



## A G E N D A

### CIBMTR WORKING COMMITTEE FOR DONOR HEALTH AND SAFETY

Salt Lake City, Utah

Monday, April 25, 2022, 12:15 pm – 1:45 pm

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#### 1. Introduction

- a. 2021 TCT Combined WC session minutes ([Attachment 1](#))

#### 2. Accrual summary ([Attachment 2](#))

#### 3. Presentations, published or submitted papers

- a. **DS05-02g** Seftel MD, Chitphakdithai P, Miller JP, Kobusingye H, Logan BR, Linenberger M, Artz AS, Haight AE, Jacobsohn DA, Litzow MR, Magalhaes-Silverman M, Selby GB, Vusirikala M, Horowitz MM, Switzer GE, Confer DL, Shaw BE, Pulsipher MA. Serious adverse events in related donors: A report from the Related Donor Safe Study. *Transplantation and Cellular Therapy*. 2021 Apr 1; 27(4):352.e1-352.e5. doi:10.1016/j.jtct.2021.01.009. Epub 2021 Jan 15. PMC8036235. Published.
- b. **DS18-02** Panch SR, Logan B, Sees JA, Bo-Subait S, Savani B, Shah NN, Hsu JW, Switzer G, Lazarus HM, Anderlini P, Hematti P, Confer D, Pulsipher MA, Shaw BE, Stroncek DF. Shorter interdonation interval contributes to lower cell counts in subsequent stem cell donations. *Transplantation and Cellular Therapy*. 2021 Jun 1; 27(6):503.e1-503.e8. doi:10.1016/j.jtct.2021.03.008. Epub 2021 Mar 9. PMC8217152. Published.
- c. **DS19-01** Hsu JW, Farhadfar N, Murthy H, Logan BR, Bo-Subait S, Frey N, Goldstein SC, Horowitz MM, Lazarus H, Schwanke JD, Shah NN, Spellman SR, Switzer GE, Devine SM, Shaw BE, Wingard JR. The effect of donor graft cryopreservation on allogeneic hematopoietic cell transplantation outcomes: A Center for International Blood and Marrow Transplant Research Analysis. Implications

**Not for publication or presentation**

during the COVID-19 pandemic. ***Transplantation and Cellular Therapy. 2021 Jun 1; 27(6):507-516. doi:10.1016/j.jtct.2021.03.015. Epub 2021 Mar 22. PMC8217124. Published.***

- d. **DS13-02** Murthy GSG, Logan BR, Bo-Subait S, Beitinjaneh A, Devine S, Farhadfar N, Gowda L, Hashmi S, Lazarus H, Nathan S, Sharma A, Yared JA, Stefanski HE, Pulsipher MA, Hsu JW, Switzer GE, Panch SR, Shaw BE. Major ABO Incompatibility Significantly Influences the Survival and Outcomes after Allogeneic Hematopoietic Cell Transplantation in Leukemia - CIBMTR Analysis. **Oral Presentation, ASH 2021.**
  - e. **DS19-02** Farhadfar N, Bo-Subait S, Ahn KW, Logan BR, Stefanski HE, Hsu JW, Panch SR, Confer DL, Anasetti C, Pulsipher MA, Shaw BE, Wingard JR, Switzer GE. The Impact of Pre-Apheresis Health Related Quality of Life on Peripheral Blood Progenitor Cell Yield and Donor's Health and Outcome: Secondary Analysis of Rdsafe and BMT CTN 0201. **Oral presentation, ASH 2021. Submitted.**
4. **Studies in progress** ([Attachment 3](#))
- a. **DS13-02** A retrospective analysis to understand the potential mechanisms underlying the clinical impact of ABO incompatibility on allogeneic transplant outcomes (Guru Murthy; Bronwen Shaw) **Submitted. Update presentation to be given.**
  - b. **DS19-02** The impact of pre-apheresis health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome (Nosha Farhadfar; John Wingard; Galen Switzer) **Manuscript preparation. Update presentation to be given.**
  - c. **DS20-01** Acute toxicities of bone marrow donation in donors with sickle cell trait (Nosha Farhadfar; John Wingard) **Data file preparation**
5. **Future/proposed studies**  
***Proposals dropped due to feasibility or overlap with existing studies***
- a. **PROP 2103-01** Impact of SARS-COV-2 (COVID 19) pandemic on cellular therapy practices and outcomes (Mariam T. Nawas; Roni Tamari; Miguel-Angel Perales)
  - b. **PROP 2110-154** Impact of Cryopreservation on Immune Reconstitution in Allogeneic Hematopoietic Cell Transplantation (Hemant Murthy; Nosha Farhadfar)
  - c. **PROP 2110-233** Impact of the COVID-19 pandemic on unrelated donor availability in different racial and ethnic groups (Nosha Farhadfar; John R. Wingard)
6. **Other business**
- a. **Review/guideline proposals**
    - i. **Review Proposal 2022-02** ([Attachment 4](#)) Reducing the Risk of Transmission of Donor Derived Malignancy: Consensus Guidelines for Donor Genetic Screening Prior to Allogeneic Stem Cell Transplant and Detection of Leukemia Origin in Relapse After Transplant (Lacey Scott Williams; Catherine Lai)
    - ii. **Review Proposal 2022-03** ([Attachment 5](#)) The safety of G-CSF (filgrastim) for mobilization in donors, both healthy donors or donors for autologous transplant. (Joseph Maakaron; Mark Juckett)

***Not for publication or presentation***

**b. Potential collaborations**

- i. **Review Proposal 2022-01** ([Attachment 6](#)) What is the relationship between donor red blood cell characteristics and collection efficiency in peripheral blood stem cell donors?(Katie Cormier; Jenna Smith; Wolfgang Rennert; Catherine Broome)
- ii. Significance of Red Blood Cell Alloimmunization in Hematopoietic Progenitor Cell Transplant Recipients (Monica Pagano)

**c. Additional business items** As needed and as time allows for discussion



## MINUTES

### CIBMTR WORKING COMMITTEE SESSION

Thursday, February 11, 2021, 1:00 - 4:00 pm

Co-Chair: Bronwen Shaw, MD, PhD; CIBMTR Statistical Center, Milwaukee, WI; E-mail: beshaw@mcw.edu

Co-Chair: John Wingard, MD; University of Florida, Gainesville, FL; E-mail: wingajr@ufl.edu

#### INTRODUCTION:

Dr. Wingard opened the virtual meeting at 1:00 pm by welcoming the working committee members and the presenters. He discussed the proposal selection and voting process. Though the pandemic amended the process for proposal selection, 368 working committee proposals were submitted and evaluated altogether by CIBMTR Working Committee Chairs and Scientific Directors. About 61% were screened out, 30% had less-relative scientific merit, and 3% were combined with overlapping proposals with relevant nature. 21 proposals (about 6%), were considered for advancing of further pro-development. The proposals were pre-recorded 5-minutes presentations of the 15 semi-finalists, which were presented by the principal investigators. Each presentation was followed by a 5-minute question and answer session, in which audience was invited to submit questions via live chat. For those not able to attend the live session, a link was posted with the session recording and voting was closed on Monday, February 15, 2021. Audience was also instructed on where to locate the scoring and voting links for the presentations. It was mentioned that over 1,000 Working Committee members voted on the first screening of these proposals. Dr. Shaw led the second part of the meeting starting with presentation #9.

#### GENERAL REMINDERS:

The following reminders were mentioned and posted via the chat option:

- a. Thank you for participating in the CIBMTR Working Committee Session! Please cast your score here: [https://mcwisc.co1.qualtrics.com/jfe/form/SV\\_7QwO1ZvzfpZV1NY](https://mcwisc.co1.qualtrics.com/jfe/form/SV_7QwO1ZvzfpZV1NY) to vote on the proposals that were presented during the session.
- b. Several presenters provided their email addresses for any future communication.

#### PRESENTATIONS:

1. **Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.** This proposal was presented by Dr. Ana Alarcon Tomas. The primary objective of this proposal is to describe the incidence rate, risk factors, characteristics, and outcomes of subsequent neoplasms in patients receiving post-transplant cyclophosphamide (PTCy) and compare it with calcineurin inhibitors-based graft-versus-host disease prophylaxis and the general population. The CIBMTR identified 64,935 patients  $\geq 18$  years of age who underwent a first allogeneic for a malignant disease between 2008-2017. 5,771 (9%) of these patients developed a subsequent neoplasm. Currently, there are no published studies on the incidence of subsequent neoplasms in patients who received post-transplant cyclophosphamide. The following questions were answered during the Q&A:
  - a. How are we going to prove that these secondary neoplasms are related to post-transplant cyclophosphamide or cyclophosphamide in conditioning and not due to "by chance" itself- as in general population? This is a case-controlled study. For example, for each patient received with a post-transplant cyclophosphamide will be matched with at least three patients who didn't receive post-transplant cyclophosphamide. Characteristics including primary disease, HLA complexity, survival, follow up time etc. would be used for matching and reviewing survival will also allow us to see that this is because of PTCy and not by coincidence.

- b. What is the median follow up time from transplant and subsequent malignancy in post-transplant cyclophosphamide group? I assume it is much shorter than other cohort? Information is not available for each median follow up time cohort. What is available is the median follow up for all patients and some numbers related to the type of diseases for each group. Dr. Rachel Phelan included in the chat that the median follow-up for the PT-Cy group is 38.2 months, and for the proposed control population is 60.3 months.
- c. How is this in comparison with matched unrelated donor and cord transplants? Cord transplants will be excluded from the analysis because we don't think we can match those patients.
- d. Do we have adequate follow up to answer this important question? We have follow-up for mantle hematological diseases but less time for solid tumors. However, when we saw the numbers that we have (around 5,000 - 5,700) subsequent neoplasms, the majority of cases occurred after the 1st - 5th year of post-transplant and have a 5-year median follow up. We think we have enough numbers to address this question now and we should not wait because it hasn't been published before. This is a noble study and if we wait for a longer median follow up, we might lose that opportunity to have it published first.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix A](#).

2. **Outcomes of chimeric antigen receptor-T cell therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome).** This proposal was presented by Dr. Farrukh Awan. The objective of this proposal is to assess outcomes in adult patients with chronic lymphocytic leukemia undergoing transformation to diffuse large B-cell lymphoma (Richter's Syndrome) and undergoing CAR-T therapy. The CIBMTR identified 36 patients underwent CAR-T for Richter's Syndrome from 2015-2019. The following questions were answered during the Q&A:

- a. I know that in the Ohio State paper have many patients that used concurrent Bruton Tyrosine Kinase (BTK) inhibitors. Will you be able to collect data on concurrent BTK inhibitors for these patients? Yes, this information is available through the CIBMTR dataset.
- b. Are you looking at diffuse large B-cell lymphoma derived Richter's Syndrome or chronic lymphocytic leukemia derived Richter's Syndrome? Yes, but it is difficult to determine a clonality between related and unrelated Richter's syndrome. Any studies that show similarities versus dissimilarities in the clone would be very helpful but unfortunately, previous studies have shown that this has been consistently difficult.
- c. You mentioned the opportunity of comparing to other treatment groups. Can you talk about that a little more? We can compare to patients with de novo diffuse large B-cell lymphoma. There are multiple approved and ongoing studies within CIBMTR of diffuse large B-cell lymphoma patients, who do undergo CAR-T therapy and look at toxicity outcomes and infectious outcomes, for example. There are efforts in place to look at outcomes of transplantation for patients with Richter's Syndrome, which can improve the impact of this project and be a competitor to those other ongoing studies.
- d. How many pts do we have? 36 patients
- e. How do you plan to deal with the very low patient numbers (n=36) to make meaningful conclusion? I agree that it is a small number, but it is substantial. Despite the small numbers, if the right competitors are used, such as those mentioned previously, this study can still provide an impactful dataset.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix B](#).

