A G E N D A
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**
   a. **Minutes and overview plan from April 2022 meeting** (Attachment 1)
   b. **Introduction of incoming co-chair:** Mark Juckett, MD
   c. **Instructions for sign-in and voting**

2. **Accrual Summary** (Attachment 2)

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

   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 (Attachment 3)

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

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)

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

Dropped Proposed Studies

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)*

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA
Salt Lake City, UT
Sunday, April 24, 2022, 12:15 p.m. – 2:15 p.m. MDT

Co-Chair:	**Ryotaro Nakamura, MD, City of Hope**
	Phone: 713-745-3055; Email: rnakamura@coh.org
Co-Chair:	**Betul Oran, MD, MD Anderson Cancer Center**
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Co-Chair:	**Bart Scott, MD, Fred Hutchinson Cancer Research Center**
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1. Introduction

*The Chronic Leukemia Working Committee (CKWC) met on **Sunday, April 24, 2022,** at 12:15 p.m. The chairs, scientific director and statisticians were all presented at the meeting. Attendees were asked to have their name badges scanned at the front gate for attendance purpose and to maintain the committee membership roster.*

As the scientific director of the CKWC, Dr. Wael Saber welcomed the attendees on behalf of the working committee leadership and presented Dr. Ryotaro Nakamura in charge or presenting the welcome slides.

2. Accrual summary

Dr. Nakamura 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 2021 were referenced, as well as abstracts that were presented at various conferences. Dr. Nakamura 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. **CK17-02:** Oran B, Ahn KW, Fretham C, Beitinjaneh A, Bashey A, Pawarode A, Wirk B, Scott BL, Savani BN, Bredeson C, Weisdorf D, Marks DI, Rizzieri D, Copelan E, Hildebrandt GC, Hale GA, Murthy HS, Lazarus HM, Cerny J, Liesveld JL, Yared JA, Yves-Cahn J, Szer J, Verdonck LF, Aljurf M, van der Poel M, Litzow M, Kalaycio M, Grunwald MR, Diaz MA, Sabloff M, Kharfan-Dabaja MA, Majhail NS, Farhadfar N, Reshef R, Olsson RF, Gale RP, Nakamura R, Seo S, Chhabra S, Hashmi S, Farhan S, Ganguly S, Nathan S, Nishihori T,

Jain T, Agrawal V, Bacher U, Popat U, Saber W. Fludarabine and melphalan compared with reduced doses of busulfan and fludarabine improve transplantation outcomes in older patients with myelodysplastic syndromes. **Transplantation and Cellular Therapy. 2021 Nov 1; 27(11):921.e1-921.e10. doi:10.1016/j.jtct.2021.08.007.** ***Epub 2021 Aug 14.***

b. **CK18-03:** Guru Murthy GS, Kim S, Hu Z-H, Estrada-Merly N, Abid MB, Aljurf M, Bacher U, Badawy SM, Beitinjaneh A, Bredeson C, Cahn J-Y, Cerny J, Diaz Perez MA, Farhadfar N, Gale RP, Ganguly S, Gergis U, Hildebrandt GC, Grunwald MR, Hashmi S, Hossain NM, Kalaycio M, Kamble RT, Kharfan-Dabaja MA, Hamilton B, Lazarus HM, Liesveld J, Litzow M, Marks DI, Murthy HS, Nathan S, Nazha A, Nishihori T, Patel SS, Pawaride A, Rizzieri D, Savani B, Seo S, Solh M, Ustun C, van der Poel M, Verdonck LF, Vij R, Wirk B, Oran B, Nakamura R, Scott B, Saber W. Relapse and disease-free survival in patients with myelodysplastic syndrome undergoing allogeneic hematopoietic cell transplantation using older matched sibling donors vs younger matched unrelated donors**. JAMA Oncology. 2022 Mar 1; 8(3):404-411. doi:10.1001/jamaoncol.2021.6846.** ***Epub 2022 Jan 13. PMC8759031.***

c. **CK19-01A:** Murthy HS, Ahn KW, Estrada-Merly N, Alkhateeb HB, Bal S, Kharfan-Dabaja MA, Dholaria B, Foss F, Gowda L, Jagadeesh D, Sauter C, Bilal Abid M, 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, Pashna N. 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.***

d. Mei M, Pillai R, Kim S, Estrada-Merly N, Afkhami M, Yang L, Meng Z, Abid MB, Aljurf M, Bacher U, Beitinjaneh A, Bredeson C, Cahn JY, Cerny J, Copelan E, Cutler C, DeFilipp Z, Diaz Perez MA, Farhadfar N, Freytes CO, Gadalla SM, Ganguly S, Gale RP, Gergis U, Grunwald MR, Hamilton BK, Hashmi S, Hildebrandt GC, Lazarus HM, Litzow M, Munker R, Murthy HS, Nathan S, Nishihori T, Patel SS, Rizzieri D, Seo S, Shah MV, Solh M, Verdonck LF, Vij R, Sobecks RM, Oran B, Scott BL, 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. 2022 Apr 21. doi: 10.3324/haematol.2021.280203.** ***Epub ahead of print. PMID: 35443559.***

e. **CK18-02:** The impact of somatic mutations on allogeneic transplant in chronic myelomonocytic leukemia. (M Mei/ R Nakamura/ R Pillai) ***Accepted in Haematologica. Oral presentation, ASH 2021.***

f. **CK16-01:** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley) ***Oral presentation, ASH 2021.***

g. **CK20-01:** Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. (G Murthy/ W Saber) ***Oral presentation, ASH 2021.***

h. **CK19-01B:** Outcomes after HCT for rare chronic leukemias: Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. (B Dholaria/B Savani/M Kharfan-Dabaja). ***Oral presentation, EBMT 2022.***

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. **CK16-01** Identification of germline predisposition mutations in young myelodysplastic syndrome patients. (L Godley). ***Submitted.***

b. **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)**.** ***Manuscript Preparation.***

c. **CK19-01b** Outcomes after HCT for rare chronic leukemias: Outcomes of chronic neutrophilic leukemia patients who underwent allogeneic hematopoietic cell transplantation. (B Dholaria/B Savani/M Kharfan-Dabaja). ***Accepted in BJH.***

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

e. **CK21-01** Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. (Tania Jain/ M Queralt Sala/V Gupta/ T Nishihori)***. Datafile Preparation.***

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. Bart Scott then announced the presenters for the first proposal and asked the audience to stand up to the microphones and present themselves before asking the presenter about their proposed studies. Also welcomed Dr. Betul Oran which attended the session virtually helped moderating the virtual chat.

a. **PROP 2110-259:** Allogeneic Hematopoietic Cell Transplantation (HCT) for the Treatment of Myelodysplastic Syndromes (MDS) in Younger Adults. (A Jimenez/T Wang) (Attachment 4)

Dr. Jimenez presented the proposal on behalf of the group. The proposal hypothesizes that Consolidation with allogeneic Hematopoietic Cell Transplant (HCT) is an effective strategy for the treatment of Myelodysplastic Syndromes (MDS) in young patients. The study aims to evaluate the clinical outcomes following allogeneic HCT in younger MDS patients (i.e., <60 years at the time of HCT). To achieve this objective, it will focus on describing clinical features and outcomes (overall survival, relapse-free survival, GVHF-free, relapse-free survival, non-relapse mortality, and cumulative incidence of relapse) in younger patients with MDS receiving allogeneic HCT consolidation. Also, evaluate differences in transplant outcomes (overall survival, relapse-free survival, cumulative incidence of relapse, cumulative incidence of non-relapse mortality and cumulative incidence of acute and chronic GVHD) between sub-cohorts stratified based on IPSS-R categories, age (AYA: 16-39, 40-49, 50-59) conditioning regimen, graft/donor source and HCT-CI. A total of 1683 MDS patients reported to CIBMTR between the period 2008 to 2019

met the selection criteria for this concept. More than a half (56%) of this patients had 50-59 years of age when transplanted.

The proposal was open for discussion. The audience asked Dr. Jimenez if there are any publications stating differences in the biology of the disease when comparing young and old patients. Other member asked on why the inclusion of patients up to 59 years, when those cases would not be considered young cases. Audience suggested looking into three age groups and characterize clinical differences and outcomes. Another member suggested obtaining supplemental genetic information and analyze the genetic profiles of the cohort.

b. **PROP 2110-308:** 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) (Attachment 5)

*Dr. Arslan presented the proposal on behalf of the group. The study hypothesizes that Allogeneic HCT is highly effective and associated with long-term survival in MDS-RS and MDS/MPD-RS-T and 2) Somatic mutations have prognostic relevance in MDS-RS and MDS/MPD-RS-T**.** The objectives of this study are to evaluate the outcome of patients with MDS-RS or MDS/MPD-RS-T who underwent allogeneic HCT and were registered in the CIBMTR database, characterize the mutation profile in the MDS-RS or MDS and MPD-RS-T in patients who underwent 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. A total of 329 cases Refractory anemia (RA), Refractory anemia with ringed sideroblasts (RARS), and MDS/MPN with ring sideroblasts and thrombocytosis (MDS/MPN–RS–T) patients, with very low, low, and intermediate risk (IPSS-r) prior to HCT reported to CIBMTR between the period 2008 to 2019 met the criteria for this study.*

The proposal was open for questions and comments. An audience members asked on the how many patients had samples and if the study could include samples from Dr. Coleman's study published. A total of 202 recipients has samples in the NMDP biorepository, some of these cases might be reanalyzed from Dr. Coleman's study. Another member asked if there is any reason to exclude PT-Cy and Haploidentical donor cases. The study will exclude depleted grafts but will include any other haploidentical patients. Another comment raised consisted of the concern for misclassification of these diagnoses.

c. **PROP 2110-163/PROP 2110-310** Combined proposal: Impact of Pre-Allogeneic Hematopoietic Stem Cell Transplantation Treatment on Outcomes of Patients with Higher-Risk MDS and CMML: A Propensity Score Analysis. (P Kongtim/S Ciurea/R Shallis/A Zeidan) (Attachment 6)
Impact of Pre-transplant Hypomethylating Treatment on Outcomes of Patients with High Risk MDS and CMML Receiving Allogeneic Hematopoietic Stem Cell Transplantation: A Propensity Score Analysis. Exploring the Impact of Frontline Therapy Intensity in Higher-Risk Myelodysplastic Syndromes or Chronic Myelomonocytic Leukemia on Post-Allogeneic Stem Cell Transplant Outcomes.

Dr. Shallis presented virtually this proposal on behalf of the group. The study hypothesizes that pre-AHCT treatment with an HMA can reduce disease burden with acceptable toxicity and results in improved outcomes after AHCT for patients with higher-risk MDS and CMML when compared with patients either treated with pre-AHCT intensive chemotherapy or, among those without excess blasts, receiving no pre-AHCT therapy. The study aims to compare post-AHCT outcomes including relapse-free survival (RFS), overall survival (OS), GvHD-free relapse-free survival (GRFS), cumulative incidence of non-relapse

mortality (NRM), relapse, acute GvHD and chronic GvHD inpatients with higher-risk MDS and CMML who received pre-AHCT treatment with HMA vs. intensive chemotherapy vs. no therapy. Lastly, to identify factors that are associated with favorable outcomes of patients with higher-risk MDS and CMML based on each type of pre-AHCT strategy. A total of 1665 cases of MDS patients with <5% marrow blasts at diagnosis AND IPSS-R intermediate/high/very high-risk disease at diagnosis reported to CIBMTR between the period 2008 to 2019. The breakdown of these patients was 1112 received HMA alone, 164 received chemotherapy and 389 did not received any treatment.

The proposal was opened for comments and questions. A member of the audience asked if higher-risk MDS and Chronic myelomonocytic leukemia (CMML) are different? Leadership mentioned that MDS and CMML are captured as different entities and should they be analyzed separately in the study. Another member of the audience asked if patients treated with HMA + Chemotherapy; specifically, Venetoclax would be excluded from the study population. The patients mentioned are planned to be included in the study, and Venetoclax will be investigated from the other drugs specified in our forms collected. Additionally, we will look at different categorizations of intensive vs less intensive treatment. Another comment from the audience suggested to look at response to HCT, this information is collected and will be looked upon the analysis. The leadership clarified that we only collect the information on patients that made it into HCT, hence we cannot determine what determine what treatment therapy is better for patients that did not receive an HCT.

d. **PROP 2110-195/PROP 2110-339** Combined proposal: Characteristics Associated with Improved Survival Following Allogeneic Hematopoietic Cell Transplant (HCT) for Myelodysplastic Syndrome/Myeloproliferative Neoplasm Overlap Syndromes. (H Elmariah/T Nishihori/L Gowda/R Shallis) (Attachment 7)
Comparison of Haploidentical Donor Allogeneic Hematopoietic Cell Transplant (HCT) with Post-Transplant Cyclophosphamide to Matched Donor HCT for Myelodysplastic Syndrome/Myeloproliferative Neoplasm Overlap Syndromes.
Does Allografting help prolong remissions for MDS-MPN.

Dr. Elmariah presented the proposal on behalf of the group. This study hypothesizes that outcomes of allogeneic (allo) hematopoietic cell transplant (HCT) for patients with myelodysplastic syndrome/myeloproliferative neoplasm overlap syndromes (MDS/MPN) will be improved with the use of myeloablative conditioning (MAC) over reduced intensity conditioning (RIC), and that haploidentical donor HCT with post-transplant cyclophosphamide (PTCy) yields similar outcomes to matched sibling and matched unrelated donor transplants. The objectives of this study are to compare outcomes by histologic category, to compare outcomes by donor platform and conditioning intensity and finally to develop a predictive model for survival post allo-HCT for MDS/MPN's. A total of 2056 patients with MDS/MPN overlap syndromes as defined by the study group were reported to CIBMTR between the period 2010 to 2019 and met the initial selection criteria requirements. Of which 1156 were registered in the TED-level track.

The floor was opened from questions and comments from the audience. A member of the audience suggested restricting this study and exclude CMML patients (n=1169), while focus on aCML, MDS/MPN and RARS-T. Main reason being that CMML has been studied and described previously. Concerns were raised about small sample size after excluding CMML cases. Another member of the audience suggested focusing analyses into conditioning regime and donor type differences.

e. **PROP 2110-287/PROP 2110-345** Combined proposal: Impact of TP53 Mutational Burden, Conditioning Regimen, and HLA Match on Cumulative Incidence of Relapse and Overall Survival after Allogeneic Stem Cell Transplant for TP53-Aberrant Myeloid Neoplasms. (S Patel/J Cerny/J Maakaron/M Juckett) (Attachment 8)

Impact of TP53 Mutational Subtype, Conditioning Regimen, and Stem Cell Donor Choice on Cumulative Incidence of Relapse and Overall Survival after Allogeneic Stem Cell Transplant for TP53-Aberrant Myeloid Neoplasms.

Matched vs. Mismatched Hematopoietic Stem Cell Transplantation (HCT) for TP53 mutated acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS).

Dr. Shyam Patel presented this proposal on behalf of the group. This study hypothesizes at higher intensity conditioning regimens are more effective at elimination of genomic MRD. We hypothesize that a graft-vs-leukemia (GvL) effect is the primary mediator of superior long-term outcomes. If so, HLA-mismatched transplant may improve the chance of a successful outcome through enhanced GvL effect. The enhanced GvL effect from a mismatched donor may be more apparent following a non-myeloablative preparative regimen. The objectives of this study are to evaluate outcomes of TP53 mutated patients, evaluate TP53 mutational burden, asses the benefit of regimen-intensity, and to evaluate the HLA-matching. A total of 331 with MDS (n=293) and MPN (n=38) patients undergoing 1st allo-HCT with TP53 mutation at any timepoint, between 2013 and 2019 met the selection criteria for this concept.

The proposal was opened for comments and questions. A comment was raised on evaluating the TP53 at time of diagnosis and HCT. A comment was raised on availability of mutation subtype on the database. Committee leadership clarified that mutation subtype is not available on the database, it was suggested to review the cytogenetics and use as surrogate. Another member of the audience asked on the availability of post-HCT data. This data is not available for this cohort of patients. A member of the audience asked how this study would be different from previous studies and a BMT-CTN study. A member suggested to restrict to complex karyotype patients but concerns on small sample size were raised.

