.8)	1397 (2.9)
AML without maturation (M1):	3364 (7.0)	7 (3.2)	3371 (7.0)

Characteristic	DDX41 not detected	DDX41 detected	Total
AML with maturation (M2):	3441 (7.2)	11 (5.0)	3452 (7.1)
acute myelomonocytic leukemia (M4):	3781 (7.9)	2 (0.9)	3783 (7.8)
acute monoblastic/monocytic leukemia (M5):	3953 (8.2)	0 (0.0)	3953 (8.2)
acute erythroid leukemia (M6):	765 (1.6)	0 (0.0)	765 (1.6)
acute megakaryoblastic leukemia (M7):	183 (0.4)	0 (0.0)	183 (0.4)
acute basophilic leukemia:	6 (0.0)	0 (0.0)	6 (0.0)
acute panmyelosis with myelofibrosis:	75 (0.2)	0 (0.0)	75 (0.2)
myeloid sarcoma:	421 (0.9)	3 (1.4)	424 (0.9)
AML with biallelic mutations of CEBPA	257 (0.5)	1 (0.5)	258 (0.5)
AML with mutated RUNX1	718 (1.5)	5 (2.3)	723 (1.5)
Graft source - no. (%)			
Bone marrow	5655 (11.8)	24 (11.0)	5679 (11.8)
Peripheral blood	39969 (83.1)	187 (85.8)	40156 (83.1)
Umbilical cord blood	2467 (5.1)	7 (3.2)	2474 (5.1)
Other	1 (0.0)	0 (0.0)	1 (0.0)
Not reported	7 (0.0)	0 (0.0)	7 (0.0)
Donor type - no. (%)			
HLA-identical sibling	14166 (29.5)	29 (13.3)	14195 (29.4)
Twin	66 (0.1)	0 (0.0)	66 (0.1)
Haploidentical	5318 (11.1)	37 (17.0)	5355 (11.1)
Other related	607 (1.3)	0 (0.0)	607 (1.3)
Mismatched related - not otherwise specified	628 (1.3)	2 (0.9)	630 (1.3)
Well-matched unrelated (8/8)	16759 (34.8)	114 (52.3)	16873 (34.9)
Partially-matched unrelated (7/8)	3056 (6.4)	24 (11.0)	3080 (6.4)
Mis-matched unrelated (<= 6/8)	211 (0.4)	2 (0.9)	213 (0.4)
Multi-donor	231 (0.5)	0 (0.0)	231 (0.5)
Unrelated (matching TBD)	4085 (8.5)	3 (1.4)	4088 (8.5)
Cord blood	2467 (5.1)	7 (3.2)	2474 (5.1)
Not reported	505 (1.0)	0 (0.0)	505 (1.0)
Conditioning regimen intensity - no. (%)			
No drugs reported	57 (0.1)	0 (0.0)	57 (0.1)
MAC	26090 (54.2)	92 (42.2)	26182 (54.2)
RIC	15308 (31.8)	94 (43.1)	15402 (31.9)
NMA	4995 (10.4)	29 (13.3)	5024 (10.4)
TBD	1649 (3.4)	3 (1.4)	1652 (3.4)
Conditioning regimen - no. (%)			
No drugs reported			
None	57 (0.1)	0 (0.0)	57 (0.1)
MAC			

Characteristic	DDX41 not detected	DDX41 detected	Total
TBI/Cy	3186 (6.6)	1 (0.5)	3187 (6.6)
TBI/Cy/Flu	633 (1.3)	0 (0.0)	633 (1.3)
TBI/Cy/Flu/TT	269 (0.6)	2 (0.9)	271 (0.6)
TBI/Cy/TT	27 (0.1)	0 (0.0)	27 (0.1)
TBI/Cy/VP	159 (0.3)	0 (0.0)	159 (0.3)
TBI/VP	239 (0.5)	0 (0.0)	239 (0.5)
TBI/Mel	98 (0.2)	0 (0.0)	98 (0.2)
TBI/Flu	1897 (3.9)	6 (2.8)	1903 (3.9)
TBI/other(s)	131 (0.3)	1 (0.5)	132 (0.3)
Bu/Cy/Mel	6 (0.0)	0 (0.0)	6 (0.0)
Bu/Cy	8161 (17.0)	18 (8.3)	8179 (16.9)
Bu/Mel	217 (0.5)	0 (0.0)	217 (0.4)
Flu/Bu/TT	733 (1.5)	14 (6.4)	747 (1.5)
Flu/Bu	9720 (20.2)	43 (19.7)	9763 (20.2)
Flu/Mel/TT	381 (0.8)	6 (2.8)	387 (0.8)
Flu/Mel	2 (0.0)	0 (0.0)	2 (0.0)
Cy/Flu	23 (0.0)	0 (0.0)	23 (0.0)
Cy alone	1 (0.0)	0 (0.0)	1 (0.0)
Mel/other(s)	11 (0.0)	0 (0.0)	11 (0.0)
Other(s)	179 (0.4)	1 (0.5)	180 (0.4)
Missing	17 (0.0)	0 (0.0)	17 (0.0)
RIC			
TBI/Cy	61 (0.1)	1 (0.5)	62 (0.1)
TBI/Cy/Flu	872 (1.8)	3 (1.4)	875 (1.8)
TBI/Cy/Flu/TT	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Cy/VP	9 (0.0)	0 (0.0)	9 (0.0)
TBI/VP	10 (0.0)	0 (0.0)	10 (0.0)
TBI/Mel	1014 (2.1)	12 (5.5)	1026 (2.1)
TBI/Flu	1301 (2.7)	9 (4.1)	1310 (2.7)
TBI/other(s)	73 (0.2)	0 (0.0)	73 (0.2)
Bu/Cy	7 (0.0)	0 (0.0)	7 (0.0)
Bu/Mel	1 (0.0)	0 (0.0)	1 (0.0)
Flu/Bu	5379 (11.2)	18 (8.3)	5397 (11.2)
Flu/Mel	6522 (13.6)	51 (23.4)	6573 (13.6)
Cy/Flu	1 (0.0)	0 (0.0)	1 (0.0)
Mel alone	2 (0.0)	0 (0.0)	2 (0.0)
Mel/other(s)	1 (0.0)	0 (0.0)	1 (0.0)
Treosulfan	4 (0.0)	0 (0.0)	4 (0.0)
Other(s)	49 (0.1)	0 (0.0)	49 (0.1)

Characteristic	DDX41 not detected	DDX41 detected	Total
Missing	1 (0.0)	0 (0.0)	1 (0.0)
NMA			
TBI/Cy	23 (0.0)	0 (0.0)	23 (0.0)
TBI/Cy/Flu	3030 (6.3)	26 (11.9)	3056 (6.3)
TBI/Cy/VP	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Mel	2 (0.0)	0 (0.0)	2 (0.0)
TBI/Flu	1066 (2.2)	2 (0.9)	1068 (2.2)
TBI/other(s)	1 (0.0)	0 (0.0)	1 (0.0)
Bu/Cy	7 (0.0)	0 (0.0)	7 (0.0)
Flu/Bu/TT	1 (0.0)	0 (0.0)	1 (0.0)
Flu/Bu	46 (0.1)	0 (0.0)	46 (0.1)
Flu/Mel	19 (0.0)	0 (0.0)	19 (0.0)
Cy/Flu	344 (0.7)	1 (0.5)	345 (0.7)
Cy alone	12 (0.0)	0 (0.0)	12 (0.0)
Treosulfan	1 (0.0)	0 (0.0)	1 (0.0)
TLI	205 (0.4)	0 (0.0)	205 (0.4)
Other(s)	236 (0.5)	0 (0.0)	236 (0.5)
Missing	1 (0.0)	0 (0.0)	1 (0.0)
TBD			
TBI/Cy	90 (0.2)	0 (0.0)	90 (0.2)
TBI/Cy/Flu	17 (0.0)	0 (0.0)	17 (0.0)
TBI/Cy/VP	5 (0.0)	0 (0.0)	5 (0.0)
TBI/Mel	7 (0.0)	0 (0.0)	7 (0.0)
TBI/Flu	171 (0.4)	2 (0.9)	173 (0.4)
TBI/other(s)	97 (0.2)	0 (0.0)	97 (0.2)
Flu/Bu	250 (0.5)	0 (0.0)	250 (0.5)
Mel/other(s)	109 (0.2)	0 (0.0)	109 (0.2)
Treosulfan	424 (0.9)	0 (0.0)	424 (0.9)
Carb/other(s)	1 (0.0)	0 (0.0)	1 (0.0)
TLI	9 (0.0)	0 (0.0)	9 (0.0)
Other(s)	468 (1.0)	1 (0.5)	469 (1.0)
Missing	1 (0.0)	0 (0.0)	1 (0.0)
GVHD prophylaxis - no. (%)			
None	239 (0.5)	1 (0.5)	240 (0.5)
Ex-vivo T-cell depletion	287 (0.6)	0 (0.0)	287 (0.6)
CD34 selection	578 (1.2)	6 (2.8)	584 (1.2)
PtCy + other(s)	8457 (17.6)	93 (42.7)	8550 (17.7)
PtCy alone	297 (0.6)	1 (0.5)	298 (0.6)
TAC + MMF +- other(s) (except PtCy)	4706 (9.8)	17 (7.8)	4723 (9.8)

Characteristic	DDX41 not detected	DDX41 detected	Total
TAC + MTX +- other(s) (except MMF, PtCy)	15704 (32.6)	69 (31.7)	15773 (32.6)
TAC + other(s) (except MMF, MTX, PtCy)	2283 (4.7)	2 (0.9)	2285 (4.7)
TAC alone	1099 (2.3)	9 (4.1)	1108 (2.3)
CSA + MMF +- other(s) (except PtCy,TAC)	4027 (8.4)	6 (2.8)	4033 (8.3)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	7339 (15.3)	14 (6.4)	7353 (15.2)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	72 (0.1)	0 (0.0)	72 (0.1)
CSA alone	2212 (4.6)	0 (0.0)	2212 (4.6)
Other(s)	799 (1.7)	0 (0.0)	799 (1.7)
Year of current transplant - no. (%)			
2008	2561 (5.3)	0 (0.0)	2561 (5.3)
2009	2700 (5.6)	0 (0.0)	2700 (5.6)
2010	2984 (6.2)	0 (0.0)	2984 (6.2)
2011	3107 (6.5)	0 (0.0)	3107 (6.4)
2012	3155 (6.6)	0 (0.0)	3155 (6.5)
2013	3303 (6.9)	0 (0.0)	3303 (6.8)
2014	3176 (6.6)	0 (0.0)	3176 (6.6)
2015	3116 (6.5)	0 (0.0)	3116 (6.4)
2016	3235 (6.7)	1 (0.5)	3236 (6.7)
2017	3555 (7.4)	4 (1.8)	3559 (7.4)
2018	3519 (7.3)	24 (11.0)	3543 (7.3)
2019	3559 (7.4)	26 (11.9)	3585 (7.4)
2020	3314 (6.9)	40 (18.3)	3354 (6.9)
2021	3350 (7.0)	56 (25.7)	3406 (7.0)
2022	3465 (7.2)	67 (30.7)	3532 (7.3)
Median follow-up of survivors (range), months - median (range)	48.3 (0.0-2199.5)	13.8 (0.0-71.8)	48.3 (0.0-2199.5)

Table 2. Characteristics of patients undergoing a 1st allo HCT for MDS with a known pathogenic DDX41 mutation or DDX41-wt status, 2008-2022

Characteristic	DDX41 not detected	DDX41 detected	Total
No. of patients	17716	29	17745
No. of centers	348	21	348
Recipient age - no. (%)			
Median (min-max)	61.3 (18.0-83.4)	66.0 (50.8-76.9)	61.3 (18.0-83.4)
18-29	752 (4.2)	0 (0.0)	752 (4.2)
30-39	906 (5.1)	0 (0.0)	906 (5.1)

Characteristic	DDX41 not detected	DDX41 detected	Total
40-49	1842 (10.4)	0 (0.0)	1842 (10.4)
50-59	4497 (25.4)	6 (20.7)	4503 (25.4)
60-69	7584 (42.8)	14 (48.3)	7598 (42.8)
>=70	2135 (12.1)	9 (31.0)	2144 (12.1)
Track - no. (%)			
TED	11144 (62.9)	15 (51.7)	11159 (62.9)
CRF	6514 (36.8)	14 (48.3)	6528 (36.8)
Not reported	58 (0.3)	0 (0.0)	58 (0.3)
CCN region at transplant - no. (%)			
US	13028 (73.5)	27 (93.1)	13055 (73.6)
Canada	862 (4.9)	0 (0.0)	862 (4.9)
Europe	1824 (10.3)	0 (0.0)	1824 (10.3)
Asia	695 (3.9)	0 (0.0)	695 (3.9)
Australia/New Zealand	657 (3.7)	2 (6.9)	659 (3.7)
Mideast/Africa	169 (1.0)	0 (0.0)	169 (1.0)
Central/South America	481 (2.7)	0 (0.0)	481 (2.7)
Sex - no. (%)			
Male	11038 (62.3)	23 (79.3)	11061 (62.3)
Female	6678 (37.7)	6 (20.7)	6684 (37.7)
Race - no. (%)			
White	13611 (76.8)	26 (89.7)	13637 (76.8)
Black or African American	641 (3.6)	0 (0.0)	641 (3.6)
Asian	1063 (6.0)	1 (3.4)	1064 (6.0)
Native Hawaiian or other Pacific Islander	49 (0.3)	0 (0.0)	49 (0.3)
American Indian or Alaska Native	37 (0.2)	0 (0.0)	37 (0.2)
More than one race	67 (0.4)	0 (0.0)	67 (0.4)
Not reported	2248 (12.7)	2 (6.9)	2250 (12.7)
Karnofsky score prior to HCT - no. (%)			
90-100%	10146 (57.3)	20 (69.0)	10166 (57.3)
< 90%	7205 (40.7)	9 (31.0)	7214 (40.7)
Not reported	365 (2.1)	0 (0.0)	365 (2.1)
HCT-CI - no. (%)			
0	4441 (25.1)	12 (41.4)	4453 (25.1)
1	2351 (13.3)	5 (17.2)	2356 (13.3)
2	2218 (12.5)	4 (13.8)	2222 (12.5)
3	2915 (16.5)	3 (10.3)	2918 (16.4)
4	1837 (10.4)	4 (13.8)	1841 (10.4)
5	1194 (6.7)	0 (0.0)	1194 (6.7)
6	928 (5.2)	0 (0.0)	928 (5.2)

Characteristic	DDX41 not detected	DDX41 detected	Total
7+	978 (5.5)	1 (3.4)	979 (5.5)
Missing/TBD	854 (4.8)	0 (0.0)	854 (4.8)
Specify ALL classification - no. (%)			
Juvenile CML:	1 (0.0)	0 (0.0)	1 (0.0)
MDS	3244 (18.3)	3 (10.3)	3247 (18.3)
Myelodysplastic syndrome with single lineage dysplasia (MDS-SLD) (RA, RCUD_RA)	789 (4.5)	2 (6.9)	791 (4.5)
CMMoL Chronic myelomonocytic leukemia:	1753 (9.9)	1 (3.4)	1754 (9.9)
RARS Acquired idiopathic sideroblastic anemia:	490 (2.8)	0 (0.0)	490 (2.8)
Myeloproliferative neoplasm(MPN),unclassifiable,MPS,NOS:	6 (0.0)	0 (0.0)	6 (0.0)
MDS with excess blasts-1 (MDS-EB-1) (RAEB-1)	3590 (20.3)	6 (20.7)	3596 (20.3)
MDS with excess blasts-2 (MDS-EB-2 (RAEB-2)	4295 (24.2)	14 (48.3)	4309 (24.3)
Myelodysplastic syndrome with multilineage dysplasia (MDS-MLD) (RCMD)	3123 (17.6)	3 (10.3)	3126 (17.6)
5q-syndrome:	320 (1.8)	0 (0.0)	320 (1.8)
Childhood myelodysplastic syndrome(Refractory cytopenia of childhood (RCC)):	7 (0.0)	0 (0.0)	7 (0.0)
Myelodysplastic/myeloproliferative neoplasm,unclassifiable:	53 (0.3)	0 (0.0)	53 (0.3)
MDS / MPN with ring sideroblasts and thrombocytosis (MDS / MPN-RS-T)	8 (0.0)	0 (0.0)	8 (0.0)
MDS-RS with single lineage dysplasia (MDS-RS-SLD)	11 (0.1)	0 (0.0)	11 (0.1)
MDS-RS with multilineage dysplasia (MDS-RS-MLD)	26 (0.1)	0 (0.0)	26 (0.1)
Graft source - no. (%)			
Bone marrow	1856 (10.5)	1 (3.4)	1857 (10.5)
Peripheral blood	15262 (86.1)	27 (93.1)	15289 (86.2)
Umbilical cord blood	597 (3.4)	1 (3.4)	598 (3.4)
Other	1 (0.0)	0 (0.0)	1 (0.0)
Donor type - no. (%)			
HLA-identical sibling	4710 (26.6)	2 (6.9)	4712 (26.6)
Twin	22 (0.1)	0 (0.0)	22 (0.1)
Haploidentical	1820 (10.3)	3 (10.3)	1823 (10.3)
Other related	227 (1.3)	0 (0.0)	227 (1.3)
Mismatched related - not otherwise specified	192 (1.1)	0 (0.0)	192 (1.1)
Well-matched unrelated (8/8)	7350 (41.5)	18 (62.1)	7368 (41.5)
Partially-matched unrelated (7/8)	1140 (6.4)	3 (10.3)	1143 (6.4)
Mis-matched unrelated (<= 6/8)	52 (0.3)	0 (0.0)	52 (0.3)
Multi-donor	84 (0.5)	0 (0.0)	84 (0.5)
Unrelated (matching TBD)	1393 (7.9)	2 (6.9)	1395 (7.9)

Characteristic	DDX41 not detected	DDX41 detected	Total
Cord blood	597 (3.4)	1 (3.4)	598 (3.4)
Not reported	129 (0.7)	0 (0.0)	129 (0.7)
Conditioning regimen intensity - no. (%)			
No drugs reported	15 (0.1)	0 (0.0)	15 (0.1)
MAC	6978 (39.4)	9 (31.0)	6987 (39.4)
RIC	7992 (45.1)	14 (48.3)	8006 (45.1)
NMA	2001 (11.3)	6 (20.7)	2007 (11.3)
TBD	730 (4.1)	0 (0.0)	730 (4.1)
Conditioning regimen - no. (%)			
No drugs reported			
None	15 (0.1)	0 (0.0)	15 (0.1)
MAC			
TBI/Cy	381 (2.2)	0 (0.0)	381 (2.1)
TBI/Cy/Flu	96 (0.5)	0 (0.0)	96 (0.5)
TBI/Cy/Flu/TT	67 (0.4)	0 (0.0)	67 (0.4)
TBI/Cy/TT	3 (0.0)	0 (0.0)	3 (0.0)
TBI/Cy/VP	1 (0.0)	0 (0.0)	1 (0.0)
TBI/VP	3 (0.0)	0 (0.0)	3 (0.0)
TBI/Mel	14 (0.1)	1 (3.4)	15 (0.1)
TBI/Flu	412 (2.3)	0 (0.0)	412 (2.3)
TBI/other(s)	16 (0.1)	0 (0.0)	16 (0.1)
Bu/Cy	2063 (11.6)	1 (3.4)	2064 (11.6)
Bu/Mel	43 (0.2)	0 (0.0)	43 (0.2)
Flu/Bu/TT	289 (1.6)	1 (3.4)	290 (1.6)
Flu/Bu	3401 (19.2)	6 (20.7)	3407 (19.2)
Flu/Mel/TT	126 (0.7)	0 (0.0)	126 (0.7)
Cy/Flu	5 (0.0)	0 (0.0)	5 (0.0)
Cy alone	1 (0.0)	0 (0.0)	1 (0.0)
Mel/other(s)	2 (0.0)	0 (0.0)	2 (0.0)
Other(s)	51 (0.3)	0 (0.0)	51 (0.3)
None	1 (0.0)	0 (0.0)	1 (0.0)
Missing	3 (0.0)	0 (0.0)	3 (0.0)
RIC			
TBI/Cy	17 (0.1)	0 (0.0)	17 (0.1)
TBI/Cy/Flu	318 (1.8)	1 (3.4)	319 (1.8)
TBI/VP	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Mel	413 (2.3)	0 (0.0)	413 (2.3)
TBI/Flu	832 (4.7)	1 (3.4)	833 (4.7)
TBI/other(s)	38 (0.2)	0 (0.0)	38 (0.2)

Characteristic	DDX41 not detected	DDX41 detected	Total
Bu/Cy	2 (0.0)	0 (0.0)	2 (0.0)
Flu/Bu	2981 (16.8)	4 (13.8)	2985 (16.8)
Flu/Mel	3359 (19.0)	8 (27.6)	3367 (19.0)
BEAM	3 (0.0)	0 (0.0)	3 (0.0)
Mel alone	1 (0.0)	0 (0.0)	1 (0.0)
Mel/other(s)	1 (0.0)	0 (0.0)	1 (0.0)
Treosulfan	1 (0.0)	0 (0.0)	1 (0.0)
TLI	1 (0.0)	0 (0.0)	1 (0.0)
Other(s)	24 (0.1)	0 (0.0)	24 (0.1)
NMA			
TBI/Cy	14 (0.1)	1 (3.4)	15 (0.1)
TBI/Cy/Flu	1249 (7.1)	5 (17.2)	1254 (7.1)
TBI/Mel	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Flu	300 (1.7)	0 (0.0)	300 (1.7)
Bu/Cy	5 (0.0)	0 (0.0)	5 (0.0)
Flu/Bu/TT	1 (0.0)	0 (0.0)	1 (0.0)
Flu/Bu	23 (0.1)	0 (0.0)	23 (0.1)
Flu/Mel	6 (0.0)	0 (0.0)	6 (0.0)
Cy/Flu	191 (1.1)	0 (0.0)	191 (1.1)
Cy alone	11 (0.1)	0 (0.0)	11 (0.1)
TLI	100 (0.6)	0 (0.0)	100 (0.6)
Other(s)	100 (0.6)	0 (0.0)	100 (0.6)
TBD			
TBI/Cy	8 (0.0)	0 (0.0)	8 (0.0)
TBI/Cy/Flu	5 (0.0)	0 (0.0)	5 (0.0)
TBI/VP	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Mel	5 (0.0)	0 (0.0)	5 (0.0)
TBI/Flu	43 (0.2)	0 (0.0)	43 (0.2)
TBI/other(s)	19 (0.1)	0 (0.0)	19 (0.1)
Flu/Bu	123 (0.7)	0 (0.0)	123 (0.7)
Mel/other(s)	39 (0.2)	0 (0.0)	39 (0.2)
Treosulfan	385 (2.2)	0 (0.0)	385 (2.2)
Carb/other(s)	1 (0.0)	0 (0.0)	1 (0.0)
TLI	4 (0.0)	0 (0.0)	4 (0.0)
Other(s)	92 (0.5)	0 (0.0)	92 (0.5)
Missing	5 (0.0)	0 (0.0)	5 (0.0)
GVHD prophylaxis - no. (%)			
None	70 (0.4)	0 (0.0)	70 (0.4)
Ex-vivo T-cell depletion	65 (0.4)	0 (0.0)	65 (0.4)

Characteristic	DDX41 not detected	DDX41 detected	Total
CD34 selection	194 (1.1)	0 (0.0)	194 (1.1)
PtCy + other(s)	3335 (18.8)	14 (48.3)	3349 (18.9)
PtCy alone	71 (0.4)	0 (0.0)	71 (0.4)
TAC + MMF +- other(s) (except PtCy)	2054 (11.6)	4 (13.8)	2058 (11.6)
TAC + MTX +- other(s) (except MMF, PtCy)	6207 (35.0)	10 (34.5)	6217 (35.0)
TAC + other(s) (except MMF, MTX, PtCy)	918 (5.2)	0 (0.0)	918 (5.2)
TAC alone	346 (2.0)	0 (0.0)	346 (1.9)
CSA + MMF +- other(s) (except PtCy,TAC)	1401 (7.9)	0 (0.0)	1401 (7.9)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	2100 (11.9)	1 (3.4)	2101 (11.8)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	29 (0.2)	0 (0.0)	29 (0.2)
CSA alone	626 (3.5)	0 (0.0)	626 (3.5)
Other(s)	300 (1.7)	0 (0.0)	300 (1.7)
Year of current transplant - no. (%)			
2008	551 (3.1)	0 (0.0)	551 (3.1)
2009	754 (4.3)	0 (0.0)	754 (4.2)
2010	847 (4.8)	0 (0.0)	847 (4.8)
2011	977 (5.5)	0 (0.0)	977 (5.5)
2012	1085 (6.1)	0 (0.0)	1085 (6.1)
2013	1172 (6.6)	0 (0.0)	1172 (6.6)
2014	1192 (6.7)	0 (0.0)	1192 (6.7)
2015	1208 (6.8)	0 (0.0)	1208 (6.8)
2016	1311 (7.4)	0 (0.0)	1311 (7.4)
2017	1473 (8.3)	0 (0.0)	1473 (8.3)
2018	1444 (8.2)	3 (10.3)	1447 (8.2)
2019	1537 (8.7)	2 (6.9)	1539 (8.7)
2020	1292 (7.3)	8 (27.6)	1300 (7.3)
2021	1394 (7.9)	9 (31.0)	1403 (7.9)
2022	1479 (8.3)	7 (24.1)	1486 (8.4)
Median follow-up of survivors (range), months - median (range)	48.5 (0.0-10861.4)	17.0 (3.3-48.6)	48.5 (0.0-10861.4)