3. **Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies.** This proposal was presented by Dr. Andrea Bauchtat. The objectives of this proposal is to determine the impact of development of grade I-II acute graft versus host disease on relapse and leukemia-free survival, to assess the impact of development of grade III-IV acute graft versus host disease on relapse and leukemia-free survival, and to determine whether the impact of graft versus host disease on

relapse and leukemia-free survival is influenced by disease risk prior to HCT. The CIBMTR identified 1,345 children <18 years who received first HCT for acute lymphoblastic leukemia and acute myeloid leukemia receiving first allogeneic transplantation between 2008 - 2017. The following questions were answered during the Q&A:

- a. What is the sample size of each sub-group: disease-risk index (DRI)-low, -intermediate, -high? Exact sample size not available but the high-risk group was less in comparison to others.
- b. How will you factor in occurrence of chronic graft versus host disease in your analysis? Our main focus is on acute graft versus host disease because it will have more impact on our clinical practice. However, we will collect the data for the interactions of chronic graft versus host disease alone, and if the patient had a history of acute.
- c. What is the biological basis for focusing this study on a pediatric population? The interest from our perspective is looking at the pediatric population compared to the adults. The literature on pediatric is severely lacking in comparison to adults and we need to expand on that for the patient population that we care for.
- d. Are you going to separate acute myeloid leukemia and acute lymphoblastic leukemia numbers at DRI level? Yes, they are already divided from DRI protocol. Our acute lymphoblastic leukemia patients are about 1,300 and the acute myeloid leukemia are about 1,200.
- e. Is the analysis going to be time dependent or landmark? Landmark
- f. Do you have the date of this max acute graft versus host disease grade to take into account the time to event aspect of the effect? No
- g. Do you have a plan to include/account for the various GVHD prophylaxis regimen "strengths?" We are taking into consideration of what GVHD prophylaxis regimen the patient uses. This data, which is already categorized, will show us the differences between trends.
- h. What is the clinical benefit besides prognostic? This will help define a better foundation of which patients will benefit more from a little bit of graft versus host disease. If we can come up with a patient category that we see is beneficial to have exposure to a little bit of graft versus host disease, it can go forward with clinical trials and GVHD prophylaxis adjustment or manipulation to improve their Leukemia-free survival.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix C](#).

4. **Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant.** This proposal was presented by Dr. Christine Camacho-Bydume. The primary objective of this proposal is to determine if HLA evolutionary divergence (HED) of HLA class I alleles of HLA-A, -B, -C and HLA class II alleles of HLA-DR is associated with overall survival and relapse. The objective is to also evaluate association of HED with acute and chronic GVHD and treatment-related mortality (TRM). The CIBMTR identified pediatric and adult patients with acute myeloid leukemia, myelodysplastic syndromes, acute lymphoblastic leukemia, chronic myeloid leukemia, or lymphoma (non-Hodgkin or Hodgkin's lymphoma), who have received initial allogeneic 8/8 HLA-matched (HLA-A, -B, -C, -DR) transplant between 2008 - 2018. The following questions were answered during the Q&A:
  - a. Could HLA diversity simply be a surrogate for race? How would you account for race in the study? Great question given there are particular HLA alleles that are more common in certain ethnic groups. We do think that evaluation of HED lows and highs within these different ethnicities can help to tease this out more, with potential to adjust for race more in this analysis. We think some of these differences in peptide binding grooves can help us to understand better the different peptides and how antigens are presented to T-cells.
  - b. Extrapolating HLA data from solid tumors and checkpoint inhibitors and their antigen presentation is slightly challenging in context of allo donor T-cell interaction with antigen presented for bone marrow origin cancers. Yes, have to consider there could be some differences. Was a small previous study that

looked at this question, saw some signals there, larger population and different types of cancers, may be able to explore that more.

- c. Leukemia (both lymphoblastic and myeloid) have low mutational burden as compared to melanoma and lung. Will the HED algorithm still work? Yes, we do expect to see differences in mutational burdens, and we do plan to look at the cohort at large to look at the disease subgroups to see more or less of this phenomenon in these groups. Do you have preliminary data in leukemias? There was a small study in Germany that looked at AML, to my knowledge only one that looked at leukemias. Mutational burden did see some differences, so we do expect it and also, besides the overall cohort, also plan to look at disease subgroups.
- d. Given HED implications for infection surveillance, are you going to look at infectious sequelae differences? No, at the moment we have initially requested information in terms of tumor control, relapse, overall survival, graft versus host disease, and TRM. Not sure of availability of the other information but would be interesting to look at if available.
- e. Would you please discuss the confounding effects of HLA mismatching for HLA-DRB3, 4, 5, DQ, and DP? Not known off the top of my head the percentages of mismatching differences in this cohort. For DR at least they will be matched, 8/8 matched, in terms of DP, don't have that info but if available it is something that can be looked at.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix D](#).

5. **Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation.** This proposal was presented by Dr. Evan C. Chen. The primary objective of this proposal is to identify differences in survival outcomes between mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients and to assess the prognostic significance of disease features in mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients. The CIBMTR identified patients  $\geq 18$  years old with a diagnosis of normal karyotype acute myeloid leukemia, receiving first allogeneic HCT during CR1 in 2013 - 2019. The following questions were answered during the Q&A:
  - a. Is there any concern that patients with IDH1/2 mutated acute myeloid leukemia would have received more intensive conditioning / therapy than IDH1/2 wild-type? Yes, and it's important to look at how conditioning intensity can be an important covariant, which is a variable captured in CIBMTR.
  - b. Will you have registry information on the type and duration of use of IDH inhibitors before/after HCT? It's currently not available with CIBMTR.
  - c. IDH mutations are usually seen in older subjects. How will you a priori adjust for this known association? Age will certainly be a covariant in our multi-variant analysis.
  - d. How reliable are the wild-type patients as some may just not be tested for IDH mutations? It is double checked. There is a datapoint in the forms that indicate whether or not testing has been done, versus if testing was done and IDH was found to be absent.
  - e. Do you have information what the numbers will be like when you divide your patient groups with concomitant mutations such FLT3 or p53 that may have an impact on outcomes? Yes, the numbers are about 20-40 for co-mutated for ITD and NPM1 patients. p53 not provided.
  - f. Is there data in CIBMTR forms that collect use of IDH inhibitors pre transplant? Will you be able to study their impact on the transplant? I'm not aware of this data point being available in the forms but it is something that we should follow up on.
  - g. How do you analyze its (or ITS?) with multiple mutations? With regards to double-mutated patients, IDH1, and IDH2 patients, which are generally rarely reported, we would look at the CIBMTR forms to ensure accurate data entry. In regard to analyzing IDH with other co-mutations, we would include co-mutations as a co-variant in a multi-variant analysis, should the sample size permit.

- h. What about other mutations in Wild type IDH? We focus on NPM1 and FLT3-ITD because they are prevalent in the cytogenetic risk population. We will look at the other mutations to see if they have any relevance at all.
- i. Do the data forms reliably collect information on use of IDH inhibitors pretransplant? Data point is not available.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix E](#).

6. **Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant.** This proposal was presented by Dr. Christin B. DeStefano. The primary objective of this proposal is to describe patient and disease related characteristics of adolescent and young adults (AYAs) with multiple myeloma treated with early high dose melphalan and AutoHCT and to characterize response to AutoHCT, survival outcomes, SPMs, and infections of AYA multiple myeloma patients and AutoHCT. The CIBMTR identified 1,142 AYA multiple myeloma patients who underwent autologous hematopoietic cell transplant) between 2008 -2018. The following questions were answered during the Q&A:
- a. What will differentiate this study from MM18-03 “To compare the outcomes in young patients with multiple myeloma at diagnosis undergoing upfront autologous hematopoietic stem cell transplant with older patients in the US: progression-free and overall survival”? There appears to be substantial population overlap. The Scientific Director clarified via the chat function that MM18-03 included the years 2013-2017 and excluded patients less than 40 years from the outcome analysis owing to small numbers.
  - b. How do you plan to control for differences between your AYA group and older control group which would be attributable to age? In total, there are about 1,700 TED and CRF cases. We can adjust the critical variables of these cases, such as stage, treatment rendered, and cytogenetics, for example, to control for differences.
  - c. Will results be stratified according to different induction regimens? Yes, we will adjust those critical variables amongst the CRF cases where this information is available.
  - d. A cohort going back to 1995 seems too outdated. What was the N for a more recent group (since 2010)? There were 1,142 AYA cases between 2008-2018.
  - e. This is a long cohort 1995-2019 with lots of changes in induction treatment, novel agents and time to bone marrow transplant. How will this be controlled for? We are going to study induction regimens, post-transplant treatment, use of tandem transplants in our analysis.
  - f. Will you be also studying the effect of post-transplant maintenance therapy? Also, any effect of extramedullary plasmacytomas in this AYA group? We will for cases where this information is available. Extramedullary plasmacytomas are a good focus, as AYA patients may have a more aggressive presentation of myeloma.
  - g. Are plasma cell leukemias included in this analysis? No

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix F](#).

7. **Impact of measurable residual disease status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT.** This proposal was presented by Dr. Firas El Chaer. The objectives of this proposal is to determine if acute myeloid leukemia measurable residual disease (MRD) analysis as currently performed has prognostic value when measured prior to AlloHCT, to explore factors that may modify the risk associated with detectable acute myeloid leukemia MRD pre-AlloHCT, and identification, using MRD combined with other clinical factors, of patients most at risk of post-AlloHCT relapse. The CIBMTR identified 753 MRD positive and 1986 MRD negative adult patients receiving first AlloHCT for de-novo AML in CR1 in 2007-2018. The following questions were answered during the Q&A:



- a. What kind of MRD data is collected? Depending on the individual participating centers, the methodology uses molecular or immunotherapy? MRD
- b. What is the rate of missing MRD status and are those patients different from those with MRD data available? The answer is not included in this study.
- c. Are you going to also study the effect of post-transplant maintenance in AML FLT3, IHD mutations on relapse and overall survival? One of the aims of this study is to have future studies look at post-transplant maintenance from this study.
- d. What do you mean by most "recent" pre-conditioning MRD assessment? Would testing need to be completed within a specific time frame before conditioning? All patients who will be receiving a stem cell transplant are required to get a bone marrow biopsy and peripheral blood aspiration before transplantation. Within a month before the transplant, we would look at data point.
- e. What is your working definition of MRD? A combination of molecular testing as well as immunotherapy by NFC.
- f. Are all mutations equivalent when thinking about MRD? Absolutely not.
- g. How sure are you that the MRD patients are really MRD negative? We can never be absolutely sure.
- h. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when? The way that CIBMTR reports the acute myeloid leukemia data is by reporting their cytogenetics and mutation analysis so we can calculate the data for this population. The point of this study is to look at the commercial availability of these tests and we can rely on it or if we should standardize one testing at all centers.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix G](#).

8. **Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.**

This proposal was presented by Dr. Noshah Farhadfar. The objectives of this proposal are to determine whether clinical manifestations and severity of chronic GVHD differ based on racial/ethnic and socioeconomic status (SES) differences, to determine whether treatment patterns of chronic GVHD differ based on racial/ethnic and SES differences, and to evaluate whether chronic GVHD treatment outcomes differ based on racial/ethnic and SES differences. The CIBMTR identified 17,665 patients, age 18 years or older, who have received first allogeneic transplant for hematologic malignancy (acute myeloid leukemia, acute lymphoblastic leukemia, myelodysplastic syndrome) between 2008 - 2019. The following questions were answered during the Q&A:

  - a. I like the idea for looking at outcomes based on race/ethnicity/SES but not sure if incidence should be a primary outcome because it will be dependent on donor type which is very different amongst the groups. The primary outcome of this study is to look at the outcome of patients who develop chronic graft versus host disease. We need to look at the whole cohort, report the incidence, and then focus on chronic graft versus host disease cohort as the primary endpoint of this study.
  - b. How will you correct for the impact of race on HLA mismatch between recipients and donors due to the lower chance of identifying a fully matched donor in non-Hispanic white patients? For the same reason, should cord blood recipients be excluded? We are going to include both the donor type, graft source and degree of HLA matching as covariables in a multi-variable analysis. Cord blood recipients should not be excluded, as there was near 14% of Non-Hispanic black, 14% Hispanic, and 15% Asian who received cord transplant. Approximately 7-8% of cord transplants were received by Non-Hispanic whites. We do have the number to look into cords but if a statistician reviews and determines we don't have the power, then we can eliminate the cords.
  - c. Is it possible to access constitutional DNA to look at ancestry information markers in this population? This information is not available for the population. The analysis will focus on self-reported race/ethnicity.
  - d. All patients in your cohort from 2008 were not reported with NIH consensus criteria for chronic GVHD. Since you have large numbers, should you limit this to more recent time period? We do have all of the

information on graft versus host disease and whether it was limited or extensive. There is information on whether graft versus host disease is progressive, de-novo or interrupted. We have organ involvement and maximum grade of chronic graft versus host disease. NIH scoring is available for at least the past 4 years and maybe we can look at that group separately. Within the past 4 years, the population limited to NIH grading only in about 1,500 non-Hispanic white, 270 non-Hispanic black, and 200 Hispanic, who have developed chronic graft versus host disease.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix H](#).

9. **Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity.** This proposal was presented by Dr. Lohith Gowda. The objectives of this proposal are to identify density and types of early and late infections (bacterial, viral and fungal) in patients that went to transplant a) <6 months b) between 6- 12 months and c) > 12 months from diagnosis; to identify T cell lymphocyte absolute numbers at days 100 and 180 and CD4/CD8 ratio for the timeline cohorts examining individual donor types; to evaluate the impact of bacterial, viral or fungal infections by day 100 and day 180 on 1-year post-transplant outcomes (relapse, non-relapse mortality, disease free survival, acute and chronic graft versus host disease); and to evaluate quantitative immunoglobulin levels at D+ 100 and + 180 if available. The CIBMTR identified 6,877  $\geq$  18 years old patients who underwent first allogeneic transplants for AML in CR1, ALL in CR1 or MDS in the United States from 2012 to 2019. The following questions were answered during the Q&A:
- How many patients in the registry have the immune parameters you wish to assess? >2100
  - How will you account for the type of treatment used prior to transplant? For example, treatments such as hypomethylating agents may require months of treatment before transplant versus induction chemo that works more quickly. We do have some variables that are available, such as types of therapy, and we can analyze levels of intensity of therapy (low to high) and post-transplantation outcomes. The exact number of how many patients who have had different intensities of therapies is not available.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix I](#).