6. **Future/proposed studies to be presented at the CIBMTR Collaborative Working Committee Study Proposals Session**

*Dr. Saber mentioned that proposal "**PROP 2110-217/PROP 2110-99** Combined proposal: Long-term Outcomes of AML/MDS Patients Receiving Allogeneic Stem Cell Transplantation using Reduced-Intensity Conditioning: A propensity score analysis." was selected to be presented at the Collaborative Session.*

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

a. **PROP 2109-17:** A personalized, machine learning derived prediction model for outcomes after allogeneic stem cell transplantation in patients with myelodysplastic/myeloproliferative overlap syndromes. ***Dropped due to low scientific impact among proposal.***

b. **PROP 2110-64:** Allogeneic stem cell transplantation for chronic myeloid leukemia 2010- 2020: How has the selection of patients and outcomes changed after the introduction of 2nd and 3rd generation TKIs? ***Dropped-supplemental data needed.***

c. **PROP 2110-76:** Early platelet count recovery before white cell count recovery after allogeneic hematopoietic cell transplantation and effect on clinical outcome. ***Dropped due to low scientific impact among proposal.***

d. **PROP 2110-129:** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis: PTCY vs ATG. ***Dropped due to overlap with current study/publication.***

e. **PROP 2110-138:** Clinical outcomes and impact of somatic mutations on outcomes of allogeneic blood or marrow transplantation in atypical chronic myeloid leukemia. ***Dropped due to small sample size.***

f. **PROP 2110-194:** Mutational Predictors of Outcomes following Allogeneic Blood or Marrow Transplantation (BMT) for Myelofibrosis (MF). ***Dropped due to small sample size.***

g. **PROP 2110-208:** Effect of pre-transplant ferritin on survival and non-transplant mortality in alternative donor types after hematopoietic stem cell transplant for myelofibrosis. ***Dropped-supplemental data needed.***

h. **PROP 2110-210:** Allogeneic Hematopoietic Cell Transplantation for Patients with Chronic Myelomonocytic Leukemia. ***Dropped due to overlap with current study/publication.***

i. **PROP 2110-213:** Impact of Measurable Residual Disease After Allo-HCT for Patients with Myelofibrosis. ***Dropped-supplemental data needed.***

j. **PROP 2110-224:** 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 due to small sample size.***

k. **PROP 2110-255:** Impact of PTCY on Outcomes in Adults with Myelofibrosis. ***Dropped due to overlap with current study/publication.***

l. **PROP 2110-265:** Sequential Allogeneic Hematopoietic Stem Cell Transplantation for Myelodisplastic Syndrome. ***Dropped due to small sample size.***

m. **PROP 2110-309:** Optimal Donor Type for Allogeneic Hematopoietic Cell Transplant for Myelodysplastic Syndrome. ***Dropped due to overlap with current study/publication.***

7. Other Business

*The meeting was adjourned at **2:15** p.m. The chairs of the working committee, scientific director and statisticians had a post-WC meeting afterwards. After the new proposals were presented, attendees had the opportunity to vote on the proposals using the Tandem app until May 2. 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 2022-2023		
Study Number and Title	**Current Status**	**Chairs Priority**
CK16-01: Identification of germline predisposition mutations in young myelodysplastic syndrome patients	Submitted	3
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 Pending	1
CK22-02: Toxicity and survival of AML/MDS patients receiving allogeneic stem cell transplantation using reduced-intensity conditioning: A propensity score analysis.	Protocol Pending	2

Working Assignments for Working Committee Leadership (May 2022)

Bart Scott	**CK16-01:** Identification of germline predisposition mutations in young MDS patients.
	CK22-02: Toxicity and survival of AML/MDS patients receiving allogeneic stem cell transplantation using reduced-intensity conditioning: A propensity score analysis.
Ryotaro Nakamura	**CK17-01:** Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation.
Betul Oran	**CK20-01:** Outcomes of allogeneic hematopoietic cell transplantation for Myelofibrosis based on the conditioning regime.
	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 2022

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	8341	1396	8702	6355
No. of centers	199	160	208	274
Age, median (range) - median (min-max)	61.7 (0.4-83.4)	44.7 (0.3-76.5)	57.7 (0.0-80.8)	52.6 (0.3-79.7)
Age, years - no. (%)				
< 10	254 (3.0)	119 (8.5)	245 (2.8)	261 (4.1)
10-19	286 (3.4)	117 (8.4)	344 (4.0)	362 (5.7)
20-29	231 (2.8)	147 (10.5)	325 (3.7)	442 (7.0)
30-39	359 (4.3)	199 (14.3)	555 (6.4)	646 (10.2)
40-49	732 (8.8)	269 (19.3)	1119 (12.9)	1112 (17.5)
50-59	1863 (22.3)	320 (22.9)	2449 (28.1)	1653 (26.0)
60-69	3515 (42.1)	204 (14.6)	2875 (33.0)	1675 (26.4)
70-79	1101 (13.2)	21 (1.5)	786 (9.0)	203 (3.2)
Not reported	0 (0.0)	0 (0.0)	4 (0.0)	1 (0.0)
Sex - no. (%)				
Male	5196 (62.3)	849 (60.8)	5246 (60.3)	3867 (60.8)
Female	3145 (37.7)	546 (39.1)	3456 (39.7)	2482 (39.1)
Not reported	0 (0.0)	1 (0.1)	0 (0.0)	6 (0.1)
Race/ethnicity - no. (%)				
White, non-Hispanics	7171 (86.0)	805 (57.7)	6979 (80.2)	2706 (42.6)
Black, non-Hispanics	370 (4.4)	14 (1.0)	409 (4.7)	51 (0.8)
Asian, non-Hispanics	233 (2.8)	383 (27.4)	287 (3.3)	648 (10.2)
Hispanics	408 (4.9)	78 (5.6)	661 (7.6)	149 (2.3)
Others	80 (1.0)	28 (2.0)	99 (1.1)	117 (1.8)
Not reported	79 (0.9)	88 (6.3)	267 (3.1)	2684 (42.2)
Disease at diagnosis - no. (%)				
MDS unclassifiable, NOS	1357 (16.3)	164 (11.7)	1893 (21.8)	1265 (19.9)
Refractory anemia (RA)	781 (9.4)	299 (21.4)	681 (7.8)	702 (11.0)
Refractory anemia excess blasts (RAEB)	3640 (43.6)	594 (42.6)	3639 (41.8)	2668 (42.0)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Chronic myelomonocytic leukemia (CMML)	756 (9.1)	133 (9.5)	893 (10.3)	536 (8.4)
Acquired idiopathic sideroblastic anemia (RARS)	320 (3.8)	40 (2.9)	223 (2.6)	135 (2.1)
Refactory anemia with multilineage dysplasia (RCMD)	1117 (13.4)	103 (7.4)	1144 (13.1)	815 (12.8)
Refactory anemia with dysplasia and ringed sideroblasts (RCMD/RS)	3 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
5q- syndrome	103 (1.2)	4 (0.3)	144 (1.7)	67 (1.1)
Other MDS, specified	264 (3.2)	59 (4.2)	85 (1.0)	167 (2.6)
Graft source - no. (%)				
Bone marrow	1585 (19.0)	444 (31.8)	1523 (17.5)	1318 (20.7)
Peripheral blood	6190 (74.2)	867 (62.1)	6827 (78.5)	4793 (75.4)
Cord blood	545 (6.5)	85 (6.1)	259 (3.0)	139 (2.2)
Not reported	21 (0.3)	0 (0.0)	93 (1.1)	105 (1.7)
Donor type - no. (%)				
HLA-identical sibling	1829 (21.9)	573 (41.0)	2744 (31.5)	2753 (43.3)
Haplo	106 (1.3)	10 (0.7)	499 (5.7)	135 (2.1)
Unrelated donor	5060 (60.7)	475 (34.0)	4408 (50.7)	2889 (45.5)
Cord blood	545 (6.5)	85 (6.1)	259 (3.0)	139 (2.2)
Other/missing	801 (9.6)	253 (18.1)	792 (9.1)	439 (6.9)
Year of transplant - no. (%)				
1995-1996	154 (1.8)	82 (5.9)	175 (2.0)	196 (3.1)
1997-1998	179 (2.1)	97 (6.9)	199 (2.3)	259 (4.1)
1999-2000	198 (2.4)	153 (11.0)	202 (2.3)	322 (5.1)
2001-2002	299 (3.6)	155 (11.1)	229 (2.6)	348 (5.5)
2003-2004	357 (4.3)	161 (11.5)	277 (3.2)	400 (6.3)
2005-2006	470 (5.6)	170 (12.2)	304 (3.5)	382 (6.0)
2007-2008	527 (6.3)	75 (5.4)	311 (3.6)	374 (5.9)
2009-2010	532 (6.4)	72 (5.2)	581 (6.7)	590 (9.3)
2011-2012	783 (9.4)	26 (1.9)	750 (8.6)	716 (11.3)
2013-2014	1208 (14.5)	121 (8.7)	642 (7.4)	565 (8.9)
2015-2016	1340 (16.1)	129 (9.2)	683 (7.8)	505 (7.9)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
2017-2018	1294 (15.5)	103 (7.4)	990 (11.4)	694 (10.9)
2019-2020	707 (8.5)	44 (3.2)	1671 (19.2)	552 (8.7)
2021-2022	293 (3.5)	8 (0.6)	1688 (19.4)	452 (7.1)

Characteristics of recipients undergoing first allogeneic HCT for MDS reported to the CIBMTR, CRF track between 2015 and 2022

Characteristic	N (%)
No. of patients	3918
No. of centers	202
Age, median (range) - median (min-max)	65.8 (1.1-82.7)
Age, years - no. (%)	
< 10	36 (0.9)
10-19	65 (1.7)
20-29	47 (1.2)
30-39	83 (2.1)
40-49	165 (4.2)
50-59	620 (15.8)
60-69	2039 (52.0)
70-79	863 (22.0)
Race/ethnicity - no. (%)	
White, non-Hispanics	3181 (81.2)
Black, non-Hispanics	178 (4.5)
Asian, non-Hispanics	226 (5.8)
Hispanics	178 (4.5)
Others	40 (1.0)
Missing	115 (2.9)
Sex - no. (%)	
Male	2519 (64.3)
Female	1399 (35.7)
Graft source - no. (%)	
Bone marrow	451 (11.5)
Peripheral blood	3286 (83.9)
Cord blood	166 (4.2)
Not reported	15 (0.4)
Disease at diagnosis - no. (%)	
MDS unclassifiable, NOS	712 (18.2)
Refractory anemia (RA)	124 (3.2)
Refractory anemia excess blasts (RAEB)	1822 (46.5)
Chronic myelomonocytic leukemia (CMML)	416 (10.6)
Acquired idiopathic sideroblastic anemia (RARS)	132 (3.4)
Refactory anemia with multilineage dysplasia (RCMD)	638 (16.3)

Characteristic	**N (%)**
5q- syndrome	74 (1.9)
Year of transplant - no. (%)	
2015-2016	1469 (37.5)
2017-2018	1397 (35.7)
2019-2020	751 (19.2)
2021-2022	301 (7.7)
Follow-up - median (range)	47.9 (0.0-82.4)

Characteristics of recipients undergoing allogeneic HCT for myelofibrosis reported to the CIBMTR between 1995 and 2022

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	2855	406	1566	1550
No. of centers	142	94	140	176
Age, median (range) - median (min-max)	61.4 (0.6-80.8)	54.1 (1.7-73.5)	58.1 (0.5-79.2)	56.0 (1.8-74.5)
Age, years - no. (%)				
< 10	11 (0.4)	3 (0.7)	17 (1.1)	12 (0.8)
10-19	15 (0.5)	6 (1.5)	10 (0.6)	27 (1.7)
20-29	14 (0.5)	11 (2.7)	23 (1.5)	36 (2.3)
30-39	66 (2.3)	24 (5.9)	53 (3.4)	115 (7.4)
40-49	311 (10.9)	96 (23.6)	232 (14.8)	276 (17.8)
50-59	848 (29.7)	155 (38.2)	574 (36.7)	566 (36.5)
60-69	1278 (44.8)	107 (26.4)	588 (37.5)	485 (31.3)
70-79	312 (10.9)	4 (1.0)	69 (4.4)	33 (2.1)
Sex - no. (%)				
Male	1652 (57.9)	259 (63.8)	929 (59.3)	965 (62.3)
Female	1203 (42.1)	147 (36.2)	637 (40.7)	585 (37.7)
Race/ethnicity - no. (%)				
White, non-Hispanics	2352 (82.4)	260 (64.0)	1296 (82.8)	638 (41.2)
Black, non-Hispanics	163 (5.7)	5 (1.2)	93 (5.9)	12 (0.8)
Asian, non-Hispanics	104 (3.6)	31 (7.6)	56 (3.6)	53 (3.4)
Hispanics	157 (5.5)	44 (10.8)	84 (5.4)	31 (2.0)
Others	34 (1.2)	11 (2.7)	13 (0.8)	20 (1.3)
Not reported	45 (1.6)	55 (13.5)	24 (1.5)	796 (51.4)
Disease at diagnosis - no. (%)				
Polycythemia vera (PV)	355 (12.4)	42 (10.3)	201 (12.8)	136 (8.8)
Essential or primary thrombocythemia (ET)	472 (16.5)	42 (10.3)	230 (14.7)	160 (10.3)
Chronic myelofibrosis	2028 (71.0)	322 (79.3)	1135 (72.5)	1254 (80.9)
Graft source - no. (%)				
Bone marrow	216 (7.6)	78 (19.2)	143 (9.1)	212 (13.7)
Peripheral blood	2566 (89.9)	319 (78.6)	1395 (89.1)	1318 (85.0)
Cord blood	57 (2.0)	8 (2.0)	19 (1.2)	9 (0.6)
Not reported	16 (0.6)	1 (0.2)	9 (0.6)	11 (0.7)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Donor type - no. (%)				
HLA-identical sibling	630 (22.1)	161 (39.7)	656 (41.9)	655 (42.3)
Haplo	134 (4.7)	1 (0.2)	36 (2.3)	37 (2.4)
Unrelated donor	1791 (62.7)	198 (48.8)	734 (46.9)	762 (49.2)
Cord blood	57 (2.0)	8 (2.0)	19 (1.2)	9 (0.6)
Other/missing	243 (8.5)	38 (9.4)	121 (7.7)	87 (5.6)
Year of transplant - no. (%)				
1995-1996	16 (0.6)	8 (2.0)	11 (0.7)	19 (1.2)
1997-1998	22 (0.8)	11 (2.7)	13 (0.8)	36 (2.3)
1999-2000	30 (1.1)	22 (5.4)	18 (1.1)	44 (2.8)
2001-2002	52 (1.8)	21 (5.2)	33 (2.1)	82 (5.3)
2003-2004	54 (1.9)	32 (7.9)	45 (2.9)	100 (6.5)
2005-2006	75 (2.6)	43 (10.6)	76 (4.9)	102 (6.6)
2007-2008	153 (5.4)	35 (8.6)	90 (5.7)	116 (7.5)
2009-2010	142 (5.0)	28 (6.9)	191 (12.2)	188 (12.1)
2011-2012	35 (1.2)	6 (1.5)	304 (19.4)	154 (9.9)
2013-2014	180 (6.3)	43 (10.6)	220 (14.0)	119 (7.7)
2015-2016	274 (9.6)	44 (10.8)	230 (14.7)	99 (6.4)
2017-2018	544 (19.1)	75 (18.5)	130 (8.3)	162 (10.5)
2019-2020	714 (25.0)	33 (8.1)	102 (6.5)	158 (10.2)
2021-2022	564 (19.8)	5 (1.2)	103 (6.6)	171 (11.0)

Characteristics of recipients undergoing allogeneic HCT for CML reported to the CIBMTR between 1995 and 2022

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	4175	3069	5001	8750
No. of centers	186	200	209	288
Age, median (range) - median (min-max)	39.9 (1.1-76.8)	35.6 (1.1-76.0)	43.0 (0.3-77.5)	36.9 (0.3-75.5)
Age, years - no. (%)				
< 10	90 (2.2)	72 (2.3)	77 (1.5)	204 (2.3)
10-19	379 (9.1)	320 (10.4)	306 (6.1)	692 (7.9)
20-29	600 (14.4)	640 (20.9)	586 (11.7)	1730 (19.8)
30-39	1032 (24.7)	920 (30.0)	1128 (22.6)	2572 (29.4)
40-49	1182 (28.3)	731 (23.8)	1416 (28.3)	2331 (26.6)
50-59	719 (17.2)	328 (10.7)	1040 (20.8)	1034 (11.8)
60-69	154 (3.7)	56 (1.8)	399 (8.0)	175 (2.0)
70-79	19 (0.5)	1 (0.0)	40 (0.8)	5 (0.1)
Not reported	0 (0.0)	1 (0.0)	9 (0.2)	7 (0.1)
Sex - no. (%)				
Male	2443 (58.5)	1879 (61.2)	2949 (59.0)	5254 (60.0)
Female	1732 (41.5)	1190 (38.8)	2045 (40.9)	3459 (39.5)
Not reported	0 (0.0)	0 (0.0)	7 (0.1)	37 (0.4)
Race/ethnicity - no. (%)				
White, non-Hispanics	3089 (74.0)	2159 (70.3)	3251 (65.0)	3846 (44.0)
Black, non-Hispanics	432 (10.3)	46 (1.5)	467 (9.3)	157 (1.8)
Asian, non-Hispanics	126 (3.0)	560 (18.2)	151 (3.0)	1012 (11.6)
Hispanics	424 (10.2)	210 (6.8)	525 (10.5)	328 (3.7)
Others	88 (2.1)	45 (1.5)	156 (3.1)	194 (2.2)
Not reported	16 (0.4)	49 (1.6)	451 (9.0)	3213 (36.7)
Graft source - no. (%)				
Bone marrow	2615 (62.6)	1814 (59.1)	2114 (42.3)	4735 (54.1)
Peripheral blood	1371 (32.8)	1180 (38.4)	2650 (53.0)	3606 (41.2)
Cord blood	184 (4.4)	70 (2.3)	151 (3.0)	106 (1.2)
Not reported	5 (0.1)	5 (0.2)	86 (1.7)	303 (3.5)
Donor type - no. (%)				
HLA-identical sibling	869 (20.8)	1600 (52.1)	2697 (53.9)	5528 (63.2)
Haplo	12 (0.3)	4 (0.1)	123 (2.5)	60 (0.7)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Unrelated donor	2827 (67.7)	992 (32.3)	1408 (28.2)	2478 (28.3)
Cord blood	184 (4.4)	70 (2.3)	151 (3.0)	106 (1.2)
Other/missing	283 (6.8)	403 (13.1)	622 (12.4)	578 (6.6)
Year of transplant - no. (%)				
1995-1996	719 (17.2)	516 (16.8)	651 (13.0)	1347 (15.4)
1997-1998	778 (18.6)	576 (18.8)	717 (14.3)	1744 (19.9)
1999-2000	687 (16.5)	667 (21.7)	605 (12.1)	1775 (20.3)
2001-2002	371 (8.9)	419 (13.7)	280 (5.6)	1210 (13.8)
2003-2004	413 (9.9)	380 (12.4)	252 (5.0)	742 (8.5)
2005-2006	318 (7.6)	274 (8.9)	173 (3.5)	428 (4.9)
2007-2008	229 (5.5)	44 (1.4)	133 (2.7)	213 (2.4)
2009-2010	236 (5.7)	47 (1.5)	160 (3.2)	275 (3.1)
2011-2012	50 (1.2)	12 (0.4)	383 (7.7)	261 (3.0)
2013-2014	122 (2.9)	43 (1.4)	326 (6.5)	166 (1.9)
2015-2016	110 (2.6)	41 (1.3)	327 (6.5)	118 (1.3)
2017-2018	65 (1.6)	24 (0.8)	340 (6.8)	139 (1.6)
2019-2020	49 (1.2)	18 (0.6)	369 (7.4)	177 (2.0)
2021-2022	28 (0.7)	8 (0.3)	285 (5.7)	155 (1.8)