Supplemental Table 1. Characteristics of patients undergoing a 1st allo HCT for AML or MDS with a known pathogenic DDX41 mutation or DDX41-wt status by track, 2008-2022

Characteristic	TED	CRF	Total
No. of patients	48528	17156	65684
No. of centers	390	271	399
Recipient age - no. (%)			

Characteristic	TED	CRF	Total
Median (min-max)	56.4 (18.0-83.5)	59.4 (18.0-87.8)	57.2 (18.0-87.8)
18-29	4362 (9.0)	1319 (7.7)	5681 (8.6)
30-39	4962 (10.2)	1354 (7.9)	6316 (9.6)
40-49	7466 (15.4)	2129 (12.4)	9595 (14.6)
50-59	12841 (26.5)	4081 (23.8)	16922 (25.8)
60-69	15286 (31.5)	6403 (37.3)	21689 (33.0)
>=70	3611 (7.4)	1870 (10.9)	5481 (8.3)
CCN region at transplant - no. (%)			
US	31414 (64.7)	15312 (89.3)	46726 (71.1)
Canada	3435 (7.1)	121 (0.7)	3556 (5.4)
Europe	6306 (13.0)	509 (3.0)	6815 (10.4)
Asia	2090 (4.3)	565 (3.3)	2655 (4.0)
Australia/New Zealand	2453 (5.1)	310 (1.8)	2763 (4.2)
Mideast/Africa	1064 (2.2)	97 (0.6)	1161 (1.8)
Central/South America	1766 (3.6)	242 (1.4)	2008 (3.1)
Sex - no. (%)			
Male	26810 (55.2)	9946 (58.0)	36756 (56.0)
Female	21718 (44.8)	7210 (42.0)	28928 (44.0)
Race - no. (%)			
White	34301 (70.7)	13957 (81.4)	48258 (73.5)
Black or African American	1797 (3.7)	1101 (6.4)	2898 (4.4)
Asian	3133 (6.5)	1255 (7.3)	4388 (6.7)
Native Hawaiian or other Pacific Islander	129 (0.3)	79 (0.5)	208 (0.3)
American Indian or Alaska Native	101 (0.2)	82 (0.5)	183 (0.3)
More than one race	192 (0.4)	115 (0.7)	307 (0.5)
Not reported	8875 (18.3)	567 (3.3)	9442 (14.4)
Karnofsky score prior to HCT - no. (%)			
90-100%	29389 (60.6)	9668 (56.4)	39057 (59.5)
< 90%	18034 (37.2)	7236 (42.2)	25270 (38.5)
Not reported	1105 (2.3)	252 (1.5)	1357 (2.1)
HCT-CI - no. (%)			
0	14083 (29.0)	4062 (23.7)	18145 (27.6)
1	7065 (14.6)	2389 (13.9)	9454 (14.4)
2	6441 (13.3)	2275 (13.3)	8716 (13.3)
3	7255 (15.0)	3033 (17.7)	10288 (15.7)
4	4729 (9.7)	1974 (11.5)	6703 (10.2)
5	2719 (5.6)	1280 (7.5)	3999 (6.1)
6	1716 (3.5)	856 (5.0)	2572 (3.9)
7+	1645 (3.4)	948 (5.5)	2593 (3.9)

Characteristic	TED	CRF	Total
Missing/TBD	2875 (5.9)	339 (2.0)	3214 (4.9)
Primary disease - no. (%)			
AML	37369 (77.0)	10628 (61.9)	47997 (73.1)
MDS	11159 (23.0)	6528 (38.1)	17687 (26.9)
Specify ALL classification - no. (%)			
AML with BCR-ABL1	97 (0.2)	15 (0.1)	112 (0.2)
AML with mutated NPM1	2195 (4.5)	330 (1.9)	2525 (3.8)
AML with t(9;11) (p22;q23);MLLT 3-MLL:	342 (0.7)	69 (0.4)	411 (0.6)
AML with t(6;9) (p23;q24); DEK-NUP214:	164 (0.3)	44 (0.3)	208 (0.3)
AML with inv(3) (q21;q26.2) or t(3;3) (q21;q26.2);RPN1-EVI1:	175 (0.4)	35 (0.2)	210 (0.3)
AML (megakaryoblastic) with t(1;22) (p13;q13);RBM15-MKL1:	2 (0.0)	0 (0.0)	2 (0.0)
Therapy related AML (t-AML):	1201 (2.5)	255 (1.5)	1456 (2.2)
AML or ANLL	122 (0.3)	2 (0.0)	124 (0.2)
Juvenile CML:	1 (0.0)	0 (0.0)	1 (0.0)
MDS	2046 (4.2)	1190 (6.9)	3236 (4.9)
Myelodysplastic syndrome with single lineage dysplasia (MDS-SLD) (RA, RCUD_RA)	522 (1.1)	270 (1.6)	792 (1.2)
CMMoL Chronic myelomonocytic leukemia:	1148 (2.4)	612 (3.6)	1760 (2.7)
RARS Acquired idiopathic sideroblastic anemia:	236 (0.5)	257 (1.5)	493 (0.8)
Myeloproliferative neoplasm(MPN),unclassifiable,MPS,NOS:	4 (0.0)	2 (0.0)	6 (0.0)
MDS with excess blasts-1 (MDS-EB-1) (RAEB-1)	2239 (4.6)	1353 (7.9)	3592 (5.5)
MDS with excess blasts-2 (MDS-EB-2 (RAEB-2)	2745 (5.7)	1592 (9.3)	4337 (6.6)
Myelodysplastic syndrome with multilineage dysplasia (MDS-MLD) (RCMD)	1961 (4.0)	1154 (6.7)	3115 (4.7)
5q-syndrome:	218 (0.4)	101 (0.6)	319 (0.5)
Childhood myelodysplastic syndrome(Refractory cytopenia of childhood (RCC)):	4 (0.0)	3 (0.0)	7 (0.0)
Myelodysplastic/myeloproliferative neoplasm,unclassifiable:	32 (0.1)	21 (0.1)	53 (0.1)
AML/ANLL, not otherwise specified:	11101 (22.9)	3231 (18.8)	14332 (21.8)
AML with t(8;21)(q22;q22)(AML1/ETO):	866 (1.8)	285 (1.7)	1151 (1.8)
AML with abnormal BM eosinophils (CBFb/MYH11):	1060 (2.2)	270 (1.6)	1330 (2.0)
AML with 11q23 (MLL) abnormalities:	1107 (2.3)	405 (2.4)	1512 (2.3)
AML with multi-lineage dysplasia:	4972 (10.2)	1420 (8.3)	6392 (9.7)
AML minimally differentiated (M0):	1084 (2.2)	293 (1.7)	1377 (2.1)
AML without maturation (M1):	2504 (5.2)	810 (4.7)	3314 (5.0)
AML with maturation (M2):	2530 (5.2)	862 (5.0)	3392 (5.2)
acute myelomonocytic leukemia (M4):	2869 (5.9)	868 (5.1)	3737 (5.7)

Characteristic	TED	CRF	Total
acute monoblastic/monocytic leukemia (M5):	3001 (6.2)	915 (5.3)	3916 (6.0)
acute erythroid leukemia (M6):	541 (1.1)	218 (1.3)	759 (1.2)
acute megakaryoblastic leukemia (M7):	147 (0.3)	36 (0.2)	183 (0.3)
acute basophilic leukemia:	6 (0.0)	0 (0.0)	6 (0.0)
acute panmyelosis with myelofibrosis:	54 (0.1)	21 (0.1)	75 (0.1)
myeloid sarcoma:	339 (0.7)	84 (0.5)	423 (0.6)
AML with biallelic mutations of CEBPA	233 (0.5)	25 (0.1)	258 (0.4)
AML with mutated RUNX1	619 (1.3)	104 (0.6)	723 (1.1)
MDS / MPN with ring sideroblasts and thrombocytosis (MDS / MPN-RS-T)	8 (0.0)	0 (0.0)	8 (0.0)
MDS-RS with single lineage dysplasia (MDS-RS-SLD)	10 (0.0)	1 (0.0)	11 (0.0)
MDS-RS with multilineage dysplasia (MDS-RS-MLD)	23 (0.0)	3 (0.0)	26 (0.0)
Graft source - no. (%)			
Bone marrow	5466 (11.3)	2048 (11.9)	7514 (11.4)
Peripheral blood	41877 (86.3)	13223 (77.1)	55100 (83.9)
Umbilical cord blood	1178 (2.4)	1883 (11.0)	3061 (4.7)
Other	2 (0.0)	0 (0.0)	2 (0.0)
Not reported	5 (0.0)	2 (0.0)	7 (0.0)
Donor type - no. (%)			
HLA-identical sibling	15034 (31.0)	3864 (22.5)	18898 (28.8)
Twin	42 (0.1)	46 (0.3)	88 (0.1)
Haploidentical	5102 (10.5)	2076 (12.1)	7178 (10.9)
Other related	506 (1.0)	328 (1.9)	834 (1.3)
Mismatched related - not otherwise specified	515 (1.1)	307 (1.8)	822 (1.3)
Well-matched unrelated (8/8)	17522 (36.1)	6715 (39.1)	24237 (36.9)
Partially-matched unrelated (7/8)	2880 (5.9)	1343 (7.8)	4223 (6.4)
Mis-matched unrelated (<= 6/8)	178 (0.4)	87 (0.5)	265 (0.4)
Multi-donor	267 (0.6)	48 (0.3)	315 (0.5)
Unrelated (matching TBD)	5114 (10.5)	364 (2.1)	5478 (8.3)
Cord blood	1178 (2.4)	1883 (11.0)	3061 (4.7)
Not reported	190 (0.4)	95 (0.6)	285 (0.4)
Presence of known pathogenic DDX41 mutation or DDX41-wt status - no. (%)			
DDX41 not detected	48337 (99.6)	17100 (99.7)	65437 (99.6)
DDX41 detected	191 (0.4)	56 (0.3)	247 (0.4)
Conditioning regimen intensity - no. (%)			
No drugs reported	66 (0.1)	6 (0.0)	72 (0.1)
MAC	25243 (52.0)	7720 (45.0)	32963 (50.2)
RIC	16630 (34.3)	6694 (39.0)	23324 (35.5)
NMA	4556 (9.4)	2407 (14.0)	6963 (10.6)

Characteristic	TED	CRF	Total
TBD	2033 (4.2)	329 (1.9)	2362 (3.6)
Conditioning regimen - no. (%)			
No drugs reported			
None	66 (0.1)	6 (0.0)	72 (0.1)
MAC			
TBI/Cy	2493 (5.1)	1045 (6.1)	3538 (5.4)
TBI/Cy/Flu	311 (0.6)	418 (2.4)	729 (1.1)
TBI/Cy/Flu/TT	225 (0.5)	112 (0.7)	337 (0.5)
TBI/Cy/TT	11 (0.0)	19 (0.1)	30 (0.0)
TBI/Cy/VP	117 (0.2)	42 (0.2)	159 (0.2)
TBI/VP	194 (0.4)	48 (0.3)	242 (0.4)
TBI/Mel	80 (0.2)	32 (0.2)	112 (0.2)
TBI/Flu	1814 (3.7)	486 (2.8)	2300 (3.5)
TBI/other(s)	116 (0.2)	32 (0.2)	148 (0.2)
Bu/Cy/Mel	4 (0.0)	2 (0.0)	6 (0.0)
Bu/Cy	7883 (16.2)	2250 (13.1)	10133 (15.4)
Bu/Mel	178 (0.4)	82 (0.5)	260 (0.4)
Flu/Bu/TT	883 (1.8)	139 (0.8)	1022 (1.6)
Flu/Bu	10394 (21.4)	2745 (16.0)	13139 (20.0)
Flu/Mel/TT	361 (0.7)	152 (0.9)	513 (0.8)
Flu/Mel	0 (0.0)	2 (0.0)	2 (0.0)
Cy/Flu	19 (0.0)	9 (0.1)	28 (0.0)
Cy alone	0 (0.0)	2 (0.0)	2 (0.0)
Mel/other(s)	12 (0.0)	1 (0.0)	13 (0.0)
Other(s)	148 (0.3)	81 (0.5)	229 (0.3)
None	0 (0.0)	1 (0.0)	1 (0.0)
Missing	0 (0.0)	20 (0.1)	20 (0.0)
RIC			
TBI/Cy	71 (0.1)	6 (0.0)	77 (0.1)
TBI/Cy/Flu	912 (1.9)	278 (1.6)	1190 (1.8)
TBI/Cy/Flu/TT	0 (0.0)	1 (0.0)	1 (0.0)
TBI/Cy/VP	7 (0.0)	2 (0.0)	9 (0.0)
TBI/VP	9 (0.0)	2 (0.0)	11 (0.0)
TBI/Mel	1065 (2.2)	374 (2.2)	1439 (2.2)
TBI/Flu	1530 (3.2)	612 (3.6)	2142 (3.3)
TBI/other(s)	73 (0.2)	38 (0.2)	111 (0.2)
Bu/Cy	4 (0.0)	5 (0.0)	9 (0.0)
Bu/Mel	1 (0.0)	0 (0.0)	1 (0.0)
Flu/Bu	5740 (11.8)	2596 (15.1)	8336 (12.7)
Flu/Mel	7199 (14.8)	2710 (15.8)	9909 (15.1)

Characteristic	TED	CRF	Total
Cy/Flu	0 (0.0)	1 (0.0)	1 (0.0)
BEAM	1 (0.0)	2 (0.0)	3 (0.0)
Mel alone	0 (0.0)	3 (0.0)	3 (0.0)
Mel/other(s)	1 (0.0)	1 (0.0)	2 (0.0)
Treosulfan	5 (0.0)	0 (0.0)	5 (0.0)
TLI	0 (0.0)	1 (0.0)	1 (0.0)
Other(s)	12 (0.0)	61 (0.4)	73 (0.1)
Missing	0 (0.0)	1 (0.0)	1 (0.0)
NMA			
TBI/Cy	27 (0.1)	11 (0.1)	38 (0.1)
TBI/Cy/Flu	2547 (5.2)	1763 (10.3)	4310 (6.6)
TBI/Cy/VP	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Mel	0 (0.0)	3 (0.0)	3 (0.0)
TBI/Flu	1080 (2.2)	284 (1.7)	1364 (2.1)
TBI/other(s)	0 (0.0)	1 (0.0)	1 (0.0)
Bu/Cy	2 (0.0)	10 (0.1)	12 (0.0)
Flu/Bu/TT	2 (0.0)	0 (0.0)	2 (0.0)
Flu/Bu	21 (0.0)	48 (0.3)	69 (0.1)
Flu/Mel	0 (0.0)	25 (0.1)	25 (0.0)
Cy/Flu	407 (0.8)	124 (0.7)	531 (0.8)
Cy alone	21 (0.0)	2 (0.0)	23 (0.0)
Treosulfan	0 (0.0)	1 (0.0)	1 (0.0)
TLI	196 (0.4)	107 (0.6)	303 (0.5)
Other(s)	252 (0.5)	27 (0.2)	279 (0.4)
Missing	0 (0.0)	1 (0.0)	1 (0.0)
TBD			
TBI/Cy	97 (0.2)	0 (0.0)	97 (0.1)
TBI/Cy/Flu	22 (0.0)	0 (0.0)	22 (0.0)
TBI/Cy/VP	3 (0.0)	2 (0.0)	5 (0.0)
TBI/Mel	11 (0.0)	1 (0.0)	12 (0.0)
TBI/Flu	199 (0.4)	16 (0.1)	215 (0.3)
TBI/other(s)	103 (0.2)	13 (0.1)	116 (0.2)
Flu/Bu	359 (0.7)	2 (0.0)	361 (0.5)
Mel/other(s)	106 (0.2)	42 (0.2)	148 (0.2)
Treosulfan	652 (1.3)	157 (0.9)	809 (1.2)
Carb/other(s)	2 (0.0)	0 (0.0)	2 (0.0)
TLI	11 (0.0)	2 (0.0)	13 (0.0)
Other(s)	468 (1.0)	88 (0.5)	556 (0.8)
Missing	0 (0.0)	6 (0.0)	6 (0.0)
GVHD prophylaxis - no. (%)			

Characteristic	TED	CRF	Total
None	252 (0.5)	50 (0.3)	302 (0.5)
Ex-vivo T-cell depletion	241 (0.5)	111 (0.6)	352 (0.5)
CD34 selection	436 (0.9)	340 (2.0)	776 (1.2)
PtCy + other(s)	8897 (18.3)	3000 (17.5)	11897 (18.1)
PtCy alone	308 (0.6)	61 (0.4)	369 (0.6)
TAC + MMF +- other(s) (except PtCy)	4168 (8.6)	2610 (15.2)	6778 (10.3)
TAC + MTX +- other(s) (except MMF, PtCy)	15529 (32.0)	6458 (37.6)	21987 (33.5)
TAC + other(s) (except MMF, MTX, PtCy)	2244 (4.6)	958 (5.6)	3202 (4.9)
TAC alone	1025 (2.1)	419 (2.4)	1444 (2.2)
CSA + MMF +- other(s) (except PtCy,TAC)	3804 (7.8)	1630 (9.5)	5434 (8.3)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	8387 (17.3)	1061 (6.2)	9448 (14.4)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	51 (0.1)	50 (0.3)	101 (0.2)
CSA alone	2330 (4.8)	197 (1.1)	2527 (3.8)
Other(s)	856 (1.8)	211 (1.2)	1067 (1.6)
Year of current transplant - no. (%)			
2008	1753 (3.6)	1315 (7.7)	3068 (4.7)
2009	2078 (4.3)	1309 (7.6)	3387 (5.2)
2010	2773 (5.7)	994 (5.8)	3767 (5.7)
2011	3339 (6.9)	713 (4.2)	4052 (6.2)
2012	3430 (7.1)	787 (4.6)	4217 (6.4)
2013	2879 (5.9)	1487 (8.7)	4366 (6.6)
2014	2616 (5.4)	1723 (10.0)	4339 (6.6)
2015	2641 (5.4)	1683 (9.8)	4324 (6.6)
2016	2948 (6.1)	1599 (9.3)	4547 (6.9)
2017	3599 (7.4)	1432 (8.3)	5031 (7.7)
2018	3688 (7.6)	1302 (7.6)	4990 (7.6)
2019	4035 (8.3)	1088 (6.3)	5123 (7.8)
2020	4035 (8.3)	617 (3.6)	4652 (7.1)
2021	4167 (8.6)	639 (3.7)	4806 (7.3)
2022	4547 (9.4)	468 (2.7)	5015 (7.6)
Median follow-up of survivors (range), months - median (range)	37.8 (0.0-2211.1)	71.8 (0.0-10861.4)	48.4 (0.0-10861.4)

Field	Response
Proposal Number	2310-62-KIM
Proposal Title	Revision Of A Disease Risk Index In Patients With Hematologic Malignancies Undergoing Allogeneic Hematopoietic Cell Transplantation
Key Words	REVISION, DISEASE RISK INDEX, ALLOGENEIC TRANSPLANTATION
Principal Investigator #1: - First and last name, degree(s)	Haesook Kim, PhD
Principal Investigator #1: - Email address	htkimc@jimmy.harvard.edu
Principal Investigator #1: - Institution name	Dana-Farber Cancer Institute
Principal Investigator #1: - Academic rank	Principal Research Scientist
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Vincent Ho, MD
Principal Investigator #2 (If applicable): - Email address:)	Vincent_Ho@dfci.harvard.edu
Principal Investigator #2 (If applicable): - Institution name:	Dana-Farber Cancer Institute
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	Yes
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Acute Leukemia
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Wael Saber, MD
RESEARCH QUESTION:	To revise the disease-risk index (DRI) developed by Armand et at (Blood, 2012; Blood 2014) to incorporate newly developed information in each disease.
RESEARCH HYPOTHESIS:	With the rapid advances in our understanding of molecular genetics and pathogenesis over the last decade, newer prognostic models have been developed in many of diseases that now incorporate molecular genetic data. We therefore believe the incorporation of molecular information into the existing DRI may further refine the risk classification.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	1.1 To revise the disease-risk index (DRI) developed by Armand et at (Blood, 2012; Blood 2014) to incorporate newly developed information in each disease for adult patients undergoing allogeneic hematopoietic cell transplantation (alloHCT) with hematologic malignancies. Endpoints to be assessed include: Progression-free survival Overall survival Disease recurrence or progression Non-relapse mortality 1.2 To explore combining revised DRI with HCT- comorbidity index for adult patients undergoing alloHCT with hematologic malignancies.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	The current DRI has been a powerful prognostic indicator for survival of patients undergoing allogeneic transplantation. We anticipate that the updated DRI will be even a stronger prognostic tool to evaluate patients eligible for alloHCT and stratify patients in clinical trials. It can provide transplantation physicians and patients the tool to more accurately predict who will benefit from alloHCT the most

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Allogeneic hematopoietic cell transplantation (HCT) has been the only curative treatment modality for many hematologic malignancies. However, the success of HCT depends on a number of patient, disease and HCT characteristics. Although many factors influence the outcome of allogeneic HCT, disease type, disease status, disease stage and cytogenetic and molecular genetic risk are among the most important prognostic factors that predict allogeneic HCT outcome. However, there existed no standardized method for stratification of patients by disease type and stage. We have previously developed the disease risk index (DRI) based on disease type and disease stage (1) to stratify patients who underwent allogeneic HCT between 2000 and 2009. Subsequently we validated the original DRI using the CIBMTR data (2). The initial and refined DRI stratified patients into 4 groups with very distinctive overall survival. However, with the rapid advances in our understanding of molecular genetics and pathogenesis over the last decade, newer prognostic models have been developed in many of these diseases that now incorporate molecular genetic data (3,4). How these molecular mutation profiles in the different diseases impact outcomes after HCT remain mostly unknown. These advances point to an urgent need for revising and updating the current DRI to incorporate new molecular information as well as other recent advances such as measurable residual disease (MRD) status in acute leukemias into the DRI classification. Indeed, we envisioned in the initial studies that this DRI should not be fixed but should be refined as new information becomes available. We thus propose to revise to incorporate widely available molecular information in many diseases including AML and MDS. The incorporation of molecular information may further refine the risk classification and alter the risk assignment. Furthermore, the derivation of the initial DRI was based solely on overall survival (OS) and did not directly take relapse risk into consideration. This was because the CIBMTR did not have the relapse information collected in the CIBMTR database in those days. Based on our experience at the Dana-Farber Cancer Institute, DRI is a risk factor for relapse and not for non-relapse mortality (NRM). In this proposal, we therefore verify that DRI is indeed a risk factor for relapse and not for NRM.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	All adult patients who underwent first allogeneic HCT from unrelated or related donors between 2017 and 2022 for hematologic malignancies (ALL, AML, CLL, CML, MDS, multiple myeloma (aka PCD), myeloproliferative neoplasms, HL, NHL, other leukemia). These are the cases in the center-specific outcomes report on whom we require the data to allow us to assign a disease risk.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	The initial DRI was developed for adult patients based on adult hematologic malignancies. Thus we hope to update DRI using the same patient population. It is possible though it can be applied to pediatric patients. But that is beyond the scope of this proposal.