10. **Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement.** This proposal was presented by Dr. Hamza Hashmi. The primary objective of this proposal. The CIBMTR identified 55 adult patients (age  $\geq$  18) who received CD19 CAR T-cell therapy for B-cell NHL with secondary central nervous system (CNS) involvement. The following questions were answered during the Q&A:
- How will you differentiate between immune effector cell-associated neurotoxicity syndrome (ICANS) and CNS relapse? ICANS will be documented as a neurotoxicity and CNS relapse will be when the form is filled out.
  - Is this active CNS disease or previously treated CNS disease? The data received from CIBMTR looks at CNS disease at the time of diagnosis and the CNS disease that is present at the time of cellular therapy.
  - Do you have any registry information on concomitant CNS therapy (chemo/radiation) pre, peri and post transplantation? Answer was not available at this time.
  - How many patients are in your study? How will you define whether the patients have cleared their CNS involvement? There are currently 60 patients in the history of this data. Of the 60, 40 had this disease at the time of diagnosis and 20 had this disease at the time of cellular therapy. Whether the patients have cleared their CNS involvement, this information is not available at the time.
  - Since this is your primary endpoint, how will you account for the differences of frequency of CRS and ICANS across different products (e.g. high in Yescarta, lower in Kymriah, low in Breynzi)? If you look at the toxicity profile of CD19 therapy, they seem to be relatively similar.

- f. Could you please include other agents such as anakinra, siltuximab, and other agents? Dasatinib for this populations for ICANS? Also, was CNS disease under control at CAR-T therapy? As for Anakinra, siltuximab, and other agents, I'm not sure if CIBMTR is capturing this data. As for dasatinib, I'm not sure if this information is available as well. Per Dr. Pasquini of CIBMTR in the live chat, he commented "we capture treatment of ICANS, like siltuximab, dasatinib has been reported as other treatment."
- g. Will you have detail on the nature and extender features of secondary CNS involvement to associate with the toxicity and outcome? I only have the essential data with me but am hopeful that this comprehensive research will have further detail.
- h. Will all the patients included have active CNS disease at the time of CAR-T or, are treated CNS disease are also included? They are both included, and we are able to tell who has had active disease with a prior history at the time they got the CAR-T therapy.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix J](#).

**11. Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis.** This proposal was presented by Dr. Tania Jain. The primary objective of this proposal is to explore the impact of donor type on overall survival of patients undergoing HCT for myelofibrosis. The CIBMTR identified 1,640 patients  $\geq 18$  years old diagnosed with primary, post-ET or post-PV myelofibrosis and undergoing first HCT between 2013 and 2019. The following questions were answered during the Q&A:

- a. Are you also going to compare the effect of pretransplant Ruxo in haplo vs MUD/MRD? Also, are you going to look for graft failures as well in these patient populations? Yes, this will be included. We also do look at graft failures in these populations.
- b. Is there a difference in time from diagnosis to HCT across the groups? The median time from diagnosis to transplant for haploidentical patients was 38 months, while for HLA- identical sibling and URD 8/8 was 21 and 24 months, respectively.
- c. Are you including all conditioning regimens types: MAC, RIC and NMA? Yes, and they will be looked at for comparison in the univariable and may be taken to the multivariable analysis as well.
- d. For the graft failure or rejection analysis are you going to include spleen size? Ideally it should be included but the spleen size measurement has many variables and it may not be a clean assessment. We don't collect precise spleen size in our forms, but it can be analyzed as spleen size as splenomegaly, no splenomegaly or splenectomy.
- e. Can you comment on the bone marrow vs peripheral blood in the three groups? Peripheral blood is more common in the donor source (about 80%).

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix K](#).

**12. Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL.**

This proposal was presented by Dr. Arushi Khurana. The objective of this proposal is to enhance our understanding of sex- and race-based differences in utilization of CAR-T vs AutoHCT and outcomes after CAR-T. The CIBMTR identified 1,133 patients to compare sex and race/ethnicity rates for first cellular infusion (AutoHCT vs. CAR-T) for relapsed/refractory non-hodgkins lymphoma patients from 2017 – 2019 (aim 1a). The CIBMTR identified 619 non-hodgkins lymphoma patients who relapse after first AutoHCT to describe subsequent treatment patterns (e.g. CAR-T, second AutoHCT, AlloHCT, other treatment, no treatment) by sex and race/ethnicity (aim 1b). The CIBMTR identified 1,253 patients to identify sex-and race-based differences in response to CD19 CAR-T in aggressive lymphomas (aim 2). The following questions were answered during the Q&A:

- a. Is there gender and race-based difference in SEER data with or without treatment for diffuse large B-cell lymphoma even before CAR T? Yes, that data does exist.

- b. Can this be stratified by center/geography (private/public, large urban/rural)? Yes, it will be shown based on zip code (of patient and of recorded center), which will allow us to differentiate from urban/rural as well.
- c. We saw almost no neurotoxicity in women so would you be plotting CRS and ICANS based on gender and race? Yes, and we believe CIBMTR is the best resource for this because of the larger numbers
- d. How do you differentiate between larger trial centers vs less resourced centers? The information is reported based on the center type. Basing on academic or zip code, or city versus rural center, that will also be a way to differentiate the centers.
- e. Would disease response status prior to cellular therapy be taken into account for analysis? Yes, that is one of the co-variants that will be included.
- f. How reliable is the data you will get to study “access”, as there are many factors, depending on patient specific factors (education, resource, finances, mobility, support, performance, etc.), center specific (criteria), and also access depends on the hematologist/oncologist who sees these patients in the community? Access to a center is not one of the main issues in this study. It is more about why some of these minorities receiving other treatments when they should be receiving cellular therapy at the time of indication.
- g. Is there any way to take into account insurance issues? We do look at the insurance statuses as one of the co-variants.
- h. Would it be possible to look at differences in access based on commercial CAR T vs. clinical trials? The majority of the patients from the forms received are from commercial CAR T.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix L](#).

13. **Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation.** This proposal was presented by Dr. Richard J. Lin. The primary objective of this proposal is to compare CRFS among patients  $\geq 60$  years old undergoing myeloablative conditioned, allogeneic hematopoietic cell transplantation with following graft versus host disease prophylaxis in 2 matched-pair analysis and to compare other transplant outcomes in the above 2 matched-pair analysis. The CIBMTR identified 1,301 patients at  $\geq 60$  years old at the time of first allo-HCT between 2010 and 2019, with any myeloablative conditioning defined by CIBMTR, 8/8 matched related or unrelated donor only, graft versus host disease prophylaxis (ex-vivo TCD/CD34+ selection versus PTCy-based versus Tac/MTX). The following questions were answered during the Q&A:

- a. What do you mean by “robust?” Is it based on KPS, HCT-CI, or just the fact that someone got MA. regimen? We use the definition of a patient getting a myelo-conditioning as a way of saying that they are robust by their transplant centers.
- b. Are patients with In-vivo T cell depletion (Campath or ATG) excluded from this analysis? T cell depletion and CD34 selection does include ATG and does not include Campath.
- c. Why do you pool post-CY and ex vivoCD34+ selection? Can we still consider ex vivoCD34 selection to be a promising transplant modality in 2021? We wanted to compare a 2-match pair analysis and not a direct comparison between CD34 selection and post-CY. We do know which will be better for an older patient.
- d. Why exclude TBI? For older patients, we don’t consider TBI to be a conditioning regimen.
- e. How many patients with Tac/methotrexate prophylaxis had ATG? Answer was not available at the time of Q&A.
- f. Do we know GFR (creatinine) coming into allo in these groups? In this study, we didn’t include the GFR (creatinine) as a variable but we have some evidence in older patients that does play a major role. I can discuss with our statistician on whether we can include this as a variable.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix M](#).

14. **Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas.** This proposal was presented by Dr. Sayeef Mirza. The primary objectives of this proposal to evaluate cumulative incidence grades, duration and median time to onset of CRS and CRES/ICANS in patients > 65 years of age receiving CD-19 directed CAR-T therapy, describe post CAR-T clinical outcomes and resource utilization in elderly, and identify disease biology, comorbidities and other clinical predictive markers of toxicity, response, and survival in elderly patients. The CIBMTR identified 1,036 patients (<65y,n=612; 65-74y, n=348; >75y, n=76) with the diagnosis of any B-cell lymphoid malignancy (indolent or aggressive lymphoma) receiving CAR-T cell product (CD19 target). The following questions were answered during the Q&A:

- a. Would you please also look at Incidence of pancytopenia, hypogammaglobulinemia and HLH in elderly versus younger in 3 cohorts <60, 60-75 ,>75? I think it's very important to look at this as the data becomes available to us. We are primarily looking at different age groups. We have 81 patients over the age of 75 and five patients over the age of 85. Overall, there are 435 (40 %) of the group are over 65 years old.
- b. How does this defer from the data presented by Dr. Pasquini last year in older patients? This data will be more helpful in including both CAR-T products.
- c. In case of CAR T was used for post-alloHCT relapse, would the donor age of the CART source be analyzed? This is something that we should include in our analysis.
- d. Are data on baseline geriatric scores or HCT-CI available for all? The answer was not available at the time of the Q&A.
- e. Do we have registry information on whether CAR-T production succeeded or not, when attempted? The answer was not available at the time of the Q&A but the moderator did state that on behalf of CIBMTR, this information is not captured.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix N](#).

15. **Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation.** This proposal was presented by Dr. Joseph Pidala. The primary objective of this proposal is to validate prediction models for immune suppression discontinuation (ISD) and ISD failure developed in prior DISCIS-defined population, explore ISD and ISD failure in a new population inclusive of full range of diversity in current HCT practices, construct and validate dynamic prediction models of ISD and ISD failure in the expanded population. The CIBMTR identified 20,031 patients with a hematologic malignancy who received an allogeneic HCT from matched sibling donor, matched or mismatched unrelated donor, umbilical cord blood or haploidentical donor between 2009-2018. The following questions were answered during the Q&A:

- a. Can you explain how the ISD data information was made feasible? We used CIBMTR follow up data in the previous analysis that led to the development of the prediction model for ISD that we intend to validate in this study.
- b. Can you provide more granularity on how the time of discontinuation of immune suppression will be defined? In the CIBMTR data, there is a hard stop date for a complete discontinuation of immune suppression. That granular data is available, and it was the data we used for the prior project. We used that hard stop of all systemic immune suppression because that's an unambiguous measure of success.
- c. Many with PTCY may be discontinuing by days 100 or 60- likely based on center practice rather than patient response, how will this be addressed? Our prior project was successfully addressed this issue, specifically within that study population. The first step in this project is to validate those findings. We will definitely be studying how immune suppression was performed and what are the subsequent outcomes.
- d. Do you plan to use age as one of the variables regarding likelihood to discontinue IST, or will you have a separate pediatric specific model? Yes, we will consider age as a variable and evaluate the need for a pediatric specific model.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in [Appendix O](#).

**CLOSING:**

Dr. Shaw, on behalf of herself and co-chair, Dr. John Wingard, did thank presenters, conference organizers, and the CIBMTR staff for having coordinated this virtual session. She did mention that this session was recorded and encouraged attendees to take survey, as access would be available until Monday, February 15, 2021.

**APPENDICES:**

- A. Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.**
1. How will authorship work for these studies? The same as usual, there are fewer studies being accepted but the process otherwise is the same
  2. What if a higher risk of cancer is related to the almost uniform use of 2GyTBI in these patients rather than PTCY?
  3. What is the breakdown of haploidentical versus matched sib/MUD in the post-transplant cyclophosphamide group?
  4. How can we r/o genetic predisposition on samples and variables of TBI based conditioning therapies?
  5. What is your sample size and follow-up period?
  6. How long post BMT you will follow up? From where will you receive the SN data?
  7. Will you be adjusting for chronic GVHD when looking at your outcome of SN?
  8. Is this study statistically powered to detect a difference between PTCY and above a certain threshold? What is the threshold?
  9. Will analysis be conducted separately for TBI/non-TBI and MAC/RIC conditioning? Are you evaluating all malignancies?
  10. Since the total CY exposure is likely not that different in PTCY vs. BU/CY or CY/TBI, is your hypothesis that the timing of exposure to CY may lead to a difference in risk? And if so, why?
  11. Information on skin cancers - ssc, bcc available?
  12. Matching for HLA matching could be a limitation because the PTCY patients are more likely to receive haploidentical grafts.
- B. Outcomes of chimeric antigen receptor-T cell (CAR-T) therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome).**
1. If patients had failed an auto or allo, how do you plan to compare to the results of auto? Isn't it a different group?
  2. Can you please provide your thoughts if the small n will be able to generate meaningful results at this time?
  3. Would you include both transformed lymphoma from other low-grade lymphoma and Richter's transformation?
  4. Are there concerns about underreporting Richter's?
  5. Since the numbers are small, can we go back to centers to establish clonality?
- C. Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies. *No additional questions***
- D. Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant.**
1. Does the HED algorithm take into account variations outside the peptide binding groove?