Characteristics of recipients undergoing allogeneic HCT for CLL reported to the CIBMTR between 1995 and 2022

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	1469	398	1967	1486
No. of centers	127	89	141	150
Age, median (range) - median (min-max)	55.5 (11.7-75.2)	53.4 (1.7-71.0)	56.7 (7.3-80.4)	53.7 (3.9-75.1)
Age, years - no. (%)				
< 10	0 (0.0)	1 (0.3)	2 (0.1)	3 (0.2)
10-19	3 (0.2)	0 (0.0)	2 (0.1)	0 (0.0)
20-29	11 (0.7)	2 (0.5)	15 (0.8)	22 (1.5)
30-39	64 (4.4)	36 (9.0)	83 (4.2)	79 (5.3)
40-49	332 (22.6)	103 (25.9)	358 (18.2)	388 (26.1)
50-59	626 (42.6)	171 (43.0)	853 (43.4)	671 (45.2)
60-69	398 (27.1)	83 (20.9)	596 (30.3)	311 (20.9)
70-79	35 (2.4)	2 (0.5)	58 (2.9)	12 (0.8)
Sex - no. (%)				
Male	1093 (74.4)	289 (72.6)	1418 (72.1)	1076 (72.4)
Female	375 (25.5)	109 (27.4)	548 (27.9)	408 (27.5)
Not reported	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.1)
Race/ethnicity - no. (%)				
White, non-Hispanics	1274 (86.7)	341 (85.7)	1697 (86.3)	755 (50.8)
Black, non-Hispanics	125 (8.5)	0 (0.0)	145 (7.4)	3 (0.2)
Asian, non-Hispanics	8 (0.5)	13 (3.3)	16 (0.8)	18 (1.2)
Hispanics	42 (2.9)	15 (3.8)	56 (2.8)	16 (1.1)
Others	8 (0.5)	4 (1.0)	13 (0.7)	5 (0.3)
Not reported	12 (0.8)	25 (6.3)	40 (2.0)	689 (46.4)
Disease at diagnosis - no. (%)				
Chronic lymphocytic leukemia, NOS	715 (48.7)	137 (34.4)	585 (29.7)	634 (42.7)
Chronic lymphocytic leukemia, B-cell	753 (51.3)	260 (65.3)	1375 (69.9)	846 (56.9)
Chronic lymphocytic leukemia, T-cell	1 (0.1)	1 (0.3)	7 (0.4)	6 (0.4)
Graft source - no. (%)				

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Bone marrow	297 (20.2)	63 (15.8)	260 (13.2)	163 (11.0)
Peripheral blood	1088 (74.1)	321 (80.7)	1665 (84.6)	1274 (85.7)
Cord blood	83 (5.7)	13 (3.3)	35 (1.8)	14 (0.9)
Not reported	1 (0.1)	1 (0.3)	7 (0.4)	35 (2.4)
Donor type - no. (%)				
HLA-identical sibling	398 (27.1)	221 (55.5)	970 (49.3)	798 (53.7)
Haplo	15 (1.0)	0 (0.0)	47 (2.4)	7 (0.5)
Unrelated donor	869 (59.2)	139 (34.9)	753 (38.3)	593 (39.9)
Cord blood	83 (5.7)	13 (3.3)	35 (1.8)	14 (0.9)
Other/missing	104 (7.1)	25 (6.3)	162 (8.2)	74 (5.0)
Year of transplant - no. (%)				
1995-1996	61 (4.2)	29 (7.3)	46 (2.3)	34 (2.3)
1997-1998	56 (3.8)	22 (5.5)	63 (3.2)	41 (2.8)
1999-2000	84 (5.7)	38 (9.5)	88 (4.5)	101 (6.8)
2001-2002	108 (7.4)	49 (12.3)	123 (6.3)	163 (11.0)
2003-2004	174 (11.8)	52 (13.1)	120 (6.1)	164 (11.0)
2005-2006	209 (14.2)	56 (14.1)	163 (8.3)	184 (12.4)
2007-2008	244 (16.6)	33 (8.3)	173 (8.8)	139 (9.4)
2009-2010	108 (7.4)	21 (5.3)	382 (19.4)	184 (12.4)
2011-2012	56 (3.8)	14 (3.5)	414 (21.0)	232 (15.6)
2013-2014	173 (11.8)	44 (11.1)	154 (7.8)	103 (6.9)
2015-2016	92 (6.3)	20 (5.0)	61 (3.1)	41 (2.8)
2017-2018	83 (5.7)	16 (4.0)	80 (4.1)	35 (2.4)
2019-2020	16 (1.1)	2 (0.5)	59 (3.0)	35 (2.4)
2021-2022	5 (0.3)	2 (0.5)	41 (2.1)	30 (2.0)

Characteristics of recipients undergoing autologous HCT for CLL reported to the CIBMTR between 1995 and 2022

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
No. of patients	85	41	272	244
No. of centers	42	14	66	58
Age, median (range) - median (min-max)	52.1 (33.2-73.0)	49.8 (38.4-67.2)	53.3 (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 (14.1)	3 (7.3)	14 (5.1)	12 (4.9)
40-49	25 (29.4)	18 (43.9)	80 (29.4)	76 (31.1)
50-59	26 (30.6)	18 (43.9)	112 (41.2)	114 (46.7)
60-69	20 (23.5)	2 (4.9)	57 (21.0)	37 (15.2)
70-79	2 (2.4)	0 (0.0)	6 (2.2)	1 (0.4)
Sex - no. (%)				
Male	62 (72.9)	33 (80.5)	190 (69.9)	194 (79.5)
Female	23 (27.1)	8 (19.5)	82 (30.1)	49 (20.1)
Not reported	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Race/ethnicity - no. (%)				
White, non-Hispanics	79 (92.9)	36 (87.8)	227 (83.5)	124 (50.8)
Black, non-Hispanics	5 (5.9)	1 (2.4)	17 (6.3)	1 (0.4)
Asian, non-Hispanics	1 (1.2)	0 (0.0)	0 (0.0)	1 (0.4)
Hispanics	0 (0.0)	4 (9.8)	4 (1.5)	4 (1.6)
Others	0 (0.0)	0 (0.0)	3 (1.1)	3 (1.2)
Not reported	0 (0.0)	0 (0.0)	21 (7.7)	111 (45.5)
Disease at diagnosis - no. (%)				
Chronic lymphocytic leukemia, NOS	22 (25.9)	24 (58.5)	86 (31.6)	48 (19.7)
Chronic lymphocytic leukemia, B-cell	62 (72.9)	17 (41.5)	181 (66.5)	195 (79.9)
Chronic lymphocytic leukemia, T-cell	1 (1.2)	0 (0.0)	5 (1.8)	1 (0.4)
Graft source - no. (%)				
Bone marrow	15 (17.6)	1 (2.4)	113 (41.5)	5 (2.0)

Characteristic	CRF / US	CRF / non-US	TED (excluding CRF) / US	TED (excluding CRF) / non-US
Peripheral blood	67 (78.8)	39 (95.1)	153 (56.3)	208 (85.2)
Not reported	3 (3.5)	1 (2.4)	6 (2.2)	31 (12.7)
Year of transplant - no. (%)				
1995-1996	15 (17.6)	3 (7.3)	43 (15.8)	14 (5.7)
1997-1998	26 (30.6)	28 (68.3)	54 (19.9)	36 (14.8)
1999-2000	18 (21.2)	6 (14.6)	72 (26.5)	90 (36.9)
2001-2002	6 (7.1)	2 (4.9)	36 (13.2)	40 (16.4)
2003-2004	4 (4.7)	1 (2.4)	27 (9.9)	22 (9.0)
2005-2006	9 (10.6)	0 (0.0)	6 (2.2)	23 (9.4)
2007-2008	3 (3.5)	0 (0.0)	5 (1.8)	4 (1.6)
2009-2010	2 (2.4)	0 (0.0)	4 (1.5)	8 (3.3)
2011-2012	0 (0.0)	0 (0.0)	9 (3.3)	5 (2.0)
2013-2014	2 (2.4)	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 (1.5)	1 (0.4)
2019-2020	0 (0.0)	0 (0.0)	2 (0.7)	0 (0.0)
2021-2022	0 (0.0)	0 (0.0)	3 (1.1)	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	13440	5788	3161
Source of data			
CRF	8377 (62)	2739 (47)	1751 (55)
TED	5063 (38)	3049 (53)	1410 (45)
Number of centers	239	211	295
Disease at transplant			
Other leukemia	1469 (11)	423 (7)	310 (10)
CML	3528 (26)	1111 (19)	1028 (33)
MDS	6936 (52)	3307 (57)	1526 (48)
MPN	1507 (11)	947 (16)	297 (9)
MDS Disease status at transplant			
Early	1480 (21)	609 (18)	351 (23)
Advanced	4487 (65)	2464 (75)	836 (55)
Missing	969 (14)	234 (7)	339 (22)
Recipient age at transplant			
0-9 years	433 (3)	103 (2)	162 (5)
10-17 years	437 (3)	134 (2)	181 (6)
18-29 years	991 (7)	290 (5)	319 (10)
30-39 years	1462 (11)	440 (8)	405 (13)
40-49 years	2146 (16)	716 (12)	560 (18)
50-59 years	3193 (24)	1230 (21)	653 (21)
60-69 years	3806 (28)	2131 (37)	701 (22)
70+ years	972 (7)	744 (13)	180 (6)
Median (Range)	54 (0-83)	60 (1-79)	49 (1-81)
Recipient race/ethnicity			
White, Non-Hispanic	11665 (87)	5073 (88)	2348 (74)
Black or African American, Non-Hispanic	561 (4)	179 (3)	140 (4)
Asian, Non-Hispanic	257 (2)	137 (2)	116 (4)
Native Hawaiian or Pacific Islander, Non-Hispanic	17 (<1)	11 (<1)	8 (<1)
American Indian or Alaska Native, Non-Hispanic	40 (<1)	21 (<1)	11 (<1)
Hispanic	472 (4)	199 (3)	101 (3)
Missing	428 (3)	168 (3)	437 (14)
Recipient sex			
Male	8174 (61)	3600 (62)	1940 (61)
Female	5266 (39)	2188 (38)	1221 (39)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Karnofsky score			
10-80	4750 (35)	2326 (40)	953 (30)
90-100	8222 (61)	3318 (57)	2044 (65)
Missing	468 (3)	144 (2)	164 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	6 (<1)	15 (<1)	2 (<1)
4/6	94 (1)	31 (1)	18 (1)
5/6	1682 (13)	511 (11)	417 (15)
6/6	11118 (86)	4171 (88)	2376 (84)
Unknown	540 (N/A)	1060 (N/A)	348 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	331 (3)	28 (1)	23 (1)
6/8	530 (4)	31 (1)	64 (3)
7/8	2308 (18)	493 (13)	365 (19)
8/8	9496 (75)	3163 (85)	1447 (76)
Unknown	775 (N/A)	2073 (N/A)	1262 (N/A)
HLA-DPB1 Match			
Double allele mismatch	3203 (29)	445 (21)	227 (25)
Single allele mismatch	6004 (54)	1089 (52)	466 (51)
Full allele matched	1912 (17)	568 (27)	214 (24)
Unknown	2321 (N/A)	3686 (N/A)	2254 (N/A)
High resolution release score			
No	3073 (23)	5757 (99)	2996 (95)
Yes	10367 (77)	31 (1)	165 (5)
KIR typing available			
No	10085 (75)	5777 (>99)	3148 (>99)
Yes	3355 (25)	11 (<1)	13 (<1)
Graft type			
Marrow	4540 (34)	1357 (23)	1267 (40)
PBSC	8874 (66)	4386 (76)	1865 (59)
BM+PBSC	3 (<1)	0	0
PBSC+UCB	10 (<1)	43 (1)	2 (<1)
Others	13 (<1)	2 (<1)	27 (1)
Conditioning regimen			
Myeloablative	7800 (58)	2707 (47)	1942 (61)
RIC/Nonmyeloablative	5598 (42)	3061 (53)	1179 (37)
TBD	42 (<1)	20 (<1)	40 (1)
Donor age at donation			
To Be Determined/NA	481 (4)	997 (17)	144 (5)
0-9 years	0	8 (<1)	2 (<1)
10-17 years	1 (<1)	5 (<1)	0
18-29 years	6139 (46)	2568 (44)	1194 (38)
30-39 years	3819 (28)	1304 (23)	963 (30)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
40-49 years	2281 (17)	673 (12)	650 (21)
50+ years	719 (5)	233 (4)	208 (7)
Median (Range)	31 (13-62)	29 (1-109)	33 (0-60)
Donor/Recipient CMV serostatus			
+/+	2720 (20)	1087 (19)	665 (21)
+/-	1471 (11)	611 (11)	312 (10)
-/+	3876 (29)	1210 (21)	844 (27)
-/-	4003 (30)	1368 (24)	854 (27)
CB - recipient +	7 (<1)	25 (<1)	2 (<1)
CB - recipient -	3 (<1)	19 (<1)	0
Missing	1360 (10)	1468 (25)	484 (15)
GvHD Prophylaxis			
No GVHD prophylaxis	42 (<1)	28 (<1)	15 (<1)
Ex vivo T-cell depletion	277 (2)	71 (1)	80 (3)
CD34 selection	152 (1)	87 (2)	26 (1)
Post-CY + other(s)	925 (7)	848 (15)	196 (6)
Post-CY alone	58 (<1)	33 (1)	15 (<1)
Tacrolimus + MMF +- others	1602 (12)	578 (10)	252 (8)
Tacrolimus + MTX +- others (except MMF)	5692 (42)	2535 (44)	891 (28)
Tacrolimus + others (except MTX, MMF)	677 (5)	414 (7)	106 (3)
Tacrolimus alone	288 (2)	117 (2)	52 (2)
CSA + MMF +- others (except Tacrolimus)	764 (6)	248 (4)	239 (8)
CSA + MTX +- others (except Tacrolimus, MMF)	2324 (17)	631 (11)	1018 (32)
CSA + others (except Tacrolimus, MTX, MMF)	258 (2)	70 (1)	108 (3)
CSA alone	110 (1)	29 (1)	91 (3)
Other GVHD prophylaxis	223 (2)	74 (1)	38 (1)
Missing	48 (<1)	25 (<1)	34 (1)
Donor/Recipient sex match			
Male-Male	5631 (42)	2170 (37)	1274 (40)
Male-Female	3001 (22)	1136 (20)	630 (20)
Female-Male	2277 (17)	909 (16)	581 (18)
Female-Female	2071 (15)	746 (13)	538 (17)
CB - recipient M	6 (<1)	31 (1)	1 (<1)
CB - recipient F	4 (<1)	13 (<1)	1 (<1)
Missing	450 (3)	783 (14)	136 (4)
Year of transplant			
1986-1990	180 (1)	24 (<1)	39 (1)
1991-1995	863 (6)	185 (3)	315 (10)
1996-2000	1331 (10)	521 (9)	434 (14)
2001-2005	1386 (10)	261 (5)	491 (16)
2006-2010	2317 (17)	466 (8)	398 (13)
2011-2015	3429 (26)	933 (16)	552 (17)
2016-2020	2966 (22)	2180 (38)	701 (22)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
2021-2022	968 (7)	1218 (21)	231 (7)
Follow-up among survivors, Months			
N Eval	5328	2706	1352
Median (Range)	61 (0-385)	24 (0-334)	48 (0-362)