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Data from the center-specific outcomes report, including patient age at transplantation, patient sex, donor sex, disease specific data (disease type, subtype, cytogenetics and molecular data, where applicable, disease status at transplantation. See Table 1 below for detail), date of transplantation, donor relationship, HLA match, graft source, CMV serostatus of patient and donor, GVHD prophylaxis regimen, conditioning intensity, HCT comorbidity index with all 17 components, Karnofsky performance score as well as HCT outcome. HCT outcome data includes survival status (alive or dead), date of last seen alive if alive, date of death if dead, cause of death, relapse status (yes or no), date of relapse if relapsed. Table 1. Disease specific data Diseases: AML, ALL, CML, CLL (or Other leukemia), MDS, MPN, HL, NHL, MM Disease Subtype: AML, ALL, CLL, MDS, MPN, HL, NHL, MM Disease status at HCT: AML, ALL, CML, CLL, MDS, MPN, HL, NHL, MM Cytogenetics at HCT: AML, ALL, CML, CLL, MDS, MPN, HL, NHL, MM Molecular marker at HCT or at DX: AML, ALL, CML, CLL, MDS, MPN Measurable residual disease at HCT: AML, ALL, CML (for pts with blast crisis only, CLL, MDS Additional information; AML: TP53 mutation, secondary AML, t-AML ALL: Philadelphia or Philadelphia-like phenotype MDS: platelet counts, t-MDS?, %BM blast, ANC(or %neutrophile), WBC, hemoglobin, IPSS-R score. IPPS-M score. TP53 mutation MPN: DIPSS+ ,MIPPS70, MIPPS70+v.2 score at HCT (if available) CLL: 17p abnormality, transformation to Richter's, prior CAR-T therapy HL: Prior autoHCT, prior checkpoint therapy NHL: Prior autoHCT, prior CART-T/BITe therapy. For DLBCL: Activated B cell type vs. germinal center B cell type. Double Hit or double expressor phenotype. Transformation from lower grade disease (CLL, FL). MM: Prior ASCT, Prior CAR-T footnote: measurable residual disease using PCR. cytogenetics testing can be done using either karyotying or FISH at the time of diagnosis or at HCT. *: if there are more than 1 abnormal karyotype, then the total number of abnormalities needs to be collected

Field	Response
REFERENCES:	1. A disease risk index for patients undergoing allogeneic stem cell transplantation. Armand P, Gibson CJ, Cutler C, Ho VT, Koreth J, Alyea EP, Ritz J, Sorror ML, Lee SJ, Deeg HJ, Storer BE, Appelbaum FR, Antin JH, Soiffer RJ, Kim HT.Blood. 2012 Jul 26;120(4):905-13. doi: 10.1182/blood-2012-03-418202. Epub 2012 Jun 18. 2. Validation and refinement of the Disease Risk Index for allogeneic stem cell transplantation.Armand P, Kim HT, Logan BR, Wang Z, Alyea EP, Kalaycio ME, Maziarz RT, Antin JH, Soiffer RJ, Weisdorf DJ, Rizzo JD, Horowitz MM, Saber W.Blood. 2014 Jun 5;123(23):3664-71. doi: 10.1182/blood-2014-01-552984. Epub 2014 Apr 1 3. Dohner H, Wei AH, Appelbaum FR, Craddock C, DiNardo CD, Dombret H, Ebert BL, Fenaux P, Godley LA, Hasserjian RP, Larson RA, Levine RL, Miyazaki Y, Niederwieser D, Ossenkoppele G, Rollig C, Sierra J, Stein EM, Tallman MS,Tien HF, Wang J, Wierzbowska A, Lowenberg B. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN blood® SPECIAL REPORT 22 SEPTEMBER 2022	VOLUME 140. 4. Bernard E, Tuechler H, Greenberg PL, Hasserjian RP, Ossa JEA, et al. Molecular International Prognostic Scoring System for Myelodysplastic Syndromes. Published June 12, 2022 NEJM Evid 2022;1(7) DOI: 10.1056/EVIDoa2200008 VOL. 1 NO. 7 5. Bejanyan N, Brunstein CG, Cao Q, Lazaryan A, Ustun C, Warlick ED, Arora M, Wagner JE, Weisdorf DJ. Predictive value of disease risk comorbidity index for overall survival after allogeneic hematopoietic transplantation. Blood Adv. 2019 Feb 12;3(3):230-236.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Table 1. Characteristics of patients undergoing a 1st allo HCT for hematologic malignancies by track, 2017-2022

Characteristic	TED	CRF	Total
No. of patients	38081	10320	48401
No. of centers	325	234	327
Recipient age - no. (%)			
Median (min-max)	56.4 (18.0-82.0)	60.9 (18.0-87.8)	57.3 (18.0-87.8)
18-29	4324 (11.4)	963 (9.3)	5287 (10.9)
30-39	4139 (10.9)	794 (7.7)	4933 (10.2)
40-49	5446 (14.3)	1098 (10.6)	6544 (13.5)
50-59	9203 (24.2)	2017 (19.5)	11220 (23.2)
60-69	11670 (30.6)	4060 (39.3)	15730 (32.5)
>=70	3299 (8.7)	1388 (13.4)	4687 (9.7)
CCN region at transplant - no. (%)			
US	26641 (70.0)	9033 (87.5)	35674 (73.7)
Canada	3167 (8.3)	43 (0.4)	3210 (6.6)
Europe	2369 (6.2)	243 (2.4)	2612 (5.4)
Asia	1002 (2.6)	266 (2.6)	1268 (2.6)
Australia/New Zealand	2148 (5.6)	298 (2.9)	2446 (5.1)
Mideast/Africa	653 (1.7)	80 (0.8)	733 (1.5)
Central/South America	2101 (5.5)	357 (3.5)	2458 (5.1)
Sex - no. (%)			
Male	22036 (57.9)	6159 (59.7)	28195 (58.3)
Female	16045 (42.1)	4161 (40.3)	20206 (41.7)
Race - no. (%)			
White	26446 (69.4)	7962 (77.2)	34408 (71.1)
Black or African American	1876 (4.9)	848 (8.2)	2724 (5.6)
Asian	1913 (5.0)	656 (6.4)	2569 (5.3)
Native Hawaiian or other Pacific Islander	119 (0.3)	56 (0.5)	175 (0.4)
American Indian or Alaska Native	115 (0.3)	72 (0.7)	187 (0.4)
More than one race	272 (0.7)	84 (0.8)	356 (0.7)
Not reported	7340 (19.3)	642 (6.2)	7982 (16.5)
Karnofsky score prior to HCT - no. (%)			
90-100%	22247 (58.4)	5396 (52.3)	27643 (57.1)
< 90%	15002 (39.4)	4756 (46.1)	19758 (40.8)
Not reported	832 (2.2)	168 (1.6)	1000 (2.1)
HCT-CI - no. (%)			
0	10013 (26.3)	2330 (22.6)	12343 (25.5)
1	5858 (15.4)	1489 (14.4)	7347 (15.2)

Characteristic	TED	CRF	Total
2	5599 (14.7)	1554 (15.1)	7153 (14.8)
3	6363 (16.7)	1847 (17.9)	8210 (17.0)
4	4248 (11.2)	1290 (12.5)	5538 (11.4)
5	2503 (6.6)	748 (7.2)	3251 (6.7)
6	1625 (4.3)	495 (4.8)	2120 (4.4)
7+	1523 (4.0)	495 (4.8)	2018 (4.2)
Missing/TBD	349 (0.9)	72 (0.7)	421 (0.9)
Primary disease - no. (%)			
Acute myelogenous leukemia or ANLL	17449 (45.8)	2914 (28.2)	20363 (42.1)
Acute lymphoblastic leukemia	6083 (16.0)	1131 (11.0)	7214 (14.9)
Other leukemia	582 (1.5)	167 (1.6)	749 (1.5)
Chronic myelogenous leukemia	1393 (3.7)	171 (1.7)	1564 (3.2)
Myelodysplastic/myeloprolifterative disorders (please classify all preleukemias)	6999 (18.4)	2435 (23.6)	9434 (19.5)
Other acute leukemia	618 (1.6)	73 (0.7)	691 (1.4)
Non-Hodgkin lymphoma	3125 (8.2)	611 (5.9)	3736 (7.7)
Hodgkin lymphoma	288 (0.8)	616 (6.0)	904 (1.9)
Plasma cell disorder/Multiple Myeloma	508 (1.3)	205 (2.0)	713 (1.5)
Other Malignancies	11 (0.0)	2 (0.0)	13 (0.0)
Myeloproliferative Neoplasms	1025 (2.7)	1995 (19.3)	3020 (6.2)
Graft source - no. (%)			
Bone marrow	3870 (10.2)	1210 (11.7)	5080 (10.5)
Peripheral blood	34209 (89.8)	9110 (88.3)	43319 (89.5)
Other	1 (0.0)	0 (0.0)	1 (0.0)
Not reported	1 (0.0)	0 (0.0)	1 (0.0)
Donor type - no. (%)			
HLA-identical sibling	10029 (26.3)	2002 (19.4)	12031 (24.9)
Twin	69 (0.2)	40 (0.4)	109 (0.2)
Haploidentical	6945 (18.2)	2346 (22.7)	9291 (19.2)
Other related	488 (1.3)	194 (1.9)	682 (1.4)
Mismatched related - not otherwise specified	371 (1.0)	245 (2.4)	616 (1.3)
Well-matched unrelated (8/8)	16203 (42.5)	4412 (42.8)	20615 (42.6)
Partially-matched unrelated (7/8)	2220 (5.8)	741 (7.2)	2961 (6.1)
Mis-matched unrelated (<= 6/8)	143 (0.4)	68 (0.7)	211 (0.4)
Unrelated (matching TBD)	1469 (3.9)	198 (1.9)	1667 (3.4)
Not reported	144 (0.4)	74 (0.7)	218 (0.5)
Conditioning regimen intensity - no. (%)			
No drugs reported	87 (0.2)	6 (0.1)	93 (0.2)
MAC	18558 (48.7)	3714 (36.0)	22272 (46.0)
RIC	13849 (36.4)	4788 (46.4)	18637 (38.5)

Characteristic	TED	CRF	Total
NMA	4270 (11.2)	1653 (16.0)	5923 (12.2)
TBD	1190 (3.1)	135 (1.3)	1325 (2.7)
Not reported	127 (0.3)	24 (0.2)	151 (0.3)
Conditioning regimen - no. (%)			
MAC			
TBI/Cy	2512 (6.6)	382 (3.7)	2894 (6.0)
TBI/Cy/Flu	94 (0.2)	33 (0.3)	127 (0.3)
TBI/Cy/Flu/TT	36 (0.1)	7 (0.1)	43 (0.1)
TBI/Cy/TT	81 (0.2)	24 (0.2)	105 (0.2)
TBI/Cy/VP	107 (0.3)	11 (0.1)	118 (0.2)
TBI/VP	533 (1.4)	68 (0.7)	601 (1.2)
TBI/Mel	75 (0.2)	18 (0.2)	93 (0.2)
TBI/Flu	2214 (5.8)	478 (4.6)	2692 (5.6)
TBI/other(s)	251 (0.7)	48 (0.5)	299 (0.6)
Bu/Cy/Mel	2 (0.0)	3 (0.0)	5 (0.0)
Bu/Cy	3881 (10.2)	721 (7.0)	4602 (9.5)
Bu/Mel	162 (0.4)	67 (0.6)	229 (0.5)
Flu/Bu/TT	986 (2.6)	215 (2.1)	1201 (2.5)
Flu/Bu	7083 (18.6)	1470 (14.2)	8553 (17.7)
Flu/Mel/TT	369 (1.0)	100 (1.0)	469 (1.0)
FCR	1 (0.0)	0 (0.0)	1 (0.0)
Cy/Flu	25 (0.1)	15 (0.1)	40 (0.1)
Cy alone	0 (0.0)	1 (0.0)	1 (0.0)
Mel alone	0 (0.0)	1 (0.0)	1 (0.0)
Mel/other(s)	15 (0.0)	0 (0.0)	15 (0.0)
TLI	0 (0.0)	1 (0.0)	1 (0.0)
Other(s)	131 (0.3)	49 (0.5)	180 (0.4)
None	0 (0.0)	2 (0.0)	2 (0.0)
RIC			
TBI/Cy	137 (0.4)	8 (0.1)	145 (0.3)
TBI/Cy/Flu	924 (2.4)	191 (1.9)	1115 (2.3)
TBI/Cy/VP	3 (0.0)	0 (0.0)	3 (0.0)
TBI/VP	26 (0.1)	5 (0.0)	31 (0.1)
TBI/Mel	1379 (3.6)	468 (4.5)	1847 (3.8)
TBI/Flu	1475 (3.9)	435 (4.2)	1910 (3.9)
TBI/other(s)	106 (0.3)	32 (0.3)	138 (0.3)
Bu/Cy	28 (0.1)	2 (0.0)	30 (0.1)
Bu/Mel	1 (0.0)	0 (0.0)	1 (0.0)
Flu/Bu/TT	1 (0.0)	0 (0.0)	1 (0.0)
Flu/Bu	3483 (9.1)	1210 (11.7)	4693 (9.7)

Characteristic	TED	CRF	Total
Flu/Mel/TT	0 (0.0)	1 (0.0)	1 (0.0)
Flu/Mel	6209 (16.3)	2377 (23.0)	8586 (17.7)
CBV	3 (0.0)	1 (0.0)	4 (0.0)
BEAM	60 (0.2)	33 (0.3)	93 (0.2)
Mel alone	0 (0.0)	3 (0.0)	3 (0.0)
Treosulfan	7 (0.0)	1 (0.0)	8 (0.0)
TLI	0 (0.0)	2 (0.0)	2 (0.0)
Other(s)	7 (0.0)	19 (0.2)	26 (0.1)
NMA			
TBI/Cy	38 (0.1)	13 (0.1)	51 (0.1)
TBI/Cy/Flu	3023 (7.9)	1320 (12.8)	4343 (9.0)
TBI/Cy/VP	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Mel	0 (0.0)	7 (0.1)	7 (0.0)
TBI/Flu	605 (1.6)	117 (1.1)	722 (1.5)
TBI/other(s)	0 (0.0)	1 (0.0)	1 (0.0)
Bu/Cy	2 (0.0)	2 (0.0)	4 (0.0)
Flu/Bu	20 (0.1)	8 (0.1)	28 (0.1)
Flu/Mel	0 (0.0)	40 (0.4)	40 (0.1)
FCR	49 (0.1)	11 (0.1)	60 (0.1)
Cy/Flu	256 (0.7)	84 (0.8)	340 (0.7)
Cy alone	50 (0.1)	3 (0.0)	53 (0.1)
Treosulfan	0 (0.0)	2 (0.0)	2 (0.0)
TLI	125 (0.3)	37 (0.4)	162 (0.3)
Other(s)	101 (0.3)	8 (0.1)	109 (0.2)
TBD			
TBI/Cy	15 (0.0)	0 (0.0)	15 (0.0)
TBI/Cy/Flu	6 (0.0)	0 (0.0)	6 (0.0)
TBI/Cy/VP	4 (0.0)	0 (0.0)	4 (0.0)
TBI/VP	6 (0.0)	0 (0.0)	6 (0.0)
TBI/Mel	18 (0.0)	2 (0.0)	20 (0.0)
TBI/Flu	82 (0.2)	12 (0.1)	94 (0.2)
TBI/other(s)	28 (0.1)	5 (0.0)	33 (0.1)
Flu/Bu	260 (0.7)	5 (0.0)	265 (0.5)
BEAM like	3 (0.0)	2 (0.0)	5 (0.0)
Mel/other(s)	17 (0.0)	6 (0.1)	23 (0.0)
Treosulfan	388 (1.0)	43 (0.4)	431 (0.9)
Carb/Etop	0 (0.0)	1 (0.0)	1 (0.0)
Carb/other(s)	2 (0.0)	0 (0.0)	2 (0.0)
TLI	12 (0.0)	2 (0.0)	14 (0.0)
Other(s)	349 (0.9)	49 (0.5)	398 (0.8)

Characteristic	TED	CRF	Total
Missing	0 (0.0)	8 (0.1)	8 (0.0)
Not reported			
Mel alone	95 (0.2)	18 (0.2)	113 (0.2)
Missing	32 (0.1)	6 (0.1)	38 (0.1)
GVHD prophylaxis - no. (%)			
None	241 (0.6)	47 (0.5)	288 (0.6)
Ex-vivo T-cell depletion	183 (0.5)	41 (0.4)	224 (0.5)
CD34 selection	205 (0.5)	113 (1.1)	318 (0.7)
PtCy + other(s)	12750 (33.5)	3971 (38.5)	16721 (34.5)
PtCy alone	170 (0.4)	77 (0.7)	247 (0.5)
TAC + MMF +- other(s) (except PtCy)	2646 (6.9)	937 (9.1)	3583 (7.4)
TAC + MTX +- other(s) (except MMF, PtCy)	11874 (31.2)	3458 (33.5)	15332 (31.7)
TAC + other(s) (except MMF, MTX, PtCy)	1529 (4.0)	462 (4.5)	1991 (4.1)
TAC alone	779 (2.0)	210 (2.0)	989 (2.0)
CSA + MMF +- other(s) (except PtCy,TAC)	1666 (4.4)	300 (2.9)	1966 (4.1)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	5225 (13.7)	559 (5.4)	5784 (12.0)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	17 (0.0)	8 (0.1)	25 (0.1)
CSA alone	427 (1.1)	32 (0.3)	459 (0.9)
Other(s)	322 (0.8)	101 (1.0)	423 (0.9)
Missing	47 (0.1)	4 (0.0)	51 (0.1)
Year of current transplant - no. (%)			
2017	5964 (15.7)	2251 (21.8)	8215 (17.0)
2018	5748 (15.1)	2199 (21.3)	7947 (16.4)
2019	6258 (16.4)	2055 (19.9)	8313 (17.2)
2020	6390 (16.8)	1336 (12.9)	7726 (16.0)
2021	6629 (17.4)	1313 (12.7)	7942 (16.4)
2022	7092 (18.6)	1166 (11.3)	8258 (17.1)
Median follow-up of survivors (range), months - median (range)	24.7 (0.0-79.3)	36.6 (0.0-79.1)	25.5 (0.0-79.3)

CIBMTR Study Proposal
(ALL SECTIONS MUST BE COMPLETED.)

Study Title:
Comparison of Reduced Intensity Conditioning Regimens for Haploidentical Donor Hematopoietic Cell Transplant with Post-Transplant Cyclophosphamide in patients with Acute Myeloid Leukemia or Myelodysplastic Syndromes

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Research Hypothesis:
We hypothesize that, in patients with acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS) who received haploidentical (haplo) donor hematopoieitic cell transplant (HCT) with post-transplant cyclophosphamide (PTCy): Fludarabine (Flu)/Melphalan (Mel)/Total Body Irradiation (TBI) based reduced intensity conditioning (RIC) will result in improved disease-free survival (DFS) compared to other frequently used RIC regimens.

Specific Aims:
1. In patients with AML or MDS who received RIC haplo HCT with PTCy, determine optimal RIC regimen that yields the best DFS.

2. In patients with AML or MDS who received haplo HCT with PTCy, compare overall survival, non-relapse mortality, relapse rate, acute graft-versus-host disease, and chronic graft-versus-host disease.

Scientific Impact:

Allogeneic haplo HCT with PTCy is an increasingly utilized platform to expand the donor pool for patients requiring transplant. This platform was initially developed with fludarabine/cyclophosphamide/total body irradiation (TBI) conditioning, while other reduced intensity conditioning regimens have been applied in subsequent studies.[1-4] A recent CIBMTR analysis showed the MAC is superior to RIC in patients $\leq$55 years with AML and MDS undergoing haplo HCT with PTCy due to improved DFS and OS.[5] However, for patients who cannot tolerate MAC, the preferred RIC regimen to use in combination with haplo HCT with PTCy for AML or MDS is unknown. As haploidentical donor HCT with PTCy for AML and MDS increases in application, identifying the optimal RIC regimen for older/less fit patients is critical for improving patient outcomes.

Scientific Justification:

The administration of high doses of PTCy has proven to be a potent intervention to prevent GVHD and allow for safe HCT even when using HLA haplo donors.[1] Multiple studies have shown that haplo HCT with PTCy results in low rates of GVHD, NRM, and comparable survival to more traditional HCT platforms.[1,6-9] A prior CIBMTR analysis suggested that haplo HCT with PTCy in patients with AML may result in lower GVHD and otherwise similar survival to matched sibling donor transplant. [10] However, relapse remains the primary driver of treatment failure.[9]

The pre-transplant conditioning regimen is a readily modifiable factor which can significantly impact relapse rates and potentially improve outcomes. The original Johns Hopkins PTCy regimen utilized RIC with fludarabine (flu) 150 mg/m^2, cyclophosphamide (cy) 29 mg/kg, and total body irradiation (TBI) 200 cGy.[1] Though this regimen has safely expanded the donor pool with low rates of NRM and GVHD, application has been marred by high rates of disease relapse in high risk diseases, exceeding 40-50% in some studies.[1,7,9,11] Myeloablative conditioning (MAC) regimens prior to haplo HCT with PTCy has been shown to reduce the risk of relapse and improve DFS.[5,12,13] However, such intensive conditioning is not feasible for older patients and those with significant comorbidities.

Hoping to find a better balance between toxicity and efficacy, the BMT Group of Georgia combined PTCy based GVHD prophylaxis with a RIC regimen consisting of flu 120 mg/m2, Cy 29 mg/kg, and busulfan (bu) 260 mg/m^2, resulting in NRM of 4% and a 2-year DFS of 64%.[2] In contrast, the group from the MD Anderson Cancer Center has attempted to implement a Mel based regimen in the setting of haplo HCT with PTCy.[14] They recently reported their experience with haplo HCT with PTCy following conditioning with flu 40 mg/m^2 Day -6 to -3, Mel 100 mg/m^2 Day -8 and either Thiotepa 5 mg/kg Day -7 or TBI 200 cGy in patients 55 years and older, resulting in relapse rates of 11-19% and NRM of 19-21%.[3,4]

Aiming to reduce the toxicity of this regimen, our group at Moffitt recently completed a clinical trial combining RIC conditioning consisting of Mel 70 mg/m^2 IV on day -6, flu 30mg/m^2 IV daily on days -6 to -2, and TBI 200 cGy on day -1 with haploidentical donor peripheral blood grafts and PTCy/sirolimus/mycophenolate mofetil (NCT04191187). The trial has met its primary endpoint with 18-month DFS of 70.5% attributable to a low relapse rate of 11.9% (Figure 1, unpublished data).

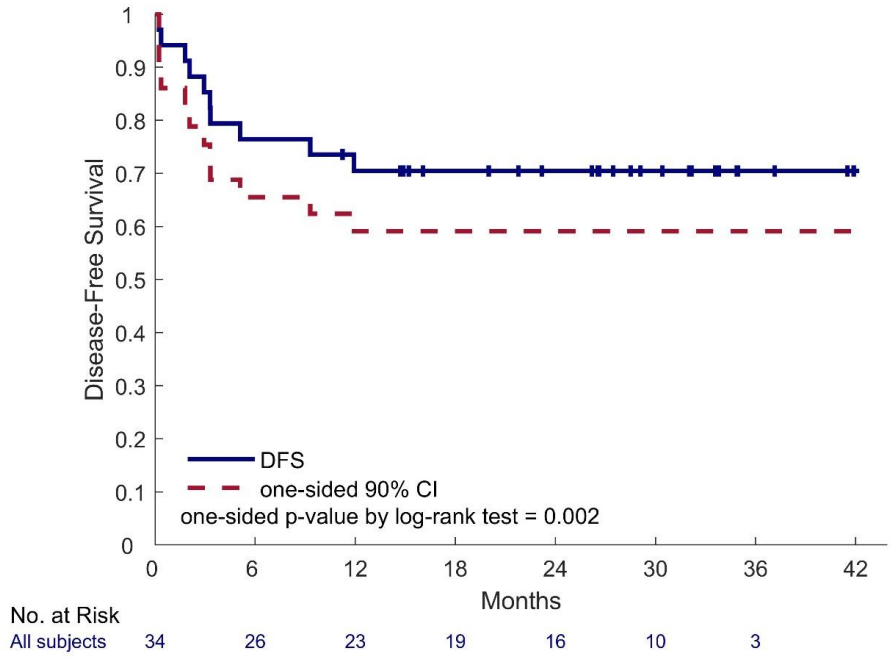

Figure 1: DFS for patients on trial NCT04191187 at the Moffitt Cancer Center

While haplo donor HCT increases in application, the optimal RIC regimen in this setting has not been identified.[5,15] Thus, we propose a retrospective CIBMTR registry analysis to compare outcomes across specific conditioning regimens in the context of haplo HCT with PTCy based GVHD prophylaxis for AML and MDS.

Patient Eligibility Population:

Inclusion:

1. Adult patients (age 18-75) who received allogeneic haplo HCT with PTCy with RIC conditioning regimen for AML or MDS between 2014 and 2022 and reported to the CIBMTR.
    a. T-cell replete Peripheral blood or marrow grafts are permitted.
    b. Donors must be haploidentical relatives.

Exclusion:

1. Transplant for conditions other than MDS or AML
2. T cell depleted grafts
3. Umbilical cord blood grafts

Data Requirements:

If supplemental data is required, please review data collection forms at:
http://www.cibmtr.org/DataManagement/DataCollectionForms/Pages/index.aspx

Bold indicates variables to be included for multivariate analysis.