2. What is the size of the cohort you are looking at?

**E. Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation. No additional questions**

**F. Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant.**

1. How do you plan to control for differences between your AYA group and older control group?

**G. Impact of MRD status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT.**

1. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when?

2. Hi Firas, How are defining the MRD?

3. The methods for MRD assessment may be quite heterogeneous, including the threshold of detection. How will you deal with the high likelihood of false MRD negative assessments from using inadequately sensitive quantification?

4. MRD test is different from different centers. How can you control for this?

5. How do you account for different MRD- cut-offs?

6. To clarify, if AML-MRD is to become a "precision medicine tool", does that mean it will be used to guide treatment decisions in addition to being prognostic?

7. How will control for the various methods for detecting MRD as different techniques have different sensitivities/accuracy?

8. if both multiparameter flow and NGS are available and are discordant on the same patient, how will that be analyzed?

9. is the MRD before alloSCT is the one to be analyzed?

10. Will this require more data from centers to answer some of the questions above?

**H. Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.**

1. Is age significantly different in your Hispanic cohort? How do you adjust for it?

2. Was the MMUD recipient cohort limited to single antigen mismatch? Or all mismatches (understanding most MMUD will likely be single antigen MM)?

3. Do you have information on health insurance? Why not to study this question in a more homogeneous patient population to avoid the complexity and interactions in different factors?

4. Are there any other sociodemographic variables available that could be used to adjust for socioeconomic status, or is median income in the patient's ZIP code the only one?

5. Baker et al 2009 demonstrated no impact of household income on GVHD (acute or chronic) and only minimal impact of race on Grade III-IV aGVHD (none of cGVHD). Why do you think this null relationship should be pursued again?

6. Is there a plan to study as per continent distribution?

7. Is there a better index to gauge SES or poverty level?

8. Are Native American/Hawaiian/Pacific islanders being grouped elsewhere?

**I. Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity.**

1. Do you plan to address the confounding influence of different factors leading to delay in transplant timing?

2. How are you going to account for number of cycles of chemotherapy versus no

chemotherapy as a confounder in the time delay?

- J. Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement.**
1. Is site-specific response (CNS vs. other lesions) and pattern of relapse/progression (CNS vs. systemic) available?
  2. Why not to consider a comparative group?
  3. Will you stratify patients according if they received IT chemo vs radiation therapy?
- K. Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis.**
1. Availability of somatic mutations?
  2. Is pretransplant Splenectomy data available? Are you going to factor this in the outcomes?
  3. At least look at splenectomies?
  4. What risk stratification is being used? DIPSS or DIPSS+?
- L. Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL.**  
*No additional questions*
- M. Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation.** *No additional questions*
- N. Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas.** *No additional questions*
- O. Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation.**
1. How is immune suppression stop defined in the CIBMTR database?
  2. How long after HCT do you expect data regarding ongoing IST usage to be reliable since many patients leave the transplant center and are managed elsewhere long-term?
  3. How long will you deal with restart IST?



## Accrual Summary for the Donor Health and Safety Working Committee

Table 1. Characteristics of domestic unrelated NMDP donors donating between 1988 and December 2020 <sup>a</sup>

Characteristic	Bone marrow	PBSC	Total
No. of patients	25377	37448	62825
<b>Characteristics</b>			
Donor age at collection - no. (%)			
Median (min-max)	34.0 (18.3-61.1)	30.8 (18.3-62.3)	32.2 (18.3-62.3)
18-29	9257 (36)	17653 (47)	26910 (43)
30-39	8471 (33)	10119 (27)	18590 (30)
40-49	5969 (24)	6834 (18)	12803 (20)
50+	1680 (7)	2842 (8)	4522 (7)
Donor sex - no. (%)			
Male	15278 (60)	23879 (64)	39157 (62)
Female	10099 (40)	13569 (36)	23668 (38)
Donor race/ethnicity - no. (%)			
Caucasian	18017 (71)	25774 (69)	43791 (70)
African/African-American	1457 (6)	1465 (4)	2922 (5)
Asian/Pacific Islander	1207 (5)	1957 (5)	3164 (5)
Hispanic	2266 (9)	3100 (8)	5366 (9)
Native American	284 (1)	279 (1)	563 (1)
Multiple/Other	1418 (6)	2870 (8)	4288 (7)
Missing	728 (3)	2003 (5)	2731 (4)
Donor CMV status - no. (%)			
Negative	14028 (55)	20816 (56)	34844 (55)
Positive	11046 (44)	16359 (44)	27405 (44)
Unknown/inconclusive	303 (1)	273 (1)	576 (1)
Year of donation - no. (%)			
1988	78 (0)	0 (0)	78 (0)
1989	176 (1)	0 (0)	176 (0)
1990	280 (1)	0 (0)	280 (0)
1991	433 (2)	0 (0)	433 (1)
1992	547 (2)	0 (0)	547 (1)
1993	640 (3)	0 (0)	640 (1)
1994	794 (3)	5 (0)	799 (1)
1995	867 (3)	21 (0)	888 (1)
1996	1039 (4)	14 (0)	1053 (2)
1997	1164 (5)	17 (0)	1181 (2)
1998	1208 (5)	29 (0)	1237 (2)
1999	1248 (5)	71 (0)	1319 (2)

Characteristic	Bone marrow	PBSC	Total
2000	1192 (5)	311 (1)	1503 (2)
2001	1063 (4)	454 (1)	1517 (2)
2002	1068 (4)	749 (2)	1817 (3)
2003	891 (4)	988 (3)	1879 (3)
2004	796 (3)	1085 (3)	1881 (3)
2005	646 (3)	1254 (3)	1900 (3)
2006	666 (3)	1374 (4)	2040 (3)
2007	643 (3)	1470 (4)	2113 (3)
2008	670 (3)	1706 (5)	2376 (4)
2009	669 (3)	1835 (5)	2504 (4)
2010	711 (3)	1954 (5)	2665 (4)
2011	753 (3)	2109 (6)	2862 (5)
2012	931 (4)	2499 (7)	3430 (5)
2013	924 (4)	2733 (7)	3657 (6)
2014	895 (4)	2635 (7)	3530 (6)
2015	805 (3)	2497 (7)	3302 (5)
2016	821 (3)	2299 (6)	3120 (5)
2017	812 (3)	2205 (6)	3017 (5)
2018	749 (3)	2259 (6)	3008 (5)
2019	661 (3)	2346 (6)	3007 (5)
2020	537 (2)	2529 (7)	3066 (5)

**Form completion**

Baseline <sup>b,c</sup> - no./total no. (%)	9268/25377 (37)	27894/37448 (74)	37162/62825 (59)
Day of collection (BM donors) <sup>b,d</sup> - no./total no. (%)	8836/25377 (35)	0/37448 (0)	8836/62825 (14)
Day 1 of collection (PBSC donors) <sup>b,e</sup> - no./total no. (%)	0/25377 (0)	26806/37448 (72)	26806/62825 (43)
Product (BM donors) <sup>b,f</sup> - no./total no. (%)	23183/25377 (91)	0/37448 (0)	23183/62825 (37)
First product (PBSC donors) <sup>b,g</sup> - no./total no. (%)	0/25377 (0)	26613/37448 (71)	26613/62825 (42)

<sup>a</sup> There have been 5927 bone marrow and 19528 PBSC international donors during this time frame.

<sup>b</sup> Completed with FormsNet1 or FormsNet2 (approximately 2004 and forward).

<sup>c</sup> Form 700 collects information related to vital signs, hematology, MTC, infection, pain, and venous access.

<sup>d</sup> Form 732 collects information related to MTC, infection, pain, vital signs, pre-collection hematology, post-collection hematology, and ABO typing.

<sup>e</sup> Form 730 collects information related to MTC, infection, pain, vital signs, pre-apheresis hematology, post-apheresis hematology, and ABO typing.

<sup>f</sup> Form 772 collects information related to marrow product analysis.

<sup>g</sup> Form 770 collects information related to PBSC product analysis.

Abbreviations: NMDP – National Marrow Donor Program; PBSC – Peripheral blood stem cell; CMV – Cytomegalovirus; MTC – Modified toxicity criteria.

**Table 2. Characteristics of domestic related NMDP donors donating between 1988 and December 2020<sup>a</sup>**

<b>Characteristic</b>	<b>Bone marrow</b>	<b>PBSC</b>	<b>Total</b>
No. of patients	96	475	571
<b><u>Characteristics</u></b>			
Donor age at collection - no. (%)			
Median (min-max)	37.1 (18.0-60.5)	50.3 (18.2-61.2)	48.5 (18.0-61.2)
18-29	31 (32)	41 (9)	72 (13)
30-39	28 (29)	91 (19)	119 (21)
40-49	15 (16)	98 (21)	113 (20)
50+	22 (23)	245 (52)	267 (47)
Donor sex - no. (%)			
Male	56 (58)	279 (59)	335 (59)
Female	40 (42)	196 (41)	236 (41)
Donor race/ethnicity - no. (%)			
Caucasian	52 (54)	331 (70)	383 (67)
African/African-American	20 (21)	33 (7)	53 (9)
Asian/Pacific Islander	2 (2)	20 (4)	22 (4)
Hispanic	16 (17)	43 (9)	59 (10)
Multiple/Other	2 (2)	29 (6)	31 (5)
Missing	4 (4)	19 (4)	23 (4)
Donor CMV status - no. (%)			
Negative	54 (56)	234 (49)	288 (50)
Positive	42 (44)	233 (49)	275 (48)
Unknown/inconclusive	0 (0)	8 (2)	8 (1)
Year of donation - no. (%)			
2009	0 (0)	1 (0)	1 (0)
2012	0 (0)	1 (0)	1 (0)
2013	0 (0)	5 (1)	5 (1)
2014	1 (1)	2 (0)	3 (1)
2015	2 (2)	7 (1)	9 (2)
2016	6 (6)	17 (4)	23 (4)
2017	23 (24)	51 (11)	74 (13)
2018	18 (19)	89 (19)	107 (19)
2019	14 (15)	94 (20)	108 (19)
2020	32 (33)	208 (44)	240 (42)
<b><u>Form completion</u></b>			
Baseline <sup>b,c</sup> - no./total no. (%)	96/96 (100)	475/475 (100)	571/571 (100)
Day of collection (BM donors) <sup>b,d</sup> - no./total no. (%)	95/96 (99)	0/475 (0)	95/571 (17)
Day 1 of collection (PBSC donors) <sup>b,d</sup> - no./total no. (%)	0/96 (0)	474/475 (100)	474/571 (83)

<b>Characteristic</b>	<b>Bone marrow</b>	<b>PBSC</b>	<b>Total</b>
Product form (BM donors) <sup>b,d</sup> - no./total no. (%)	96/96 (100)	0/475 (0)	96/571 (17)
First product form (PBSC donors) <sup>b,d</sup> - no./total no. (%)	0/96 (0)	471/475 (99)	471/571 (82)

<sup>a</sup> There have been 1 bone marrow and 13 PBSC international donors during this time frame.

<sup>b</sup> Completed with FormsNet2 (approximately 2009 and forward). Similar data are collected prior to 2009.

<sup>c</sup> Form 700 collects information related to vital signs, hematology, MTC, infection, pain, and venous access.

<sup>d</sup> Form 732 collects information related to MTC, infection, pain, vital signs, pre-collection hematology, post-collection hematology, and ABO typing.

<sup>e</sup> Form 730 collects information related to MTC, infection, pain, vital signs, pre-apheresis hematology, post-apheresis hematology, and ABO typing.

<sup>f</sup> Form 772 collects information related to marrow product analysis.

<sup>g</sup> Form 770 collects information related to PBSC product analysis.

Abbreviations: NMDP – National Marrow Donor Program; PBSC – Peripheral blood stem cell; CMV – Cytomegalovirus; MTC – Modified toxicity criteria.