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	841	250	286
Source of data			
CRF	614 (73)	174 (70)	126 (44)
TED	227 (27)	76 (30)	160 (56)
Number of centers	122	78	112
Disease at transplant			
Other leukemia	98 (12)	30 (12)	37 (13)
CML	132 (16)	36 (14)	57 (20)
MDS	559 (66)	168 (67)	172 (60)
MPN	52 (6)	16 (6)	20 (7)
MDS Disease status at transplant			
Early	173 (31)	41 (24)	72 (42)
Advanced	337 (60)	113 (67)	78 (45)
Missing	49 (9)	14 (8)	22 (13)
Recipient age at transplant			
0-9 years	122 (15)	35 (14)	52 (18)
10-17 years	59 (7)	14 (6)	25 (9)
18-29 years	74 (9)	12 (5)	20 (7)
30-39 years	79 (9)	23 (9)	30 (10)
40-49 years	118 (14)	34 (14)	39 (14)
50-59 years	180 (21)	55 (22)	64 (22)
60-69 years	173 (21)	64 (26)	53 (19)
70+ years	36 (4)	13 (5)	3 (1)
Median (Range)	48 (0-80)	51 (1-76)	45 (0-73)
Recipient race/ethnicity			
White, Non-Hispanic	503 (60)	168 (67)	166 (58)
Black or African American, Non-Hispanic	144 (17)	33 (13)	35 (12)
Asian, Non-Hispanic	53 (6)	18 (7)	20 (7)
Native Hawaiian or Pacific Islander, Non-Hispanic	7 (1)	0	2 (1)
American Indian or Alaska Native, Non-Hispanic	4 (<1)	1 (<1)	2 (1)
Hispanic	102 (12)	24 (10)	21 (7)
Missing	28 (3)	6 (2)	40 (14)
Recipient sex			
Male	499 (59)	150 (60)	171 (60)
Female	342 (41)	100 (40)	115 (40)
Karnofsky score			
10-80	219 (26)	77 (31)	88 (31)
90-100	604 (72)	159 (64)	176 (62)
Missing	18 (2)	14 (6)	22 (8)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
HLA-A B DRB1 groups - low resolution			
<=3/6	15 (2)	13 (6)	1 (<1)
4/6	357 (44)	101 (50)	136 (53)
5/6	358 (44)	79 (39)	105 (41)
6/6	75 (9)	10 (5)	13 (5)
Unknown	36 (N/A)	47 (N/A)	31 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	427 (60)	98 (65)	132 (63)
6/8	173 (24)	32 (21)	52 (25)
7/8	75 (11)	17 (11)	19 (9)
8/8	36 (5)	4 (3)	6 (3)
Unknown	130 (N/A)	99 (N/A)	77 (N/A)
HLA-DPB1 Match			
Double allele mismatch	127 (44)	14 (41)	21 (40)
Single allele mismatch	138 (47)	17 (50)	27 (52)
Full allele matched	26 (9)	3 (9)	4 (8)
Unknown	550 (N/A)	216 (N/A)	234 (N/A)
High resolution release score			
No	649 (77)	246 (98)	284 (99)
Yes	192 (23)	4 (2)	2 (1)
KIR typing available			
No	682 (81)	250 (100)	285 (>99)
Yes	159 (19)	0	1 (<1)
Graft type			
UCB	770 (92)	206 (82)	263 (92)
PBSC+UCB	70 (8)	43 (17)	22 (8)
Others	1 (<1)	1 (<1)	1 (<1)
Number of cord units			
1	676 (80)	0	231 (81)
2	164 (20)	0	54 (19)
Unknown	1 (N/A)	250 (N/A)	1 (N/A)
Conditioning regimen			
Myeloablative	455 (54)	125 (50)	148 (52)
RIC/Nonmyeloablative	385 (46)	124 (50)	137 (48)
TBD	1 (<1)	1 (<1)	1 (<1)
Donor age at donation			
To Be Determined/NA	625 (74)	72 (29)	223 (78)
0-9 years	168 (20)	136 (54)	53 (19)
10-17 years	10 (1)	13 (5)	1 (<1)
18-29 years	12 (1)	9 (4)	2 (1)
30-39 years	11 (1)	8 (3)	1 (<1)
40-49 years	9 (1)	4 (2)	1 (<1)
50+ years	6 (1)	8 (3)	5 (2)
Median (Range)	4 (0-67)	5 (0-72)	4 (0-63)
Donor/Recipient CMV serostatus			
CB - recipient +	506 (60)	158 (63)	170 (59)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CB - recipient -	328 (39)	83 (33)	106 (37)
CB - recipient CMV unknown	7 (1)	9 (4)	10 (3)
GvHD Prophylaxis			
No GVHD prophylaxis	2 (<1)	0	1 (<1)
Ex vivo T-cell depletion	1 (<1)	1 (<1)	0
CD34 selection	39 (5)	29 (12)	13 (5)
Post-CY + other(s)	1 (<1)	3 (1)	1 (<1)
Tacrolimus + MMF +- others	285 (34)	83 (33)	57 (20)
Tacrolimus + MTX +- others (except MMF)	26 (3)	5 (2)	10 (3)
Tacrolimus + others (except MTX, MMF)	33 (4)	11 (4)	14 (5)
Tacrolimus alone	27 (3)	11 (4)	4 (1)
CSA + MMF +- others (except Tacrolimus)	351 (42)	88 (35)	140 (49)
CSA + MTX +- others (except Tacrolimus, MMF)	8 (1)	2 (1)	5 (2)
CSA + others (except Tacrolimus, MTX, MMF)	26 (3)	10 (4)	25 (9)
CSA alone	9 (1)	1 (<1)	9 (3)
Other GVHD prophylaxis	33 (4)	6 (2)	6 (2)
Missing	0	0	1 (<1)
Donor/Recipient sex match			
CB - recipient M	499 (59)	150 (60)	171 (60)
CB - recipient F	342 (41)	100 (40)	115 (40)
Year of transplant			
1996-2000	0	0	1 (<1)
2001-2005	16 (2)	7 (3)	4 (1)
2006-2010	249 (30)	70 (28)	77 (27)
2011-2015	363 (43)	74 (30)	116 (41)
2016-2020	178 (21)	80 (32)	64 (22)
2021-2022	35 (4)	19 (8)	24 (8)
Follow-up among survivors, Months			
N Eval	326	113	138
Median (Range)	64 (0-170)	49 (3-175)	46 (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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	2482	381	183
Source of data			
CRF	1059 (43)	133 (35)	85 (46)
TED	1423 (57)	248 (65)	98 (54)
Number of centers	76	48	38
Disease at transplant			
Other leukemia	205 (8)	41 (11)	19 (10)
CML	337 (14)	45 (12)	24 (13)
MDS	1483 (60)	226 (59)	111 (61)
MPN	457 (18)	69 (18)	29 (16)
MDS Disease status at transplant			
Early	253 (17)	31 (14)	20 (18)
Advanced	1177 (79)	183 (81)	85 (77)
Missing	53 (4)	12 (5)	6 (5)
Recipient age at transplant			
0-9 years	54 (2)	13 (3)	2 (1)
10-17 years	67 (3)	6 (2)	6 (3)
18-29 years	99 (4)	17 (4)	7 (4)
30-39 years	114 (5)	21 (6)	11 (6)
40-49 years	268 (11)	27 (7)	17 (9)
50-59 years	684 (28)	105 (28)	47 (26)
60-69 years	974 (39)	165 (43)	81 (44)
70+ years	222 (9)	27 (7)	12 (7)
Median (Range)	60 (1-78)	60 (1-76)	60 (7-74)
Recipient race/ethnicity			
White, Non-Hispanic	1806 (73)	241 (63)	138 (75)
Black or African American, Non-Hispanic	224 (9)	43 (11)	14 (8)
Asian, Non-Hispanic	108 (4)	21 (6)	7 (4)
Native Hawaiian or Pacific Islander, Non-Hispanic	9 (<1)	3 (1)	0
American Indian or Alaska Native, Non-Hispanic	8 (<1)	2 (1)	1 (1)
Hispanic	252 (10)	57 (15)	20 (11)
Missing	75 (3)	14 (4)	3 (2)
Recipient sex			
Male	1511 (61)	237 (62)	122 (67)
Female	971 (39)	144 (38)	61 (33)
Karnofsky score			
10-80	1053 (42)	180 (47)	91 (50)
90-100	1363 (55)	186 (49)	81 (44)
Missing	66 (3)	15 (4)	11 (6)
HLA-A B DRB1 groups - low resolution			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
<=3/6	495 (23)	56 (20)	40 (30)
4/6	139 (6)	30 (10)	12 (9)
5/6	33 (2)	8 (3)	4 (3)
6/6	1484 (69)	192 (67)	78 (58)
Unknown	331 (N/A)	95 (N/A)	49 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	604 (29)	74 (28)	45 (39)
6/8	17 (1)	10 (4)	4 (3)
7/8	27 (1)	4 (2)	1 (1)
8/8	1436 (69)	173 (66)	65 (57)
Unknown	398 (N/A)	120 (N/A)	68 (N/A)
HLA-DPB1 Match			
Double allele mismatch	2 (<1)	0	0
Single allele mismatch	164 (22)	4 (40)	0
Full allele matched	567 (77)	6 (60)	4 (100)
Unknown	1749 (N/A)	371 (N/A)	179 (N/A)
High resolution release score			
No	1071 (43)	374 (98)	179 (98)
Yes	1411 (57)	7 (2)	4 (2)
Graft type			
Marrow	390 (16)	48 (13)	33 (18)
PBSC	2076 (84)	327 (86)	149 (81)
UCB (related)	0	2 (1)	0
BM+PBSC	5 (<1)	0	0
BM+UCB	0	1 (<1)	0
PBSC+UCB	0	0	1 (1)
Others	11 (<1)	3 (1)	0
Conditioning regimen			
Myeloablative	1159 (47)	170 (45)	75 (41)
RIC/Nonmyeloablative	1321 (53)	211 (55)	107 (58)
TBD	2 (<1)	0	1 (1)
Donor age at donation			
To Be Determined/NA	5 (<1)	3 (1)	2 (1)
0-9 years	37 (1)	9 (2)	2 (1)
10-17 years	61 (2)	10 (3)	3 (2)
18-29 years	279 (11)	35 (9)	26 (14)
30-39 years	328 (13)	62 (16)	30 (16)
40-49 years	444 (18)	53 (14)	28 (15)
50+ years	1328 (54)	209 (55)	92 (50)
Median (Range)	52 (0-82)	52 (0-76)	50 (7-73)
Donor/Recipient CMV serostatus			
+/+	976 (39)	156 (41)	53 (29)
+/-	292 (12)	28 (7)	20 (11)
-/+	584 (24)	94 (25)	42 (23)
-/-	588 (24)	89 (23)	51 (28)
CB - recipient +	0	3 (1)	1 (1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	42 (2)	11 (3)	16 (9)
GvHD Prophylaxis			
No GVHD prophylaxis	13 (1)	6 (2)	0
Ex vivo T-cell depletion	10 (<1)	1 (<1)	3 (2)
CD34 selection	13 (1)	6 (2)	0
Post-CY + other(s)	876 (35)	106 (28)	70 (38)
Post-CY alone	20 (1)	2 (1)	2 (1)
Tacrolimus + MMF +- others	186 (7)	20 (5)	5 (3)
Tacrolimus + MTX +- others (except MMF)	958 (39)	156 (41)	79 (43)
Tacrolimus + others (except MTX, MMF)	201 (8)	57 (15)	17 (9)
Tacrolimus alone	17 (1)	5 (1)	1 (1)
CSA + MMF +- others (except Tacrolimus)	36 (1)	5 (1)	2 (1)
CSA + MTX +- others (except Tacrolimus, MMF)	107 (4)	12 (3)	1 (1)
CSA + others (except Tacrolimus, MTX, MMF)	1 (<1)	1 (<1)	0
CSA alone	8 (<1)	0	1 (1)
Other GVHD prophylaxis	25 (1)	1 (<1)	2 (1)
Missing	11 (<1)	3 (1)	0
Donor/Recipient sex match			
Male-Male	850 (34)	136 (36)	67 (37)
Male-Female	502 (20)	72 (19)	30 (16)
Female-Male	646 (26)	97 (25)	49 (27)
Female-Female	465 (19)	69 (18)	26 (14)
CB - recipient M	0	2 (1)	1 (1)
CB - recipient F	0	1 (<1)	0
Missing	19 (1)	4 (1)	10 (5)
Year of transplant			
2006-2010	147 (6)	20 (5)	14 (8)
2011-2015	813 (33)	97 (25)	42 (23)
2016-2020	1132 (46)	186 (49)	93 (51)
2021-2022	390 (16)	78 (20)	34 (19)
Follow-up among survivors, Months			
N Eval	1320	204	108
Median (Range)	36 (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: 2022 Studies in Progress Summary

CK17-01 Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation. (T Roni/SA Giralt/J Palmer) The primary objective of the study is to identify patient-, disease-, and transplant-specific factors that positively associate with overall survival after allo-HCT for patients with myelofibrosis; the secondary objective is to develop a scoring system prognostic of OS post allo-HCT; the third objective is to validate the scoring system in an independent dataset. This study is in collaboration with the EBMT. The PI is currently working on the manuscript preparation. The goal of this study is to have the manuscript published by June 2023.

CK20-01 Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. (G Murthy/ W Saber) The primary objectives of this study are to determine clinical outcomes based on the choice of conditioning regimen used in MAC and RIC setting, for patients with MF undergoing allo-HCT for: overall survival (OS), disease free survival (DFS), non-relapse mortality (NRM), relapse, incidence of graft failure, incidence of acute graft versus host disease (GVHD), incidence of Chronic GVHD and GRFS. The manuscript has been accepted and is currently in press. The goal of this study is to have the manuscript published by June 2023.

CK21-01 Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. (Tania Jain/ M Queralt Sala/V Gupta/ T Nishihori) 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 on data file preparation stage. The goal of this study is to have the manuscript published by June 2023.

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). Also, we aim 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.

TO: Chronic Leukemia Working Committee

To: Bart Scott, MD, Betul Oran, MD, Ryotaro Nakamura, MD

STUDY PIs (Alphabetical Order): Amar Harry Kelkar, MD, FACP, Aref AlKali, MD, Talha Badar, MD, Corey S. Cutler, MD, MPH, Mohamed Kharfan Dabaja, MD, Haesook T Kim, PhD, R Coleman Lindsley, MD, PhD, Guru Subramanian Guru Murthy, MD, Wael Saber, MD, Srinivasa Reddy Sanikommu, MD

DATE: December 2, 2022

RE: Developing a Molecular Risk Score for Patients with Myelodysplastic Syndrome undergoing Allogeneic Hematopoietic Cell Transplantation (MRS-MDS-HCT)

Hypothesis:

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).

Specific aims:

- 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.

- To further validate this new clinical prediction rule compared with the revised international prognostic scoring system (IPSS-R) in prognosticating clinical outcomes of patients with MDS undergoing allogeneic HCT.

- To determine mutation-specific outcomes for patients with MDS undergoing allogeneic HCT.

- To 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. (if mutation data for calculating IPSS-M are available in the dataset)

Developing a Molecular Risk Score for Patients with Myelodysplastic Syndrome undergoing Allogeneic Hematopoietic Cell Transplantation (MRS-MDS-HCT)

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Key Words: Myelodysplastic Syndromes; Stem Cell Transplantation; Hematopoietic Stem Cell Transplantation; Transplantation, Homologous; Clinical Decision Rules

1.0 Research Question

1.1 Can pre-transplant mutation data, in conjunction with clinical, cytogenetic, and routine laboratory data, be used to develop a clinical prediction rule for outcomes in patients with myelodysplastic syndrome (MDS) undergoing allogeneic hematopoietic cell transplantation (HCT)?

1.2 Could this pre-transplant molecular-based clinical prediction rule in patients with MDS be more predictive of allogeneic HCT outcomes than the Revised International Prognostic Scoring System (IPSS-R) score?

1.3 What are the mutation-specific outcomes of patients with MDS undergoing allogeneic HCT?

1.4 Does the pre-transplant Molecular International Prognostic Scoring System (IPSS-M) predict outcomes following allogeneic hematopoietic stem cell transplantation (HCT) for myelodysplastic syndromes (MDS)? (if mutation data for calculating IPSS-M are available in the dataset)

1.5 If the pre-transplant IPSS-M is predictive of MDS allogeneic HCT outcomes, is it more predictive than the pre-transplant IPSS-R score? (if mutation data for calculating IPSS-M are available in the dataset)

2.0 Research Hypothesis

2.1 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 in patients with MDS.

2.2 A clinical prediction rule using pre-transplant molecular data is more predictive of allogeneic HCT outcomes in patients with MDS than the R-IPSS.

2.3 The pre-transplant IPSS-M is predictive of allogeneic HCT outcomes in patients with MDS.

2.4 The pre-transplant IPSS-M is a superior tool to the pre-transplant IPSS-R for risk stratification and predicting outcomes of patients with MDS undergoing allogeneic HCT.