Patient Related Variables:

1. **Age**: continuous, divided by decade
2. Gender: male vs. female
3. **Race/ethnicity: Hispanic vs. non Hispanic White vs. non Hispanic Black vs. non Hispanic Asian vs. non Hispanic other**
4. **Karnofsky performance score** (KPS): KPS < 90 vs. 90-100
5. **Hematopoietic cell transplant comorbidity** index (HCT-CI)[16]: 0-2 versus 3+

Disease Related Variables:

6. Treatments prior to HCT
    a. Chemotherapy: yes vs. no
    b. Hypomethylating therapy: yes vs. no
    c. Other therapies
7. Number of lines of therapy: continuous
8. **ELN 2022 risk for AML**
9. **R-IPSS for MDS**
10. **Time between diagnosis and HCT for AML CR1**
11. **MRD for AML CR1/CR2**
12. **Time between diagnosis and HCT for MDS**

BMT Related Variables:

1. **RIC regimen (main effect):** Flu/Cy/TBI versus Flu/Mel/TBI versus Flu/Mel versus Flu/Bu +/- TBI versus Flu/Bu/Cy
2. Donor age: continuous divided by decade
3. **Donor/recipient gender:** M/M vs M/F vs. F/F vs. F/M
4. Donor relationship: sibling, parent, children, other
5. **Donor/Recipient cytomegalovirus matching**: +/+, +/-, -/+, -/-
6. Donor/recipient ABO compatibility
7. **Graft source** (peripheral blood vs. marrow)
8. **GVHD prophylactic regimen** (including duration): PTCY-TAC -based vs. PTCY-sirolimus-based vs. other PTCy-based
9. **Year of HCT**
10. **Center effect**

Outcomes

1. Overall survival (OS): Time from allogeneic HCT to death from any cause. Patients will be censored at the time of last follow up.
2. Non-relapse mortality (NRM): Death due to any cause in the first 28 days or death due to conditions

other than disease relapse or progression beyond 28 days. Events will be summarized by the cumulative incidence estimate with relapse as a competing risk.

3. Disease-free survival (DFS): Time from allogeneic HCT to death or relapse. Patients will be censored at the time of last follow up.
4. Relapse/progression: Development of relapse/progression as defined by the CIBMTR. The event will be summarized by the cumulative incidence estimate. NRM will be a competing risk for this outcome.
5. Acute GVHD: Time to development of grade II-IV acute GVHD using the Glucksberg grading system. The event will be summarized by the cumulative incidence estimate, where death and relapse without grade II-IV acute GVHD will be treated as a competing risk.
6. Chronic GVHD: 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 the competing risk. Patients will be censored at second transplant or date of last follow-up. This will have both univariate and multivariate analyses.
7. Acute and chronic GVHD, relapse-free survival (GRFS): Survival without acute grade III-IV GVHD plus chronic GVHD plus disease relapse or progression or death
8. Graft failure: Primary and secondary graft failure are considered as one outcome. Primary graft failure is defined as failure to achieve absolute neutrophil count (ANC) of 0.5 x 10^9/L or donor chimerism <5% in any compartment (T-cell chimerism ≤5%, unsorted blood or marrow chimerism). Secondary graft failure is defined as initial engraftment followed by graft loss evidenced by sustained drop in neutrophil recovery to less than 0.5 x 10^9/L or loss of donor chimerism to <5% in any compartment (T-cell chimerism ≤5%, unsorted blood or marrow chimerism) or a second infusion within the first year after transplant in patients with documented clinical remission. When there is recurrent disease it is assumed that graft failure is related to disease recurrence and not considered an event for this study. Time to graft failure is the interval between date of chimerism/date of ANC decline/date of second infusion and date of transplant; patients who are engrafted (full donor or mixed) are censored at 12 months.
9. Cause of death: causes of death will be presented in a table

Sample Requirements:

N/A

Study Design:

This is a retrospective data review of all patients who have undergone haplo HCT with PTCy-based GVHD prophylaxis for AML or MDS within the CIBMTR database. The primary endpoint is DFS. Other endpoints of interest will include OS, relapse rates, NRM, GVHD, engraftment, and GRFS, all calculated from the time of HCT. Survival endpoints will be calculated using the Kaplan-Meier method. Cumulative Incidences of other endpoints including GVHD, relapse rates, and NRM will be determined. Outcomes will be compared based on specific conditioning regimen to determine the optimal RIC regimen. Within the RIC cohort, regimens will include Flu/Cy/TBI versus Flu/Mel/TBI (reference group) versus Flu/Mel versus Flu/Bu +/- TBI versus Flu/Bu/Cy. If feasible, a subgroup analysis of patients receiving Flu/Mel/TBI will be pursued comparing different Mel doses. Univariate and multivariate analyses will be pursued to determine variables associated with outcomes. For comparisons, p-values $\leq$ 0.05 will be considered significant.

Non-CIBMTR Data Source:

None

Conflicts of Interest:

☐ Yes

X No

Proposal submission: E-mail your observational study proposal to: proposals.cibmtr@mcw.edu

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Table 1. Characteristics of patients undergoing a 1st allo HCT for AML or MDS with PTCy-based GVHD prophylaxis, 2014-2022

Characteristic	Flu/Cy/TBI	Flu/Mel + TBI	Flu/Mel - TBI	Flu/Bu +/- TBI
No. of patients	2272	477	154	237
No. of centers	147	59	38	47
Recipient age - no. (%)				
Median (min-max)	64.3 (18.2-74.9)	61.3 (19.2-74.6)	59.0 (18.8-74.0)	62.1 (18.9-74.7)
18-29	55 (2.4)	28 (5.9)	13 (8.4)	20 (8.4)
30-39	88 (3.9)	27 (5.7)	12 (7.8)	16 (6.8)
40-49	148 (6.5)	49 (10.3)	17 (11.0)	17 (7.2)
50-59	440 (19.4)	103 (21.6)	40 (26.0)	45 (19.0)
60-69	1094 (48.2)	231 (48.4)	54 (35.1)	111 (46.8)
>=70	447 (19.7)	39 (8.2)	18 (11.7)	28 (11.8)
CCN region at transplant - no. (%)				
US	2085 (91.8)	381 (79.9)	140 (90.9)	130 (54.9)
Canada	7 (0.3)	0 (0.0)	0 (0.0)	65 (27.4)
Europe	10 (0.4)	0 (0.0)	1 (0.6)	1 (0.4)
Asia	11 (0.5)	23 (4.8)	5 (3.2)	12 (5.1)
Australia/New Zealand	83 (3.7)	27 (5.7)	1 (0.6)	6 (2.5)
Mideast/Africa	8 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Central/South America	68 (3.0)	46 (9.6)	7 (4.5)	23 (9.7)
Sex - no. (%)				
Male	1369 (60.3)	301 (63.1)	80 (51.9)	139 (58.6)
Female	903 (39.7)	176 (36.9)	74 (48.1)	98 (41.4)
Race - no. (%)				
White	1629 (71.7)	323 (67.7)	101 (65.6)	148 (62.4)
Black or African American	315 (13.9)	58 (12.2)	36 (23.4)	21 (8.9)
Asian	140 (6.2)	29 (6.1)	14 (9.1)	10 (4.2)
Native Hawaiian or other Pacific Islander	14 (0.6)	4 (0.8)	0 (0.0)	1 (0.4)
American Indian or Alaska Native	2 (0.1)	5 (1.0)	0 (0.0)	1 (0.4)
More than one race	10 (0.4)	8 (1.7)	0 (0.0)	1 (0.4)
Not reported	162 (7.1)	50 (10.5)	3 (1.9)	55 (23.2)
Karnofsky score prior to HCT - no. (%)				
90-100%	1158 (51.0)	232 (48.6)	75 (48.7)	139 (58.6)
< 90%	1071 (47.1)	225 (47.2)	77 (50.0)	90 (38.0)
Not reported	43 (1.9)	20 (4.2)	2 (1.3)	8 (3.4)
HCT-CI - no. (%)				
0	453 (19.9)	104 (21.8)	16 (10.4)	55 (23.2)

Characteristic	Flu/Cy/TBI	Flu/Mel + TBI	Flu/Mel - TBI	Flu/Bu +/- TBI
1	316 (13.9)	77 (16.1)	20 (13.0)	31 (13.1)
2	280 (12.3)	56 (11.7)	15 (9.7)	35 (14.8)
3	380 (16.7)	86 (18.0)	35 (22.7)	40 (16.9)
4	314 (13.8)	61 (12.8)	19 (12.3)	29 (12.2)
5	209 (9.2)	43 (9.0)	13 (8.4)	20 (8.4)
6	134 (5.9)	17 (3.6)	16 (10.4)	17 (7.2)
7+	159 (7.0)	27 (5.7)	19 (12.3)	8 (3.4)
Missing/TBD	27 (1.2)	6 (1.3)	1 (0.6)	2 (0.8)
Primary disease - no. (%)				
AML	1568 (69.0)	338 (70.9)	119 (77.3)	166 (70.0)
MDS	704 (31.0)	139 (29.1)	35 (22.7)	71 (30.0)
Specify ALL classification - no. (%)				
AML with BCR-ABL1	6 (0.3)	3 (0.6)	2 (1.3)	0 (0.0)
AML with mutated NPM1	169 (7.4)	36 (7.5)	9 (5.8)	15 (6.3)
AML with t(9;11) (p22;q23);MLLT 3-MLL:	12 (0.5)	2 (0.4)	1 (0.6)	1 (0.4)
AML with t(6;9) (p23;q24); DEK-NUP214:	11 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)
AML with inv(3) (q21;q26.2) or t(3;3) (q21;q26.2);RPN1-EVI1:	9 (0.4)	1 (0.2)	0 (0.0)	1 (0.4)
Therapy related AML (t-AML):	96 (4.2)	16 (3.4)	6 (3.9)	10 (4.2)
MDS	119 (5.2)	24 (5.0)	3 (1.9)	10 (4.2)
Myelodysplastic syndrome with single lineage dysplasia (MDS-SLD) (RA, RCUD_RA)	31 (1.4)	2 (0.4)	0 (0.0)	3 (1.3)
CMMoL Chronic myelomonocytic leukemia:	97 (4.3)	17 (3.6)	6 (3.9)	10 (4.2)
RARS Acquired idiopathic sideroblastic anemia:	22 (1.0)	0 (0.0)	1 (0.6)	2 (0.8)
MDS with excess blasts-1 (MDS-EB-1) (RAEB-1)	147 (6.5)	25 (5.2)	8 (5.2)	12 (5.1)
MDS with excess blasts-2 (MDS-EB-2 (RAEB-2)	172 (7.6)	39 (8.2)	10 (6.5)	24 (10.1)
Myelodysplastic syndrome with multilineage dysplasia (MDS-MLD) (RCMD)	101 (4.4)	30 (6.3)	8 (5.2)	10 (4.2)
5q-syndrome:	11 (0.5)	1 (0.2)	0 (0.0)	2 (0.8)
Myelodysplastic/myeloproliferative neoplasm,unclassifiable:	2 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)
AML/ANLL, not otherwise specified:	473 (20.8)	106 (22.2)	24 (15.6)	57 (24.1)
AML with t(8;21)(q22;q22)(AML1/ETO):	33 (1.5)	6 (1.3)	1 (0.6)	4 (1.7)
AML with abnormal BM eosinophils (CBFb/MYH11):	58 (2.6)	6 (1.3)	5 (3.2)	0 (0.0)
AML with 11q23 (MLL) abnormalities:	36 (1.6)	9 (1.9)	4 (2.6)	4 (1.7)
AML with multi-lineage dysplasia:	314 (13.8)	59 (12.4)	31 (20.1)	28 (11.8)

Characteristic	Flu/Cy/TBI	Flu/Mel + TBI	Flu/Mel - TBI	Flu/Bu +/- TBI
AML minimally differentiated (M0):	19 (0.8)	8 (1.7)	1 (0.6)	1 (0.4)
AML without maturation (M1):	46 (2.0)	11 (2.3)	5 (3.2)	8 (3.4)
AML with maturation (M2):	48 (2.1)	10 (2.1)	7 (4.5)	6 (2.5)
acute myelomonocytic leukemia (M4):	64 (2.8)	17 (3.6)	4 (2.6)	14 (5.9)
acute monoblastic/monocytic leukemia (M5):	79 (3.5)	23 (4.8)	8 (5.2)	11 (4.6)
acute erythroid leukemia (M6):	6 (0.3)	3 (0.6)	2 (1.3)	0 (0.0)
acute megakaryoblastic leukemia (M7):	4 (0.2)	1 (0.2)	1 (0.6)	0 (0.0)
acute panmyelosis with myelofibrosis:	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
myeloid sarcoma:	19 (0.8)	5 (1.0)	0 (0.0)	1 (0.4)
AML with biallelic mutations of CEBPA	13 (0.6)	3 (0.6)	3 (1.9)	0 (0.0)
AML with mutated RUNX1	51 (2.2)	10 (2.1)	4 (2.6)	3 (1.3)
MDS / MPN with ring sideroblasts and thrombocytosis (MDS / MPN-RS-T)	2 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
MDS-RS with multilineage dysplasia (MDS-RS-MLD)	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
Graft source - no. (%)				
Bone marrow	532 (23.4)	129 (27.0)	19 (12.3)	13 (5.5)
Peripheral blood	1740 (76.6)	348 (73.0)	135 (87.7)	224 (94.5)
Donor type - no. (%)				
Haploidentical	2272 (100)	477 (100)	154 (100)	237 (100)
Conditioning regimen intensity - no. (%)				
RIC	394 (17.3)	476 (99.8)	154 (100)	234 (98.7)
NMA	1878 (82.7)	1 (0.2)	0 (0.0)	3 (1.3)
TBI dose, cGy - no. (%)				
RIC				
100	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
200	2 (0.1)	451 (94.5)	1 (0.6)	105 (44.3)
220	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
300	54 (2.4)	1 (0.2)	0 (0.0)	0 (0.0)
400	337 (14.8)	21 (4.4)	0 (0.0)	12 (5.1)
600	1 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)
Not reported	0 (0.0)	0 (0.0)	153 (99.4)	114 (48.1)
NMA				
200	1878 (82.7)	1 (0.2)	0 (0.0)	0 (0.0)
Not reported	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)
GVHD prophylaxis - no. (%)				
PtCy + other(s)	2265 (99.7)	477 (100)	153 (99.4)	236 (99.6)
PtCy alone	7 (0.3)	0 (0.0)	1 (0.6)	1 (0.4)

Characteristic	Flu/Cy/TBI	Flu/Mel + TBI	Flu/Mel - TBI	Flu/Bu +/- TBI
Year of current transplant - no. (%)				
2014	84 (3.7)	6 (1.3)	8 (5.2)	5 (2.1)
2015	160 (7.0)	18 (3.8)	11 (7.1)	12 (5.1)
2016	219 (9.6)	19 (4.0)	15 (9.7)	17 (7.2)
2017	257 (11.3)	20 (4.2)	14 (9.1)	25 (10.5)
2018	344 (15.1)	35 (7.3)	10 (6.5)	34 (14.3)
2019	293 (12.9)	77 (16.1)	18 (11.7)	33 (13.9)
2020	334 (14.7)	107 (22.4)	21 (13.6)	38 (16.0)
2021	327 (14.4)	90 (18.9)	33 (21.4)	36 (15.2)
2022	254 (11.2)	105 (22.0)	24 (15.6)	37 (15.6)
Median follow-up of survivors (range), months - median (range)	36.9 (0.0-103.8)	24.5 (0.0-96.0)	27.8 (0.0-97.1)	24.9 (0.0-96.4)

Table 2. Characteristics of patients undergoing a 1st allo HCT for AML or MDS with PTCy-based GVHD prophylaxis by track, 2014-2022

Characteristic	TED	CRF	Total
No. of patients	2320	1000	3320
No. of centers	179	124	187
Recipient age - no. (%)			
Median (min-max)	62.9 (18.2-74.9)	64.6 (18.9-74.9)	63.4 (18.2-74.9)
18-29	83 (3.6)	47 (4.7)	130 (3.9)
30-39	119 (5.1)	33 (3.3)	152 (4.6)
40-49	193 (8.3)	50 (5.0)	243 (7.3)
50-59	496 (21.4)	168 (16.8)	664 (20.0)
60-69	1053 (45.4)	523 (52.3)	1576 (47.5)
>=70	376 (16.2)	179 (17.9)	555 (16.7)
CCN region at transplant - no. (%)			
US	1980 (85.3)	913 (91.3)	2893 (87.1)
Canada	67 (2.9)	8 (0.8)	75 (2.3)
Europe	8 (0.3)	5 (0.5)	13 (0.4)
Asia	28 (1.2)	25 (2.5)	53 (1.6)
Australia/New Zealand	93 (4.0)	27 (2.7)	120 (3.6)
Mideast/Africa	9 (0.4)	0 (0.0)	9 (0.3)
Central/South America	135 (5.8)	22 (2.2)	157 (4.7)
Sex - no. (%)			
Male	1376 (59.3)	627 (62.7)	2003 (60.3)
Female	944 (40.7)	373 (37.3)	1317 (39.7)

Characteristic	TED	CRF	Total
Race - no. (%)			
White	1599 (68.9)	724 (72.4)	2323 (70.0)
Black or African American	323 (13.9)	138 (13.8)	461 (13.9)
Asian	134 (5.8)	73 (7.3)	207 (6.2)
Native Hawaiian or other Pacific Islander	10 (0.4)	9 (0.9)	19 (0.6)
American Indian or Alaska Native	3 (0.1)	5 (0.5)	8 (0.2)
More than one race	14 (0.6)	7 (0.7)	21 (0.6)
Not reported	237 (10.2)	44 (4.4)	281 (8.5)
Karnofsky score prior to HCT - no. (%)			
90-100%	1223 (52.7)	458 (45.8)	1681 (50.6)
< 90%	1035 (44.6)	528 (52.8)	1563 (47.1)
Not reported	62 (2.7)	14 (1.4)	76 (2.3)
HCT-CI - no. (%)			
0	488 (21.0)	182 (18.2)	670 (20.2)
1	315 (13.6)	154 (15.4)	469 (14.1)
2	293 (12.6)	124 (12.4)	417 (12.6)
3	403 (17.4)	156 (15.6)	559 (16.8)
4	311 (13.4)	131 (13.1)	442 (13.3)
5	202 (8.7)	97 (9.7)	299 (9.0)
6	143 (6.2)	56 (5.6)	199 (6.0)
7+	140 (6.0)	88 (8.8)	228 (6.9)
Missing/TBD	25 (1.1)	12 (1.2)	37 (1.1)
Primary disease - no. (%)			
AML	1664 (71.7)	643 (64.3)	2307 (69.5)
MDS	656 (28.3)	357 (35.7)	1013 (30.5)
Specify ALL classification - no. (%)			
AML with BCR-ABL1	9 (0.4)	2 (0.2)	11 (0.3)
AML with mutated NPM1	201 (8.7)	39 (3.9)	240 (7.2)
AML with t(9;11) (p22;q23);MLLT 3-MLL:	13 (0.6)	5 (0.5)	18 (0.5)
AML with t(6;9) (p23;q24); DEK-NUP214:	10 (0.4)	3 (0.3)	13 (0.4)
AML with inv(3) (q21;q26.2) or t(3;3) (q21;q26.2);RPN1-EVI1:	10 (0.4)	1 (0.1)	11 (0.3)
Therapy related AML (t-AML):	101 (4.4)	34 (3.4)	135 (4.1)
MDS	101 (4.4)	61 (6.1)	162 (4.9)
Myelodysplastic syndrome with single lineage dysplasia (MDS-SLD) (RA, RCUD_RA)	23 (1.0)	15 (1.5)	38 (1.1)
CMMoL Chronic myelomonocytic leukemia:	93 (4.0)	42 (4.2)	135 (4.1)
RARS Acquired idiopathic sideroblastic anemia:	7 (0.3)	18 (1.8)	25 (0.8)
MDS with excess blasts-1 (MDS-EB-1) (RAEB-1)	137 (5.9)	73 (7.3)	210 (6.3)
MDS with excess blasts-2 (MDS-EB-2 (RAEB-2)	165 (7.1)	99 (9.9)	264 (8.0)

Characteristic	TED	CRF	Total
Myelodysplastic syndrome with multilineage dysplasia (MDS-MLD) (RCMD)	117 (5.0)	46 (4.6)	163 (4.9)
5q-syndrome:	9 (0.4)	5 (0.5)	14 (0.4)
Myelodysplastic/myeloproliferative neoplasm,unclassifiable:	3 (0.1)	0 (0.0)	3 (0.1)
AML/ANLL, not otherwise specified:	496 (21.4)	200 (20.0)	696 (21.0)
AML with t(8;21)(q22;q22)(AML1/ETO):	33 (1.4)	12 (1.2)	45 (1.4)
AML with abnormal BM eosinophils (CBFb/MYH11):	55 (2.4)	17 (1.7)	72 (2.2)
AML with 11q23 (MLL) abnormalities:	40 (1.7)	18 (1.8)	58 (1.7)
AML with multi-lineage dysplasia:	330 (14.2)	126 (12.6)	456 (13.7)
AML minimally differentiated (M0):	23 (1.0)	8 (0.8)	31 (0.9)
AML without maturation (M1):	39 (1.7)	32 (3.2)	71 (2.1)
AML with maturation (M2):	44 (1.9)	30 (3.0)	74 (2.2)
acute myelomonocytic leukemia (M4):	70 (3.0)	34 (3.4)	104 (3.1)
acute monoblastic/monocytic leukemia (M5):	90 (3.9)	36 (3.6)	126 (3.8)
acute erythroid leukemia (M6):	2 (0.1)	10 (1.0)	12 (0.4)
acute megakaryoblastic leukemia (M7):	6 (0.3)	0 (0.0)	6 (0.2)
acute panmyelosis with myelofibrosis:	0 (0.0)	2 (0.2)	2 (0.1)
myeloid sarcoma:	17 (0.7)	10 (1.0)	27 (0.8)
AML with biallelic mutations of CEBPA	19 (0.8)	3 (0.3)	22 (0.7)
AML with mutated RUNX1	53 (2.3)	19 (1.9)	72 (2.2)
MDS / MPN with ring sideroblasts and thrombocytosis (MDS / MPN-RS-T)	2 (0.1)	0 (0.0)	2 (0.1)
MDS-RS with multilineage dysplasia (MDS-RS-MLD)	2 (0.1)	0 (0.0)	2 (0.1)
Graft source - no. (%)			
Bone marrow	453 (19.5)	262 (26.2)	715 (21.5)
Peripheral blood	1867 (80.5)	738 (73.8)	2605 (78.5)
Donor type - no. (%)			
Haploidentical	2320 (100)	1000 (100)	3320 (100)
Conditioning regimen intensity - no. (%)			
RIC	1042 (44.9)	317 (31.7)	1359 (40.9)
NMA	1278 (55.1)	683 (68.3)	1961 (59.1)
Conditioning regimen - no. (%)			
RIC			
Flu/Cy/TBI	327 (14.1)	67 (6.7)	394 (11.9)
Flu/Mel + TBI	369 (15.9)	107 (10.7)	476 (14.3)
Flu/Mel - TBI	106 (4.6)	48 (4.8)	154 (4.6)
Flu/Bu +/- TBI	154 (6.6)	80 (8.0)	234 (7.0)
Not reported	86 (3.7)	15 (1.5)	101 (3.0)
NMA			

Characteristic	TED	CRF	Total
Flu/Cy/TBI	1216 (52.4)	662 (66.2)	1878 (56.6)
Flu/Mel + TBI	0 (0.0)	1 (0.1)	1 (0.0)
Flu/Bu +/- TBI	1 (0.0)	2 (0.2)	3 (0.1)
Not reported	61 (2.6)	18 (1.8)	79 (2.4)
GVHD prophylaxis - no. (%)			
PtCy + other(s)	2311 (99.6)	998 (99.8)	3309 (99.7)
PtCy alone	9 (0.4)	2 (0.2)	11 (0.3)
Year of current transplant - no. (%)			
2014	41 (1.8)	62 (6.2)	103 (3.1)
2015	98 (4.2)	106 (10.6)	204 (6.1)
2016	143 (6.2)	132 (13.2)	275 (8.3)
2017	174 (7.5)	151 (15.1)	325 (9.8)
2018	259 (11.2)	179 (17.9)	438 (13.2)
2019	259 (11.2)	179 (17.9)	438 (13.2)
2020	443 (19.1)	90 (9.0)	533 (16.1)
2021	451 (19.4)	77 (7.7)	528 (15.9)
2022	452 (19.5)	24 (2.4)	476 (14.3)
Median follow-up of survivors (range), months - median (range)	25.1 (0.0-103.4)	48.6 (0.0-103.8)	36.1 (0.0-103.8)

CIBMTR Study Proposal
(ALL SECTIONS MUST BE COMPLETED.)

Study Title:
Identifying the Optimal Stem Cell Dosing for Peripheral Blood Stem Cell Transplantation with Post-Transplant Cyclophosphamide

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Research Hypothesis:
We hypothesize that CD34+ cell dose of >5x10^6 CD34+ cells/kg leads to improved overall survival (OS) in the setting of allogeneic donor peripheral blood stem cell transplant (PBSCT) with post-transplant cyclophosphamide (PTCy).

Specific Aims:
1. Determine the impact of infused CD34+ cell dose on OS following allogeneic PBSCT with PTCy.
2. Determine the impact of infused CD34+ cell dose on other transplant outcomes (engraftment, graft-versus-host disease (GVHD), relapse, non-relapse mortality, disease free survival (DFS), and GVHD-free relapse free survival (GRFS) following allogeneic PBSCT with PTCy.
3. Determine the impact of infused CD34+ cell dose on OS following haploidentical related and mismatched unrelated donor PBSCT with PTCy.