Table 3. Characteristics of Related Donors from the RCI-BMT 06-DON (RDSafe) Study

Variable	<u>GMARROW<sup>a</sup></u>	<u>MARROW</u>	<u>PBSC</u>	<u>Total</u>
	N (%)	N (%)	N (%)	N (%)
Number of donors	20	404	1256	1680
Donor age at time of donation				
0 to 5	2 (10)	59 (15)	1 (<1)	62 ( 4)
6 to 10	2 (10)	93 (23)	4 (<1)	99 ( 6)
11 to 17	5 (25)	115 (28)	13 ( 1)	133 ( 8)
18 to 30	3 (15)	59 (15)	122 (10)	184 (11)
31 to 40	1 ( 5)	21 ( 5)	149 (12)	171 (10)
41 to 50	2 (10)	22 ( 5)	278 (22)	302 (18)
51 to 55	2 (10)	12 ( 3)	221 (18)	235 (14)
56 to 60	3 (15)	14 ( 3)	212 (17)	229 (14)
61 to 65	0	6 ( 1)	147 (12)	153 ( 9)
66 to 70	0	2 (<1)	82 ( 7)	84 ( 5)
≥ 71	0	1 (<1)	27 ( 2)	28 ( 2)
Median (Range)	21 (4-57)	14 (0-77)	53 (6-79)	48 (0-79)
Donor race/ethnicity				
Caucasian	17 (85)	238 (59)	1048 (83)	1303 (78)
Hispanic	1 ( 5)	49 (12)	75 ( 6)	125 ( 7)
Black / African American	2 (10)	90 (22)	72 ( 6)	164 (10)
Asian / Pacific Islander	0	11 ( 3)	39 ( 3)	50 ( 3)
American Indian / Alaska Native	0	5 ( 1)	7 ( 1)	12 ( 1)
Other / multiple race	0	8 ( 2)	9 ( 1)	17 ( 1)
Decline / unknown	0	3 ( 1)	6 (<1)	9 ( 1)
Donor sex				
Female	11 (55)	194 (48)	568 (45)	773 (46)
Male	9 (45)	210 (52)	688 (55)	907 (54)
First or second donation				
First donation	19 (95)	396 (98)	1226 (98)	1641 (98)
Second donation	1 ( 5)	8 ( 2)	30 ( 2)	39 ( 2)
Year of donation				
2010	4 (20)	44 (11)	146 (12)	194 (12)
2011	10 (50)	105 (26)	399 (32)	514 (31)
2012	2 (10)	126 (31)	489 (39)	617 (37)
2013	3 (15)	88 (22)	219 (17)	310 (18)
2014	1 ( 5)	41 (10)	3 (<1)	45 ( 3)

<sup>a</sup> GCSF-primed marrow

**Table 4. 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	<u>Samples Available for Recipient and Donor</u>		<u>Samples Available for Donor Only</u>
	N (%)	N (%)	N (%)
Number of patients	44543	15903	8657
Source of data			
CRF	24072 (54)	6924 (44)	4451 (51)
TED	20471 (46)	8979 (56)	4206 (49)
Number of centers	258	232	351
Disease at transplant			
AML	15294 (34)	5896 (37)	2918 (34)
ALL	6535 (15)	2123 (13)	1370 (16)
Other leukemia	1408 (3)	385 (2)	249 (3)
CML	3509 (8)	1045 (7)	695 (8)
MDS	6346 (14)	2568 (16)	1072 (12)
Other acute leukemia	462 (1)	185 (1)	106 (1)
NHL	4032 (9)	1194 (8)	710 (8)
Hodgkin Lymphoma	917 (2)	220 (1)	160 (2)
Plasma Cell Disorders, MM	892 (2)	270 (2)	159 (2)
Other malignancies	59 (<1)	13 (<1)	18 (<1)
Breast cancer	7 (<1)	3 (<1)	1 (<1)
SAA	1428 (3)	485 (3)	344 (4)
Inherited abnormalities erythrocyte diff fxn	727 (2)	251 (2)	157 (2)
Inherited bone marrow failure syndromes	9 (<1)	9 (<1)	11 (<1)
Hemoglobinopathies	8 (<1)	6 (<1)	4 (<1)
Paroxysmal nocturnal hemoglobinuria	1 (<1)	4 (<1)	0
SCIDs	780 (2)	280 (2)	253 (3)
Inherited abnormalities of platelets	40 (<1)	14 (<1)	11 (<1)
Inherited disorders of metabolism	292 (1)	79 (<1)	95 (1)
Histiocytic disorders	376 (1)	107 (1)	94 (1)
Autoimmune disorders	22 (<1)	12 (<1)	5 (<1)
Other	51 (<1)	21 (<1)	19 (<1)
MPN	1347 (3)	733 (5)	204 (2)

Variable	<u>Samples Available for Recipient and Donor</u>		<u>Samples Available for Donor Only</u>
	N (%)	N (%)	N (%)
Disease missing	1 (N/A)	0 (N/A)	2 (N/A)
AML Disease status at transplant			
CR1	8061 (53)	3434 (58)	1439 (49)
CR2	2975 (19)	1072 (18)	590 (20)
CR3+	330 (2)	95 (2)	67 (2)
Advanced or active disease	3783 (25)	1262 (21)	767 (26)
Missing	145 (1)	33 (1)	55 (2)
ALL Disease status at transplant			
CR1	3206 (49)	1180 (56)	585 (43)
CR2	1873 (29)	548 (26)	393 (29)
CR3+	558 (9)	157 (7)	139 (10)
Advanced or active disease	852 (13)	222 (10)	217 (16)
Missing	46 (1)	16 (1)	36 (3)
MDS Disease status at transplant			
Early	1380 (22)	488 (19)	256 (24)
Advanced	4003 (63)	1854 (72)	592 (55)
Missing	963 (15)	226 (9)	224 (21)
NHL Disease status at transplant			
CR1	556 (14)	205 (17)	90 (13)
CR2	741 (18)	223 (19)	117 (17)
CR3+	345 (9)	102 (9)	66 (9)
PR	439 (11)	110 (9)	76 (11)
Advanced	1866 (47)	531 (45)	346 (49)
Missing	65 (2)	15 (1)	12 (2)
Recipient age at transplant			
0-9 years	3829 (9)	1110 (7)	1068 (12)
10-19 years	3937 (9)	1138 (7)	978 (11)
20-29 years	4617 (10)	1454 (9)	981 (11)
30-39 years	5099 (11)	1604 (10)	1015 (12)
40-49 years	6813 (15)	2184 (14)	1294 (15)
50-59 years	9175 (21)	3138 (20)	1573 (18)
60-69 years	9168 (21)	4145 (26)	1465 (17)
70+ years	1905 (4)	1130 (7)	283 (3)
Median (Range)	47 (0-84)	52 (0-82)	43 (0-81)
Recipient race/ethnicity			
Caucasian, non-Hispanic	36965 (83)	13172 (83)	6184 (71)

Variable	<u>Samples Available for Recipient and Donor</u>		<u>Samples Available for Donor Only</u>
	N (%)	N (%)	N (%)
African-American, non-Hispanic	2018 (5)	651 (4)	388 (4)
Asian, non-Hispanic	1027 (2)	498 (3)	331 (4)
Pacific islander, non-Hispanic	55 (<1)	25 (<1)	23 (<1)
Native American, non-Hispanic	168 (<1)	66 (<1)	33 (<1)
Hispanic	2662 (6)	861 (5)	468 (5)
Missing	1648 (4)	630 (4)	1230 (14)
Recipient sex			
Male	25968 (58)	9313 (59)	5132 (59)
Female	18575 (42)	6590 (41)	3525 (41)
Karnofsky score			
10-80	15260 (34)	5968 (38)	2755 (32)
90-100	27634 (62)	9412 (59)	5408 (62)
Missing	1649 (4)	523 (3)	494 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	28 (<1)	37 (<1)	3 (<1)
4/6	235 (1)	102 (1)	45 (1)
5/6	6059 (14)	1819 (13)	1217 (15)
6/6	37443 (86)	12508 (86)	6817 (84)
Unknown	778 (N/A)	1437 (N/A)	575 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	884 (2)	102 (1)	45 (1)
6/8	1724 (4)	139 (1)	152 (3)
7/8	8420 (20)	1863 (16)	1254 (22)
8/8	31783 (74)	9524 (82)	4335 (75)
Unknown	1732 (N/A)	4275 (N/A)	2871 (N/A)
HLA-DPB1 Match			
Double allele mismatch	10933 (29)	1275 (23)	590 (26)
Single allele mismatch	20128 (54)	2834 (51)	1199 (52)
Full allele matched	6179 (17)	1427 (26)	512 (22)
Unknown	7303 (N/A)	10367 (N/A)	6356 (N/A)
High resolution release score			
No	9149 (21)	15838 (>99)	8450 (98)
Yes	35394 (79)	65 (<1)	207 (2)
KIR typing available			
No	30764 (69)	15880 (>99)	8609 (99)
Yes	13779 (31)	23 (<1)	48 (1)



Variable	<u>Samples Available for Recipient and Donor</u>		<u>Samples Available for Donor Only</u>
	N (%)	N (%)	N (%)
<b>Graft type</b>			
Marrow	16082 (36)	4740 (30)	3436 (40)
PBSC	28404 (64)	11007 (69)	5187 (60)
BM+PBSC	11 (<1)	7 (<1)	3 (<1)
PBSC+UCB	27 (<1)	137 (1)	5 (<1)
Others	19 (<1)	12 (<1)	26 (<1)
<b>Conditioning regimen</b>			
Myeloablative	27651 (62)	8835 (56)	5389 (62)
RIC/Nonmyeloablative	16685 (37)	7019 (44)	3146 (36)
TBD	207 (<1)	49 (<1)	122 (1)
<b>Donor age at donation</b>			
To Be Determined/NA	410 (1)	1434 (9)	126 (1)
0-9 years	8 (<1)	36 (<1)	3 (<1)
10-19 years	1223 (3)	550 (3)	184 (2)
20-29 years	20165 (45)	7124 (45)	3529 (41)
30-39 years	12640 (28)	3985 (25)	2591 (30)
40-49 years	7729 (17)	2111 (13)	1682 (19)
50+ years	2368 (5)	663 (4)	542 (6)
Median (Range)	30 (0-69)	29 (0-109)	32 (0-67)
<b>Donor/Recipient CMV serostatus</b>			
+/+	11076 (25)	4431 (28)	2157 (25)
+/-	5279 (12)	2016 (13)	1101 (13)
-/+	14617 (33)	4780 (30)	2679 (31)
-/-	12957 (29)	4204 (26)	2327 (27)
CB - recipient +	3 (<1)	17 (<1)	0
CB - recipient -	1 (<1)	8 (<1)	0
CB - recipient CMV unknown	0	1 (<1)	0
Missing	610 (1)	446 (3)	393 (5)
<b>GvHD Prophylaxis</b>			
No GvHD Prophylaxis	146 (<1)	65 (<1)	45 (1)
TDEPLETION alone	100 (<1)	31 (<1)	31 (<1)
TDEPLETION +- other	1068 (2)	278 (2)	261 (3)
CD34 select alone	272 (1)	129 (1)	62 (1)
CD34 select +- other	881 (2)	628 (4)	194 (2)
Cyclophosphamide alone	785 (2)	676 (4)	226 (3)
Cyclophosphamide +- others	2016 (5)	1404 (9)	426 (5)

Variable	<u>Samples Available for Recipient and Donor</u>		<u>Samples Available for Donor Only</u>
	N (%)	N (%)	N (%)
FK506 + MMF +- others	4990 (11)	1515 (10)	694 (8)
FK506 + MTX +- others(not MMF)	18673 (42)	6475 (41)	2380 (27)
FK506 +- others(not MMF,MTX)	2264 (5)	958 (6)	320 (4)
FK506 alone	1019 (2)	361 (2)	147 (2)
CSA + MMF +- others(not FK506)	2904 (7)	746 (5)	700 (8)
CSA + MTX +- others(not MMF,FK506)	6888 (15)	1819 (11)	2318 (27)
CSA +- others(not FK506,MMF,MTX)	1112 (2)	333 (2)	299 (3)
CSA alone	448 (1)	121 (1)	292 (3)
Other GVHD Prophylaxis	735 (2)	250 (2)	145 (2)
Missing	242 (1)	114 (1)	117 (1)
Donor/Recipient sex match			
Male-Male	18261 (41)	6197 (39)	3395 (39)
Male-Female	11147 (25)	3783 (24)	1963 (23)
Female-Male	7474 (17)	2729 (17)	1655 (19)
Female-Female	7249 (16)	2505 (16)	1506 (17)
CB - recipient M	13 (<1)	78 (<1)	0
CB - recipient F	14 (<1)	67 (<1)	6 (<1)
Missing	385 (1)	544 (3)	132 (2)
Year of transplant			
1986-1990	383 (1)	49 (<1)	53 (1)
1991-1995	1959 (4)	460 (3)	503 (6)
1996-2000	3363 (8)	1200 (8)	823 (10)
2001-2005	5238 (12)	1036 (7)	1553 (18)
2006-2010	9426 (21)	1872 (12)	1486 (17)
2011-2015	13159 (30)	3524 (22)	1900 (22)
2016-2020	10087 (23)	6869 (43)	2066 (24)
2021	928 (2)	893 (6)	273 (3)
Follow-up among survivors, Months			
N Eval	18378	7541	3603
Median (Range)	63 (0-385)	36 (0-362)	47 (0-365)

