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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

A G E N D A
CIBMTR WORKING COMMITTEE FOR DONOR HEALTH AND SAFETY
Houston, TX
Saturday, February 23, 2019, 12:15 – 2:15 pm

Co-Chair:	**Michael Pulsipher, MD, Children's Hospital of Los Angeles, Los Angeles, CA; Telephone: 323-361-2121; E-mail: mpulsipher@chla.usc.edu**
Co-Chair:	**Galen Switzer, PhD, University of Pittsburgh, Pittsburgh, PA; Telephone: 412-246-6564; E-mail: gswitzer@pitt.edu**
Co-Chair:	**Nirali Shah, MD, MHSc, National Cancer Institute – NIH, Bethesda, MD; Telephone: 301-451-0390; E-mail: nirali.shah@nih.gov**
Scientific Director:	**Bronwen Shaw, MD, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0700; E-mail: beshaw@mcw.edu**
Ex Officio Senior Advisor:	**Dennis Confer, CIBMTR Statistical Center, Minneapolis, MN; Telephone: 763-406-3425; E-mail: dconfer@nmdp.org**
Statistical Director:	**Brent Logan, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-955-8849; E-mail: blogan@mcw.edu**
Statisticians:	**Jennifer Sees, MPH, CIBMTR Statistical Center, Minneapolis, MN; Telephone: 763-406-8673; E-mail: jsees@nmdp.org** **Pintip Chitphakdithai, PhD, CIBMTR Statistical Center, Minneapolis, MN; Telephone: 763-406-8309; E-mail: pchitpha@nmdp.org**

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1. **Introduction**
   a. Minutes and Overview Plan from February 2018 meeting (Attachment 1)
   b. Introduction of incoming elected Co-Chair: **Jack Hsu,** MD, Shands HealthCare and University of Florida, Gainesville, FL; Telephone: 352-273-7832; E-mail: hsujw@medicine.ufl.edu

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

3. **Presentations, published or submitted papers**
   a. **DS17-02** Farhadfar N, Murthy H, Khanal M, Ahn KW, Logan BR, Sees JA, Chitphakdithai P, Confer DL, Pulsipher MA, Shah N, Switzer GE, Shaw BE, Wingard JR. Impact of Autologous Blood Transfusion after Bone Marrow Harvest on Donor Health and Outcome. ***Poster Presentation at TCT 2019 in Houston, TX.***
   b. **DS16-01** Hsu JW, Kim S, Logan BR, Sees JA, Chitphakdithai P, Confer DL, Pulsipher MA, Shah N, Switzer GE, Shaw BE, Wingard JR. Peripheral Blood Stem Cell Collection in One Day is Preferable to Two Days in Unrelated Donors. ***Poster Presentation at TCT 2019 in Houston, TX.***
   c. **DS05-02e** Pulsipher MA, Logan BR, Kiefer DM, Chitphakdithai P, Riches ML, Rizzo JD, Anderlini P, Leitman SF, Varni JW, Kobusingye H, Besser RM, Miller JP, Drexler RJ, Abdel-Mageed A, Ahmed IA, Ball ED, Bolwell BJ, Bunin NJ, Cheerva A, Delgado DC, Dvorak CC, Gillio AP, Hahn TE, Hale GA, Haight AE, Hayes-Lattin BM, Kasow KA, Linenberger M, Magalhaes-Silverman M, Mori S, Prasad VK, Quigg TC, Sahdev I, Schriber JR, Shenoy S, Tse WT, Yanik GA, Navarro WH,

Horowitz MM, Confer DL, Shaw BE, Switzer GE. Higher risks of toxicity and incomplete recovery in 13-17 year old females after marrow donation: RDSafe peds results. ***Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2018.12.765. Epub 2018 Dec 31.***

d. **DS16-S1** Wiener L, Hoag JA, Pelletier W, Shah NN, Shaw BE, Pulsipher MA, Bruce J, Bader P, Willasch AM, Dalissier A, Guilcher G, Anthias C, Confer DL, Sees JA, Logan B, Switzer GE. Transplant Center Practices for Psychosocial Assessment and Management of Pediatric Hematopoietic Stem Cell (HSC) Donors. ***Submitted to BBMT Nov 2018***

e. **DS05-02a** Pulsipher MA, Logan BR, Chitphakdithai P, Kiefer DM, Riches ML, Rizzo JD, Anderlini P, Leitman SF, Varni JW, Kobusingye H, Besser RM, Miller JP, Drexler RJ, Abdel-Mageed A, Ahmed IA, Akard LP, Artz AS, Ball ED, Bayer R-L, Bigelow C, Bolwell BJ, Broun ER, Bunin NJ, Delgado DC, Duckworth K, Dvorak CC, Hahn TE, Haight AE, Hari PN, Hayes-Lattin BM, Jacobsohn DA, Jakubowski AA, Kasow KA, Lazarus HM, Liesveld JL, Linenberger M, Litzow MR, Longo W, Magalhaes-Silverman M, McCarty JM, McGuirk JP, Mori S, Prasad VK, Rowley SD, Rybka WB, Sahdev I, Schriber JR, Selby GB, Shaughnessy PJ, Shenoy S, Spitzer T, Tse WT, Uberti JP, Vusirikala M, Waller EK, Weisdorf DJ, Yanik GA, Navarro WH, Horowitz MM, Switzer GE, Shaw BE, Confer DL. The effect of aging and pre-donation comorbidities on the related pbsc donor experience: A report from the Related Donor Safety Study (RDSafe). ***Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2018.11.004. Epub 2018 Nov 10.***