Scientific Impact:

Post-transplant cyclophosphamide (PTCy) has been established as the new standard of care for graft versus-host disease (GVHD) prophylaxis.[1] Though this platform was initially developed with bone marrow grafts, peripheral blood stem cell grafts are commonly substituted due to potential improvements in engraftment and relapse.[2] Elmariah, et al. from the Moffitt Cancer Center published internal data suggesting that cell dose significantly impacts survival after allogeneic PBSCT with PTCy. However, these findings merit confirmation through a larger, multicenter dataset. As cell dose is a Modifiable variable, identifying the optimal cell dose would result in a feasible strategy to improve outcomes for patients receiving allogeneic PBSCT with PTCy.

Scientific Justification:

The administration of high doses of post-transplant cyclophosphamide (PTCy) has proven to be a potent intervention to control donor/recipient alloreactivity and allow for safe HCT even when using HLA disparate donors.[3] A recent phase III multicenter trial confirmed that PTCy results in lower risks of GVHD and improved GVHD-free relapse free survival (GRFS) compared to tacrolimus/methotrexate in the setting of reduced intensity condition, matched donor PBSCT.[1] These results have established PTCy as the new standard of care GVHD prophylaxis regimen in this setting. As the field transitions towards increased adoption of PTCy for GVHD prophylaxis, identifying other factors that improve outcomes with this regimen is warranted.

Optimization of the graft source is one strategy to potentially improve the efficacy of HCT with PTCy. McCurdy, et al. demonstrated that administration of higher total nucleated cell dose with haplo bone marrow transplant (BMT) with PTCy yields decreased relapse rates and improved progression free survival (PFS) and overall survival (OS), without increased GVHD.[4] However, this study did not address the use of peripheral blood stem cell grafts with PTCy. Subsequently, Bashey, et al. demonstrated that using peripheral blood stem cell transplant (PBSCT) with PTCy instead of bone marrow may reduce relapse rates and improve PFS in high risk diseases, though does result in higher rates of GVHD.[2]

In light of these results, many institutions prefer PBSCT as the graft source for haplo HCT with PTCy. Published trials have set varying caps on infused doses, though no study has compared outcomes based on cell dose to identify the optimal dose cap.[5,6] Single institution data published by our center suggested that patients receiving allogeneic HCT with PTCy and a CD34+ cell dose $<5x10^6$/kg had worse non-relapse mortality (HR = 4.51, 95% CI: 1.92-10.58, $p < 0.001$), progression- free survival (HR = 4.11, 95% CI: 2.07-8.15, $p < 0.001$), and overall survival (HR = 4.06, 95% CI: 2.00-8.25, $p \leq 0.001$) compared to higher CD34+ cell doses.[7] Larger studies are warranted to confirm this finding.

Existing data suggests that cell dose is likely to impact outcomes of allogeneic PBSCT with PTCy. Thus, we propose to better characterize this impact in order to identify optimal cell doses and improve outcomes in patients receiving allogeneic PBSCT with PTCy.

Patient Eligibility Population:

Inclusion

1. Patients having received allogeneic PBSCT with PTCy for hematologic malignancy
2. Patients age 18 or older
3. January 2014 to July 2022

Exclusion

1. Second allogeneic transplant
2. Use of anti-thymocyte globulin

Data Requirements:

If supplemental data is required, please review data collection forms at:
http://www.cibmtr.org/DataManagement/DataCollectionForms/Pages/index.aspx

Variables for multivariate analysis are in bold.

Patient Related Variables:

1. **Age: continuous, divided by decade**
2. Gender: male vs. female
3. **Race/ethnicity: Hispanic vs. non Hispanic White vs. non Hispanic Black vs. non Hispanic Asian vs. non Hispanic other**
4. **Functional status Karnofsky performance score (KPS): KPS < 90 vs. 90-100**
5. **Hematopoietic cell transplant comorbidity index (HCT-CI)[8]: 0-2 versus 3+**

Disease Related Variables:

1. Disease type: MDS, AML, ALL, CML, Myelofibrosis,
2. **BMT Disease Risk Index (DRI)[9]: low vs. intermediate vs. high vs. very high**
3. Number of lines of prior therapy (continuous)

BMT Related Variables:

1. **Conditioning intensity (myeloablative, reduced intensity, nonmyeloablative)**
2. **Donor: matched related, matched unrelated, haploidentical related and mismatched unrelated**
3. **Donor age for unrelated donors (continuous)**
4. **Donor-recipient gender match**
5. **Graft cell dose (CD34+ cells) as continuous variables and quartiles**
6. **Year of transplant**
7. **Donor/Recipient Cytomegalovirus matching: +/+, +/-, -/+, -/-**
8. **Center effect**
9. Donor/recipient ABO compatibility: major, minor, bidirectional, match
10. **PTCy/calcineurin inhibitor versus PTCy/sirolimus**
11. Healthcare utilization/intensive care unit utilization

Outcomes

1. Overall survival (OS): Time from allogeneic HCT to death from any cause. Patients will be censored

at the time of last follow up.

2. Non-relapse mortality (NRM): Death due to any cause in the first 28 days or death due to conditions other than disease relapse or progression beyond 28 days. Events will be summarized by the cumulative incidence estimate with relapse as a competing risk.
3. Progression-free survival (PFS): Time from allogeneic HCT to death or relapse. Patients will be censored at the time of last follow up.
4. Relapse/progression: Development of relapse/progression as defined by the CIBMTR. The event will be summarized by the cumulative incidence estimate. NRM will be a competing risk for this outcome.
5. Acute GVHD: Time to development of grade II-IV acute GVHD using the Glucksberg grading system. The event will be summarized by the cumulative incidence estimate, where death and relapse without grade II-IV acute GVHD will be treated as a competing risk.
6. Chronic GVHD: 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 the competing risk. Patients will be censored at second transplant or date of last follow-up. This will have both univariate and multivariate analyses.
7. Acute and chronic GVHD, relapse-free survival (GRFS): Survival without acute grade III-IV GVHD plus chronic GVHD plus disease relapse or progression or death
8. Graft failure: Primary and secondary graft failure are considered as one outcome. Primary graft failure is defined as failure to achieve absolute neutrophil count (ANC) of 0.5 x 10^9/L or donor chimerism <5% in any compartment (T-cell chimerism ≤5%, unsorted blood or marrow chimerism). Secondary graft failure is defined as initial engraftment followed by graft loss evidenced by sustained drop in neutrophil recovery to less than 0.5 x 10^9/L or loss of donor chimerism to <5% in any compartment (T-cell chimerism ≤5%, unsorted blood or marrow chimerism) or a second infusion within the first year after transplant in patients with documented clinical remission. When there is recurrent disease it is assumed that graft failure is related to disease recurrence and not considered an event for this study. Time to graft failure is the interval between date of chimerism/date of ANC decline/date of second infusion and date of transplant; patients who are engrafted (full donor or mixed) are censored at 12 months.
9. Cause of death: causes of death will be presented in a table
10. Cytokine release syndrome: Cumulative incidence of grade 2-5 cytokine release syndrome within 1 week of stem cell infusion.
11. Cumulative incidence of major infectious complications including bacterial, fungal, or viral within 100 days post stem cell infusion.

Sample Requirements:

N/A

Study Design:

This is a retrospective data review of all patients who have undergone allogeneic PBSCT with PTCy within the CIBMTR database. The primary endpoint is progression free survival (PFS). Other endpoints of interest will include OS, relapse rates, NRM, GVHD, engraftment, GRFS, and cytokine release syndrome, all calculated from the time of HCT. Survival endpoints will be calculated using the Kaplan-Meier method. Cumulative Incidences (CuI) of other endpoints including GVHD, relapse rates, cytokine release syndrome, and NRM will be determined. Outcomes will be compared based on the total nucleated cell dose, the CD34+ cell dose, and the CD3+ cell dose given with the graft in order to determine the impact

of these cell doses on outcomes. Univariate and multivariate analyses will be pursued to determine variables associated with outcomes. For comparisons, p-values ≤ 0.05 will be considered significant. Subgroup analyses evaluating haploidentical related and mismatched unrelated donor transplants will also be evaluated.

Non-CIBMTR Data Source:
None

Conflicts of Interest:

☐ Yes

X No

Proposal submission: E-mail your observational study proposal to: proposals.cibmtr@mcw.edu

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Table 1. Characteristics of patients undergoing a 1st allo HCT for any hematological malignancy with PTCy-based GVHD prophylaixs by track, 2014-2022

Characteristic	TED	CRF	Total
No. of patients	11648	4091	15739
No. of centers	262	176	270
Recipient age - no. (%)			
Median (min-max)	56.6 (18.0-81.1)	59.9 (18.0-82.2)	57.4 (18.0-82.2)
18-29	1321 (11.3)	437 (10.7)	1758 (11.2)
30-39	1256 (10.8)	366 (8.9)	1622 (10.3)
40-49	1656 (14.2)	442 (10.8)	2098 (13.3)
50-59	2715 (23.3)	805 (19.7)	3520 (22.4)
60-69	3556 (30.5)	1556 (38.0)	5112 (32.5)
>=70	1144 (9.8)	485 (11.9)	1629 (10.4)
CCN region at transplant - no. (%)			
US	9528 (81.8)	3594 (87.9)	13122 (83.4)
Canada	317 (2.7)	35 (0.9)	352 (2.2)
Europe	497 (4.3)	113 (2.8)	610 (3.9)
Asia	202 (1.7)	112 (2.7)	314 (2.0)
Australia/New Zealand	415 (3.6)	106 (2.6)	521 (3.3)
Mideast/Africa	46 (0.4)	5 (0.1)	51 (0.3)
Central/South America	643 (5.5)	126 (3.1)	769 (4.9)
Sex - no. (%)			
Male	6887 (59.1)	2448 (59.8)	9335 (59.3)
Female	4761 (40.9)	1643 (40.2)	6404 (40.7)
Race - no. (%)			
White	8328 (71.5)	2988 (73.0)	11316 (71.9)
Black or African American	1130 (9.7)	538 (13.2)	1668 (10.6)
Asian	590 (5.1)	245 (6.0)	835 (5.3)
Native Hawaiian or other Pacific Islander	32 (0.3)	30 (0.7)	62 (0.4)
American Indian or Alaska Native	47 (0.4)	27 (0.7)	74 (0.5)
More than one race	81 (0.7)	28 (0.7)	109 (0.7)
Not reported	1440 (12.4)	235 (5.7)	1675 (10.6)
Karnofsky score prior to HCT - no. (%)			
90-100%	6625 (56.9)	2129 (52.0)	8754 (55.6)
< 90%	4742 (40.7)	1910 (46.7)	6652 (42.3)
Not reported	281 (2.4)	52 (1.3)	333 (2.1)
HCT-CI - no. (%)			
0	2901 (24.9)	914 (22.3)	3815 (24.2)
1	1739 (14.9)	591 (14.4)	2330 (14.8)

Characteristic	TED	CRF	Total
2	1757 (15.1)	641 (15.7)	2398 (15.2)
3	1974 (16.9)	686 (16.8)	2660 (16.9)
4	1413 (12.1)	495 (12.1)	1908 (12.1)
5	770 (6.6)	334 (8.2)	1104 (7.0)
6	491 (4.2)	201 (4.9)	692 (4.4)
7+	502 (4.3)	200 (4.9)	702 (4.5)
Missing/TBD	101 (0.9)	29 (0.7)	130 (0.8)
Primary disease - no. (%)			
Acute myelogenous leukemia or ANLL	5166 (44.4)	1440 (35.2)	6606 (42.0)
Acute lymphoblastic leukemia	1884 (16.2)	499 (12.2)	2383 (15.1)
Other leukemia	188 (1.6)	62 (1.5)	250 (1.6)
Chronic myelogenous leukemia	447 (3.8)	80 (2.0)	527 (3.3)
Myelodysplastic/myeloprolifterative disorders (please classify all preleukemias)	2189 (18.8)	841 (20.6)	3030 (19.3)
Other acute leukemia	197 (1.7)	29 (0.7)	226 (1.4)
Non-Hodgkin lymphoma	977 (8.4)	266 (6.5)	1243 (7.9)
Hodgkin lymphoma	150 (1.3)	273 (6.7)	423 (2.7)
Plasma cell disorder/Multiple Myeloma	201 (1.7)	53 (1.3)	254 (1.6)
Other Malignancies	5 (0.0)	2 (0.0)	7 (0.0)
Myeloproliferative Neoplasms	244 (2.1)	546 (13.3)	790 (5.0)
Graft source - no. (%)			
Peripheral blood	11648 (100)	4091 (100)	15739 (100)
CD34 cell doses (peripheral blood, x 10/kg) - no. (%)			
0-2 x 10/kg	70 (0.6)	123 (3.0)	193 (1.2)
2-4 x 10/kg	224 (1.9)	300 (7.3)	524 (3.3)
4-8 x 10/kg	1077 (9.2)	1376 (33.6)	2453 (15.6)
> 8 x 10/kg	466 (4.0)	596 (14.6)	1062 (6.7)
Not reported	9811 (84.2)	1696 (41.5)	11507 (73.1)
CD34 cell doses (peripheral blood, x 10/kg) - median (min-max)	5.7 (0.0-48.3)	5.4 (0.0-70.3)	5.5 (0.0-70.3)
Donor type - no. (%)			
HLA-identical sibling	1416 (12.2)	322 (7.9)	1738 (11.0)
Twin	2 (0.0)	1 (0.0)	3 (0.0)
Haploidentical	5644 (48.5)	2258 (55.2)	7902 (50.2)
Other related	238 (2.0)	105 (2.6)	343 (2.2)
Mismatched related - not otherwise specified	275 (2.4)	192 (4.7)	467 (3.0)
Well-matched unrelated (8/8)	2828 (24.3)	785 (19.2)	3613 (23.0)
Partially-matched unrelated (7/8)	952 (8.2)	354 (8.7)	1306 (8.3)
Mis-matched unrelated (<= 6/8)	68 (0.6)	26 (0.6)	94 (0.6)
Multi-donor	16 (0.1)	5 (0.1)	21 (0.1)

Characteristic	TED	CRF	Total
Unrelated (matching TBD)	179 (1.5)	30 (0.7)	209 (1.3)
Not reported	30 (0.3)	13 (0.3)	43 (0.3)
Conditioning regimen intensity - no. (%)			
No drugs reported	41 (0.4)	2 (0.0)	43 (0.3)
MAC	5197 (44.6)	1480 (36.2)	6677 (42.4)
RIC	3455 (29.7)	1338 (32.7)	4793 (30.5)
NMA	2753 (23.6)	1252 (30.6)	4005 (25.4)
TBD	178 (1.5)	15 (0.4)	193 (1.2)
Not reported	24 (0.2)	4 (0.1)	28 (0.2)
Conditioning regimen - no. (%)			
No drugs reported			
None	41 (0.4)	2 (0.0)	43 (0.3)
MAC			
TBI/Cy	102 (0.9)	31 (0.8)	133 (0.8)
TBI/Cy/Flu	63 (0.5)	15 (0.4)	78 (0.5)
TBI/Cy/Flu/TT	0 (0.0)	1 (0.0)	1 (0.0)
TBI/VP	30 (0.3)	2 (0.0)	32 (0.2)
TBI/Mel	16 (0.1)	6 (0.1)	22 (0.1)
TBI/Flu	1433 (12.3)	475 (11.6)	1908 (12.1)
TBI/other(s)	206 (1.8)	32 (0.8)	238 (1.5)
Bu/Cy/Mel	1 (0.0)	1 (0.0)	2 (0.0)
Bu/Cy	884 (7.6)	279 (6.8)	1163 (7.4)
Bu/Mel	45 (0.4)	8 (0.2)	53 (0.3)
Flu/Bu/TT	537 (4.6)	156 (3.8)	693 (4.4)
Flu/Bu	1617 (13.9)	398 (9.7)	2015 (12.8)
Flu/Mel/TT	235 (2.0)	59 (1.4)	294 (1.9)
Cy/Flu	17 (0.1)	12 (0.3)	29 (0.2)
Mel/other(s)	5 (0.0)	0 (0.0)	5 (0.0)
Other(s)	6 (0.1)	4 (0.1)	10 (0.1)
None	0 (0.0)	1 (0.0)	1 (0.0)
RIC			
TBI/Cy	52 (0.4)	4 (0.1)	56 (0.4)
TBI/Cy/Flu	602 (5.2)	135 (3.3)	737 (4.7)
TBI/VP	2 (0.0)	1 (0.0)	3 (0.0)
TBI/Mel	676 (5.8)	257 (6.3)	933 (5.9)
TBI/Flu	359 (3.1)	160 (3.9)	519 (3.3)
TBI/other(s)	29 (0.2)	4 (0.1)	33 (0.2)
Bu/Cy	3 (0.0)	3 (0.1)	6 (0.0)
Flu/Bu	502 (4.3)	266 (6.5)	768 (4.9)
Flu/Mel	1221 (10.5)	495 (12.1)	1716 (10.9)

Characteristic	TED	CRF	Total
Cy/Flu	0 (0.0)	1 (0.0)	1 (0.0)
BEAM	5 (0.0)	4 (0.1)	9 (0.1)
Mel alone	0 (0.0)	2 (0.0)	2 (0.0)
Treosulfan	1 (0.0)	1 (0.0)	2 (0.0)
Other(s)	3 (0.0)	5 (0.1)	8 (0.1)
NMA			
TBI/Cy	24 (0.2)	8 (0.2)	32 (0.2)
TBI/Cy/Flu	2564 (22.0)	1177 (28.8)	3741 (23.8)
TBI/Cy/VP	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Mel	0 (0.0)	6 (0.1)	6 (0.0)
TBI/Flu	60 (0.5)	21 (0.5)	81 (0.5)
Bu/Cy	0 (0.0)	1 (0.0)	1 (0.0)
Flu/Bu	6 (0.1)	3 (0.1)	9 (0.1)
Flu/Mel	0 (0.0)	11 (0.3)	11 (0.1)
FCR	3 (0.0)	0 (0.0)	3 (0.0)
Cy/Flu	66 (0.6)	21 (0.5)	87 (0.6)
Cy alone	9 (0.1)	1 (0.0)	10 (0.1)
Treosulfan	0 (0.0)	1 (0.0)	1 (0.0)
TLI	4 (0.0)	0 (0.0)	4 (0.0)
Other(s)	16 (0.1)	2 (0.0)	18 (0.1)
TBD			
TBI/Cy	1 (0.0)	0 (0.0)	1 (0.0)
TBI/Cy/Flu	4 (0.0)	0 (0.0)	4 (0.0)
TBI/Mel	13 (0.1)	0 (0.0)	13 (0.1)
TBI/Flu	33 (0.3)	3 (0.1)	36 (0.2)
TBI/other(s)	5 (0.0)	0 (0.0)	5 (0.0)
Flu/Bu	33 (0.3)	1 (0.0)	34 (0.2)
Mel/other(s)	1 (0.0)	0 (0.0)	1 (0.0)
Treosulfan	53 (0.5)	9 (0.2)	62 (0.4)
TLI	1 (0.0)	0 (0.0)	1 (0.0)
Other(s)	34 (0.3)	2 (0.0)	36 (0.2)
Not reported			
Mel alone	23 (0.2)	3 (0.1)	26 (0.2)
Missing	1 (0.0)	1 (0.0)	2 (0.0)
GVHD prophylaxis - no. (%)			
PtCy + other(s)	11550 (99.2)	4075 (99.6)	15625 (99.3)
PtCy alone	98 (0.8)	16 (0.4)	114 (0.7)
Year of current transplant - no. (%)			
2014	172 (1.5)	156 (3.8)	328 (2.1)
2015	340 (2.9)	319 (7.8)	659 (4.2)

Characteristic	TED	CRF	Total
2016	535 (4.6)	330 (8.1)	865 (5.5)
2017	955 (8.2)	485 (11.9)	1440 (9.1)
2018	1108 (9.5)	604 (14.8)	1712 (10.9)
2019	1386 (11.9)	727 (17.8)	2113 (13.4)
2020	2111 (18.1)	491 (12.0)	2602 (16.5)
2021	2359 (20.3)	474 (11.6)	2833 (18.0)
2022	2682 (23.0)	505 (12.3)	3187 (20.2)
Median follow-up of survivors (range), months - median (range)	24.3 (0.0-114.5)	37.0 (0.0-102.9)	24.9 (0.0-114.5)

Supplemental table 1. CD34 cell dose information by region of tx

Characteristic	TED	CRF	Total
CD34 cell doses (peripheral blood, x 10/kg) - no. (%)			
US			
0-2 x 10/kg	70 (0.6)	78 (1.9)	148 (0.9)
2-4 x 10/kg	223 (1.9)	272 (6.6)	495 (3.1)
4-8 x 10/kg	1069 (9.2)	1234 (30.2)	2303 (14.6)
> 8 x 10/kg	461 (4.0)	470 (11.5)	931 (5.9)
Not reported	7705 (66.1)	1540 (37.6)	9245 (58.7)
Canada			
0-2 x 10/kg	0 (0.0)	3 (0.1)	3 (0.0)
2-4 x 10/kg	0 (0.0)	2 (0.0)	2 (0.0)
4-8 x 10/kg	1 (0.0)	26 (0.6)	27 (0.2)
> 8 x 10/kg	0 (0.0)	2 (0.0)	2 (0.0)
Not reported	316 (2.7)	2 (0.0)	318 (2.0)
Europe			
0-2 x 10/kg	0 (0.0)	3 (0.1)	3 (0.0)
2-4 x 10/kg	1 (0.0)	4 (0.1)	5 (0.0)
4-8 x 10/kg	4 (0.0)	29 (0.7)	33 (0.2)
> 8 x 10/kg	3 (0.0)	47 (1.1)	50 (0.3)
Not reported	489 (4.2)	30 (0.7)	519 (3.3)
Asia			
0-2 x 10/kg	0 (0.0)	12 (0.3)	12 (0.1)
2-4 x 10/kg	0 (0.0)	2 (0.0)	2 (0.0)
4-8 x 10/kg	0 (0.0)	25 (0.6)	25 (0.2)
> 8 x 10/kg	0 (0.0)	46 (1.1)	46 (0.3)
Not reported	202 (1.7)	27 (0.7)	229 (1.5)
Australia/New Zealand			

Characteristic	TED	CRF	Total
0-2 x 10/kg	0 (0.0)	4 (0.1)	4 (0.0)
2-4 x 10/kg	0 (0.0)	11 (0.3)	11 (0.1)
4-8 x 10/kg	2 (0.0)	40 (1.0)	42 (0.3)
> 8 x 10/kg	1 (0.0)	18 (0.4)	19 (0.1)
Not reported	412 (3.5)	33 (0.8)	445 (2.8)
Mideast/Africa			
4-8 x 10/kg	0 (0.0)	1 (0.0)	1 (0.0)
> 8 x 10/kg	1 (0.0)	1 (0.0)	2 (0.0)
Not reported	45 (0.4)	3 (0.1)	48 (0.3)
Central/South America			
0-2 x 10/kg	0 (0.0)	23 (0.6)	23 (0.1)
2-4 x 10/kg	0 (0.0)	9 (0.2)	9 (0.1)
4-8 x 10/kg	1 (0.0)	21 (0.5)	22 (0.1)
> 8 x 10/kg	0 (0.0)	12 (0.3)	12 (0.1)
Not reported	642 (5.5)	61 (1.5)	703 (4.5)

Field	Response
Proposal Number	2310-166-LAW
Proposal Title	Predictive factors and outcomes of patients who experience graft failure after allogeneic stem cell transplant for primary Myelofibrosis.
Key Words	Myelofibrosis, allogeneic transplantation, graft failure, transplant outcomes
Principal Investigator #1: - First and last name, degree(s)	Arjun Datt Law, MBBS, MD, DM, DRCPC
Principal Investigator #1: - Email address	Arjun.Law@uhn.ca
Principal Investigator #1: - Institution name	Princess Margaret Cancer Centre
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Tommy Alfaro Moya, MD
Principal Investigator #2 (If applicable): - Email address:)	tommy.alfaromoya@uhn.ca
Principal Investigator #2 (If applicable): - Institution name:	Princess Margaret Cancer Centre
Principal Investigator #2 (If applicable): - Academic rank:	Clinical Fellow
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Both authors are Principal Investigators on LKWC study number LK23-01 The impact of allogeneic stem cell transplantation on acute myeloid leukemia and myelodysplastic syndrome with chromosome 3 abnormalities.
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Morbidity, Recovery and Survivorship
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	What are the predictive factors for primary graft failure in patients who undergo allogeneic stem cell transplantation for primary myelofibrosis and what are the outcomes of those patients who present it?
RESEARCH HYPOTHESIS:	In patients with primary myelofibrosis the incidence of graft failure after allogeneic stem cell transplant is higher than in other conditions. We hypothesize that the rates of overall survival and disease-free survival will vary significantly based on donor type, age, and disease stage at the time of the second transplant.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	• To assess overall survival and disease-free survival of patients with primary myelofibrosis who develop primary graft failure after allogeneic stem cell transplantation. • To investigate the incidence and severity of complications, such as graft-versus-host disease (GVHD), infections, graft failure, and relapse in patients receiving a second allogeneic stem cell transplant. • To identify prognostic factors for graft failure in primary myelofibrosis patients, including donor type, age, disease stage, use of pre transplant JAK2 inhibitors, and previous transplant history.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	This study will provide valuable insights into the management of patient with graft failure and in particular the efficacy and safety of second allogeneic stem cell transplants for primary myelofibrosis patients. It may lead to improved treatment strategies for patients who require a second transplant due to graft failure. This study aims to determine predictive factors for the development of primary graft failure. By identifying prognostic factors, this research can help clinicians better stratify patients who are most likely to benefit from a second transplant and those who may not, thus optimizing treatment decisions.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	The therapeutic management of patients with primary or secondary myelofibrosis (MF) who experience relapse or graft failure following allogeneic hematopoietic cell transplantation (allo-HCT) is diverse. MF is a chronic myeloproliferative neoplasm characterized by abnormal clonal stem cell-derived myeloid proliferation, marrow fibrosis, and inflammation, leading to symptoms like ineffective hematopoiesis, splenomegaly, and constitutional symptoms (1,2). After the discovery of the JAK2 mutation and the development of its inhibitors the treatment of this condition has changed radically (3,4). However, Allo-HCT is the only curative option. The decision to transplant patients with myelofibrosis is based on scoring systems such as IPSS/DIPSS(2). Transplant is considered for intermediate to high-risk patients, after taking into account factors like age, clinical phenotype, comorbidities, and donor availability. Graft failure is relatively frequent among patients who undergo transplantation for myelofibrosis with incidences reported in the literature ranging from 2-24% of the cases (5,6). Graft failure is defined as the finding of neutrophils <0.5x109/L, Hb <80g/L, and platelets <20x109/L by day + 28(7). Poor graft function is the Multiple strategies have been developed to try to reduce the incidence of graft failure. Pre-transplant splenectomy is not currently recommended but several studies have explored its influence on the outcomes of transplantation with controversial results (6,8). Other used strategies include JAK inhibitors to reduce splenomegaly, splenic radiation, evaluation of donor-specific antibodies for mismatched donors, intensifying conditioning, and T-cell depletion (3). Salvage treatment with a second allo-HCT is typically considered for patients with good clinical status and no major comorbidities. Strategies such as CD34+ boost infusion have been utilized for patients with poor graft function (persistent cytopenias with donor chimerism) (9). There are several studies that have looked at the outcomes of patients who underwent a second transplant for MF. Long intervals since the first transplant have been found to be predictors of better relapse-free survival (RFS) and non-relapse mortality (NRM). Most patients who undergo a second alloHCT will receive a reduced intensity conditioning (RIC), the use of the same donor has not been shown to be detrimental to the outcomes of the second transplant (10).