**Table 5. Unrelated Cord 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	<u>Samples Available for</u>	<u>Samples Available</u>	<u>Samples Available</u>
	<u>Recipient and Donor</u>	<u>for Recipient Only</u>	<u>for Donor Only</u>
	N (%)	N (%)	N (%)
Number of patients	5894	1566	1557
Source of data			
CRF	4361 (74)	1124 (72)	947 (61)
TED	1533 (26)	442 (28)	610 (39)
Number of centers	152	138	201
Disease at transplant			
AML	2221 (38)	529 (34)	505 (32)
ALL	1222 (21)	344 (22)	347 (22)
Other leukemia	93 (2)	30 (2)	27 (2)
CML	128 (2)	35 (2)	38 (2)
MDS	523 (9)	151 (10)	119 (8)
Other acute leukemia	93 (2)	26 (2)	28 (2)
NHL	394 (7)	89 (6)	100 (6)
Hodgkin Lymphoma	97 (2)	27 (2)	27 (2)
Plasma Cell Disorders, MM	37 (1)	12 (1)	11 (1)
Other malignancies	11 (<1)	1 (<1)	1 (<1)
SAA	93 (2)	31 (2)	27 (2)
Inherited abnormalities erythrocyte diff fxn	165 (3)	50 (3)	33 (2)
Inherited bone marrow failure syndromes	2 (<1)	2 (<1)	1 (<1)
Hemoglobinopathies	1 (<1)	0	0
SCIDs	262 (4)	87 (6)	122 (8)
Inherited abnormalities of platelets	20 (<1)	5 (<1)	7 (<1)
Inherited disorders of metabolism	361 (6)	105 (7)	105 (7)
Histiocytic disorders	105 (2)	27 (2)	38 (2)
Autoimmune disorders	9 (<1)	0	2 (<1)
Other	11 (<1)	2 (<1)	5 (<1)
MPN	46 (1)	13 (1)	14 (1)
AML Disease status at transplant			
CR1	1147 (52)	287 (54)	241 (48)
CR2	608 (27)	139 (26)	139 (28)

Variable	<u>Samples Available for</u>	<u>Samples Available</u>	<u>Samples Available</u>
	<u>Recipient and Donor</u>	<u>for Recipient Only</u>	<u>for Donor Only</u>
	N (%)	N (%)	N (%)
CR3+	62 (3)	8 (2)	22 (4)
Advanced or active disease	398 (18)	93 (18)	101 (20)
Missing	6 (<1)	2 (<1)	2 (<1)
<b>ALL Disease status at transplant</b>			
CR1	550 (45)	146 (42)	146 (42)
CR2	451 (37)	124 (36)	125 (36)
CR3+	143 (12)	51 (15)	48 (14)
Advanced or active disease	77 (6)	21 (6)	28 (8)
Missing	1 (<1)	2 (1)	0
<b>MDS Disease status at transplant</b>			
Early	163 (31)	41 (27)	52 (44)
Advanced	315 (60)	95 (63)	48 (40)
Missing	45 (9)	15 (10)	19 (16)
<b>NHL Disease status at transplant</b>			
CR1	60 (15)	6 (7)	18 (18)
CR2	74 (19)	20 (22)	31 (31)
CR3+	44 (11)	10 (11)	9 (9)
PR	67 (17)	12 (13)	11 (11)
Advanced	146 (37)	40 (45)	28 (28)
Missing	0	1 (1)	2 (2)
<b>Recipient age at transplant</b>			
0-9 years	1776 (30)	580 (37)	578 (37)
10-19 years	776 (13)	175 (11)	211 (14)
20-29 years	556 (9)	110 (7)	131 (8)
30-39 years	569 (10)	141 (9)	153 (10)
40-49 years	623 (11)	154 (10)	144 (9)
50-59 years	803 (14)	190 (12)	184 (12)
60-69 years	683 (12)	188 (12)	145 (9)
70+ years	108 (2)	28 (2)	11 (1)
Median (Range)	27 (0-83)	22 (0-76)	19 (0-78)
<b>Recipient race/ethnicity</b>			
Caucasian, non-Hispanic	3254 (55)	917 (59)	834 (54)
African-American, non-Hispanic	841 (14)	204 (13)	176 (11)
Asian, non-Hispanic	340 (6)	107 (7)	105 (7)
Pacific islander, non-Hispanic	30 (1)	3 (<1)	16 (1)
Native American, non-Hispanic	42 (1)	9 (1)	18 (1)
Hispanic	1054 (18)	229 (15)	209 (13)

Variable	<u>Samples Available for</u>	<u>Samples Available</u>	<u>Samples Available</u>
	<u>Recipient and Donor</u>	<u>for Recipient Only</u>	<u>for Donor Only</u>
	N (%)	N (%)	N (%)
Missing	333 (6)	97 (6)	199 (13)
Recipient sex			
Male	3249 (55)	892 (57)	879 (56)
Female	2645 (45)	674 (43)	678 (44)
Karnofsky score			
10-80	1563 (27)	400 (26)	391 (25)
90-100	4149 (70)	1075 (69)	1056 (68)
Missing	182 (3)	91 (6)	110 (7)
HLA-A B DRB1 groups - low resolution			
<=3/6	97 (2)	38 (3)	12 (1)
4/6	2341 (41)	537 (40)	555 (39)
5/6	2550 (45)	566 (42)	647 (46)
6/6	718 (13)	191 (14)	202 (14)
Unknown	188 (N/A)	234 (N/A)	141 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2777 (55)	537 (56)	609 (54)
6/8	1193 (24)	228 (24)	279 (25)
7/8	701 (14)	129 (13)	166 (15)
8/8	333 (7)	70 (7)	79 (7)
Unknown	890 (N/A)	602 (N/A)	424 (N/A)
HLA-DPB1 Match			
Double allele mismatch	815 (39)	97 (43)	109 (39)
Single allele mismatch	1065 (51)	108 (48)	145 (51)
Full allele matched	199 (10)	21 (9)	28 (10)
Unknown	3815 (N/A)	1340 (N/A)	1275 (N/A)
High resolution release score			
No	4378 (74)	1500 (96)	1539 (99)
Yes	1516 (26)	66 (4)	18 (1)
KIR typing available			
No	4634 (79)	1560 (>99)	1545 (99)
Yes	1260 (21)	6 (<1)	12 (1)
Graft type			
UCB	5557 (94)	1429 (91)	1472 (95)
BM+UCB	1 (<1)	0	0
PBSC+UCB	307 (5)	137 (9)	78 (5)
Others	29 (<1)	0	7 (<1)
Number of cord units			

Variable	<u>Samples Available for</u>	<u>Samples Available</u>	<u>Samples Available</u>
	<u>Recipient and Donor</u>	<u>for Recipient Only</u>	<u>for Donor Only</u>
	N (%)	N (%)	N (%)
1	4944 (84)	0	1310 (84)
2	946 (16)	0	247 (16)
3	2 (<1)	0	0
Unknown	2 (N/A)	1566 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	3852 (65)	1008 (64)	978 (63)
RIC/Nonmyeloablative	2029 (34)	554 (35)	570 (37)
TBD	13 (<1)	4 (<1)	9 (1)
Donor age at donation			
To Be Determined/NA	209 (4)	113 (7)	120 (8)
0-9 years	5183 (88)	1205 (77)	1316 (85)
10-19 years	296 (5)	141 (9)	70 (4)
20-29 years	65 (1)	35 (2)	11 (1)
30-39 years	56 (1)	34 (2)	18 (1)
40-49 years	39 (1)	17 (1)	8 (1)
50+ years	46 (1)	21 (1)	14 (1)
Median (Range)	3 (0-72)	5 (0-73)	3 (0-69)
Donor/Recipient CMV serostatus			
+/+	1338 (23)	309 (20)	307 (20)
+/-	573 (10)	148 (9)	145 (9)
-/+	1084 (18)	283 (18)	267 (17)
-/-	724 (12)	195 (12)	201 (13)
CB - recipient +	1253 (21)	336 (21)	339 (22)
CB - recipient -	828 (14)	238 (15)	238 (15)
CB - recipient CMV unknown	94 (2)	57 (4)	60 (4)
GvHD Prophylaxis			
No GvHD Prophylaxis	21 (<1)	8 (1)	9 (1)
TDEPLETION alone	1 (<1)	0	0
TDEPLETION +- other	27 (<1)	9 (1)	5 (<1)
CD34 select alone	0	2 (<1)	2 (<1)
CD34 select +- other	287 (5)	136 (9)	84 (5)
Cyclophosphamide alone	0	0	2 (<1)
Cyclophosphamide +- others	47 (1)	27 (2)	53 (3)
FK506 + MMF +- others	1622 (28)	415 (27)	260 (17)
FK506 + MTX +- others(not MMF)	214 (4)	56 (4)	71 (5)
FK506 +- others(not MMF,MTX)	221 (4)	63 (4)	65 (4)
FK506 alone	139 (2)	43 (3)	23 (1)

Variable	<u>Samples Available for</u>	<u>Samples Available</u>	<u>Samples Available</u>
	<u>Recipient and Donor</u>	<u>for Recipient Only</u>	<u>for Donor Only</u>
	N (%)	N (%)	N (%)
CSA + MMF +- others(not FK506)	2689 (46)	610 (39)	707 (45)
CSA + MTX +- others(not MMF,FK506)	99 (2)	33 (2)	41 (3)
CSA +- others(not FK506,MMF,MTX)	333 (6)	124 (8)	151 (10)
CSA alone	50 (1)	18 (1)	50 (3)
Other GVHD Prophylaxis	132 (2)	19 (1)	25 (2)
Missing	12 (<1)	3 (<1)	9 (1)
Donor/Recipient sex match			
CB - recipient M	3249 (55)	892 (57)	878 (56)
CB - recipient F	2645 (45)	674 (43)	678 (43)
CB - recipient sex unknown	0	0	1 (<1)
Year of transplant			
1996-2000	1 (<1)	2 (<1)	5 (<1)
2001-2005	115 (2)	108 (7)	27 (2)
2006-2010	1811 (31)	413 (26)	492 (32)
2011-2015	2613 (44)	501 (32)	608 (39)
2016-2020	1300 (22)	506 (32)	389 (25)
2021	54 (1)	36 (2)	36 (2)
Follow-up among survivors, Months			
N Eval	2805	808	788
Median (Range)	66 (1-196)	56 (3-213)	52 (1-240)

**Table 6. 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 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	9695	1555	646
Source of data			
CRF	3455 (36)	446 (29)	245 (38)
TED	6240 (64)	1109 (71)	401 (62)
Number of centers	90	72	59
Disease at transplant			
AML	3214 (33)	506 (33)	206 (32)
ALL	1578 (16)	299 (19)	124 (19)
Other leukemia	189 (2)	35 (2)	14 (2)
CML	314 (3)	36 (2)	20 (3)
MDS	1277 (13)	191 (12)	92 (14)
Other acute leukemia	133 (1)	29 (2)	7 (1)
NHL	856 (9)	141 (9)	61 (9)
Hodgkin Lymphoma	188 (2)	37 (2)	17 (3)
Plasma Cell Disorders, MM	254 (3)	40 (3)	18 (3)
Other malignancies	24 (<1)	0	0
Breast cancer	1 (<1)	0	0
SAA	442 (5)	62 (4)	20 (3)
Inherited abnormalities erythrocyte diff fxn	484 (5)	69 (4)	20 (3)
Inherited bone marrow failure syndromes	7 (<1)	1 (<1)	0
Hemoglobinopathies	35 (<1)	7 (<1)	2 (<1)
Paroxysmal nocturnal hemoglobinuria	2 (<1)	0	0
SCIDs	201 (2)	33 (2)	11 (2)
Inherited abnormalities of platelets	10 (<1)	0	0
Inherited disorders of metabolism	14 (<1)	3 (<1)	2 (<1)
Histiocytic disorders	57 (1)	6 (<1)	3 (<1)
Autoimmune disorders	11 (<1)	0	1 (<1)
Other	11 (<1)	3 (<1)	1 (<1)
MPN	393 (4)	57 (4)	27 (4)
AML Disease status at transplant			
CR1	2063 (64)	340 (67)	134 (65)