3.0 Specific Objectives

3.1 To develop and validate an accessible clinical prediction rule for outcome in patients with MDS undergoing allogeneic HCT that utilizes pre-transplant molecular data in addition to clinical, cytogenetic, and routine laboratory data.

- 3.1.1 To describe the clinical outcomes of patients with MDS undergoing allogeneic HCT based on this new molecular-based clinical prediction rule, with clinical outcomes stratified by risk group to include: overall survival (OS), disease-free survival (DFS), non-relapse mortality (NRM), and relapse.
  - 3.1.1.1 OS, defined as time to death from any cause with surviving patients censored at last follow-up.
  - 3.1.1.2 DFS, defined as time to relapse or death from any cause, with surviving patients in CR censored at last follow-up.

3.1.1.3 Disease relapse, defined as any reported events of recurrent MDS or leukemia incidence, with NRM and death as competing events.

3.2 To compare the effectiveness of this new pre-transplant molecular-based clinical prediction rule with the IPSS-R in prognosticating clinical outcomes of patients with MDS undergoing allogeneic HCT.

3.3 To determine mutation-specific outcomes for patients with MDS undergoing allogeneic HCT.

3.4 To evaluate prognostic value of molecular international prognostic scoring system (IPSS-M) predicting clinical outcomes of patients with MDS undergoing allogeneic hematopoietic cell transplantation (if mutation data for calculating IPSS-M are available in the dataset)

3.4.1 To describe clinical outcomes stratified by IPSS-M risk group to include: OS, DFS, NRM, and relapse.

3.4.2 To compare the predictability of the pre-transplant IPSS-M risk group for allogeneic HCT relapse to the IPSS-R risk group with regards to OS, DFS, NRM, and relapse.

3.5 Assess post-transplant health states (alive without relapse, alive with relapse, acute GVHD, chronic GVHD, dead) by the pre-transplant molecular-based clinical prediction rule risk group or score.

3.6 To define the situations and cutoff values in this new pre-transplant molecular-based clinical prediction rule that could help guide allogeneic HCT decision-making in patients with MDS. (exploratory)

4.0 Scientific Impact

4.1 The findings from this study will help to refine MDS allogeneic HCT decision-making. The recently developed IPSS-M has not been validated in the population of patients with MDS undergoing allogeneic HCT. Its utility is also limited because much of the mutation data needed is not routinely tested. Developing a clinical decision rule using commonly tested pre-transplant molecular, cytogenetic, routine laboratory, and clinical data, would result in a more accessible tool for clinicians than the IPSS-M. This could be called the Molecular Risk Score for Patients with Myelodysplastic Syndrome undergoing Allogeneic Hematopoietic Cell Transplantation (MRS-MDS-HCT).

Within the same study, a comparative analysis would be performed to demonstrate that this Center for International Blood and Marrow Transplantation Research (CIBMTR) pre-transplant molecular-based prognostic risk scoring system adds value over risk stratification with IPSS-R that is the current standard of practice. This tool could then be used to model decision-making that incorporates molecular data to determine the optimal situations to take patients with MDS for allogeneic HCT.

5.0 Scientific Justification

5.1 Pre-leukemic abnormalities of myeloid lineages of hematopoiesis are characterized as a group of diseases known as MDS.[1] MDS is a disease of aging with a median age of diagnosis of 71 and few cases before the age of 50.[2] It is characterized by persistent cytopenias of one or more myeloid lineages and concurrent morphologic dysplasia in one or more cell lines.[1] MDS represents a group of clonal hematopoietic stem cell disorders, characterized by dysplasia, ineffective hematopoiesis, cytopenia, transfusion dependency and risk of transformation to acute myeloid leukemia (AML).[3] MDS is a very heterogenous disease with variable outcomes.[3-5] This certainly dictates a risk-adapted treatment approach.[6]

Different risk-stratification tools have been designed to assess the risk of progression to leukemia. Approximately, 2 decades ago Greenberg *et al* [7] developed the International Prognostic Scoring System (IPSS) based on bone marrow blasts, cytogenetic abnormalities and cytopenias. The IPSS demonstrated its utility in predicting survival and progression to leukemia in MDS and has been a reference for clinical management for patients with MDS. Also, additional factors were found to have prognostic value including multilineage dysplasia, transfusion dependency and cytogenetic sub-groups.[8-10] Thus the IPSS was revised and was validated as the IPSS-R.[8]

These outcomes have been further evaluated by decision analyses to demonstrate the optimal levels of risk to refer patients for allogeneic HCT.[11,12] Based on the strategies favored in these analyses, allogeneic HCT has been recommended for IPSS Intermediate-2 and IPSS-R Intermediate risk groups and higher.[12] These strategies were subsequently evaluated prospectively and were shown to improve OS.[13] For a decade IPSS-R has been used for risk stratification, clinical trial design, and treatment recommendations.

Somatic myeloid mutations have been shown to have valuable prognostic value in multiple studies[14-17] but this was not included in the IPSS-R and had not been formally used for treatment recommendations.[18] Most recently, Bernard *et al* [18] studied 2957 patients under the guidance of the International Working Group for Prognosis in MDS (IWG-PM) to develop the IPSS-Molecular (IPSS-M) model and validated it in 754 patients. The model uses blood counts, marrow blasts, the five IPSS-R cytogenetic categories, 16 main effect genes, and 15 residual genes (NRAS). *TP53*^{multihit}, *FLT3* mutations, and *MLL*^{PTD} were strong predictors of adverse outcomes, highlighting the importance of screening for those mutations at diagnosis.

Analyses to demonstrate the utility of IPSS-M to predict allogeneic HCT outcomes have not yet been performed. The primary limitation is data availability. Molecular panels at many transplant centers do not test for all the genes or specific mutations included in the IPSS-M. The CIBMTR is uniquely positioned to solve this issue due to it large, longitudinal database. The CIBMTR has extensive molecular data that could be leveraged to improve the prognostication of patients MDS undergoing allogeneic HCT. Thus, we propose utilizing the CIBMTR database to develop an accessible pre-transplant molecular-based clinical decision rule to risk stratify patients with MDS undergoing allogeneic HCT.

6.0 Participant Selection Criteria

6.1 Inclusion Criteria

- 6.1.1 Diagnosis of MDS receiving their first allogeneic stem cell transplantation (allo-HSCT) between 2012 and 2021.
- 6.1.2 Age ≥ 18 years.
- 6.1.3 Patients receiving a graft from a human leukocyte antigen (HLA)-matched sibling, fully matched unrelated donor, mismatched unrelated donors, umbilical cord blood (UCB) graft, and haploidentical donors are eligible for study.

6.2 Exclusion Criteria

- 6.2.1 Recipients of second allogeneic HCT.

7.0 Data Requirements

7.1 Patient-related:

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

7.2 Disease-related:

- 7.2.1 IPSS-R risk group
- 7.2.2 Disease state at time of transplant
- 7.2.3 Time from diagnosis to HCT
- 7.2.4 Number of pre-transplant lines of therapy
- 7.2.5 Complete blood counts including hemoglobin, platelet count, absolute neutrophil count at diagnosis and/or pre-transplant
- 7.2.6 Bone marrow blast count at diagnosis and/or pre-transplant
- 7.2.7 Karyotype and cytogenetic abnormalities at diagnosis and/or pre-treatment
- 7.2.8 All available diagnosis and/or pre-transplant data on mutation profile, including TP53 number of mutations and locus loss of heterozygosity, MLL PTD, FLT3 TKD and ITD, ASXL1, CBL, DNMT3A, ETV6, EZH2, IDH2, KRAS, NPM1, NRAS, RUNX1, SF3B1, SRSF2, U2AF1, BCOR, BCORL1, CEBPA, ETNK1, GATA2, GNB1, IDH1, NF1, PHF6, PPM1D, PRPF8, PTPN11, SETBP1, STAG2, WT1
- 7.2.9 Measurable residual disease (MRD) status pre-transplant (if available)
- 7.2.10 Serum ferritin levels pre-transplant

7.3 Transplant-related:

- 7.3.1 Cell source: bone marrow vs. peripheral blood
- 7.3.2 Transplant donor type: Match related donor vs. match unrelated donor vs. mismatch unrelated donor vs haploidentical donor vs cord blood
- 7.3.3 Conditioning intensity: myeloablative vs. reduced intensity/nonmyeloablative conditioning
- 7.3.4 Total Body Irradiation: TBI vs non-TBI based conditioning regimen
- 7.3.5 GVHD prophylaxis: CNI + MTX ± others except MMF, post Cy vs. CNI + MMF ±others except post Cy vs. CNI + others except MMF, MTX vs. missing vs. other
- 7.3.6 Donor-recipient sex match: male-male vs. male-female vs. female-male vs. female-female vs. missing

7.3.7 CMV serostatus matching (+/-, +/+, -/-, -/+) between donor and recipient
7.3.8 ABO compatibility: Minor vs Major vs matched
7.3.9 Year of transplant: continuous
7.3.10 Post-transplant treatment: maintenance therapy vs DLI vs others vs None

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Table. Baseline characteristics of MDS patients first allo HCT from 2017-2019

Characteristic	MDS
No. of patients	1673
No. of centers	142
Patient age - median (min-max)	66.3 (18.0-82.7)
Age - no. (%)	
Median (min-max)	6.0 (2.0-7.0)
18-29	24 (1.4)
30-39	26 (1.6)
40-49	64 (3.8)
50-59	255 (15.2)
60-69	926 (55.3)
70-80	378 (22.6)
Sex - no. (%)	
Male	1085 (64.9)
Female	588 (35.1)
Race - no. (%)	
White	1432 (85.6)
Black or African American	90 (5.4)
Asian	79 (4.7)
Native Hawaiian or other Pacific Islander	9 (0.5)
American Indian or Alaska Native	9 (0.5)
More than one race	5 (0.3)
Not reported	49 (2.9)
Karnofsky score - no. (%)	
90-100	824 (49.3)
< 90	829 (49.6)
Not reported	20 (1.2)
HCT-CI - no. (%)	
0	252 (15.1)
1	212 (12.7)
2	204 (12.2)
3+	983 (58.8)
TBD, review needed for history of malignancies	1 (0.1)
TBD, inconsistencies between parent and sub-questions	21 (1.3)
Therapy related (AML/MDS) - no. (%)	
No	1357 (81.1)
Yes	270 (16.1)

Characteristic	MDS
Missing	46 (2.7)
Cytogenetic score - no. (%)	
Favorable	723 (43.2)
Intermediate	338 (20.2)
Poor	599 (35.8)
TBD (needs rev.)	3 (0.2)
Not tested	3 (0.2)
Not reported	7 (0.4)
IPSS-R cytogenetic score - no. (%)	
Very good	26 (1.6)
Good	751 (44.9)
Intermediate	330 (19.7)
Poor	190 (11.4)
Very poor	363 (21.7)
TBD (needs rev.)	3 (0.2)
Not tested	3 (0.2)
Not reported	7 (0.4)
Disease risk - no. (%)	
MDS early	588 (35.1)
MDS advanced	1068 (63.8)
Other	17 (1.0)
Blast in marrow prior to HCT - no. (%)	
< 5%	1611 (96.3)
Not reported	62 (3.7)
Blast in blood prior to HCT - no. (%)	
<= 3%	1230 (73.5)
> 3%	100 (6.0)
Not reported	343 (20.5)
Hb count prior to HCT - no. (%)	
>= 100 g/L	735 (43.9)
< 100 g/L	930 (55.6)
Not reported	8 (0.5)
ANC prior to HCT - no. (%)	
>= 1500 /uL	620 (37.1)
< 1500 /uL	973 (58.2)
Not reported	80 (4.8)
Platelet count prior to HCT - no. (%)	
>= 100 x 10/L	817 (48.8)

Characteristic	MDS
< 100 x 10/L	838 (50.1)
Not reported	18 (1.1)
IPSS prior to HCT - no. (%)	
Low	325 (19.4)
Intermediate-1	921 (55.1)
Intermediate-2	330 (19.7)
Not reported	97 (5.8)
IPSS-R prior to HCT - no. (%)	
Very low	280 (16.7)
Low	484 (28.9)
Intermediate	493 (29.5)
High	220 (13.2)
Very high	56 (3.3)
Not reported	140 (8.4)
Time from diagnosis to HCT - median (min-max)	8.5 (0.3-690.3)
Conditioning regimen intensity - no. (%)	
MAC	447 (26.7)
RIC	918 (54.9)
NMA	274 (16.4)
TBD	18 (1.1)
Missing	16 (1.0)
Conditioning regimen - no. (%)	
TBI/Cy	8 (0.5)
TBI/Cy/Flu	265 (15.8)
TBI/Cy/Flu/TT	9 (0.5)
TBI/Cy/TT	1 (0.1)
TBI/Mel	60 (3.6)
TBI/Flu	147 (8.8)
TBI/other(s)	9 (0.5)
Bu/Cy	96 (5.7)
Bu/Mel	7 (0.4)
Flu/Bu/TT	21 (1.3)
Flu/Bu	584 (34.9)
Flu/Mel/TT	18 (1.1)
Flu/Mel	393 (23.5)
Cy/Flu	13 (0.8)
Mel/other(s)	1 (0.1)
Treosulfan	7 (0.4)

Characteristic	MDS
TLI	8 (0.5)
Other(s)	10 (0.6)
None	3 (0.2)
Missing	13 (0.8)
Donor type - no. (%)	
HLA-identical sibling	317 (18.9)
Twin	2 (0.1)
Other related	366 (21.9)
Multi-donor	2 (0.1)
Unrelated (matching TBD)	928 (55.5)
Cord blood	58 (3.5)
Donor/recipient sex match - no. (%)	
M-M	338 (20.2)
M-F	149 (8.9)
F-M	199 (11.9)
F-F	118 (7.1)
CB - recipient M	34 (2.0)
CB - recipient F	24 (1.4)
Not reported	811 (48.5)
Donor/recipient CMV serostatus - no. (%)	
+/+	511 (30.5)
+/-	196 (11.7)
-/+	429 (25.6)
-/-	465 (27.8)
CB - recipient +	30 (1.8)
CB - recipient -	28 (1.7)
Not reported	14 (0.8)
Graft source - no. (%)	
Bone marrow	226 (13.5)
Peripheral blood	1389 (83.0)
Cord blood	58 (3.5)
GVHD prophylaxis - no. (%)	
No GVHD prophylaxis	5 (0.3)
Ex-vivo T-cell depletion	5 (0.3)
CD34 selection	27 (1.6)
Post-CY + other(s)	479 (28.6)
Post-CY alone	7 (0.4)
TAC + MMF +- other(s) (except post-CY)	240 (14.3)

Characteristic	MDS
TAC + MTX +- other(s) (except MMF, post-CY)	634 (37.9)
TAC + other(s) (except MMF, MTX, post-CY)	111 (6.6)
TAC alone	13 (0.8)
CSA + MMF +- other(s) (except post-CY)	74 (4.4)
CSA + MTX +- other(s) (except MMF, post-CY)	30 (1.8)
CSA alone	1 (0.1)
Other(s)	20 (1.2)
Not reported	27 (1.6)
ATG/Campath - no. (%)	
ATG alone	315 (18.8)
CAMPATH alone	18 (1.1)
No ATG or CAMPATH	1300 (77.7)
Not reported	40 (2.4)
Year of HCT - no. (%)	
2017	644 (38.5)
2018	578 (34.5)
2019	451 (27.0)
ASXL1 - no. (%)	
No	280 (16.7)
Yes	139 (8.3)
Not done	1253 (74.9)
Missing	1 (0.1)
JAK2 - no. (%)	
No	59 (3.5)
Yes	24 (1.4)
Not done	1139 (68.1)
Missing	451 (27.0)
ETV6 - no. (%)	
No	344 (20.6)
Yes	19 (1.1)
Not done	1309 (78.2)
Missing	1 (0.1)
EZH2 - no. (%)	
No	362 (21.6)
Yes	32 (1.9)
Not done	1279 (76.4)
P53 - no. (%)	
No	281 (16.8)

Characteristic	MDS
Yes	91 (5.4)
Not done	1300 (77.7)
Missing	1 (0.1)
RUNX1 - no. (%)	
No	344 (20.6)
Yes	79 (4.7)
Not done	1250 (74.7)
UAF1 - no. (%)	
No	419 (25.0)
Yes	45 (2.7)
Not done	1209 (72.3)
SRSF2 - no. (%)	
No	414 (24.7)
Yes	50 (3.0)
Not done	1209 (72.3)
CALR - no. (%)	
No	447 (26.7)
Yes	17 (1.0)
Not done	1209 (72.3)
IDH1 - no. (%)	
No	436 (26.1)
Yes	28 (1.7)
Not done	1209 (72.3)
IDH2 - no. (%)	
No	429 (25.6)
Yes	35 (2.1)
Not done	1209 (72.3)
DMNT3A - no. (%)	
No	394 (23.6)
Yes	70 (4.2)
Not done	1209 (72.3)
FLT3 - no. (%)	
No	418 (25.0)
Yes	46 (2.7)
Not done	1209 (72.3)
TET - no. (%)	
No	373 (22.3)
Yes	91 (5.4)