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	1. All patients, irrespective of age who experienced graft failure after allogeneic stem cell transplantation for primary Myelofibrosis will be included in the analyses
Does this study include pediatric patients?	Yes
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Data on the following will be retrieved: age, sex, diagnosis, date of diagnosis, prior treatment received before transplant, number of prior HSCT (auto and/or allo HSCT), disease status at time of transplant, KPS at time of transplant, date of transplant, date of transplant, donor (related, unrelated, haploidentical, cord), HLA match, donor sex, donor and recipient CMV status, product type of stem cells (bone marrow, peripheral blood, single cord, double cord), conditioning regimen, GVHD prophylaxis, time to neutrophil and platelet engraftment, aGVHD grade and cGVHD grade, date of diagnosis of aGVHD and cGVHD, date of relapse, and date and cause of death.
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A desc	Not required
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	Not required
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary o	Not required
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	Not required

Field	Response
REFERENCES:	1. Nabergoj M, Mauff K, Robin M, Kröger N, Angelucci E, Poiré X, et al. Outcomes following second allogeneic haematopoietic cell transplantation in patients with myelofibrosis: a retrospective study of the Chronic Malignancies Working Party of EBMT. Bone Marrow Transplant. 2021 Aug;56(8):1944–52. 2. Gowin K, Ballen K, Ahn KW, Hu ZH, Ali H, Arcasoy MO, et al. Survival following allogeneic transplant in patients with myelofibrosis. Blood Adv. 2020 May 12;4(9):1965–73. 3. McLornan DP, Hernandez-Boluda JC, Czerw T, Cross N, Joachim Deeg H, Ditschkowski M, et al. Allogeneic haematopoietic cell transplantation for myelofibrosis: proposed definitions and management strategies for graft failure, poor graft function and relapse: best practice recommendations of the EBMT Chronic Malignancies Working Party. Leukemia. 2021 Sep;35(9):2445–59. 4. McLornan DP, Yakoub-Agha I, Robin M, Chalandon Y, Harrison CN, Kroger N. State-of-the-art review: allogeneic stem cell transplantation for myelofibrosis in 2019. Haematologica. 2019 Apr;104(4):659–68. 5. Ballen KK, Shrestha S, Sobocinski KA, Zhang MJ, Bashey A, Bolwell BJ, et al. Outcome of Transplantation for Myelofibrosis. Biol Blood Marrow Transplant. 2010 Mar;16(3):358–67. 6. Zhang L, Yang F, Feng S. Allogeneic hematopoietic stem-cell transplantation for myelofibrosis. Ther Adv Hematol. 7. Carreras E, Dufour C, Mohty M, Kröger N, editors. The EBMT Handbook: Hematopoietic Stem Cell Transplantation and Cellular Therapies [Internet]. Cham: Springer International Publishing; 2019 [cited 2023 Mar 24]. Available from: http://link.springer.com/10.1007/978-3-030-02278-5 8. Keyzner A, Han S, Shapiro S, Moshier E, Schorr E, Petersen B, et al. Outcome of Allogeneic Hematopoietic Stem Cell Transplantation for Patients with Chronic and Advanced Phase Myelofibrosis. Biol Blood Marrow Transplant. 2016 Dec;22(12):2180–6. 9. Ali H, Bacigalupo A. 2021 Update on allogeneic hematopoietic stem cell transplant for myelofibrosis: A review of current data and applications on risk stratification and management. Am J Hematol. 2021 Nov;96(11):1532–8. 10. Jain T, Mesa RA, Palmer JM. Allogeneic Stem Cell Transplantation in Myelofibrosis. Biol Blood Marrow Transplant. 2017 Sep;23(9):1429–36.

Field	Response
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Table 1. Characteristics of patients who experienced graft failure after an allo-HCT for primary myelofibrosis by track, 2008-2022

Characteristic	TED	CRF	Total
No. of patients	1491	2120	3611
No. of centers	216	168	260
Recipient age - no. (%)			
Median (min-max)	58.7 (0.5-75.6)	62.5 (1.1-80.8)	60.8 (0.5-80.8)
<10	9 (0.6)	6 (0.3)	15 (0.4)
10-17	3 (0.2)	5 (0.2)	8 (0.2)
18-29	15 (1.0)	9 (0.4)	24 (0.7)
30-39	65 (4.4)	33 (1.6)	98 (2.7)
40-49	202 (13.5)	197 (9.3)	399 (11.0)
50-59	534 (35.8)	592 (27.9)	1126 (31.2)
60-69	612 (41.0)	1028 (48.5)	1640 (45.4)
>=70	51 (3.4)	250 (11.8)	301 (8.3)
CCN region at transplant - no. (%)			
US	589 (39.5)	1941 (91.6)	2530 (70.1)
Canada	233 (15.6)	14 (0.7)	247 (6.8)
Europe	351 (23.5)	64 (3.0)	415 (11.5)
Asia	55 (3.7)	24 (1.1)	79 (2.2)
Australia/New Zealand	141 (9.5)	40 (1.9)	181 (5.0)
Mideast/Africa	25 (1.7)	6 (0.3)	31 (0.9)
Central/South America	97 (6.5)	31 (1.5)	128 (3.5)
Sex - no. (%)			
Male	945 (63.4)	1279 (60.3)	2224 (61.6)
Female	546 (36.6)	841 (39.7)	1387 (38.4)
Race - no. (%)			
White	862 (57.8)	1777 (83.8)	2639 (73.1)
Black or African American	44 (3.0)	123 (5.8)	167 (4.6)
Asian	78 (5.2)	86 (4.1)	164 (4.5)
Native Hawaiian or other Pacific Islander	5 (0.3)	16 (0.8)	21 (0.6)
American Indian or Alaska Native	3 (0.2)	8 (0.4)	11 (0.3)
More than one race	4 (0.3)	12 (0.6)	16 (0.4)
Not reported	495 (33.2)	98 (4.6)	593 (16.4)
Karnofsky score prior to HCT - no. (%)			
90-100%	938 (62.9)	1054 (49.7)	1992 (55.2)
< 90%	532 (35.7)	1038 (49.0)	1570 (43.5)
Not reported	21 (1.4)	28 (1.3)	49 (1.4)
HCT-CI - no. (%)			

Characteristic	TED	CRF	Total
0	497 (33.3)	499 (23.5)	996 (27.6)
1	204 (13.7)	278 (13.1)	482 (13.3)
2	196 (13.1)	342 (16.1)	538 (14.9)
3	215 (14.4)	407 (19.2)	622 (17.2)
4	111 (7.4)	279 (13.2)	390 (10.8)
5	54 (3.6)	136 (6.4)	190 (5.3)
6	50 (3.4)	91 (4.3)	141 (3.9)
7+	25 (1.7)	73 (3.4)	98 (2.7)
Missing/TBD	139 (9.3)	15 (0.7)	154 (4.3)
Myelofibrosis - no. (%)			
Primary MFS	1491 (100)	2120 (100)	3611 (100)
Did the recipient receive a subsequent HCT since the date of last report? - no. (%)			
No	1259 (84.4)	1900 (89.6)	3159 (87.5)
Yes	100 (6.7)	164 (7.7)	264 (7.3)
Not reported	132 (8.9)	56 (2.6)	188 (5.2)
Graft source - no. (%)			
Bone marrow	103 (6.9)	88 (4.2)	191 (5.3)
Peripheral blood	1379 (92.5)	2004 (94.5)	3383 (93.7)
Umbilical cord blood	8 (0.5)	28 (1.3)	36 (1.0)
Not reported	1 (0.1)	0 (0.0)	1 (0.0)
Donor type - no. (%)			
HLA-identical sibling	539 (36.2)	489 (23.1)	1028 (28.5)
Twin	1 (0.1)	4 (0.2)	5 (0.1)
Haploidentical	95 (6.4)	242 (11.4)	337 (9.3)
Other related	14 (0.9)	24 (1.1)	38 (1.1)
Mismatched related - not otherwise specified	31 (2.1)	12 (0.6)	43 (1.2)
Well-matched unrelated (8/8)	451 (30.2)	1096 (51.7)	1547 (42.8)
Partially-matched unrelated (7/8)	76 (5.1)	155 (7.3)	231 (6.4)
Mis-matched unrelated (<= 6/8)	4 (0.3)	6 (0.3)	10 (0.3)
Multi-donor	9 (0.6)	2 (0.1)	11 (0.3)
Unrelated (matching TBD)	260 (17.4)	54 (2.5)	314 (8.7)
Cord blood	8 (0.5)	28 (1.3)	36 (1.0)
Not reported	3 (0.2)	8 (0.4)	11 (0.3)
Conditioning regimen intensity - no. (%)			
No drugs reported	2 (0.1)	1 (0.0)	3 (0.1)
MAC	660 (44.3)	794 (37.5)	1454 (40.3)
RIC	693 (46.5)	1154 (54.4)	1847 (51.1)
NMA	74 (5.0)	157 (7.4)	231 (6.4)
TBD	62 (4.2)	11 (0.5)	73 (2.0)

Characteristic	TED	CRF	Total
Not reported	0 (0.0)	3 (0.1)	3 (0.1)
Conditioning regimen - no. (%)			
No drugs reported			
None	2 (0.1)	1 (0.0)	3 (0.1)
MAC			
TBI/Cy	19 (1.3)	14 (0.7)	33 (0.9)
TBI/Cy/Flu	3 (0.2)	12 (0.6)	15 (0.4)
TBI/Cy/Flu/TT	3 (0.2)	1 (0.0)	4 (0.1)
TBI/Flu	46 (3.1)	30 (1.4)	76 (2.1)
TBI/other(s)	0 (0.0)	3 (0.1)	3 (0.1)
Bu/Cy/Mel	1 (0.1)	0 (0.0)	1 (0.0)
Bu/Cy	138 (9.3)	176 (8.3)	314 (8.7)
Bu/Mel	2 (0.1)	7 (0.3)	9 (0.2)
Flu/Bu/TT	51 (3.4)	86 (4.1)	137 (3.8)
Flu/Bu	391 (26.2)	440 (20.8)	831 (23.0)
Flu/Mel/TT	4 (0.3)	13 (0.6)	17 (0.5)
Cy/Flu	2 (0.1)	2 (0.1)	4 (0.1)
Other(s)	0 (0.0)	8 (0.4)	8 (0.2)
None	0 (0.0)	2 (0.1)	2 (0.1)
RIC			
TBI/Cy	0 (0.0)	4 (0.2)	4 (0.1)
TBI/Cy/Flu	11 (0.7)	44 (2.1)	55 (1.5)
TBI/Mel	27 (1.8)	105 (5.0)	132 (3.7)
TBI/Flu	91 (6.1)	111 (5.2)	202 (5.6)
TBI/other(s)	1 (0.1)	5 (0.2)	6 (0.2)
Flu/Bu	235 (15.8)	242 (11.4)	477 (13.2)
Flu/Mel	327 (21.9)	640 (30.2)	967 (26.8)
TLI	1 (0.1)	0 (0.0)	1 (0.0)
Other(s)	0 (0.0)	3 (0.1)	3 (0.1)
NMA			
TBI/Cy	0 (0.0)	2 (0.1)	2 (0.1)
TBI/Cy/Flu	34 (2.3)	104 (4.9)	138 (3.8)
TBI/Mel	0 (0.0)	1 (0.0)	1 (0.0)
TBI/Flu	12 (0.8)	18 (0.8)	30 (0.8)
Bu/Cy	0 (0.0)	1 (0.0)	1 (0.0)
Flu/Bu	1 (0.1)	6 (0.3)	7 (0.2)
Flu/Mel	0 (0.0)	9 (0.4)	9 (0.2)
Cy/Flu	10 (0.7)	10 (0.5)	20 (0.6)
Cy alone	1 (0.1)	0 (0.0)	1 (0.0)
TLI	3 (0.2)	2 (0.1)	5 (0.1)

Characteristic	TED	CRF	Total
Other(s)	13 (0.9)	4 (0.2)	17 (0.5)
TBD			
TBI/Cy	2 (0.1)	0 (0.0)	2 (0.1)
TBI/Mel	0 (0.0)	1 (0.0)	1 (0.0)
TBI/Flu	3 (0.2)	1 (0.0)	4 (0.1)
TBI/other(s)	5 (0.3)	0 (0.0)	5 (0.1)
Flu/Bu	24 (1.6)	1 (0.0)	25 (0.7)
Mel/other(s)	3 (0.2)	1 (0.0)	4 (0.1)
Treosulfan	20 (1.3)	5 (0.2)	25 (0.7)
Other(s)	5 (0.3)	1 (0.0)	6 (0.2)
Missing	0 (0.0)	1 (0.0)	1 (0.0)
Not reported			
Mel alone	0 (0.0)	2 (0.1)	2 (0.1)
Missing	0 (0.0)	1 (0.0)	1 (0.0)
GVHD prophylaxis - no. (%)			
None	8 (0.5)	4 (0.2)	12 (0.3)
Ex-vivo T-cell depletion	1 (0.1)	2 (0.1)	3 (0.1)
CD34 selection	9 (0.6)	25 (1.2)	34 (0.9)
PtCy + other(s)	167 (11.2)	480 (22.6)	647 (17.9)
PtCy alone	4 (0.3)	6 (0.3)	10 (0.3)
TAC + MMF +- other(s) (except PtCy)	96 (6.4)	245 (11.6)	341 (9.4)
TAC + MTX +- other(s) (except MMF, PtCy)	392 (26.3)	961 (45.3)	1353 (37.5)
TAC + other(s) (except MMF, MTX, PtCy)	58 (3.9)	112 (5.3)	170 (4.7)
TAC alone	18 (1.2)	44 (2.1)	62 (1.7)
CSA + MMF +- other(s) (except PtCy,TAC)	154 (10.3)	70 (3.3)	224 (6.2)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	411 (27.6)	127 (6.0)	538 (14.9)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	1 (0.1)	3 (0.1)	4 (0.1)
CSA alone	123 (8.2)	15 (0.7)	138 (3.8)
Other(s)	28 (1.9)	23 (1.1)	51 (1.4)
Missing	21 (1.4)	3 (0.1)	24 (0.7)
Year of current transplant - no. (%)			
2008	60 (4.0)	62 (2.9)	122 (3.4)
2009	89 (6.0)	62 (2.9)	151 (4.2)
2010	132 (8.9)	19 (0.9)	151 (4.2)
2011	117 (7.8)	14 (0.7)	131 (3.6)
2012	141 (9.5)	9 (0.4)	150 (4.2)
2013	118 (7.9)	40 (1.9)	158 (4.4)
2014	65 (4.4)	103 (4.9)	168 (4.7)
2015	81 (5.4)	98 (4.6)	179 (5.0)
2016	98 (6.6)	104 (4.9)	202 (5.6)

Characteristic	TED	CRF	Total
2017	85 (5.7)	194 (9.2)	279 (7.7)
2018	75 (5.0)	208 (9.8)	283 (7.8)
2019	85 (5.7)	272 (12.8)	357 (9.9)
2020	83 (5.6)	301 (14.2)	384 (10.6)
2021	125 (8.4)	319 (15.0)	444 (12.3)
2022	137 (9.2)	315 (14.9)	452 (12.5)
Median follow-up of survivors (range), months - median (range)	35.9 (0.0-172.4)	36.1 (0.0-176.7)	36.1 (0.0-176.7)

Field	Response
Proposal Number	2310-183-MINAGAWA
Proposal Title	Impact of Splenomegaly on Graft Failure in Chronic Leukemia Patients Using Post-transplant Cyclophosphamide
Key Words	Splenomegaly, Graft Failure, Post-transplant Cyclophosphamide, Myeloproliferative neoplasms, Chronic Myelogenous Leukemia, Myelodysplastic Syndrome
Principal Investigator #1: - First and last name, degree(s)	Kentaro Minagawa, M.D., Ph.D.
Principal Investigator #1: - Email address	kminagawa@pennstatehealth.psu.edu
Principal Investigator #1: - Institution name	Penn State Cancer Institute
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Shin Mineishi, M.D.
Principal Investigator #2 (If applicable): - Email address:)	smineishi@pennstatehealth.psu.edu
Principal Investigator #2 (If applicable): - Institution name:	Penn State Cancer Institute
Principal Investigator #2 (If applicable): - Academic rank:	Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	Yes
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Kentaro Minagawa
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Chronic Leukemia
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	Is splenomegaly a risk factor for graft failure in MPNs, CML, MDS and CMML patients using PTCy for GVHD prophylaxis?
RESEARCH HYPOTHESIS:	Splenomegaly is a risk factor for graft failure in MPNs, CML, MDS and CMML patients using PTCy for GVHD prophylaxis.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Graft failure (GF) is a relatively rare complication in allogeneic hematopoietic cell transplant (allo-HCT). Post-transplantation cyclophosphamide (PTCy) is considered to be the best option in graft-versus-host disease (GVHD) prophylaxis. However, there is a concern that GF could increase as high dose chemotherapy is given after stem cell infusion, although its risk factors are unclear in PTCy setting. On the other hand, splenomegaly before allo-HCT is considered a risk factor for GF in non-PTCy setting in myeloproliferative neoplasms (MPN) such as myelofibrosis (MF), chronic myelogenous leukemia (CML), or myelodysplastic syndrome (MDS) patients. Therefore, the risk of GF may be exaggerated in these patients who have splenomegaly in PTCy setting, but there are few reports that have investigated this point. In this study, we defied that the primary endpoint was the cumulative incidence of all GF (including both primary and secondary GF), and the secondary endpoints were 1) the cumulative incidence of primary and secondary GF, 2) the cumulative incidence of non-relapse mortality and relapse, and 3) the probability of overall survival. We will evaluate the differences in these outcomes depending on the presence or absence of splenomegaly and spleen size before allo-HCT.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	We conducted a single center retrospective study (Reference #) and found that splenomegaly before allo-HCT was frequently observed not only MPN but also in acute leukemias and lymphomas, and spleen size was an independent risk factor for GF in PTCy setting and affect the transplant outcome. Since then we obtain non-contrast CT scans pretransplant and if more than moderate splenomegaly is found, PTCy is avoided as much as possible. If our finding is confirmed in using CIBMTR database, it may be practice changing.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	PTCY is considered to be the best method for GVHD prophylaxis and widely used in not only haploidentical also in HLA matched or mismatched allo-HCT.[1] Although PTCy produces better GVHD-free relapse-free survival, overall or disease-free survival were not much different compared to those of conventional GVHD prophylaxis, because PTCy patients may succumb to other causes.[1] GF may be one of them. It is a relatively rare complication in HLA-matched non-PTCy setting, as it has been reported in 0-13% HLA-mismatched PTCy setting.[2-5] Several risk factors for GF have been reported; age[6, 7], stem cell doses[8], HLA-mismatched transplant[9], CMV viremia or infection[6, 10, 11], donor-recipients ABO mismatch[6, 10], non-myeloablative or reduced-intensity conditioning[12], presence of donor-specific HLA antibody[13], and acute GVHD.[10, 11] However, these reports were based on non-PTCy setting, and few studies focused on the GF in PTCy setting. Splenomegaly is commonly observed in MPNs such as MF or CML, MDS and CMML, splenomegaly before allo-HCT has been reported as a risk factor for engraftment failure in non-PTCy setting.[7, 8] We conducted a single center retrospective study and found that splenomegaly before allo-HCT was frequently observed not only chronic myeloproliferative tumors but also acute leukemia and lymphoma (Figure 1) and spleen size was an independent risk factor for GF in PTCy setting (Table 1). Since then we obtain non-contrast CT scans pretransplant and if more than moderate splenomegaly is found, PTCy is avoided as much as possible (submitted for publication)[14]. According to the CIBMT Working Committee Study # CK21-01 (Haploidentical donor transplantation versus matched donor allogeneic hematopoietic cell transplantation outcomes in patients with myelofibrosis) the incidence of primary GF was very high at 19 (95%CI: 13-27) % in PTCy-based haploidentical transplant in MF.[15] However this study did not analyze the relationship of spleen size as the risk factor of graft failure. Kunte, et al reported the effect of splenomegaly on allo-HCT outcomes in MF patients.[16] This study, on the other hand, focused on relapse of MF not graft failure, only included MF not CML, MDS and CMML, and small sample size (N=69). In other words, there have been no studies that evaluated the relationship between spleen size and GF in allo-HCT using PTCy for MF, CML, CMML, and MDS. As stated above, this study may be practice changing. Besides, study CK21-01 already collected similar data sets, thus this study can be conducted by modifying the existing database.

Field	Response
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Id	F_21u3hGc7wwwW4SW
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Name	Presentation1.jpg
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Size	111944
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Type	image/jpeg
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria • Adults • Patients with myelofibrosis, chronic myelogenous leukemia, myelodysplastic syndrome and chronic myelomonocytic leukaemia • Patients who received their first allo-HCT • Patients who used PTCy for GVHD prophylaxis • Patients with documented presence or absence of splenomegaly before allo-HCT Exclusion criteria • Cord blood transplantation • Patients who did not measure spleen size by ultrasound or CT within 1 month before allo-HCT • Patients for whom GVHD prophylaxis is unknown • Patients whose engraftment status and date of engraftment are unknown
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	This study targets diseases that are common among adults, especially the elderly.

DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	• Basic required data collection forms (minimum) 1. Form no. 2000 -- Recipient Baseline Data (Rev: 6.0) 2. Form no. 2006 -- Hematopoietic Stem Cell Transplant Infusion (Rev: 6.0) 3. Form no. 2400 -- Pre-Transplant Essential Data (Rev: 10.0) 4. Form no. 2450 -- Post-Transplant Essential Data (Rev: 7.0) 5. Form no. 2100 -- Post-HSCT Data (Rev: 8.0) 6. Form no. 2900 -- Recipient Death Data (Rev: 5.0) 7. Form no. 2012 -- Chronic Myelogenous Leukemia Pre-Infusion (Rev: 3.0) 8. Form no. 2014 -- Myelodysplastic Syndrome Pre-Infusion (Rev: 4.0) 9. Form no. 2057 -- Myeloproliferative Neoplasms Pre-Infusion (Rev: 1.0) • Required additional data collection This study requires collecting information on spleen size by ultrasound or CT measured within 1 month before stem cell infusion. However, for MDS, additional data collection is not entirely necessary as the form (Form no. 2014) already has spleen size information. • Variables to be analyzed 1. Patient factors 1) Age at HCT 2) Gender (both recipient and donor) 3) Race 4) KPS at HCT 5) HCT-CI score 2. Disease factors 1)Disease diagnosis 2) Disease risk (as defined by the DRI) 3) Disease stage (as defined by the DRI) 4) Spleen size (maximum diameter) and measurement method (ultrasound or CT) -- required additional data collection in some patients 5) Presence or absence of splenectomy 6) Presence or absence of splenic radiation 7) Presence or absence of iron overload 8) Presence or absence of receiving JAK 1 or 2 inhibitor treatment prior allo-HCT 9) Pre-HCT Ferritin 3. Donor related factors 1) Donor type (related or unrelated) 2) Donor age 3) Source of stem cell (bone marrow or peripheral blood) 4) Dose of stem cell (TNC and/or CD34 counts) 5) HLA compatibility 6) ABO donor and recipient matching 7) CMV status of donor and recipient 4. Transplant related factors 1) Conditioning intensity (MAC vs RIC vs NMA) 2)Conditioning Regimen 3) TBI use 4) TBI dose 5) GVHD prophylaxis 5. Outcomes variables 1) Date of transplant 2) Presence or absence of hematopoietic recovery 3) Date of hematopoietic recovery 4) Achieve or not achieve of platelet count

Field	Response
	≥ 20 x109/L 5) Date of achieve of platelet count ≥ 20 x109/L 6) Presence or absence of clinical/hematological relapse or progression 7) Date of clinical/hematological relapse or progression 8) Status at last follow up (Alive/Died) 9) Date of last follow up 10) Cause of death
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A desc	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary o	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A

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Field	Response
	128-35. 13. Spellman, S., et al., The detection of donor-directed, HLA-specific alloantibodies in recipients of unrelated hematopoietic cell transplantation is predictive of graft failure. Blood, 2010. 115(13): p. 2704-8. 14. Emma Zulch, J.C., Kevin Rakszawski, Myles Nickolich, W Christopher Ehmann, Baldeep Wirk, Seema Naik, Witold Rybka, Hong Zheng, Hiroko Shike, Jeffery Sivik, Joseph Mierski, Brooke Silar, Robert Greiner, Valerie I. Brown, Leonard Tuanquin, David F Claxton, Shin Mineishi, Kentaro Minagawa, Splenomegaly Predisposes Graft Failure in Ptcy Transplant, in 2022 Tandem Meetings. 2022. 15. Tania Jain, N.E.-M., Soyoung Kim, Maria Queralt Salas, Marcio Andrade Campos, Hany Elmariah, Rajat Kumar, Nelli Bejanyan, Richard J Jones, Taiga Nishihori. Betul Oran, Ryotaro Nakamura, Bart Scott, Vikas Gupta, Wael Saber, Posttransplant Cyclophosphamide-Based Transplantation from Haploidentical Donors Has Similar Outcomes As Unrelated Donor Transplantation in Myelofibrosis: A Center for International BMT Research (CIBMTR) Study, in 2023 Tandem Meetings. 2023. 16. Kunte, S., et al., Allogeneic blood or marrow transplantation with haploidentical donor and post-transplantation cyclophosphamide in patients with myelofibrosis: a multicenter study. Leukemia, 2022. 36(3): p. 856-864.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Table 1. Characteristics of patients who underwent a first allo-HCT for myelofibrosis with PTCy-based GVHD prophylaxis, 2008-2022

Characteristic	Spleen response/no splenomegaly prior to preparative regimen	No spleen response/splenomegaly prior to preparative regimen	Splenectomy
No. of patients	138	344	4
No. of centers	52	99	4
Recipient age - no. (%)			
Median (min-max)	63.3 (32.1-75.9)	62.7 (32.7-76.9)	52.6 (46.9-76.2)
30-39	3 (2.2)	5 (1.5)	0 (0.0)
40-49	16 (11.6)	37 (10.8)	1 (25.0)
50-59	37 (26.8)	82 (23.8)	2 (50.0)
60-69	57 (41.3)	186 (54.1)	0 (0.0)
>=70	25 (18.1)	34 (9.9)	1 (25.0)
Track - no. (%)			
TED	22 (15.9)	69 (20.1)	0 (0.0)
CRF	116 (84.1)	275 (79.9)	4 (100)
CCN region at transplant - no. (%)			
US	137 (99.3)	299 (86.9)	4 (100)
Canada	1 (0.7)	20 (5.8)	0 (0.0)
Europe	0 (0.0)	9 (2.6)	0 (0.0)
Asia	0 (0.0)	2 (0.6)	0 (0.0)
Australia/New Zealand	0 (0.0)	9 (2.6)	0 (0.0)
Mideast/Africa	0 (0.0)	1 (0.3)	0 (0.0)
Central/South America	0 (0.0)	4 (1.2)	0 (0.0)
Sex - no. (%)			
Male	82 (59.4)	223 (64.8)	1 (25.0)
Female	56 (40.6)	121 (35.2)	3 (75.0)
Race - no. (%)			
White	109 (79.0)	257 (74.7)	4 (100)
Black or African American	19 (13.8)	31 (9.0)	0 (0.0)
Asian	4 (2.9)	21 (6.1)	0 (0.0)
Native Hawaiian or other Pacific Islander	1 (0.7)	4 (1.2)	0 (0.0)
American Indian or Alaska Native	0 (0.0)	2 (0.6)	0 (0.0)
More than one race	1 (0.7)	1 (0.3)	0 (0.0)
Not reported	4 (2.9)	28 (8.1)	0 (0.0)
Karnofsky score prior to HCT - no. (%)			

Characteristic	Spleen response/no splenomegaly prior to preparative regimen	No spleen response/splenomegaly prior to preparative regimen	Splenectomy
90-100%	81 (58.7)	169 (49.1)	2 (50.0)
< 90%	57 (41.3)	169 (49.1)	2 (50.0)
Not reported	0 (0.0)	6 (1.7)	0 (0.0)
HCT-CI - no. (%)			
0	29 (21.0)	61 (17.7)	0 (0.0)
1	20 (14.5)	59 (17.2)	1 (25.0)
2	31 (22.5)	53 (15.4)	1 (25.0)
3	21 (15.2)	73 (21.2)	0 (0.0)
4	16 (11.6)	37 (10.8)	2 (50.0)
5	9 (6.5)	20 (5.8)	0 (0.0)
6	5 (3.6)	27 (7.8)	0 (0.0)
7+	7 (5.1)	13 (3.8)	0 (0.0)
Missing/TBD	0 (0.0)	1 (0.3)	0 (0.0)
Myelofibrosis - no. (%)			
Primary MFS	93 (67.4)	301 (87.5)	3 (75.0)
Secondary MFS	45 (32.6)	43 (12.5)	1 (25.0)
Graft source - no. (%)			
Bone marrow	6 (4.3)	24 (7.0)	0 (0.0)
Peripheral blood	132 (95.7)	320 (93.0)	4 (100)
Donor type - no. (%)			
HLA-identical sibling	18 (13.0)	40 (11.6)	0 (0.0)
Haploidentical	64 (46.4)	169 (49.1)	2 (50.0)
Other related	6 (4.3)	1 (0.3)	0 (0.0)
Mismatched related - not otherwise specified	3 (2.2)	8 (2.3)	1 (25.0)
Well-matched unrelated (8/8)	37 (26.8)	89 (25.9)	1 (25.0)
Partially-matched unrelated (7/8)	8 (5.8)	33 (9.6)	0 (0.0)
Mis-matched unrelated (<= 6/8)	0 (0.0)	2 (0.6)	0 (0.0)
Unrelated (matching TBD)	1 (0.7)	1 (0.3)	0 (0.0)
Not reported	1 (0.7)	1 (0.3)	0 (0.0)
Method used to measure spleen size - no. (%)			
Physical assessment	0 (0.0)	70 (20.3)	0 (0.0)
Ultrasound	0 (0.0)	64 (18.6)	0 (0.0)
CT/MRI	0 (0.0)	70 (20.3)	0 (0.0)
N/A, splenectomy or no splenomegaly at evaluation of spleen size	138 (100)	0 (0.0)	4 (100)

Characteristic	Spleen response/no splenomegaly prior to preparative regimen	No spleen response/splenomegaly prior to preparative regimen	Splenectomy
Not reported	0 (0.0)	140 (40.7)	0 (0.0)
Conditioning regimen intensity - no. (%)			
MAC	66 (47.8)	137 (39.8)	3 (75.0)
RIC	37 (26.8)	144 (41.9)	1 (25.0)
NMA	35 (25.4)	62 (18.0)	0 (0.0)
Not reported	0 (0.0)	1 (0.3)	0 (0.0)
Conditioning regimen - no. (%)			
MAC			
TBI/Cy/Flu	0 (0.0)	1 (0.3)	0 (0.0)
TBI/Flu	3 (2.2)	11 (3.2)	2 (50.0)
TBI/other(s)	0 (0.0)	1 (0.3)	0 (0.0)
Bu/Cy	10 (7.2)	9 (2.6)	0 (0.0)
Bu/Mel	2 (1.4)	0 (0.0)	0 (0.0)
Flu/Bu/TT	21 (15.2)	57 (16.6)	0 (0.0)
Flu/Bu	28 (20.3)	54 (15.7)	0 (0.0)
Flu/Mel/TT	2 (1.4)	4 (1.2)	1 (25.0)
RIC			
TBI/Cy	0 (0.0)	2 (0.6)	0 (0.0)
TBI/Cy/Flu	9 (6.5)	22 (6.4)	1 (25.0)
TBI/Mel	10 (7.2)	38 (11.0)	0 (0.0)
TBI/Flu	5 (3.6)	17 (4.9)	0 (0.0)
Flu/Bu	7 (5.1)	16 (4.7)	0 (0.0)
Flu/Mel	6 (4.3)	49 (14.2)	0 (0.0)
NMA			
TBI/Cy	0 (0.0)	1 (0.3)	0 (0.0)
TBI/Cy/Flu	33 (23.9)	57 (16.6)	0 (0.0)
TBI/Flu	0 (0.0)	1 (0.3)	0 (0.0)
Flu/Bu	0 (0.0)	2 (0.6)	0 (0.0)
Flu/Mel	0 (0.0)	1 (0.3)	0 (0.0)
Cy/Flu	2 (1.4)	0 (0.0)	0 (0.0)
Not reported			
Missing	0 (0.0)	1 (0.3)	0 (0.0)
GVHD prophylaxis - no. (%)			
PtCy + other(s)	138 (100)	340 (98.8)	4 (100)
PtCy alone	0 (0.0)	4 (1.2)	0 (0.0)

Characteristic	Spleen response/no splenomegaly prior to preparative regimen	No spleen response/splenomegaly prior to preparative regimen	Splenectomy
Year of current transplant - no. (%)			
2013	0 (0.0)	3 (0.9)	0 (0.0)
2014	1 (0.7)	4 (1.2)	0 (0.0)
2015	3 (2.2)	4 (1.2)	0 (0.0)
2016	4 (2.9)	6 (1.7)	1 (25.0)
2017	22 (15.9)	28 (8.1)	2 (50.0)
2018	36 (26.1)	32 (9.3)	1 (25.0)
2019	48 (34.8)	56 (16.3)	0 (0.0)
2020	17 (12.3)	53 (15.4)	0 (0.0)
2021	5 (3.6)	73 (21.2)	0 (0.0)
2022	2 (1.4)	85 (24.7)	0 (0.0)
Median follow-up of survivors (range), months - median (range)	47.7 (3.4-74.3)	24.0 (1.6-99.7)	66.0 (60.0-72.1)

Table 2. Characteristics of patients who underwent a first allo-HCT for myelofibrosis with PTCy-based GVHD prophylaxis by track, 2008-2022

Characteristic	TED	CRF	Total
No. of patients	91	395	486
No. of centers	24	94	108
Recipient age - no. (%)			
Median (min-max)	58.6 (32.7-74.4)	63.9 (32.1-76.9)	62.7 (32.1-76.9)
30-39	3 (3.3)	5 (1.3)	8 (1.6)
40-49	14 (15.4)	40 (10.1)	54 (11.1)
50-59	36 (39.6)	85 (21.5)	121 (24.9)
60-69	35 (38.5)	208 (52.7)	243 (50.0)
>=70	3 (3.3)	57 (14.4)	60 (12.3)
CCN region at transplant - no. (%)			
US	62 (68.1)	378 (95.7)	440 (90.5)
Canada	18 (19.8)	3 (0.8)	21 (4.3)
Europe	0 (0.0)	9 (2.3)	9 (1.9)
Asia	2 (2.2)	0 (0.0)	2 (0.4)
Australia/New Zealand	5 (5.5)	4 (1.0)	9 (1.9)
Mideast/Africa	1 (1.1)	0 (0.0)	1 (0.2)

Characteristic	TED	CRF	Total
Central/South America	3 (3.3)	1 (0.3)	4 (0.8)
Sex - no. (%)			
Male	57 (62.6)	249 (63.0)	306 (63.0)
Female	34 (37.4)	146 (37.0)	180 (37.0)
Race - no. (%)			
White	62 (68.1)	308 (78.0)	370 (76.1)
Black or African American	6 (6.6)	44 (11.1)	50 (10.3)
Asian	5 (5.5)	20 (5.1)	25 (5.1)
Native Hawaiian or other Pacific Islander	1 (1.1)	4 (1.0)	5 (1.0)
American Indian or Alaska Native	0 (0.0)	2 (0.5)	2 (0.4)
More than one race	0 (0.0)	2 (0.5)	2 (0.4)
Not reported	17 (18.7)	15 (3.8)	32 (6.6)
Karnofsky score prior to HCT - no. (%)			
90-100%	61 (67.0)	191 (48.4)	252 (51.9)
< 90%	26 (28.6)	202 (51.1)	228 (46.9)
Not reported	4 (4.4)	2 (0.5)	6 (1.2)
HCT-CI - no. (%)			
0	15 (16.5)	75 (19.0)	90 (18.5)
1	23 (25.3)	57 (14.4)	80 (16.5)
2	17 (18.7)	68 (17.2)	85 (17.5)
3	15 (16.5)	79 (20.0)	94 (19.3)
4	9 (9.9)	46 (11.6)	55 (11.3)
5	3 (3.3)	26 (6.6)	29 (6.0)
6	7 (7.7)	25 (6.3)	32 (6.6)
7+	2 (2.2)	18 (4.6)	20 (4.1)
Missing/TBD	0 (0.0)	1 (0.3)	1 (0.2)
Myelofibrosis - no. (%)			
Primary MFS	70 (76.9)	327 (82.8)	397 (81.7)
Secondary MFS	21 (23.1)	68 (17.2)	89 (18.3)
Graft source - no. (%)			
Bone marrow	7 (7.7)	23 (5.8)	30 (6.2)
Peripheral blood	84 (92.3)	372 (94.2)	456 (93.8)
Donor type - no. (%)			
HLA-identical sibling	24 (26.4)	34 (8.6)	58 (11.9)
Haploidentical	38 (41.8)	197 (49.9)	235 (48.4)
Other related	1 (1.1)	6 (1.5)	7 (1.4)
Mismatched related - not otherwise specified	0 (0.0)	12 (3.0)	12 (2.5)
Well-matched unrelated (8/8)	24 (26.4)	103 (26.1)	127 (26.1)
Partially-matched unrelated (7/8)	4 (4.4)	37 (9.4)	41 (8.4)
Mis-matched unrelated (<= 6/8)	0 (0.0)	2 (0.5)	2 (0.4)

Characteristic	TED	CRF	Total
Unrelated (matching TBD)	0 (0.0)	2 (0.5)	2 (0.4)
Not reported	0 (0.0)	2 (0.5)	2 (0.4)
Spleen status prior to preparative regimen - no. (%)			
Spleen response/no splenomegaly prior to preparative regimen	22 (24.2)	116 (29.4)	138 (28.4)
No spleen response/splenomegaly prior to preparative regimen	69 (75.8)	275 (69.6)	344 (70.8)
Splenectomy	0 (0.0)	4 (1.0)	4 (0.8)
Method used to measure spleen size - no. (%)			
Physical assessment	27 (29.7)	43 (10.9)	70 (14.4)
Ultrasound	15 (16.5)	49 (12.4)	64 (13.2)
CT/MRI	7 (7.7)	63 (15.9)	70 (14.4)
N/A, splenectomy or no splenomegaly at evaluation of spleen size	22 (24.2)	120 (30.4)	142 (29.2)
Not reported	20 (22.0)	120 (30.4)	140 (28.8)
Conditioning regimen intensity - no. (%)			
MAC	60 (65.9)	146 (37.0)	206 (42.4)
RIC	23 (25.3)	159 (40.3)	182 (37.4)
NMA	8 (8.8)	89 (22.5)	97 (20.0)
Not reported	0 (0.0)	1 (0.3)	1 (0.2)
Conditioning regimen - no. (%)			
MAC			
TBI/Cy/Flu	0 (0.0)	1 (0.3)	1 (0.2)
TBI/Flu	3 (3.3)	13 (3.3)	16 (3.3)
TBI/other(s)	0 (0.0)	1 (0.3)	1 (0.2)
Bu/Cy	0 (0.0)	19 (4.8)	19 (3.9)
Bu/Mel	0 (0.0)	2 (0.5)	2 (0.4)
Flu/Bu/TT	29 (31.9)	49 (12.4)	78 (16.0)
Flu/Bu	28 (30.8)	54 (13.7)	82 (16.9)
Flu/Mel/TT	0 (0.0)	7 (1.8)	7 (1.4)
RIC			
TBI/Cy	0 (0.0)	2 (0.5)	2 (0.4)
TBI/Cy/Flu	1 (1.1)	31 (7.8)	32 (6.6)
TBI/Mel	8 (8.8)	40 (10.1)	48 (9.9)
TBI/Flu	7 (7.7)	15 (3.8)	22 (4.5)
Flu/Bu	5 (5.5)	18 (4.6)	23 (4.7)
Flu/Mel	2 (2.2)	53 (13.4)	55 (11.3)
NMA			
TBI/Cy	0 (0.0)	1 (0.3)	1 (0.2)
TBI/Cy/Flu	7 (7.7)	83 (21.0)	90 (18.5)

Characteristic	TED	CRF	Total
TBI/Flu	0 (0.0)	1 (0.3)	1 (0.2)
Flu/Bu	0 (0.0)	2 (0.5)	2 (0.4)
Flu/Mel	0 (0.0)	1 (0.3)	1 (0.2)
Cy/Flu	1 (1.1)	1 (0.3)	2 (0.4)
Not reported			
Missing	0 (0.0)	1 (0.3)	1 (0.2)
GVHD prophylaxis - no. (%)			
PtCy + other(s)	91 (100)	391 (99.0)	482 (99.2)
PtCy alone	0 (0.0)	4 (1.0)	4 (0.8)
Year of current transplant - no. (%)			
2013	0 (0.0)	3 (0.8)	3 (0.6)
2014	0 (0.0)	5 (1.3)	5 (1.0)
2015	0 (0.0)	7 (1.8)	7 (1.4)
2016	0 (0.0)	11 (2.8)	11 (2.3)
2017	7 (7.7)	45 (11.4)	52 (10.7)
2018	11 (12.1)	58 (14.7)	69 (14.2)
2019	15 (16.5)	89 (22.5)	104 (21.4)
2020	13 (14.3)	57 (14.4)	70 (14.4)
2021	22 (24.2)	56 (14.2)	78 (16.0)
2022	23 (25.3)	64 (16.2)	87 (17.9)
Median follow-up of survivors (range), months - median (range)	24.4 (1.6-76.3)	36.7 (2.6-99.7)	35.9 (1.6-99.7)

Field	Response
Proposal Number	2310-180-ALI
Proposal Title	Impact of spleen size reduction using JAK inhibitors, spleen irradiation, or splenectomy on allogeneic hematopoietic cellular transplantation outcomes in myelofibrosis.
Key Words	myelofibrosis, splenomegaly, ruxolitinib, fedratinib, pacritinib, JAK inhibitors, hydroxyurea, interferon, spleen irradiation, splenectomy, splenic embolization, allo-HCT
Principal Investigator #1: - First and last name, degree(s)	Alaa Ali
Principal Investigator #1: - Email address	alaa.ali@gunet.georgetown.edu
Principal Investigator #1: - Institution name	Georgetown Lombardi Comprehensive Cancer Center
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Anne S. Renteria
Principal Investigator #2 (If applicable): - Email address:)	anne.renteria@medstar.net
Principal Investigator #2 (If applicable): - Institution name:	Georgetown Lombardi Comprehensive Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Chronic Leukemia
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	What is the impact of different spleen size reduction strategies on engraftment, graft failure, poor graft function, relapse rate, non-relapse mortality (NRM) and overall survival (OS) post allogeneic hematopoietic cellular transplantation (allo-HCT)?

Field	Response
RESEARCH HYPOTHESIS:	Splenomegaly has been associated with worse outcomes after allo-HCT when compared to patients without significant splenomegaly. Several strategies have been employed during the pre-HCT period in attempting to reduce spleen size but currently no clear consensus exists on how to best manage splenomegaly prior to allo-HCT. In the absence of solid prospective data, a large retrospective registry study might help identify circumstances where one of these interventions can improve outcomes following HCT. We propose to investigate the survival of patients diagnosed with primary or secondary myelofibrosis and with splenomegaly who undergo allo-HCT. We hypothesize that the addition of JAK inhibitors to previously available spleen-reducing strategies has significantly impacted patients' outcomes and that different strategies might best apply to specific populations of patients with myelofibrosis.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Compare the outcomes of patients diagnosed with primary or secondary myelofibrosis and splenomegaly who responded to spleen size reducing treatment (JAK inhibitors including second-generation agents, hydroxyurea, interferon, spleen irradiation, splenic embolization, or splenectomy) versus patients who did not respond or did not receive such treatment prior to undergoing allo-HCT in terms of: Primary endpoint: Overall survival (OS) Secondary endpoints: o 1-year TRM, 1-year OS, and relapse rate o Event free survival: time from HCT until relapse/progression or death o Rate of graft failure, poor graft function, delayed engraftment and mixed chimerism. o OS based on best spleen response to spleen reducing strategies and to best spleen response to allo-HCT. o OS based on the duration of JAK inhibition exposure prior to transplant and number of lines of JAK inhibitors that patients required. o Grade II-IV aGVHD. 2-year cumulative incidence of cGVHD o Grade 2 or higher infection, including viral reactivation. o Spleen size response with different conditioning regimens. o Rate of organ toxicities and failure (e.g, liver)

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Once the aim of the project is completed, it will provide treating clinicians with evidence (although retrospective) on whether any of the spleen reducing strategies might benefit a particular group of patients with myelofibrosis in terms of improving survival and other transplant outcomes. It may allow the identification of an optimal timing for allo-HCT when related to spleen size, optimal duration of JAK inhibition prior to transplant, and other spleen size reducing strategies.
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Splenomegaly is a hallmark of myelofibrosis and more than 80% of patients present with variable degrees of splenomegaly at diagnosis. [1] Nevertheless, it is not included in risk scores, including The Myelofibrosis Transplant Scoring System (MTSS). [2] Splenomegaly affects engraftment and relapse after allo-HCT, but it is unclear whether that translates into an impact on mortality or overall survival.[3, 4] Furthermore, it remains debatable whether pharmacological or other interventions (surgery, splenic embolization or radiation) to reduce spleen size prior to allo HCT can improve the outcomes of patients, and a wide range of practices is encountered among transplant centers in Europe and the US. Previous small prospective or retrospective studies have not been able to provide conclusive evidence and carry multiple limitations. Much of that literature emerged from European centers where conditioning and GVHD prevention strategies tend to be rather different from those applied in the US. [4-8] Moreover, second-generation JAK inhibitors are being increasingly used prior to transplant and they seem to be more effective than ruxolitinib in reducing splenomegaly [9, 10], but their impact in the setting of a transplant has not been examined yet. In addition, although post-transplant cyclophosphamide (PTCy) for GVHD prevention is increasingly utilized in non-haploidentical allo-HCT and is effective in reducing acute and chronic GVHD, it has been associated with higher incidence rates of secondary graft rejection, slower hematologic recovery, delayed engraftment, and higher infection rates. [11, 12] The benefit of reducing the size of splenomegaly, a known risk factor for graft failure and poor graft function in myelofibrosis patients, might be more prominent when PTCy is used for GVHD prevention. Graft failure, poor graft function and delayed hematopoietic recovery are major challenges in allo-HCT for myelofibrosis.[13] Interventions that decrease the impact of these challenges have the potential to improve the outcomes of patients with myelofibrosis undergoing allo-HCT.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: - Patients with primary myelofibrosis or post polycythemia vera or essential thrombocythemia myelofibrosis who underwent allo HCT. - Presence of splenomegaly at diagnosis - Received or did not receive: ruxolitinib, fedratinib, pacritinib, hydroxyurea, interferon, spleen irradiation, splenic embolization or splenectomy. - Related or unrelated donor - Matched or mismatched donor - Any conditioning regimen - Any GVHD prevention strategy Exclusion criteria: - Myelofibrosis with accelerated or blast phase transformation.
Does this study include pediatric patients?	Yes
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Form 2057 (Myeloproliferative Neoplasms Pre-Infusion) - Splenomegaly at diagnosis: method used to measure spleen size, spleen size - Maximum DIPSS - Molecular studies, driver mutation, cytogenetics - Systemic therapy: ruxulitinib, fedratinib, other JAK 1 or JAK2 inhibitor, hydroxyurea, other - Best response to therapy - Was spleen response achieved? - Splenic radiation - Splenectomy: date performed - Portal HTN at HCT infusion Form 2157 (Myeloproliferative Neoplasms Post-Infusion) - Best response to HCT - Was a spleen response achieved? Method used to measure splenomegaly, spleen size. Form 2400 (pre-transplant essential data) - Donor (allogeneic unrelated) - Product type (bone marrow, PBSC) - Unrelated donor type (matched, mismatched) - Preparative regimen (myeloablative, non-myeloablative, reduced intensity) - GVHD prophylaxis Form 2450 (post-transplant essential data), Form 2100 (post-HSCT data), Form 2900 (recipient death data) - Initial ANC and platelet recovery - aGVHD occurrence, persistence, grade and organ stage at diagnosis, maximum grade and stage - cGVHD occurrence, persistence, maximum grade, steroids treatment, other immunosuppressants - Chimerism - Survival status - Primary cause of death