Variable	Samples Available for	Samples Available	Samples Available
	Recipient and Donor N (%)	for Recipient Only N (%)	for Donor Only N (%)
CR2	486 (15)	66 (13)	26 (13)
CR3+	38 (1)	13 (3)	1 (<1)
Advanced or active disease	619 (19)	83 (16)	45 (22)
Missing	8 (<1)	4 (1)	0
ALL Disease status at transplant			
CR1	974 (62)	195 (65)	76 (61)
CR2	437 (28)	69 (23)	31 (25)
CR3+	88 (6)	13 (4)	10 (8)
Advanced or active disease	78 (5)	22 (7)	7 (6)
Missing	1 (<1)	0	0
MDS Disease status at transplant			
Early	209 (16)	26 (14)	18 (20)
Advanced	1026 (80)	154 (81)	69 (75)
Missing	42 (3)	11 (6)	5 (5)
NHL Disease status at transplant			
CR1	154 (18)	32 (23)	11 (18)
CR2	162 (19)	31 (22)	8 (13)
CR3+	93 (11)	15 (11)	2 (3)
PR	67 (8)	13 (9)	5 (8)
Advanced	371 (44)	49 (35)	34 (56)
Missing	5 (1)	0	1 (2)
Recipient age at transplant			
0-9 years	961 (10)	137 (9)	48 (7)
10-19 years	1139 (12)	139 (9)	56 (9)
20-29 years	829 (9)	169 (11)	51 (8)
30-39 years	763 (8)	137 (9)	66 (10)
40-49 years	1226 (13)	196 (13)	77 (12)
50-59 years	2129 (22)	350 (23)	133 (21)
60-69 years	2254 (23)	369 (24)	190 (29)
70+ years	394 (4)	58 (4)	25 (4)
Median (Range)	50 (0-82)	50 (0-76)	52 (0-83)
Recipient race/ethnicity			
Caucasian, non-Hispanic	6077 (63)	825 (53)	421 (65)
African-American, non-Hispanic	1174 (12)	188 (12)	55 (9)
Asian, non-Hispanic	438 (5)	116 (7)	31 (5)
Pacific islander, non-Hispanic	30 (<1)	3 (<1)	1 (<1)
Native American, non-Hispanic	37 (<1)	4 (<1)	2 (<1)

Variable	Samples Available for	Samples Available	Samples Available
	Recipient and Donor N (%)	for Recipient Only N (%)	for Donor Only N (%)
Hispanic	1434 (15)	298 (19)	102 (16)
Missing	505 (5)	121 (8)	34 (5)
Recipient sex			
Male	5676 (59)	917 (59)	380 (59)
Female	4019 (41)	638 (41)	266 (41)
Karnofsky score			
10-80	3458 (36)	625 (40)	284 (44)
90-100	5979 (62)	887 (57)	338 (52)
Missing	258 (3)	43 (3)	24 (4)
Graft type			
Marrow	2780 (29)	348 (22)	168 (26)
PBSC	6834 (70)	1181 (76)	464 (72)
UCB (related)	2 (<1)	10 (1)	0
BM+PBSC	8 (<1)	4 (<1)	1 (<1)
BM+UCB	38 (<1)	11 (1)	2 (<1)
PBSC+UCB	0	0	11 (2)
Others	33 (<1)	1 (<1)	0
Conditioning regimen			
Myeloablative	5411 (56)	862 (55)	327 (51)
RIC/Nonmyeloablative	4233 (44)	683 (44)	307 (48)
TBD	51 (1)	10 (1)	12 (2)
Donor age at donation			
To Be Determined/NA	16 (<1)	10 (1)	1 (<1)
0-9 years	659 (7)	89 (6)	28 (4)
10-19 years	983 (10)	140 (9)	56 (9)
20-29 years	1354 (14)	231 (15)	97 (15)
30-39 years	1382 (14)	246 (16)	121 (19)
40-49 years	1574 (16)	258 (17)	88 (14)
50+ years	3727 (38)	581 (37)	255 (39)
Median (Range)	43 (0-82)	43 (0-79)	43 (1-76)
Donor/Recipient CMV serostatus			
+/+	3949 (41)	706 (45)	248 (38)
+/-	1079 (11)	127 (8)	60 (9)
-/+	2411 (25)	368 (24)	163 (25)
-/-	2115 (22)	325 (21)	151 (23)
CB – recipient +	0	3 (<1)	0
CB – recipient -	0	0	3 (<1)

Variable	Samples Available for	Samples Available	Samples Available
	Recipient and Donor N (%)	for Recipient Only N (%)	for Donor Only N (%)
Missing	141 (1)	26 (2)	21 (3)
GvHD Prophylaxis			
No GvHD Prophylaxis	103 (1)	14 (1)	6 (1)
TDEPLETION alone	40 (<1)	17 (1)	4 (1)
TDEPLETION +- other	63 (1)	19 (1)	7 (1)
CD34 select alone	77 (1)	20 (1)	6 (1)
CD34 select +- other	371 (4)	86 (6)	47 (7)
Cyclophosphamide alone	261 (3)	50 (3)	24 (4)
Cyclophosphamide +- others	2500 (26)	360 (23)	176 (27)
FK506 + MMF +- others	690 (7)	73 (5)	19 (3)
FK506 + MTX +- others(not MMF)	3524 (36)	478 (31)	233 (36)
FK506 +- others(not MMF,MTX)	713 (7)	253 (16)	49 (8)
FK506 alone	67 (1)	9 (1)	3 (<1)
CSA + MMF +- others(not FK506)	223 (2)	33 (2)	12 (2)
CSA + MTX +- others(not MMF,FK506)	666 (7)	83 (5)	33 (5)
CSA +- others(not FK506,MMF,MTX)	80 (1)	10 (1)	1 (<1)
CSA alone	76 (1)	9 (1)	3 (<1)
Other GVHD Prophylaxis	136 (1)	16 (1)	12 (2)
Missing	105 (1)	25 (2)	11 (2)
Donor/Recipient sex match			
Male-Male	3212 (33)	546 (35)	222 (34)
Male-Female	2068 (21)	313 (20)	136 (21)
Female-Male	2436 (25)	350 (23)	150 (23)
Female-Female	1934 (20)	317 (20)	125 (19)
CB - recipient M	24 (<1)	15 (1)	8 (1)
CB - recipient F	16 (<1)	6 (<1)	5 (1)
Missing	5 (<1)	8 (1)	0
Year of transplant			
2006-2010	604 (6)	72 (5)	38 (6)
2011-2015	3665 (38)	491 (32)	181 (28)
2016-2020	4930 (51)	874 (56)	361 (56)
2021	496 (5)	118 (8)	66 (10)
Follow-up among survivors, Months			
N Eval	5758	893	368
Median (Range)	37 (1-150)	29 (0-124)	27 (2-143)



**TO:** Donor Health and Safety Working Committee Members

**FROM:** Heather Stefanski, MD, PhD; Scientific Director for the Donor Health and Safety Working Committee

**RE:** Studies in Progress Summary

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**DS13-02: A retrospective analysis to understand the potential mechanisms underlying the clinical impact of ABO incompatibility on allogeneic transplant outcomes** (G Murthy/B Shaw). The primary aim of this study is to examine the impact of ABO mismatching (match, major mismatch, minor mismatch, bidirectional mismatch) on overall survival. Secondary aims are to investigate the impact of ABO incompatibility on disease-free survival, engraftment, non-relapse mortality, relapse, and acute and chronic GVHD, and to understand the impact on graft processing and manipulation. This study was accepted as at ASH as an oral presentation and is currently in manuscript preparation. We aim to have the manuscript submitted by July 2022.

**DS19-02: The Impact of pre-apheresis Health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome** (N Farhadfar/J Wingard/G Switzer). This study aims to determine the impact of pre-procedural health related quality of life (HRQoL) on peri-collection pain and acute toxicities experienced in PBSC donors, and to determine the impact of pre-apheresis HRQoL on incidence of hospitalizations and peripheral blood progenitor cell yield. This manuscript is currently submitted.

**DS20-01: Acute toxicities of bone marrow donation in donors with sickle cell trait** (N Farhadfar/ J Wingard). This study primarily aims to evaluate the impact of present of sickle cell trait on per-donation toxicity experienced by unrelated bone marrow donors. Secondary aims are to evaluate the impact of sickle cell trait on time to complete recovery from donation-associated symptoms and to compare the BM collected yield between unrelated donors with and without sickle cell trait. This study is in data file preparation and we aim to submit the manuscript by July 2022.



**CIBMTR Donor Safety Working Committee Review Proposal**  
**(ALL SECTIONS MUST BE COMPLETED.)**

**Review Topic**

Reducing the Risk of Transmission of Donor Derived Malignancy: Consensus Guidelines for Donor Genetic Screening Prior to Allogeneic Stem Cell Transplant and Detection of Leukemia Origin in Relapse After Transplant

**1st PI Information:**

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**3rd PI Information if applicable:**

PI Name (First, Middle, Last):  
 Degree(s):  
 Academic Rank:  
 Email Address:  
 Institution Name:

**Type of Review**

Expert Opinion/Consensus Guidelines  
 Comprehensive Review  
 Meta-Analysis  
 Narrative  
 Cochrane  
 Scoping

**Brief Summary and/or Brief Outline of Review:**

A. Brief overview of topic

- When/if a similar review has been published previously and/or in a different patient population
  - We published a review of the genetics reported for donor-derived cases of MDS and AML after allogeneic stem cell transplantation (ASCT) reported in the literature through 2020. This review serves as a foundational article for our proposed broader review of donor-derived leukemia (acute myelogenous leukemia AML, acute lymphoblastic leukemia ALL, and myelodysplastic syndrome MDS) and consensus guidelines for donor selection.

- We propose a broader review of the donor sources, genetics, treatment and maintenance strategies used, theories of donor cell leukemia development, and guidelines for donor genetic screening for ASCT to reduce likelihood of donor-derived leukemia relapse after ASCT. Further, we aim to put forth consensus recommendations for molecular analysis at time of leukemia relapse after ASCT for detection of cell origin, which is not yet common practice at all centers.
- Current gaps in the literature
  - The true incidence of donor derived leukemia remains unclear because many of the frequency estimates were evaluated before the advent of molecular testing in the last decade, which has enhanced ability to differentiate relapse of original disease ASCT versus leukemia development from the donor graft cells. Further, completion of molecular analysis at time of relapse to assess leukemia origin remains inconsistent.
  - Donor screening for selection for ASCT after leukemia remission includes immunologic compatibility and personal medical status, but usually does not include detailed family history or donor genetic analysis. By convening transplant and leukemia specialists, we would like to put forth best practices for genetic screening of donors related to risk factors for development of donor derived leukemia leukemia.
  - There is not standard molecular analysis completed at time of leukemia relapse after ASCT to detect cell origin of the recurrent leukemia.

#### B. Main objective(s) of review

- Focus (cause, prognosis, diagnosis, management/treatment, prevention)
  - Comprehensive review of donor derived leukemia (ALL, AML, MDS) including donor sources, genetics, treatment and maintenance strategies, pathophysiology, and guidelines for genetic screening of donors for ASCT to reduce likelihood of donor derived leukemia relapse after ASCT.
- Study population (adult/peds, allo/auto)
  - Adults and children who have received allogenic stem cell transplant and subsequently developed donor derived leukemia

#### C. Methodology

- Search strategy including selection/inclusion and analytic steps used based on the type of review proposed.
  - PubMed, OVID, general web search for retrospective analyses of donor derived leukemia development after ASCT from large cohorts, as well as cases of donor cell leukemia reported individually
  - Articles will be selected that are available in the English language, or language that can be reliably interpreted for for inclusion
- Study Selection
  - Type of Study (prospective, retrospective, etc.)
    - Retrospective studies and case reports will be included
  - Assessment of quality of studies
    - Because donor derived leukemia is rare and detection methods for cell of origin are not used in all cases of leukemia relapse after ASCT, often case reports are the primary source of clinical details for patients with donor derived leukemia

#### D. Expected Scientific Impact

Relapse of leukemia is a significant cause of morbidity and mortality after bone marrow transplant. Though accounting for a small portion of relapse leukemia after transplant, donor derived leukemia is estimated in up to 2-5% of those relapses<sup>1,2</sup>. Donor derived leukemia carries a very poor prognosis with life expectancy approximately 9 months in cases reported in the literature, and genetic screening of donors is infrequent<sup>2</sup>. The proposed article aims to put forth consensus guidelines for standard molecular analysis for leukemia relapse after ASCT to enable more accurate determination of incidence of donor derived leukemia. Further, donor genetic screening guidelines will provide means to reduce the likelihood of transplantation of pre-leukemic disease during ASCT. For example, germline *GATA2* have been reported in 8 families, including ASCT resulting in donor derived leukemia<sup>3</sup>.

These consensus guidelines will parse out the role of detailed family history, germline genetic screening, and benefit of testing for somatic mutations and clonal hematopoiesis for donors prior to ASCT. The guidelines will also standardize molecular analysis to detect donor derived malignancy among relapse leukemia after ASCT.