Characteristic	MDS
Not done	1209 (72.3)
BCOR - no. (%)	
No	423 (25.3)
Yes	41 (2.5)
Not done	1209 (72.3)
MLL - no. (%)	
No	460 (27.5)
Yes	4 (0.2)
Not done	1209 (72.3)
CBL - no. (%)	
No	437 (26.1)
Yes	27 (1.6)
Not done	1209 (72.3)
KRAS - no. (%)	
No	439 (26.2)
Yes	25 (1.5)
Not done	1209 (72.3)
NPM - no. (%)	
No	439 (26.2)
Yes	25 (1.5)
Not done	1209 (72.3)
NRAS - no. (%)	
No	434 (25.9)
Yes	30 (1.8)
Not done	1209 (72.3)
SF3BL - no. (%)	
No	434 (25.9)
Yes	30 (1.8)
Not done	1209 (72.3)
CEBPA - no. (%)	
No	440 (26.3)
Yes	24 (1.4)
Not done	1209 (72.3)
ETNKL - no. (%)	
No	440 (26.3)
Yes	24 (1.4)
Not done	1209 (72.3)
GATA2 - no. (%)	

Characteristic	MDS
No	447 (26.7)
Yes	17 (1.0)
Not done	1209 (72.3)
GNBL - no. (%)	
No	464 (27.7)
Not done	1209 (72.3)
PPML - no. (%)	
No	452 (27.0)
Yes	12 (0.7)
Not done	1209 (72.3)
PRPF - no. (%)	
No	462 (27.6)
Yes	2 (0.1)
Not done	1209 (72.3)
PTPN - no. (%)	
No	462 (27.6)
Yes	2 (0.1)
Not done	1209 (72.3)
SETBP - no. (%)	
No	441 (26.4)
Yes	23 (1.4)
Not done	1209 (72.3)
STAG - no. (%)	
No	439 (26.2)
Yes	25 (1.5)
Not done	1209 (72.3)
WT1 - no. (%)	
No	455 (27.2)
Yes	9 (0.5)
Not done	1209 (72.3)

Table. Samples available in MDS patients with first allo HCT from 2017-2021

Characteristic	TED	CRF
No. of patients	6113	2343
No. of centers	284	181
Samples available - no. (%)		
No Sample	3334 (54.5)	773 (33.0)
Recipient and Donor	1422 (23.3)	932 (39.8)
Recipient Only	1042 (17.0)	536 (22.9)
Donor Only	315 (5.2)	102 (4.4)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Identifying the Optimal Graft-versus-Host Disease Regimen in Allogeneic Transplantation for Myelofibrosis

Q2. Key Words

graft-versus-host disease, myelofibrosis, allogeneic transplant

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Sagar Patel, MD
Email address:	sagar.patel@hci.utah.edu
Institution name:	Huntsman Cancer Institute, University of Utah
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Daniel Couriel, MD, MS, MBA
Email address:	dan.couriel@hci.utah.edu
Institution name:	Huntsman Cancer Institute, University of Utah
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

Sagar Patel

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Chronic Leukemia

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

What is the optimal graft-versus-host disease (GVHD) prophylaxis strategy in allogeneic hematopoietic cell transplantation (alloHCT) for primary and secondary myelofibrosis (MF)?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that a graft-versus-host disease (GVHD) prophylaxis strategy in allogeneic hematopoietic cell transplantation (alloHCT) 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 in regards to graft-versus-host disease-free/relapse-free survival (GFRS) as well as acute and chronic GVHD incidence and severity.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary Aim:

1. Identify the optimal GVHD prophylaxis strategy in alloHCT for primary and secondary myelofibrosis as assessed by GFRS, acute and chronic GVHD incidence and severity.

Secondary Aims:

1. Evaluate risk factors for engraftment failure after alloHCT in those receiving ATG vs PTCY
2. Evaluate GFRS, acute and chronic GVHD incidence and severity in MF patients with impaired renal function
3. Assess the impact of pre-transplant ruxolitinib use on engraftment and GFRS
4. Impact of GVHD prophylaxis on overall survival (OS), non-relapse mortality (NRM), relapse-free survival (RFS)

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Transplantation for primary and secondary MF creates unique challenges when selecting the optimal GVHD prophylaxis strategy. First, alloHCT outcomes remain historically poor in MF patients in part due to the older age of these patients and baseline impairments in other organs due to the disease, such as the spleen or kidneys. This translates into higher rates of engraftment failure and treatment-related toxicity. Second, efforts to avoid GVHD agents that may precipitate or contribute to engraftment failure and treatment-related toxicity are critical and have not been well-studied with no uniform standard amongst centers. Third, there is heterogeneity amongst centers in use of pre-transplant ruxolitinib on engraftment and GVHD. Fourth, contemporary practice often includes the use of ATG and PTCY in non-haploidentical donor settings, particularly with matched unrelated donors.

A comprehensive analysis through the CIBMTR is needed to appropriately identify the optimal GVHD prophylaxis strategy. Most centers see a limited number of patients given the relative rarity of the disease, which lends itself well to investigation by large registries such as the CIBMTR. Our study seeks to investigate the impact on outcomes amongst various GVHD prophylaxis approaches irrespective of conditioning regimen/intensity or donor type. Given the older age of MF patients, they are less likely to have optimal recovery from acute or chronic GVHD and given the predominant use of PBSC, this emphasizes the need for prevention via the optimal primary prophylaxis approach.

Thus, this study is critically important to address ways by which myelofibrosis outcomes can be improved through appropriate GVHD prophylaxis selection. Such results consequently can help provide the foundation for future prospective, randomized studies.

Q19. 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.

Myelofibrosis (MF) is a myeloproliferative neoplasm marked by cytopenias, splenomegaly, and constitutional symptoms. It is characterized by extensive fibrous scarring in the bone marrow typically driven by mutations in either JAK2, MPL, CALR, TET2, or in some cases no known mutation is identified. MF can develop de novo or secondary to essential thrombocythemia or polycythemia vera. AlloHCT remains the only potentially curative treatment for primary and secondary MF.

While more patients are now able to receive an alloHCT with the advent of reduced-intensity conditioning (RIC) rather than the traditional myeloablative conditioning regimen (MAC), it remains unknown the optimal GVHD prophylaxis agents. Historically, outcomes after transplant for myelofibrosis have been poor regardless of the GVHD prophylaxis and conditioning regimen approach.

A previous CIBMTR study from a decade ago showed transplant-related mortality rates of 18% for HLA-identical sibling transplants, 35% for unrelated transplants, and 19% for alternative donor transplants. Notably, OS rates were dismal at 37%, 30%, and 40%, respectively. In addition, graft failure was substantially higher for patients with matched unrelated donors than in those with matched sibling donors (20% vs. 9%). Given the high risk of graft failure, current practice reflects greater use of PBSC rather than BM given the faster engraftment rates, however large-scale studies are limited. These poor outcomes may reflect the challenges inherent with a fibrotic marrow. A comprehensive study in this challenging population is needed given the substantial and immediate impact such results would have on alloHCT strategies for these patients.

A previous CIBMTR study investigating some of the outcomes of the proposed study included patients from 1982, prior to widespread use of ruxolitinib and contemporary transplant practices. The proposed questions is not directly addressed in the CK17-01 study, which is focused on developing a prognostic scoring system in MF. The CK20-01 focuses on outcomes in MF by conditioning regimen. Finally, the CK21-01 study focuses on haploidentical versus matched related donors in MF.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion:

- Disease diagnosis of primary or secondary (post-essential thrombocythemia or polycythemia vera) myelofibrosis
- Received a first allogeneic HCT from 2000-2020 with at least 1 year of follow-up
- All graft sources, donor relationships, conditioning regimens/intensities

Exclusion:

- Patients with missing GVHD prophylaxis data

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Data to be analyzed will only be from CIBMTR report forms. No supplemental data will be required.
Required Forms:
- Myelodysplasia / Myeloproliferative Disorders Pre-HSCT Data (Form 2014)
- Pre-Transplant Essential Data (Form 2400)
- Myelodysplasia / Myeloproliferative Disorders Post-HCT Data (Form 2114)
- Post-Transplant Essential Data (Form 2450)
- Post-HCT Follow-up Data (Form 2100)

Q23. 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 description of the hypothesis specific to PROS.

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. 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 of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/A

Q25. 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, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

1. Ballen KK, Shrestha S, Sobocinski KA, et al. Outcome of transplantation for myelofibrosis. Biol Blood Marrow Transplant. 2010;16(3):358-367.
2. Mesa RA, Silverstein MN, Jacobsen SJ, Wollan PC, Tefferi A. Population-based incidence and survival figures in essential thrombocythemia and agnogenic myeloid metaplasia: an Olmsted County Study, 1976-1995. Am J Hematol. 1999;61(1):10-15.
3. Tefferi A. Primary myelofibrosis: 2019 update on diagnosis, risk-stratification and management. Am J Hematol. 2018;93(12):1551-1560.
4. Gupta V, Malone AK, Hari PN, et al. Reduced-intensity hematopoietic cell transplantation for patients with primary myelofibrosis: a cohort analysis from the center for international blood and marrow transplant research. Biol Blood Marrow Transplant. 2014;20(1):89-97.
5. Olsson R, Remberger M, Schaffer M, et al. Graft failure in the modern era of allogeneic hematopoietic SCT. Bone Marrow Transplant. 2013;48(4):537-543.
XIII.

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table. Baseline characteristics of MF patients undergoing 1st allo-HCT with PTCY vs ATG between 2008 and 2019

Characteristic	TAC-Based (No PTCY)	CSA-Based (No PTCY)	PTCy-based	Other
No. of patients	1131	233	137	34
No. of centers	106	72	46	18
Age at HCT - median (min-max)	61.2 (3.0-77.9)	58.3 (1.1-74.1)	61.0 (16.3-77.3)	59.5 (25.0-76.7)
Age at HCT - no. (%)				
<10	1 (0.1)	4 (1.7)	0 (0.0)	0 (0.0)
10-17	3 (0.3)	3 (1.3)	1 (0.7)	0 (0.0)
18-29	3 (0.3)	4 (1.7)	0 (0.0)	1 (2.9)
30-39	16 (1.4)	7 (3.0)	3 (2.2)	1 (2.9)
40-49	113 (10.0)	41 (17.6)	18 (13.1)	1 (2.9)
50-59	368 (32.5)	73 (31.3)	39 (28.5)	15 (44.1)
60-69	531 (46.9)	97 (41.6)	58 (42.3)	13 (38.2)
>=70	96 (8.5)	4 (1.7)	18 (13.1)	3 (8.8)
Recipient sex - no. (%)				
Male	648 (57.3)	140 (60.1)	78 (56.9)	18 (52.9)
Female	483 (42.7)	93 (39.9)	59 (43.1)	16 (47.1)
Race - no. (%)				
White	1010 (89.3)	172 (73.8)	116 (84.7)	30 (88.2)
Black or African-American	48 (4.2)	5 (2.1)	12 (8.8)	1 (2.9)
Asian	40 (3.5)	10 (4.3)	3 (2.2)	0 (0.0)
Native Hawaiian or other Pacific Islander	7 (0.6)	4 (1.7)	2 (1.5)	0 (0.0)
American Indian or Alaska Native	3 (0.3)	1 (0.4)	0 (0.0)	0 (0.0)
Other	5 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	18 (1.6)	41 (17.6)	4 (2.9)	3 (8.8)
Subdisease - no. (%)				
Myelofibrosis	768 (67.9)	171 (73.4)	89 (65.0)	24 (70.6)
Polycythemia vera	150 (13.3)	35 (15.0)	16 (11.7)	2 (5.9)
Essential thrombocythemia	196 (17.3)	23 (9.9)	28 (20.4)	7 (20.6)
Not reported	17 (1.5)	4 (1.7)	4 (2.9)	1 (2.9)
Graft type - no. (%)				
Bone marrow	57 (5.0)	21 (9.0)	8 (5.8)	1 (2.9)
Peripheral blood	1056 (93.4)	197 (84.5)	129 (94.2)	28 (82.4)
Cord blood	18 (1.6)	15 (6.4)	0 (0.0)	5 (14.7)

Characteristic	TAC-Based (No PTCY)	CSA-Based (No PTCY)	PTCy-based	Other
HCT-CI - no. (%)				
0	262 (23.2)	90 (38.6)	27 (19.7)	9 (26.5)
1	148 (13.1)	27 (11.6)	19 (13.9)	7 (20.6)
2	179 (15.8)	37 (15.9)	24 (17.5)	6 (17.6)
3	227 (20.1)	27 (11.6)	27 (19.7)	7 (20.6)
4	141 (12.5)	19 (8.2)	19 (13.9)	2 (5.9)
5	70 (6.2)	10 (4.3)	10 (7.3)	2 (5.9)
6+	88 (7.8)	12 (5.2)	10 (7.3)	1 (2.9)
Missing	16 (1.4)	11 (4.7)	1 (0.7)	0 (0.0)
Time from diagnosis to HCT (months) - median (min-max)	30.7 (1.9-593.9)	25.6 (2.3-378.0)	36.9 (1.6-398.1)	29.2 (4.8-301.4)
Cytogenetic score - no. (%)				
Favorable	637 (56.3)	126 (54.1)	86 (62.8)	19 (55.9)
Intermediate	211 (18.7)	39 (16.7)	21 (15.3)	9 (26.5)
Poor	159 (14.1)	28 (12.0)	18 (13.1)	3 (8.8)
TBD (needs rev.)	66 (5.8)	13 (5.6)	11 (8.0)	2 (5.9)
Not reported	58 (5.1)	27 (11.6)	1 (0.7)	1 (2.9)
Donor/recipient sex match - no. (%)				
M-M	427 (37.8)	86 (36.9)	54 (39.4)	5 (14.7)
M-F	304 (26.9)	44 (18.9)	30 (21.9)	5 (14.7)
F-M	208 (18.4)	49 (21.0)	24 (17.5)	10 (29.4)
F-F	170 (15.0)	37 (15.9)	29 (21.2)	9 (26.5)
CB - recipient M	10 (0.9)	5 (2.1)	0 (0.0)	3 (8.8)
CB - recipient F	8 (0.7)	10 (4.3)	0 (0.0)	2 (5.9)
Not reported	4 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)
Donor type - no. (%)				
HLA-identical sibling	332 (29.4)	99 (42.5)	36 (26.3)	7 (20.6)
Well-matched unrelated (8/8)	681 (60.2)	83 (35.6)	79 (57.7)	19 (55.9)
Partially-matched unrelated (7/8)	93 (8.2)	22 (9.4)	21 (15.3)	3 (8.8)
Mis-matched unrelated (<= 6/8)	2 (0.2)	3 (1.3)	0 (0.0)	0 (0.0)
Unrelated (matching TBD)	5 (0.4)	11 (4.7)	1 (0.7)	0 (0.0)
Cord blood	18 (1.6)	15 (6.4)	0 (0.0)	5 (14.7)
Conditioning intensity - no. (%)				
No drugs reported	1 (0.1)	1 (0.4)	0 (0.0)	0 (0.0)

Characteristic	TAC-Based (No PTCY)	CSA-Based (No PTCY)	PTCy-based	Other
MAC	500 (44.2)	90 (38.6)	86 (62.8)	18 (52.9)
RIC	598 (52.9)	114 (48.9)	41 (29.9)	16 (47.1)
NMA	23 (2.0)	20 (8.6)	10 (7.3)	0 (0.0)
TBD	9 (0.8)	7 (3.0)	0 (0.0)	0 (0.0)
Not reported	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Conditioning regimen - no. (%)				
TBI/Cy	17 (1.5)	2 (0.9)	0 (0.0)	0 (0.0)
TBI/Cy/Flu	10 (0.9)	15 (6.4)	11 (8.0)	3 (8.8)
TBI/Cy/Flu/TT	1 (0.1)	0 (0.0)	0 (0.0)	1 (2.9)
TBI/Mel	22 (1.9)	1 (0.4)	4 (2.9)	3 (8.8)
TBI/Flu	77 (6.8)	16 (6.9)	6 (4.4)	0 (0.0)
TBI/other(s)	3 (0.3)	3 (1.3)	0 (0.0)	0 (0.0)
Bu/Cy	152 (13.4)	25 (10.7)	6 (4.4)	3 (8.8)
Bu/Mel	0 (0.0)	1 (0.4)	0 (0.0)	9 (26.5)
Flu/Bu/TT	4 (0.4)	1 (0.4)	13 (9.5)	0 (0.0)
Flu/Bu	464 (41.0)	87 (37.3)	74 (54.0)	9 (26.5)
Flu/Mel/TT	0 (0.0)	0 (0.0)	5 (3.6)	0 (0.0)
Flu/Mel	369 (32.6)	64 (27.5)	18 (13.1)	6 (17.6)
Cy/Flu	4 (0.4)	6 (2.6)	0 (0.0)	0 (0.0)
Cy alone	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Mel alone	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Mel/other(s)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Treosulfan	1 (0.1)	3 (1.3)	0 (0.0)	0 (0.0)
TLI	0 (0.0)	3 (1.3)	0 (0.0)	0 (0.0)
Other(s)	4 (0.4)	4 (1.7)	0 (0.0)	0 (0.0)
None	1 (0.1)	1 (0.4)	0 (0.0)	0 (0.0)
In-vivo T-cell depletion (ATG/alemtuzumab) - no. (%)				
No	775 (68.5)	124 (53.2)	132 (96.4)	15 (44.1)
Yes	356 (31.5)	109 (46.8)	5 (3.6)	19 (55.9)
Ruxolitinib (Jakafi) used in prior therapy (MFS, CRF track) - no. (%)				
No	479 (42.4)	128 (54.9)	41 (29.9)	12 (35.3)
Yes	610 (53.9)	76 (32.6)	90 (65.7)	18 (52.9)
Not reported	42 (3.7)	29 (12.4)	6 (4.4)	4 (11.8)
DIPSS score prior to HCT (MFS, CRF track) - no. (%)				