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Field	Response
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CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Table 1. Characteristics of patients undergoing a 1st allo HCT for myelofibrosis that did not have splenomegaly resolve between diagnosis and the preparative regimen, 2008-2019

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Hydroxyurea	No/other therapy*	Total
No. of patients	294	31	52	126	503
No. of centers	93	19	34	63	115
Recipient age - no. (%)					
Median (min-max)	61.7 (25.0-75.4)	62.0 (44.6-72.1)	56.9 (32.6-69.4)	60.1 (1.1-75.8)	60.8 (1.1-75.8)
<10	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)	2 (0.4)
10-17	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.2)
18-29	2 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
30-39	2 (0.7)	0 (0.0)	2 (3.8)	2 (1.6)	6 (1.2)
40-49	26 (8.8)	6 (19.4)	12 (23.1)	22 (17.5)	66 (13.1)
50-59	95 (32.3)	7 (22.6)	17 (32.7)	35 (27.8)	154 (30.6)
60-69	146 (49.7)	16 (51.6)	21 (40.4)	59 (46.8)	242 (48.1)
>=70	23 (7.8)	2 (6.5)	0 (0.0)	5 (4.0)	30 (6.0)
Track - no. (%)					
TED	12 (4.1)	0 (0.0)	3 (5.8)	4 (3.2)	19 (3.8)
CRF	282 (95.9)	31 (100)	49 (94.2)	122 (96.8)	484 (96.2)
CCN region at transplant - no. (%)					
US	272 (92.5)	27 (87.1)	37 (71.2)	112 (88.9)	448 (89.1)
Canada	1 (0.3)	0 (0.0)	0 (0.0)	3 (2.4)	4 (0.8)
Europe	10 (3.4)	3 (9.7)	2 (3.8)	5 (4.0)	20 (4.0)
Asia	1 (0.3)	0 (0.0)	1 (1.9)	4 (3.2)	6 (1.2)
Australia/New Zealand	5 (1.7)	0 (0.0)	7 (13.5)	1 (0.8)	13 (2.6)
Mideast/Africa	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.2)
Central/South America	5 (1.7)	1 (3.2)	5 (9.6)	0 (0.0)	11 (2.2)
Sex - no. (%)					
Male	198 (67.3)	16 (51.6)	33 (63.5)	85 (67.5)	332 (66.0)
Female	96 (32.7)	15 (48.4)	19 (36.5)	41 (32.5)	171 (34.0)
Race - no. (%)					
White	260 (88.4)	24 (77.4)	45 (86.5)	104 (82.5)	433 (86.1)
Black or African American	11 (3.7)	2 (6.5)	3 (5.8)	6 (4.8)	22 (4.4)
Asian	9 (3.1)	1 (3.2)	0 (0.0)	9 (7.1)	19 (3.8)
Native Hawaiian or other Pacific Islander	3 (1.0)	0 (0.0)	3 (5.8)	1 (0.8)	7 (1.4)
American Indian or Alaska Native	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.8)	2 (0.4)
More than one race	1 (0.3)	0 (0.0)	0 (0.0)	2 (1.6)	3 (0.6)

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Hydroxyurea	No/other therapy*	Total
Not reported	9 (3.1)	4 (12.9)	1 (1.9)	3 (2.4)	17 (3.4)
Karnofsky score prior to HCT - no. (%)					
90-100%	140 (47.6)	6 (19.4)	33 (63.5)	71 (56.3)	250 (49.7)
< 90%	151 (51.4)	25 (80.6)	19 (36.5)	53 (42.1)	248 (49.3)
Not reported	3 (1.0)	0 (0.0)	0 (0.0)	2 (1.6)	5 (1.0)
HCT-CI - no. (%)					
0	58 (19.7)	7 (22.6)	17 (32.7)	45 (35.7)	127 (25.2)
1	37 (12.6)	3 (9.7)	8 (15.4)	13 (10.3)	61 (12.1)
2	64 (21.8)	4 (12.9)	5 (9.6)	15 (11.9)	88 (17.5)
3	51 (17.3)	11 (35.5)	11 (21.2)	24 (19.0)	97 (19.3)
4	36 (12.2)	0 (0.0)	6 (11.5)	14 (11.1)	56 (11.1)
5	19 (6.5)	2 (6.5)	1 (1.9)	7 (5.6)	29 (5.8)
6	12 (4.1)	2 (6.5)	2 (3.8)	4 (3.2)	20 (4.0)
7+	17 (5.8)	2 (6.5)	1 (1.9)	4 (3.2)	24 (4.8)
Missing/TBD	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	1 (0.2)
Primary disease - no. (%)					
Myelodysplastic/myeloprolifterative disorders (please classify all preleukemias)	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	1 (0.2)
Myeloproliferative Neoplasms	294 (100)	31 (100)	51 (98.1)	126 (100)	502 (99.8)
Graft source - no. (%)					
Bone marrow	14 (4.8)	0 (0.0)	3 (5.8)	8 (6.3)	25 (5.0)
Peripheral blood	280 (95.2)	31 (100)	49 (94.2)	118 (93.7)	478 (95.0)
Donor type - no. (%)					
HLA-identical sibling	81 (27.6)	4 (12.9)	15 (28.8)	42 (33.3)	142 (28.2)
Twin	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.2)
Haploidentical	26 (8.8)	3 (9.7)	4 (7.7)	11 (8.7)	44 (8.7)
Other related	2 (0.7)	0 (0.0)	2 (3.8)	1 (0.8)	5 (1.0)
Mismatched related - not otherwise specified	4 (1.4)	1 (3.2)	0 (0.0)	0 (0.0)	5 (1.0)
Well-matched unrelated (8/8)	155 (52.7)	19 (61.3)	21 (40.4)	58 (46.0)	253 (50.3)
Partially-matched unrelated (7/8)	19 (6.5)	2 (6.5)	7 (13.5)	11 (8.7)	39 (7.8)
Mis-matched unrelated (<= 6/8)	0 (0.0)	1 (3.2)	1 (1.9)	1 (0.8)	3 (0.6)
Unrelated (matching TBD)	7 (2.4)	0 (0.0)	2 (3.8)	1 (0.8)	10 (2.0)
Not reported	0 (0.0)	1 (3.2)	0 (0.0)	0 (0.0)	1 (0.2)
Conditioning regimen intensity - no. (%)					
MAC	121 (41.2)	11 (35.5)	20 (38.5)	64 (50.8)	216 (42.9)

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Hydroxyurea	No/other therapy*	Total
RIC	155 (52.7)	18 (58.1)	28 (53.8)	58 (46.0)	259 (51.5)
NMA	16 (5.4)	2 (6.5)	3 (5.8)	4 (3.2)	25 (5.0)
TBD	2 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
Not reported	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	1 (0.2)
Conditioning regimen - no. (%)					
MAC					
TBI/Cy	1 (0.3)	0 (0.0)	1 (1.9)	4 (3.2)	6 (1.2)
TBI/Cy/Flu	2 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
TBI/Cy/Flu/TT	0 (0.0)	1 (3.2)	0 (0.0)	0 (0.0)	1 (0.2)
TBI/Flu	2 (0.7)	0 (0.0)	1 (1.9)	0 (0.0)	3 (0.6)
Bu/Cy	23 (7.8)	0 (0.0)	5 (9.6)	21 (16.7)	49 (9.7)
Flu/Bu/TT	10 (3.4)	2 (6.5)	1 (1.9)	3 (2.4)	16 (3.2)
Flu/Bu	80 (27.2)	8 (25.8)	11 (21.2)	34 (27.0)	133 (26.4)
Flu/Mel/TT	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.8)	2 (0.4)
Other(s)	2 (0.7)	0 (0.0)	0 (0.0)	1 (0.8)	3 (0.6)
None	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	1 (0.2)
RIC					
TBI/Cy/Flu	4 (1.4)	0 (0.0)	0 (0.0)	1 (0.8)	5 (1.0)
TBI/Mel	10 (3.4)	1 (3.2)	3 (5.8)	2 (1.6)	16 (3.2)
TBI/Flu	16 (5.4)	1 (3.2)	3 (5.8)	7 (5.6)	27 (5.4)
TBI/other(s)	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	2 (0.4)
Flu/Bu	33 (11.2)	4 (12.9)	6 (11.5)	15 (11.9)	58 (11.5)
Flu/Mel	92 (31.3)	12 (38.7)	14 (26.9)	32 (25.4)	150 (29.8)
Other(s)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.2)
NMA					
TBI/Cy/Flu	15 (5.1)	0 (0.0)	1 (1.9)	2 (1.6)	18 (3.6)
TBI/Flu	1 (0.3)	1 (3.2)	2 (3.8)	1 (0.8)	5 (1.0)
Flu/Bu	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.2)
Cy/Flu	0 (0.0)	1 (3.2)	0 (0.0)	0 (0.0)	1 (0.2)
TBD					
Treosulfan	2 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
Not reported					
Mel alone	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	1 (0.2)
GVHD prophylaxis - no. (%)					
None	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.2)
Ex-vivo T-cell depletion	0 (0.0)	1 (3.2)	0 (0.0)	0 (0.0)	1 (0.2)
CD34 selection	4 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.8)

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Hydroxyurea	No/other therapy*	Total
PtCy + other(s)	62 (21.1)	3 (9.7)	7 (13.5)	20 (15.9)	92 (18.3)
PtCy alone	0 (0.0)	1 (3.2)	0 (0.0)	0 (0.0)	1 (0.2)
TAC + MMF +- other(s) (except PtCy)	42 (14.3)	5 (16.1)	9 (17.3)	10 (7.9)	66 (13.1)
TAC + MTX +- other(s) (except MMF, PtCy)	135 (45.9)	15 (48.4)	21 (40.4)	67 (53.2)	238 (47.3)
TAC + other(s) (except MMF, MTX, PtCy)	20 (6.8)	1 (3.2)	0 (0.0)	5 (4.0)	26 (5.2)
TAC alone	8 (2.7)	1 (3.2)	0 (0.0)	4 (3.2)	13 (2.6)
CSA + MMF +- other(s) (except PtCy,TAC)	9 (3.1)	1 (3.2)	2 (3.8)	5 (4.0)	17 (3.4)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	13 (4.4)	1 (3.2)	12 (23.1)	9 (7.1)	35 (7.0)
CSA alone	0 (0.0)	1 (3.2)	1 (1.9)	1 (0.8)	3 (0.6)
Other(s)	1 (0.3)	1 (3.2)	0 (0.0)	4 (3.2)	6 (1.2)
Year of current transplant - no. (%)					
2008	1 (0.3)	3 (9.7)	6 (11.5)	12 (9.5)	22 (4.4)
2009	0 (0.0)	1 (3.2)	13 (25.0)	12 (9.5)	26 (5.2)
2010	0 (0.0)	0 (0.0)	1 (1.9)	5 (4.0)	6 (1.2)
2011	0 (0.0)	0 (0.0)	2 (3.8)	2 (1.6)	4 (0.8)
2012	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	1 (0.2)
2013	4 (1.4)	0 (0.0)	3 (5.8)	11 (8.7)	18 (3.6)
2014	20 (6.8)	5 (16.1)	5 (9.6)	12 (9.5)	42 (8.3)
2015	26 (8.8)	1 (3.2)	5 (9.6)	12 (9.5)	44 (8.7)
2016	33 (11.2)	2 (6.5)	3 (5.8)	6 (4.8)	44 (8.7)
2017	56 (19.0)	10 (32.3)	7 (13.5)	19 (15.1)	92 (18.3)
2018	72 (24.5)	4 (12.9)	3 (5.8)	17 (13.5)	96 (19.1)
2019	82 (27.9)	5 (16.1)	3 (5.8)	18 (14.3)	108 (21.5)
Median follow-up of survivors (range), months - median (range)	54.2 (6.4-102.6)	36.7 (3.3-98.4)	72.6 (24.0-169.7)	81.6 (12.1-174.2)	60.1 (3.3-174.2)

***No therapy = 75; Thalidomide = 3; Erythopoietin = 4; Decitabine = 5; Corticosteroids = 2; Azacytidine = 4; Other drug = 15; 2 or more drugs given = 18**

Table 2. Characteristics of patients undergoing a 1st allo HCT for myelofibrosis that had splenomegaly resolve between diagnosis and the preparative regimen, 2008-2019

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Splenectomy	Hydroxyurea	No/other therapy*	Total
No. of patients	117	2	37	16	46	218
No. of centers	52	2	29	14	31	74
Recipient age - no. (%)						
Median (min-max)	61.7 (16.2-74.8)	51.1 (38.5-63.7)	59.4 (36.5-71.2)	59.2 (42.5-70.2)	57.9 (40.3-73.7)	60.4 (16.2-74.8)
10-17	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
30-39	1 (0.9)	1 (50.0)	1 (2.7)	0 (0.0)	0 (0.0)	3 (1.4)
40-49	7 (6.0)	0 (0.0)	8 (21.6)	3 (18.8)	11 (23.9)	29 (13.3)
50-59	39 (33.3)	0 (0.0)	11 (29.7)	7 (43.8)	17 (37.0)	74 (33.9)
60-69	55 (47.0)	1 (50.0)	14 (37.8)	5 (31.3)	16 (34.8)	91 (41.7)
>=70	14 (12.0)	0 (0.0)	3 (8.1)	1 (6.3)	2 (4.3)	20 (9.2)
Track - no. (%)						
TED	9 (7.7)	0 (0.0)	0 (0.0)	1 (6.3)	4 (8.7)	14 (6.4)
CRF	108 (92.3)	2 (100)	37 (100)	15 (93.8)	42 (91.3)	204 (93.6)
CCN region at transplant - no. (%)						
US	116 (99.1)	1 (50.0)	35 (94.6)	13 (81.3)	44 (95.7)	209 (95.9)
Canada	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.3)	0 (0.0)	1 (0.5)
Europe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	1 (0.5)
Asia	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.3)	1 (2.2)	2 (0.9)
Australia/New Zealand	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Mideast/Africa	0 (0.0)	1 (50.0)	1 (2.7)	0 (0.0)	0 (0.0)	2 (0.9)
Central/South America	0 (0.0)	0 (0.0)	1 (2.7)	1 (6.3)	0 (0.0)	2 (0.9)
Sex - no. (%)						
Male	70 (59.8)	2 (100)	18 (48.6)	10 (62.5)	20 (43.5)	120 (55.0)
Female	47 (40.2)	0 (0.0)	19 (51.4)	6 (37.5)	26 (56.5)	98 (45.0)
Race - no. (%)						
White	104 (88.9)	2 (100)	36 (97.3)	12 (75.0)	39 (84.8)	193 (88.5)
Black or African American	6 (5.1)	0 (0.0)	0 (0.0)	2 (12.5)	2 (4.3)	10 (4.6)
Asian	5 (4.3)	0 (0.0)	0 (0.0)	1 (6.3)	1 (2.2)	7 (3.2)

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Splenectomy	Hydroxyurea	No/other therapy*	Total
More than one race	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	1 (0.5)
Not reported	2 (1.7)	0 (0.0)	1 (2.7)	1 (6.3)	3 (6.5)	7 (3.2)
Karnofsky score prior to HCT - no. (%)						
90-100%	66 (56.4)	1 (50.0)	18 (48.6)	10 (62.5)	35 (76.1)	130 (59.6)
< 90%	50 (42.7)	1 (50.0)	18 (48.6)	6 (37.5)	11 (23.9)	86 (39.4)
Not reported	1 (0.9)	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	2 (0.9)
HCT-CI - no. (%)						
0	23 (19.7)	1 (50.0)	8 (21.6)	4 (25.0)	14 (30.4)	50 (22.9)
1	21 (17.9)	0 (0.0)	5 (13.5)	1 (6.3)	8 (17.4)	35 (16.1)
2	17 (14.5)	1 (50.0)	8 (21.6)	1 (6.3)	7 (15.2)	34 (15.6)
3	26 (22.2)	0 (0.0)	10 (27.0)	3 (18.8)	7 (15.2)	46 (21.1)
4	17 (14.5)	0 (0.0)	4 (10.8)	3 (18.8)	5 (10.9)	29 (13.3)
5	8 (6.8)	0 (0.0)	1 (2.7)	0 (0.0)	3 (6.5)	12 (5.5)
6	4 (3.4)	0 (0.0)	0 (0.0)	2 (12.5)	1 (2.2)	7 (3.2)
7+	1 (0.9)	0 (0.0)	1 (2.7)	2 (12.5)	1 (2.2)	5 (2.3)
Primary disease - no. (%)						
Myeloproliferative Neoplasms	117 (100)	2 (100)	37 (100)	16 (100)	46 (100)	218 (100)
Graft source - no. (%)						
Bone marrow	7 (6.0)	0 (0.0)	1 (2.7)	2 (12.5)	3 (6.5)	13 (6.0)
Peripheral blood	110 (94.0)	2 (100)	36 (97.3)	14 (87.5)	43 (93.5)	205 (94.0)
Donor type - no. (%)						
HLA-identical sibling	27 (23.1)	1 (50.0)	10 (27.0)	4 (25.0)	12 (26.1)	54 (24.8)
Haploidentical	13 (11.1)	1 (50.0)	2 (5.4)	3 (18.8)	6 (13.0)	25 (11.5)
Other related	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	2 (0.9)
Mismatched related - not otherwise specified	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Well-matched unrelated (8/8)	67 (57.3)	0 (0.0)	18 (48.6)	7 (43.8)	23 (50.0)	115 (52.8)
Partially-matched unrelated (7/8)	7 (6.0)	0 (0.0)	5 (13.5)	0 (0.0)	3 (6.5)	15 (6.9)

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Splenectomy	Hydroxyurea	No/other therapy*	Total
Unrelated (matching TBD)	1 (0.9)	0 (0.0)	1 (2.7)	1 (6.3)	1 (2.2)	4 (1.8)
Not reported	0 (0.0)	0 (0.0)	1 (2.7)	1 (6.3)	0 (0.0)	2 (0.9)
Conditioning regimen intensity - no. (%)						
MAC	53 (45.3)	0 (0.0)	17 (45.9)	11 (68.8)	25 (54.3)	106 (48.6)
RIC	51 (43.6)	0 (0.0)	17 (45.9)	5 (31.3)	18 (39.1)	91 (41.7)
NMA	12 (10.3)	2 (100)	3 (8.1)	0 (0.0)	2 (4.3)	19 (8.7)
TBD	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	2 (0.9)
Conditioning regimen - no. (%)						
MAC						
TBI/Cy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	1 (0.5)
TBI/Flu	2 (1.7)	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	3 (1.4)
Bu/Cy	17 (14.5)	0 (0.0)	6 (16.2)	3 (18.8)	4 (8.7)	30 (13.8)
Bu/Mel	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)	1 (2.2)	2 (0.9)
Flu/Bu/TT	3 (2.6)	0 (0.0)	1 (2.7)	1 (6.3)	2 (4.3)	7 (3.2)
Flu/Bu	31 (26.5)	0 (0.0)	7 (18.9)	6 (37.5)	17 (37.0)	61 (28.0)
Flu/Mel/TT	0 (0.0)	0 (0.0)	1 (2.7)	1 (6.3)	0 (0.0)	2 (0.9)
RIC						
TBI/Cy/Flu	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)	1 (2.2)	2 (0.9)
TBI/Mel	3 (2.6)	0 (0.0)	1 (2.7)	0 (0.0)	1 (2.2)	5 (2.3)
TBI/Flu	8 (6.8)	0 (0.0)	3 (8.1)	0 (0.0)	2 (4.3)	13 (6.0)
Flu/Bu	14 (12.0)	0 (0.0)	4 (10.8)	1 (6.3)	4 (8.7)	23 (10.6)
Flu/Mel	26 (22.2)	0 (0.0)	8 (21.6)	4 (25.0)	10 (21.7)	48 (22.0)
NMA						
TBI/Cy/Flu	8 (6.8)	1 (50.0)	0 (0.0)	0 (0.0)	2 (4.3)	11 (5.0)
TBI/Flu	1 (0.9)	1 (50.0)	1 (2.7)	0 (0.0)	0 (0.0)	3 (1.4)
Flu/Bu	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	1 (0.5)
Cy/Flu	2 (1.7)	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	3 (1.4)
Other(s)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
TBD						
TBI/Mel	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
TBI/Flu	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	1 (0.5)
GVHD prophylaxis - no. (%)						
PtCy + other(s)	30 (25.6)	1 (50.0)	2 (5.4)	5 (31.3)	9 (19.6)	47 (21.6)

Characteristic	Ruxolitinib or JAK1/2 inhibitor	Splenic radiation	Splenectomy	Hydroxyurea	No/other therapy*	Total
TAC + MMF +- other(s) (except PtCy)	12 (10.3)	0 (0.0)	6 (16.2)	1 (6.3)	2 (4.3)	21 (9.6)
TAC + MTX +- other(s) (except MMF, PtCy)	61 (52.1)	0 (0.0)	19 (51.4)	6 (37.5)	28 (60.9)	114 (52.3)
TAC + other(s) (except MMF, MTX, PtCy)	7 (6.0)	0 (0.0)	2 (5.4)	1 (6.3)	3 (6.5)	13 (6.0)
TAC alone	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
CSA + MMF +- other(s) (except PtCy,TAC)	2 (1.7)	1 (50.0)	5 (13.5)	0 (0.0)	0 (0.0)	8 (3.7)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	3 (2.6)	0 (0.0)	2 (5.4)	3 (18.8)	4 (8.7)	12 (5.5)
Other(s)	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	1 (0.5)
Year of current transplant - no. (%)						
2008	0 (0.0)	0 (0.0)	6 (16.2)	0 (0.0)	2 (4.3)	8 (3.7)
2009	0 (0.0)	1 (50.0)	4 (10.8)	1 (6.3)	1 (2.2)	7 (3.2)
2010	0 (0.0)	0 (0.0)	4 (10.8)	0 (0.0)	1 (2.2)	5 (2.3)
2011	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	1 (0.5)
2013	2 (1.7)	0 (0.0)	2 (5.4)	0 (0.0)	5 (10.9)	9 (4.1)
2014	6 (5.1)	0 (0.0)	5 (13.5)	1 (6.3)	1 (2.2)	13 (6.0)
2015	6 (5.1)	0 (0.0)	3 (8.1)	2 (12.5)	1 (2.2)	12 (5.5)
2016	13 (11.1)	0 (0.0)	2 (5.4)	2 (12.5)	5 (10.9)	22 (10.1)
2017	31 (26.5)	1 (50.0)	5 (13.5)	0 (0.0)	8 (17.4)	45 (20.6)
2018	23 (19.7)	0 (0.0)	4 (10.8)	7 (43.8)	4 (8.7)	38 (17.4)
2019	36 (30.8)	0 (0.0)	2 (5.4)	3 (18.8)	17 (37.0)	58 (26.6)
Median follow-up of survivors (range), months - median (range)	59.9 (6.1-95.6)	119.9 (119.9-119.9)	96.7 (34.3-168.6)	58.4 (12.5-96.2)	60.1 (26.2-176.7)	60.8 (6.1-176.7)

***No therapy = 22; Thalidomide = 2; Lenalidomide = 2; Erythopoietin = 1; Decitabine = 3; Corticosteroids = 3; Azacytidine = 4; Other drug = 4; 2 or more drugs given = 5**