E. Implications for Research/Practice/Policy:

These consensus guidelines would influence best practice for donor selection. Detection of germline or somatic genetic mutations in donors presents ethical considerations for disclosing this information to the donors, which must be assessed by the expert panel. These additional steps in donor selection also increase the logistical and financial impact of donor selection. Given the poor prognosis of median life expectancy of 9 months after donor derived leukemia diagnosis, this diagnosis presents a large burden for the patient's life and the financial structure for treating the recurrent leukemia. Thus while adding donor selection guidelines increases financial and logistical requirements, there is high level of need to address the role of genetic screening of donors prior to ASCT.

### References:

- 1 Wiseman DH. Donor cell leukemia: a review. *Biol Blood Marrow Transplant J Am Soc Blood Marrow Transplant* 2011; **17**: 771–789.
- 2 Williams L, Doucette K, Karp JE, Lai C. Genetics of donor cell leukemia in acute myelogenous leukemia and myelodysplastic syndrome. *Bone Marrow Transplant* 2021; **56**: 1535–1549.
- 3 Galera P, Hsu AP, Wang W, Droll S, Chen R, Schwartz JR *et al*. Donor-derived MDS/AML in families with germline GATA2 mutation. *Blood* 2018; **132**: 1994–1998.

### Are you a Young Investigator (Within 10 years of obtaining an MD, PhD, RN, or other)?

Yes

No

### Conflicts of Interest:

*Do you have any conflicts of interest pertinent to this proposal concerning:*

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

Yes

No

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

**Deadline for submission: 1/15/22**

**E-mail your completed form to:**

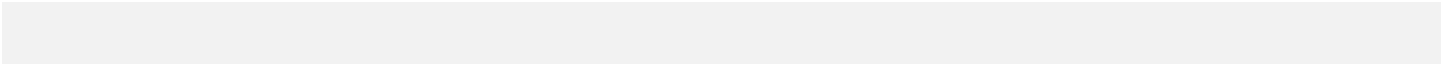
Alyssa Carlson [Alyssa.Carlson@NMDP.ORG](mailto:Alyssa.Carlson@NMDP.ORG)

**Contact Information:** [Lacey.S.Williams@Medstar.Net](mailto:Lacey.S.Williams@Medstar.Net)

**Lacey Williams, MD**

**Hematology, Oncology Fellow**

**Medstar Georgetown University Hospital**







**CIBMTR Donor Safety Working Committee Review Proposal**  
**(ALL SECTIONS MUST BE COMPLETED.)**

**Review Topic**

We would like to review the safety of G-CSF (filgrastim) for mobilization in donors, both healthy donors or donors for autologous transplant.

Proposed title, tentative

Myeloid Growth Factors for Mobilization of Stem Cells: Do We Know the Whole Story Yet?

- G-CSF is almost used exclusively for the mobilization of healthy donors. It has been associated, and in some cases, even “rumored” to have several side effects. Listed here briefly: pulmonary hypersensitivity, splenic rupture, induction/contribution to pathogenesis of myeloid neoplasms such as AML or MDS, induction/contribution to the pathogenesis of autoimmune diseases, hyperviscosity. It certainly causes bony pain and the management and recovery from that is not clear (2 days vs 5 days, need for narcotic pain medications, time off work, etc).
- Furthermore, in BMT in particular, there are more concerns about contamination of grafts in recipients of autologous grafts with tumor cells. There are concerns for donor safety when it comes to allogeneic grafts. Several of these concerns are not well founded in the literature.
- There has not been any recent review in the literature that I can find about this
- There are newer agents available now with longer half-lives, different formulations, biosimilars
- The use of them have become widespread and they frequently used in oncology, but also in benign conditions
- New research has come out to other beneficial pleiotropic effects such as help with cardiac remodeling
- Most recently, impact of G-CSF on inducing “cytokine storm” in the setting of past COVID infections (extrapolated from GM-CSF’s role in CAR-T)

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Academic Rank:

Email Address:

Institution Name:

**Type of Review**

- Expert Opinion/Consensus Guidelines  
 Comprehensive Review  
 Meta-Analysis  
 Narrative  
 Cochrane  
 Scoping

**Brief Summary and/or Brief Outline of Review:**

## A. Brief overview of topic

- When/if a similar review has been published previously and/or in a different patient population
- Current gaps in the literature

The most relevant review that I can find is in 2007 and still not exactly on point:  
 (Tigue et al., 2007)

## B. Main objective(s) of review

- Focus (cause, prognosis, diagnosis, management/treatment, prevention)
- Study population (adult/peds, allo/auto)

The main objective will be to review available literature about the safety of Filgrastim and other relevant growth factors and conclude with expert guidelines about the use in healthy donors as well as in oncology and other fields.

## C. Methodology

- Search strategy including selection/inclusion and analytic steps used based on the type of review proposed.
- Study Selection
  - Type of Study (prospective, retrospective, etc.)
  - Assessment of quality of studies

We will search the relevant databases using MeSH terms “myeloid growth factor”, “filgrastim”, “pegfilgrastim”, “linograstim”, “G-CSF”, and review relevant data, summarize and tabulate, and issue guidelines.

We will also want to review all data available to the donor safety committee on long-term impact of G-CSF.

## D. Expected Scientific Impact

As research around the role of myeloid cells in various disease states evolves, the manipulation of these cells is only going to increase. I expect this review to be heavily cited as we aim to make it comprehensive in regards to what is available in the literature and what experts who utilize these medications everyday think.

## E. Implications for Research/Practice/Policy:

This would help counsel patients better prior to initiation of G-CSF. It would also help with future research looking for a clear document regarding the use of G-CSF, in addition to potential effects of supra- and sub-physiologic doses of it.

**References:**

Cesaro, S., Marson, P., Gazzola, M. V., De Silvestro, G., Destro, R., Pillon, M., Calore, E., Messina, C., & Zanesco, L. (2002). The use of cytokine-stimulated healthy donors in allogeneic stem cell

transplantation. *Haematologica*, 87(8 Suppl), 35–41.

DiPersio, J. F., Ho, A. D., Hanrahan, J., Hsu, F. J., & Fruehauf, S. (2011). Relevance and clinical implications of tumor cell mobilization in the autologous transplant setting. *Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation*, 17(7), 943–955. <https://doi.org/10.1016/j.bbmt.2010.10.018>

Kobbe, G., Bruns, I., Fenk, R., Czibere, A., & Haas, R. (2009). Pegfilgrastim for PBSC mobilization and autologous haematopoietic SCT. *Bone Marrow Transplantation*, 43(9), 669–677. <https://doi.org/10.1038/bmt.2009.59>

Tabbara, I. A., Ghazal, C. D., & Ghazal, H. H. (1997). The role of granulocyte colony-stimulating factor in hematopoietic stem cell transplantation. *Cancer Investigation*, 15(4), 353–357. <https://doi.org/10.3109/07357909709039739>

Takano, H., Ohtsuka, M., Akazawa, H., Toko, H., Harada, M., Hasegawa, H., Nagai, T., & Komuro, I. (2003). Pleiotropic effects of cytokines on acute myocardial infarction: G-CSF as a novel therapy for acute myocardial infarction. *Current Pharmaceutical Design*, 9(14), 1121–1127. <https://doi.org/10.2174/1381612033455008>

Takano, H., Ueda, K., Hasegawa, H., & Komuro, I. (2007). G-CSF therapy for acute myocardial infarction. *Trends in Pharmacological Sciences*, 28(10), 512–517. <https://doi.org/10.1016/j.tips.2007.09.002>

Tigue, C. C., McKoy, J. M., Evens, A. M., Trifilio, S. M., Tallman, M. S., & Bennett, C. L. (2007). Granulocyte-colony stimulating factor administration to healthy individuals and persons with chronic neutropenia or cancer: An overview of safety considerations from the Research on Adverse Drug Events and Reports project. *Bone Marrow Transplantation*, 40(3), 185–192. <https://doi.org/10.1038/sj.bmt.1705722>

**Are you a Young Investigator (Within 10 years of obtaining an MD, PhD, RN, or other)?**

Yes

No

**Conflicts of Interest:**

*Do you have any conflicts of interest pertinent to this proposal concerning:*

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

Yes

No

*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.*

Insert here

**Deadline for submission: 1/15/22**

**E-mail your completed form to:**

**Contact Information:**

**Alyssa Carlson [Alyssa.Carlson@NMDP.ORG](mailto:Alyssa.Carlson@NMDP.ORG)**



**CIBMTR Donor Safety Working Committee Review Proposal**  
**(ALL SECTIONS MUST BE COMPLETED.)**

**Review Topic**

What is the relationship between donor red blood cell characteristics and collection efficiency in peripheral blood stem cell donors?

**1st PI Information:**

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**4th PI Information if applicable:**

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Institution Name: Medstar Georgetown University Hospital

**Type of Review**

- Expert Opinion/Consensus Guidelines
- Comprehensive Review
- Meta-Analysis
- Narrative
- Cochrane
- Scoping

**Brief Summary and/or Brief Outline of Review:**

Brief overview of topic:

Venous leukapheresis of stimulated hematopoietic stem cells has become an important instrument for stem cell transplantation. Stem cell mobilization is measured by the degree of leukocytosis and number of CD34+ cells mobilized to the peripheral blood after five days of high dose filgrastim. Collection efficiency can be calculated by comparing the CD34+ count in the peripheral blood to the overall apheresis product yield. Collection efficiency can be impacted by a variety of variables to include quality of the venous access, apheresis machine settings/collection preference, and donor's peripheral white blood cell (WBC), red blood cell (RBC), and CD34+ counts.

Cell layer separation during leukapheresis can also be affected by red cell abnormalities, particularly when red cell mean corpuscular volumes (MCV) are decreased. This can lead to lower than expected CD34 cell yields (Constaninou et al, 2017; Wang et al, 2013). Under these circumstances extended apheresis periods may be required, imposing an undue burden on allogeneic stem cell donors. Clear guidelines correlating apheresis machine cell separation settings with red cell MCVs are missing.

Main objective(s) of review:

The objective of this study is to determine if there is a correlation between CD34 cell yield and red cell abnormalities in stimulated peripheral leukapheresis using red cell MCV as a surrogate marker. A secondary outcome is to identify a critical MCV level at which cell separation settings of apheresis machines should be adjusted towards smaller cell volumes.

Methodology:

224 consecutive donors (related and unrelated) who underwent a peripheral stem cell harvest between January 2021 and December 2021 at the Georgetown University Blood and Marrow Collection Program (BMCP) will be analyzed by retrospective chart review. Data will be extracted manually from electronic medical records. Linear and multivariate regression analysis will be performed to correlate CD34+ yields in the HPCA product with donor red cell MCV and peripheral CD34 levels.

Expected Scientific Impact:

We aim to provide insight and guidance for collection centers to manage donors with lower MCV counts and to successfully meet transplant center's hematopoietic progenitor cell (HPC) request (Bryant et al, 2009). We also aim to establish guidelines for optimal apheresis settings for a variety of red cell MCV levels. Guidelines could serve to improve collection yields and prevent donors from having to undergo extended apheresis with additional stem cell mobilization.

Implications for Research/Practice/Policy:

This study has the potential to impact future practice leading to multiple benefits for collection centers, transplant centers, and stem cell donors. The primary outcome is to facilitate the generation of a higher quality stem cell product which will be beneficial to the transplant center (Kalwak, 2010). Preventing additional days of apheresis can benefit the collection centers in essential areas such as staff, supplies and resources. Lastly, the donors will benefit by avoiding a second day of collection which delays donor travel, reduces donor satisfaction, and prolongs recovery.

**References:**

Bryant B, Hopkins J, Arceo S, Leitman S. Evaluation of low red cell mean corpuscular volume in an apheresis donor population. *Transfusion*. 2009; 49: 1971-1976.

Constatinou, V. Bouinta, A. Karponi, G. Zervou, F. Papayanni, P. et al. Poor stem cell harvest may not always be related to poor mobilization: lessons gained from a mobilization study in patients with B-thalassemia major. Transfusion and Cellular Engineering. 2017,54:1031-1039

Kalwak, K, Porwolik J, Mielcarek M, Gorczynska E, Owoc-Lempach J, Ussowicz M et al. Higher incidence of severe acute or chronic graft versus-host disease after in vivo T cell-depleted unrelated donor hematopoietic stem cell transplantation in children. Biol Blood Marrow Transplant. 2010; 16: 1388-1401.

Wang, T, Cheng, S, Yang, S, Su, Y, Chu, S, Li, D. Poor harvest of peripheral blood stem cell in donors with microcytic red blood cells. Transplantation and Cellular Engineering. 2013; 53:91-95.

**Are you a Young Investigator (Within 10 years of obtaining an MD, PhD, RN, or other)?**

Yes

No

**Conflicts of Interest:**

*Do you have any conflicts of interest pertinent to this proposal concerning:*

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

Yes

No

*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.*

Insert here

**Deadline for submission: 1/15/22**

**E-mail your completed form to:**

**Contact Information:**

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