Characteristic	TAC-Based (No PTCY)	CSA-Based (No PTCY)	PTCy-based	Other
Low	117 (10.3)	16 (6.9)	14 (10.2)	2 (5.9)
Intermediate-1	385 (34.0)	57 (24.5)	52 (38.0)	13 (38.2)
Intermediate-2	422 (37.3)	91 (39.1)	55 (40.1)	8 (23.5)
High	13 (1.1)	4 (1.7)	2 (1.5)	0 (0.0)
Not reported	194 (17.2)	65 (27.9)	14 (10.2)	11 (32.4)
Splenomegaly (MFS, CRF track) - no. (%)				
No	267 (23.6)	60 (25.8)	34 (24.8)	7 (20.6)
Yes	742 (65.6)	129 (55.4)	94 (68.6)	20 (58.8)
Splenectomy	26 (2.3)	9 (3.9)	0 (0.0)	1 (2.9)
Not reported	96 (8.5)	35 (15.0)	9 (6.6)	6 (17.6)
Year of HCT - no. (%)				
2008	67 (5.9)	20 (8.6)	0 (0.0)	2 (5.9)
2009	55 (4.9)	26 (11.2)	0 (0.0)	0 (0.0)
2010	27 (2.4)	8 (3.4)	0 (0.0)	0 (0.0)
2011	15 (1.3)	3 (1.3)	0 (0.0)	0 (0.0)
2012	6 (0.5)	7 (3.0)	0 (0.0)	1 (2.9)
2013	37 (3.3)	6 (2.6)	3 (2.2)	1 (2.9)
2014	96 (8.5)	29 (12.4)	5 (3.6)	3 (8.8)
2015	94 (8.3)	24 (10.3)	6 (4.4)	4 (11.8)
2016	113 (10.0)	23 (9.9)	4 (2.9)	4 (11.8)
2017	184 (16.3)	28 (12.0)	31 (22.6)	6 (17.6)
2018	201 (17.8)	34 (14.6)	37 (27.0)	7 (20.6)
2019	236 (20.9)	25 (10.7)	51 (37.2)	6 (17.6)
Follow-up - median (range)	48.9 (3.2-174.2)	58.9 (3.2-168.3)	37.6 (1.6-99.7)	48.1 (6.4-99.0)

I. Study Title

Allogeneic Stem Cell Transplant Outcomes for Patients with *TP53*-Mutant Myelodysplastic Syndrome and Myeloproliferative Neoplasm: A CIBMTR Analysis

II. Key Words

TP53
myelodysplastic syndrome
myeloproliferative neoplasm
conditioning regimen
human leukocyte antigen

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V. Research Question

For allogeneic transplant recipients with *TP53*-mutant myelodysplastic syndrome (MDS) or myeloproliferative neoplasm (MPN), what is the impact of (1) conditioning regimen, (2) stem cell donor source, and (3) graft-versus-host disease (GvHD) prophylaxis regimen on disease-free survival (DFS), overall survival (OS), non-relapse mortality (NRM), and incidence of GvHD?

VI. Research Hypothesis

We hypothesize 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. We hypothesize that a tailored approach to selection of transplant factors should be considered, given the heterogeneity within this genetically defined subset.

VII. Specific Objectives/Outcomes to be Investigated

We will examine data from transplant recipients with MDS and MPN from 2005-2022. This study has 3 independent variables:

<u>Independent variable 1: Conditioning regimen</u>
We will perform subgroup analysis for myeloablative conditioning (MAC), reduced-intensity conditioning (RIC), and non-myeloablative (NMA) conditioning, by CIBMTR definitions. These regimens within the CIBMTR dataset include various combinations of cyclophosphamide, fludarabine, melphalan, busulfan, thiotepa, treosulfan, total lymphoid irradiation, and/or total body irradiation. We will specifically assess the outcomes of MAC vs. RIC/NMA for *TP53*-mutant MDS and MPN.

<u>Independent variable 2: Stem cell donor source</u>
We will perform subgroup analysis for stem cell donor subtype, including HLA match status. HLA match options available in this *TP53*-mutant CIBMTR dataset include HLA-identical sibling donor, haploidentical related donor, well-matched unrelated donor (8/8 match), partially-matched unrelated donor (7/8 match), mis-matched unrelated donor (≤6/8 match), and cord blood donor. We will also assess the impact of sex match (male or female) and graft source (bone marrow, peripheral blood, or cord blood) on outcomes.

<u>Independent variable 3: GvHD prophylaxis regimen</u>
We will perform subgroup analysis for the effect of the intensity of the GvHD prophylaxis regimen. Such regimens in this *TP53*-mutant CIBMTR dataset include various combinations of post-transplant cyclophosphamide, tacrolimus, mycophenolate mofetil, methotrexate, cyclosporine A, anti-thymocyte globulin, alemtuzumab, *ex vivo* T cell depletion, and CD34(+) cell selection.

This study has 2 dependent variables:

Primary endpoints: DFS and OS
We will evaluate the DFS and OS at 30 days, 100 days, 6 months, 1 year, and 5 years. We will also assess durability of cytogenetic remission and molecular remission, if CIBMTR data is available. OS refers to death from any cause. Patient who are alive will be censored at the time of last clinic follow up or the date of last contact, whichever is later. Univariate vs. multivariate analysis will depend on accrual and we will collaborate with our statistician. Kaplan-Meier curves will be generated for subgroups of each of the independent variables. Hazard ratio with 95% confidence interval (CI) will be obtained.

Secondary endpoints: NRM and Incidence of GvHD
We will evaluate NRM and incidence of GvHD at 30 days, 100 days, 6 months, 1 year, and 5 years. NRM is defined at death due to transplant-related factors in the absence of disease relapse.

VIII. Scientific Impact

TP53-mutant MDS and MPN represent an area of unmet need, with very few impactful discoveries described recently.[1,2] First, a major step forward in 2022 has been the validation of IPSS-M data for precision prognostics in MDS: this data showed definitively that *TP53* mutation carries the highest adjusted hazard ratio for survival.[1] Another major improvement in our understanding has been the official recognition of *TP53* mutation in top-line pathology diagnoses in the International Consensus Classification.[2] Several small and mostly single-center studies have shown positive impact of allogeneic transplant for *TP53*-mutant myeloid neoplasms (both MDS and AML). We propose to investigate factors impacting survival in patients with *TP53*-mutant MDS and MPN undergoing allogenic transplant. The CIBMTR database offers the largest collection of transplant-related data about *TP53*-mutated patients and is the most valuable tool that would allow us to identify potential prognostic factors that would help in clinical practice. Specifically, the findings of this CIBMTR investigative effort will be impactful because they will:

- help clinicians decide on transplant candidacy for patients with MDS or MPN with *TP53* disruption
- guide selection of the optimal conditioning regimen for transplant-eligible patients
- guide selection of the optimal donor and HLA haplotype for transplant-eligible patients
- inform translational investigations (including phase III clinical trials) of targeted therapy for this subset of patients with MDS and MPN in need of better outcomes
- inform decisions about post-transplant maintenance for this mutational subset

IX. Scientific Justification

It has been well-known that *TP53* aberrations have been associated with adverse outcomes for MDS and MPN, and no targeted therapies are commercially available. The leading pharmacologic agent in late 2020 had been APR-246 (eprenatapopt), but this agent failed to meet the primary endpoint in phase III data, leaving us with no precision approaches for *TP53*-aberrant myeloid neoplasms. Data for magrolimab plus azacitidine in *TP53*-mutant AML was presented at European Hematology Association (EHA) Congress and American Society of

Clinical Oncology (ASCO) in June 2022, though the data is not mature and this medication may not available to the community in the near future.[3-5] Since transplant outcomes data is a mandatory reporting requirement to the CIBMTR, many centers might choose to not offer transplant to this exceptionally high-risk subset of patients with myeloid neoplasms carrying *TP53* aberrations, since long-term outcomes have historically been poor. Instead, a management plan is often designed with palliative intent and frequently includes temporizing rather than definitive interventions.

Prior CIBMTR studies involving 1514 MDS patients with (19% with *TP53*-mutation) showed that this mutational cohort has shorter survival (3-year OS of 20%) compared to wild-type *TP53*, and relapse rates were high.[6] The group of researchers at UMass has recently shown improvement in OS with transplant (compared to no transplant) for *TP53*-mutant myeloid neoplasm (14.7 vs. 5.1 months) and compared this to MD Anderson data.[7,8] To understand the basis for the improved OS with transplant, clonal dynamics were modeled by annotating copy number variation analysis against *TP53* VAF to infer clonality. The study showed that *TP53*-mutant clone(s) persisted during morphologic remission and fueled relapse (with heterogenous descendant clones), but the *TP53*-mutant clones and descendant clones were eliminated only after allogeneic transplant. This concept may justify transplant, as transplant confers the highest chance of eliminating genomic MRD. The sample size was relatively small (n = 40 total and n = 11 who were transplanted). This study was similar to that of Yale Cancer Center, who also transplanted n = 11 patients and showed improvement in OS with transplant.[9] This CIBMTR proposal will impart a much higher power for analysis.

Much of the uncharted territory within *TP53*-mutant myeloid neoplasms includes the translational significance of allelic status (monoallelic vs. biallelic *TP53* hit) and the concurrent cytogenetics.[10] This year at ASH 2022, we will be presenting our data on clinical outcomes of patients with monoallelic, biallelic, and multi-hit states of *TP53*-mutant MDS and AML (Abstract #2792). However, we are limited with regard to studying transplant outcomes with single-institutional data, since there are so few transplant recipients.

Data from TCT 2021 on a similar topic was important, but our analysis will differ and add to the literature because we are performing centralized data collection with a broader range of patients, in contrast to a multicenter retrospective analysis. Our proposal will request a higher sample size and thus may garner more power for analysis.[11]

In summary, the scientific justification and novelty for this proposal is:

- CIBMTR registry data has thus far not been systematically analyzed for outcomes for patients with *TP53*-mutant MDS or MPN, and this is the largest database that would allow us to determine prognostic factors.
- The analysis would allow us to determine which specific subgroups of *TP53*-mutant MDS or MPN may derive benefit from specific conditioning regimens or HLA haplotypes. Aggregate outcomes data for this mutational subset may inform rational therapeutic design towards precision medicine or towards post-transplant maintenance.

X. Participant Selection Criteria

Inclusion criteria:

- Age ≥ 18 years at the time of diagnosis
- Diagnosis of MDS or MPN between 2005 and 2022, per WHO 2016 classification
- History of allogeneic stem cell transplantation between 2005 and 2022
- Mutated TP53 or deletion of chromosome 17p

Exclusion criteria:

- Age < 18 years
- No documented evidence of *TP53* mutation or deletion of chromosome 17p

XI. Data Requirements

Recipient data:
Age
Sex
Race
Ethnicity
Cytogenetics
NGS results at the time of diagnosis
Depth of remission prior to transplant
Hematopoietic cell transplant (HCT) comorbidity index
Time from diagnosis to HCT
Bone marrow blast percentage
Stem cell source (BM, PBSC, cord blood)
Conditioning regimen
GVHD prophylaxis regimen
Date of transplant
Time to neutrophil engraftment
Time to platelet engraftment
Immune recovery (T_{reg} frequency, CD4(+) cell frequency)
Mixed chimerism at 30 days, 100 days, 6 months, 1 year, and 5 years
Post-transplant infection (bacteria, fungal and/or viral)
Durability of remission
NGS results and MRD status at 30 days, 100 days, 6 months, 1 year, and 5 years
Disease-free survival at 30 days, 100 days, 6 months, 1 year, and 5 years
Incidence of GvHD at 30 days, 100 days, 6 months, 1 year, and 5 years
OS at 30 days, 100 days, 6 months, 1 year, and 5 years
Date of Death
Date of Relapse

Donor data:
Age
Sex
Race
Ethnicity
Degree of HLA match to recipient

CMV status

Statistical analysis:
The probabilities for DFS and OS will be calculated using the Kaplan-Meier estimator. Cumulative incidence estimates will be used for competing risks outcomes, including NRM and incidence of GvHD. Cox proportional hazards regression will be used to identify independent prognostic factors associated with the outcomes. The proportional hazards assumption for each factor will be checked. When the proportional hazards assumption is violated, a time-varying effect will be considered. The stepwise selection method will be used to identify significant factors associated with the outcomes at a significance level $p < 0.05$. Interactions between main effects and significant factors will be tested. Center effects will be tested using the score test of homogeneity.

XII. Patient-Reported Outcome (PRO) Requirements

This is not applicable. The study does not require patient-reported outcomes.

XIII. Sample Requirements

This is not applicable. The study does not require biologic samples from the CIBMTR Repository.

XIV. Non-CIBMTR Data Source

This is not applicable. There is no external data source to which the CIBMTR data will be linked.

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XVI. Conflicts of Interest

The investigators declare no relevant conflicts of interest.

Table 1. Baseline characteristics of MDS and MPN patients undergoing 1st allo-HCT with TP53 mutation at any timepoint, between 2008 and 2019

Characteristic	MDS
No. of patients	301
No. of centers	79
Patient age - median (min-max)	66 (18-83)
Age - no. (%)	
Median (min-max)	6 (2-7)
18-29	4 (1)
30-39	2 (1)
40-49	11 (4)
50-59	52 (17)
60-69	164 (54)
70-80	68 (23)
Sex - no. (%)	
Male	185 (61)
Female	116 (39)
Race - no. (%)	
White	269 (89)
Black or African American	10 (3)
Asian	11 (4)
Native Hawaiian or other Pacific Islander	1 (0)
American Indian or Alaska Native	3 (1)
More than one race	1 (0)
Missing	6 (2)
Karnofsky score - no. (%)	
90-100	143 (48)
< 90	154 (51)
Missing	4 (1)
HCT-CI - no. (%)	
0	29 (10)
1	37 (12)
2	42 (14)
3+	191 (63)
TBD, review needed for history of malignancies	1 (0)
TBD, inconsistencies between parent and sub-questions	1 (0)
Therapy related (AML/MDS) - no. (%)	
No	188 (62)

Characteristic	MDS
Yes	105 (35)
Missing	8 (3)
Cytogenetic score - no. (%)	
Favorable	36 (12)
Intermediate	21 (7)
Poor	244 (81)
Disease risk - no. (%)	
MDS early	114 (38)
MDS advanced	184 (61)
Other	3 (1)
Blast in marrow prior to HCT - no. (%)	
< 5%	286 (95)
5-10%	2 (1)
11-20%	1 (0)
Missing	12 (4)
Blast in blood prior to HCT - no. (%)	
<= 3%	238 (79)
> 3%	12 (4)
Missing	51 (17)
Hb count prior to HCT - no. (%)	
>= 100 g/L	145 (48)
< 100 g/L	156 (52)
ANC prior to HCT - no. (%)	
>= 1500 /uL	97 (32)
< 1500 /uL	193 (64)
Missing	11 (4)
Platelet count prior to HCT - no. (%)	
>= 100 x 10/L	159 (53)
< 100 x 10/L	141 (47)
Missing	1 (0)
Time from diagnosis to HCT - median (min-max)	6 (1-153)
Conditioning regimen intensity - no. (%)	
MAC	82 (27)
RIC	177 (59)
NMA	36 (12)
TBD	3 (1)
Missing	3 (1)
Conditioning regimen - no. (%)	

Characteristic	MDS
TBI/Cy	2 (1)
TBI/Cy/Flu	36 (12)
TBI/Cy/Flu/TT	1 (0)
TBI/Mel	12 (4)
TBI/Flu	23 (8)
TBI/other(s)	1 (0)
Bu/Cy	16 (5)
Bu/Mel	5 (2)
Flu/Bu/TT	4 (1)
Flu/Bu	106 (35)
Flu/Mel/TT	7 (2)
Flu/Mel	79 (26)
Cy/Flu	1 (0)
Mel/other(s)	1 (0)
Treosulfan	1 (0)
TLI	1 (0)
Other(s)	2 (1)
None	1 (0)
Missing	2 (1)
Donor type - no. (%)	
HLA-identical sibling	60 (20)
Other related	48 (16)
Well-matched unrelated (8/8)	162 (54)
Partially-matched unrelated (7/8)	15 (5)
Mis-matched unrelated (<= 6/8)	3 (1)
Cord blood	13 (4)
Donor/recipient sex match - no. (%)	
M-M	139 (46)
M-F	77 (26)
F-M	37 (12)
F-F	35 (12)
CB - recipient M	9 (3)
CB - recipient F	4 (1)
Donor/recipient CMV serostatus - no. (%)	
+/+	74 (25)
+/-	34 (11)
-/+	81 (27)
-/-	97 (32)

Characteristic	MDS
CB - recipient +	3 (1)
CB - recipient -	10 (3)
Missing	2 (1)
Graft source - no. (%)	
Bone marrow	31 (10)
Peripheral blood	257 (85)
Cord blood	13 (4)
GVHD prophylaxis - no. (%)	
Ex-vivo T-cell depletion	1 (0)
CD34 selection	9 (3)
Post-CY + other(s)	71 (24)
TAC + MMF +- other(s) (except post-CY)	51 (17)
TAC + MTX +- other(s) (except MMF, post-CY)	126 (42)
TAC + other(s) (except MMF, MTX, post-CY)	23 (8)
TAC alone	3 (1)
CSA + MMF +- other(s) (except post-CY)	9 (3)
CSA + MTX +- other(s) (except MMF, post-CY)	2 (1)
Other(s)	2 (1)
Missing	4 (1)
ATG/Campath - no. (%)	
ATG alone	70 (23)
CAMPATH alone	5 (2)
No ATG or CAMPATH	219 (73)
Missing	7 (2)
Year of HCT - no. (%)	
2009	1 (0)
2012	3 (1)
2013	4 (1)
2014	9 (3)
2015	29 (10)
2016	40 (13)
2017	70 (23)
2018	84 (28)
2019	61 (20)
Follow-up - median (range)	48 (5-96)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

The mutational landscape in Myelodysplastic Syndrome arising from Aplastic Anemia and its impact on Allogeneic Stem Cell Transplantation Outcomes.

Q2. Key Words

Aplastic Anemia, MDS, mutational profiling, allogeneic stem cell transplantation

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Brian Ball, MD
Email address:	brball@coh.org
Institution name:	City of Hope
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Ryotaro Nakamura
Email address:	rnakamura@coh.org
Institution name:	City of Hope
Academic rank:	Director, Center for Stem Cell Transplantation

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

brball@coh.org

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Chronic Leukemia

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Among patients with myelodysplastic syndrome arising from prior aplastic anemia, who undergo allogeneic stem cell transplantation, what is the frequency and impact of myeloid molecular abnormalities on post-transplant outcomes?

Q16. RESEARCH HYPOTHESIS:

Somatic gene mutations detected in patients with MDS arising from aplastic anemia prior to allogeneic stem cell transplantation impact post-transplant outcomes.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary Objectives:
1) To determine the impact of IPSS, IPSS-R, and IPSS-M assessed prior to conditioning on overall survival among patients with post-AA MDS undergoing alloHCT
Secondary Objectives:
1) To determine the impact of IPSS, IPSS-R, and IPSS-M assessed prior to conditioning on Disease-free survival, relapse/progression, non-relapse mortality.
2). To determine the mutational landscape of mutations among patients with post-AA MDS undergoing alloHCT
3) To determine the mutational burden (allele fraction) of myeloid mutations among patients MDS arising from aplastic anemia
4) To determine correlation between mutations and disease phenotype

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Myelodysplastic syndrome (MDS) arising from an antecedent aplastic anemia (Post-AA MDS) represents a unique disease subset, developing as a consequence of immunologic dysfunction. Somatic gene mutations are recognized as important prognostic factors in myelodysplastic syndrome (MDS) and have been incorporated into the Molecular International Prognostic Scoring System (IPSS-M). However, limited data are available regarding the impact of these mutations in patients with post-AA MDS on outcomes after allogeneic hematopoietic cell transplantation (alloHCT). Performing next generation sequencing on DNA isolated from blood of patients with Post-AA MDS prior to alloHCT will inform the landscape of mutations, their prognostic impact, and whether the IPSS-M MDS risk stratification systems predict outcomes.

Q19. 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.

Acquired aplastic anemia is a bone marrow failure disorder arising from immune mediated destruction of hematopoietic stem and progenitor cells.1 Although allogeneic stem cell transplant is a curative frontline approach, immunosuppressive therapy is an effective treatment for older patients and those without an HLA-matched donor.2 Among those receiving immunosuppressive therapy, somatic mutations in myeloid genes, in particular ASXL1 and DNMT3A are common and have prognostic implications.3 These mutations are associated decreased responses to immunosuppressive therapy, decreased progression-free survival and overall survival.3 Further, the ASXL1 and DNMT3A mutated clones tend to expand in size over the course of treatment. Long-term follow-up of patients receiving immunosuppressive therapy has shown transformation to a myeloid neoplasm occurring in ~13-20% of patients.4,5 As a result of their unique pathogenesis, post-AA MDS patients have distinct molecular features from de Novo MDS. Cytogenetic and molecular profiling of post-aplastic anemia (Post-AA) MDS patients demonstrated increased chromosome 7 aberrations, ASXL1 and RUNX1 mutations, and higher R-IPSS scores when compared to de-novo MDS patients.4 In a matched pair analysis of post-AA MDS and de novo MDS patents undergoing alloHCT, the post-AA cohort had more patients with poor-risk cytogenetics. In this study, there was no difference in relapse risk, non-relapse mortality, relapse free survival, or overall survival between post-AA MDS and de Novo MDS cohorts.6 However, this analysis did not assess the impact of somatic mutations on post-AA MDS outcomes. The recently developed Molecular International Prognostic Scoring System (IPSS-M) is the first MDS risk stratification system to incorporate recurrent somatic gene mutations.7 While this has changed the prognostication of MDS in the non-transplant setting, limited data are available regarding the impact of somatic mutations or this molecularly informed prognostic model in patients with MDS undergoing alloHCT. Even less is known about the impact of somatic mutations among patients with post-AA MDS undergoing alloHCT.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Enrolled in the Center for International Blood and Marrow Transplant Research (CIBMTR) Repository
Patients developing myelodysplastic syndrome from an antecedent aplastic anemia, who underwent allogeneic stem cell transplant during 2001 – 2022 will be included.
Pre-conditioning peripheral blood sample available.
Patients with AML, CMML, or other types of MDS are excluded.

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient related variables (age, Sex, race, Karnofsky performance status, Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI)
Disease-related factors (Hgb, platelet count, bone marrow blasts, IPSS-R score, IPSS score, Time from diagnosis to HCT)
Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI)
Transplant-related factors (conditioning regimens, Graft type, donor type, GVHD prophylaxis, in-vivo T-cell depletion, ex-vivo T-cell depletion, Year of transplant

Q23. **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 description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

Not applicable

Q24. 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 of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

1) Mutation analysis will be performed centrally at City of Hope on DNA isolated from whole blood aliquots collected and stored according to the protocol of the CIBMTR research sample repository. Our method for mutation analysis has previously been described by Mei M et al (Reference below). Next-generation sequencing (NGS) libraries will be prepared from genomic DNA (40 ng) using the SureSelect target enrichment system (Agilent Technologies Inc.) after transposase-based fragmentation and adapter ligation. The adapter-ligated library will be amplified by polymerase chain reaction, and quality control will be performed for sizing and concentration. Target regions will be captured using a customized SureSelect library (Agilent Technologies) for all coding exons plus 10 flanking bases of 523 genes. After hybridization of 750 ng of adapter-ligated library with biotin-labeled probes that are specific to target regions, the dual-index tag will be added during post-capture polymerase chain reaction amplification. The amplified captured libraries are quality-controlled using a high sensitivity DNA Bioanalyzer kit (Agilent Technologies Inc.) then pooled and sequenced using HiSeq 150 bp paired-end sequencing. Alignment of sequence reads to the human genome (GRCh37/hg19), variant calling and annotation will be performed independently using two software applications – CLC Biomedical Workbench (CLC Bio, Aarhus, Denmark) and NextGENe (SoftGenetics, State Collage, PA, USA). Annotated variants are processed using previously published criteria.(24, 25) Synonymous variants, variants located >2 bp outside protein-coding regions, polymorphisms present in >1% in population databases including ExAC, gnomAD, Exome Variant Server and the 1000 Genomes Project, and variants with <30x coverage will be filtered. The remaining variants will be evaluated using tumor-specific databases (COSMIC, cBioPortal), information retrieved from literature, sequence conservation, and in silico prediction algorithms, including SIFT, Polyphen-2, and FATHMM, for clinical significance.
2) These assays will be performed centrally at COH by the molecular pathology department.

Q25. 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, i.e., neither database contains all the data required to answer the study question.

Not applicable

Q26. REFERENCES:

1. Young NS. Aplastic Anemia. New England Journal of Medicine 2018;379:1643-56.
2. Townsley DM, Scheinberg P, Winkler T, et al. Eltrombopag Added to Standard Immunosuppression for Aplastic Anemia. New England Journal of Medicine 2017;376:1540-50.
3. Yoshizato T, Dumitriu B, Hosokawa K, et al. Somatic Mutations and Clonal Hematopoiesis in Aplastic Anemia. New England Journal of Medicine 2015;373:35-47.
4. Gurnari C, Pagliuca S, Prata PH, et al. Clinical and Molecular Determinants of Clonal Evolution in Aplastic Anemia and Paroxysmal Nocturnal Hemoglobinuria. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2022:Jco2200710.
5. Sun L, Babushok DV. Secondary myelodysplastic syndrome and leukemia in acquired aplastic anemia and paroxysmal nocturnal hemoglobinuria. Blood 2020;136:36-49.
6. Kim SY, Le Rademacher J, Antin JH, et al. Myelodysplastic syndrome evolving from aplastic anemia treated with immunosuppressive therapy: efficacy of hematopoietic stem cell transplantation. Haematologica 2014;99:1868-75.
7. Bernard E, Tuechler H, Greenberg Peter L, et al. Molecular International Prognostic Scoring System for Myelodysplastic Syndromes. NEJM Evidence 2022;1:EVIDoa2200008.
8. Mei M, Pillai R, Kim S, et al. 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 2022.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Characteristics of MDS cases arising from Aplastic Anemia reported to CIBMTR between the period 2001 to 2019.

Characteristic	TED	CRF	Total
No. of patients	146	126	272
No. of centers	89	70	119
Samples available - no. (%)			
No Sample	78 (53)	45 (36)	123 (45)
Recipient and Donor	45 (31)	58 (46)	103 (38)
Recipient Only	14 (10)	18 (14)	32 (12)
Donor Only	9 (6)	5 (4)	14 (5)
Subdisease - no. (%)			
MDS, NOS	62 (42)	41 (33)	103 (38)
RA Refractory anemia	12 (8)	12 (10)	24 (9)
CMMoL Chronic myelomonocytic leukemia	7 (5)	5 (4)	12 (4)
RARS Acquired idiopathic sideroblastic anemia	2 (1)	7 (6)	9 (3)
RAEB-1	21 (14)	16 (13)	37 (14)
RAEB-2	11 (8)	9 (7)	20 (7)
RCMD	26 (18)	29 (23)	55 (20)
RCMD / RS	0 (0)	1 (1)	1 (0)
5q-syndrome	1 (1)	2 (2)	3 (1)
Other MDS, spec (02CORE)	0 (0)	2 (2)	2 (1)
68	3 (2)	1 (1)	4 (1)
Other MFS/MPS, specify (02CORE)	1 (1)	1 (1)	2 (1)
Age - median (min-max)	45 (3-74)	51 (10-75)	47 (3-75)
Age - no. (%)			
<18	6 (4)	1 (1)	7 (3)
18-29	31 (21)	29 (23)	60 (22)
30-39	23 (16)	13 (10)	36 (13)
40-49	31 (21)	17 (13)	48 (18)
50-59	26 (18)	21 (17)	47 (17)
60-69	25 (17)	35 (28)	60 (22)
>= 70	4 (3)	10 (8)	14 (5)
Sex - no. (%)			
Male	82 (56)	72 (57)	154 (57)
Female	64 (44)	54 (43)	118 (43)
Region - no. (%)			
US	102 (70)	107 (85)	209 (77)
Canada	8 (5)	0 (0)	8 (3)

Characteristic	TED	CRF	Total
Europe	4 (3)	3 (2)	7 (3)
Asia	8 (5)	8 (6)	16 (6)
Australia/New Zealand	10 (7)	2 (2)	12 (4)
Mideast/Africa	4 (3)	1 (1)	5 (2)
Central/South America	10 (7)	5 (4)	15 (6)
Race - no. (%)			
White	98 (67)	95 (75)	193 (71)
Black or African American	9 (6)	10 (8)	19 (7)
Asian	11 (8)	13 (10)	24 (9)
Native Hawaiian or other Pacific Islander	0 (0)	1 (1)	1 (0)
American Indian or Alaska Native	0 (0)	1 (1)	1 (0)
More than one race	0 (0)	2 (2)	2 (1)
Missing	28 (19)	4 (3)	32 (12)
Karnofsky score - no. (%)			
90-100	84 (58)	73 (58)	157 (58)
< 90	60 (41)	52 (41)	112 (41)
Missing	2 (1)	1 (1)	3 (1)
Time from diagnosis to HCT - median (min-max)	6 (1-358)	5 (0-142)	6 (0-358)
Graft source - no. (%)			
Bone marrow	31 (21)	27 (21)	58 (21)
Peripheral blood	108 (74)	87 (69)	195 (72)
Cord blood	7 (5)	12 (10)	19 (7)
Conditioning regimen intensity (F2400 pre-TED data) - no. (%)			
MAC	71 (49)	50 (40)	121 (44)
RIC	32 (22)	51 (40)	83 (31)
NMA	35 (24)	18 (14)	53 (19)
TBD	6 (4)	3 (2)	9 (3)
Missing	2 (1)	4 (3)	6 (2)
Conditioning regimen - no. (%)			
TBI/Cy	3 (2)	8 (6)	11 (4)
TBI/Cy/Flu	22 (15)	13 (10)	35 (13)
TBI/Cy/Flu/TT	2 (1)	0 (0)	2 (1)
TBI/Mel	5 (3)	5 (4)	10 (4)
TBI/Flu	11 (8)	18 (14)	29 (11)
TBI/other(s)	0 (0)	1 (1)	1 (0)
Bu/Cy/Mel	1 (1)	0 (0)	1 (0)
Bu/Cy	29 (20)	13 (10)	42 (15)
Bu/Mel	5 (3)	2 (2)	7 (3)

Characteristic	TED	CRF	Total
Flu/Bu/TT	0 (0)	2 (2)	2 (1)
Flu/Bu	35 (24)	39 (31)	74 (27)
Flu/Mel/TT	2 (1)	2 (2)	4 (1)
Flu/Mel	11 (8)	14 (11)	25 (9)
Cy/Flu	11 (8)	5 (4)	16 (6)
Cy alone	0 (0)	1 (1)	1 (0)
Mel alone	1 (1)	0 (0)	1 (0)
Mel/other(s)	2 (1)	0 (0)	2 (1)
Treosulfan	3 (2)	2 (2)	5 (2)
TLI	1 (1)	1 (1)	2 (1)
Other(s)	1 (1)	0 (0)	1 (0)
None	1 (1)	0 (0)	1 (0)
computed GVHD - no. (%)			
TDEPLETION +- other	0 (0)	1 (1)	1 (0)
CD34 select alone	4 (3)	3 (2)	7 (3)
CD34 select +- other	7 (5)	4 (3)	11 (4)
Cyclophosphamide alone	0 (0)	1 (1)	1 (0)
Cyclophosphamide +- others	33 (23)	17 (13)	50 (18)
FK506 + MMF +- others	14 (10)	16 (13)	30 (11)
FK506 + MTX +- others(not MMF)	37 (25)	48 (38)	85 (31)
FK506 +- others(not MMF,MTX)	6 (4)	7 (6)	13 (5)
FK506 alone	5 (3)	5 (4)	10 (4)
CSA + MMF +- others(not FK506)	5 (3)	9 (7)	14 (5)
CSA + MTX +- others(not MMF,FK506)	33 (23)	11 (9)	44 (16)
CSA alone	0 (0)	2 (2)	2 (1)
Other GVHD Prophylaxis	1 (1)	2 (2)	3 (1)
Missing	1 (1)	0 (0)	1 (0)
Year of HCT - no. (%)			
2002	0 (0)	1 (1)	1 (0)
2005	0 (0)	1 (1)	1 (0)
2006	0 (0)	1 (1)	1 (0)
2007	0 (0)	2 (2)	2 (1)
2008	1 (1)	11 (9)	12 (4)
2009	0 (0)	14 (11)	14 (5)
2010	0 (0)	4 (3)	4 (1)
2011	0 (0)	4 (3)	4 (1)
2012	0 (0)	5 (4)	5 (2)
2013	1 (1)	11 (9)	12 (4)

Characteristic	TED	CRF	Total
2014	24 (16)	17 (13)	41 (15)
2015	14 (10)	14 (11)	28 (10)
2016	17 (12)	15 (12)	32 (12)
2017	22 (15)	9 (7)	31 (11)
2018	17 (12)	6 (5)	23 (8)
2019	17 (12)	8 (6)	25 (9)
2020	33 (23)	3 (2)	36 (13)
Follow-up - median (range)	34 (3-97)	67 (3-174)	48 (3-174)