f. **DS17-01** Farhadfar N, Hsu JW, Logan BR, Sees JA, Chitphakdithai P, Confer DL, Pulsipher MA, Shah NN, Switzer GE, Shaw BE, Wingard JR. Weighty choices: selecting optimal G-CSF doses for stem cell mobilization to optimize yield. ***Oral Presentation at ASH 2018 in San Diego, CA.***

g. **DS13-01** Prokopishyn N. The Quality of Harvested Bone Marrow for Transplantation Has Decreased Over Time -Implications & Solutions. ***Oral Presentation at NMDP Council 2018 in Minneapolis, MN.***

h. **DS16-01** Hsu J. One versus Two day apheresis in unrelated donors ***Oral Presentation at NMDP Council 2018 in Minneapolis, MN.***

i. **DS13-01** Prokopishyn NL, Logan BR, Kiefer DM, Sees JA, Chitphakdithai P, Ahmed IA, Anderlini PN, Beitinjaneh AM, Bredeson C, Cerny J, Chhabra S, Daly A, Diaz MA, Farhadfar N, Frangoul HA, Ganguly S, Gastineau DA, Gergis U, Hale GA, Hematti P, Kamble RT, Kasow KA, Lazarus HM, Liesveld JL, Murthy HS, Norkin M, Olsson RF, Papari M, Savani BN, Szer J, Waller EK, Wirk B, Yared JA, Pulsipher MA, Shah NN, Switzer GE, O'Donnell PV, Confer DL, Shaw BE. The concentration of total nucleated cells in harvested bone marrow for transplantation has decreased over time. ***Submitted to BBMT Nov 2018.***

j. **DS05-02c** Pulsipher MA, Logan BR, Kiefer DM, Chitphakdithai P, Riches ML, Rizzo JD, Anderlini P, Leitman SF, Kobusingye H, Besser RM, Miller JP, Drexler RJ, Abdel-Mageed A, Ahmed IA, Akard LP, Artz AS, Ball ED, Bayer R-L, Bigelow C, Bolwell BJ, Broun ER, Delgado DC, Duckworth K, Dvorak CC, Hahn TE, Haight AE, Hari PN, Hayes-Lattin BM, Jacobsohn DA, Jakubowski AA, Kasow KA, Lazarus HM, Liesveld JL, Linenberger M, Litzow MR, Longo W, Magalhaes-Silverman M, McCarty JM, McGuirk JP, Mori S, Parameswaran V, Prasad VK, Rowley SD, Rybka WB, Sahdev I, Schriber JR, Selby GB, Shaughnessy PJ, Shenoy S, Spitzer T, Tse WT, Uberti JP, Vusirikala M, Waller EK, Weisdorf DJ, Yanik GA, Navarro WH, Horowitz MM, Switzer GE, Confer DL, Shaw BE. Related peripheral blood stem cell donors experience more severe symptoms and less complete recovery at 1-year compared to unrelated donors Haematologica. doi:10.3324/haematol.2018.200121. Epub 2018 Oct 31.

k. **DS16-S2** Steftel M, Formanek M, Burns L, Chitphakdithai P, Confer D, Kiefer D, Lee S, Logan B, O'Donnell P, Pulsipher M, Shah N, Switzer G, Shaw B. Screening And Management For Clonal

Hematopoiesis In Related Allogeneic Donors: An International Survey on Behalf of the CIBMTR. ***Poster Presentation at CBMTG 2018 in Ottawa, Canada.***

l. **DS16-S1** Wiener L, Hoag JA, Pelletier W, Shah NN, Shaw BE, Pulsipher MA, Bruce J, Bader P, Willasch AM, Dalissier A, Guilcher G, Anthias C, Confer DL, Sees JA, Logan B, Switzer GE. Transplant Center Practices for Psychosocial Assessment and Management of Pediatric HSC Donors. ***Poster Presentation at ASPHO/PBMTC 2018 in Pittsburgh, PA.***

m. **DS16-S2** Steftel M, Formanek M, Burns L, Chitphakdithai P, Confer D, Kiefer D, Lee S, Logan B, O'Donnell P, Pulsipher M, Shah N, Switzer G, Shaw B. Screening And Management For Clonal Hematopoiesis In Related Allogeneic Donors: An International Survey on Behalf of the CIBMTR. ***Poster Presentation at EMBT 2018 in Lisbon, Portugal.***

4. Studies in progress (Attachment 3)

a. **DS05-02d** RDSafe-d: QoL for related adult donors compared to unrelated adult donors (G Switzer/M Pulsipher) **Manuscript Prep**

b. **DS05-02g** RDSafe-g: Late toxicities and SAE for related donors (M Pulsipher) **Analysis**

c. **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) **Protocol Development**

d. **DS16-01** One vs two day apheresis in URD (J Hsu/J Wingard) **Manuscript Prep**

e. **DS16-S2** Survey of the screening and management for clonal disorders of hematopoiesis in related ALLO donors (M Seftel) **Manuscript Prep**

f. **DS17-01** The impact of donor body mass index on collection of Filgrastim (G-CSF) mobilized peripheral blood progenitor cells from unrelated donors (N Farhadfar/J Hsu/JR Wingard) **Manuscript Prep**

g. **DS17-02** Impact of Collection of Autologous Blood prior to Bone Marrow Harvest on Unrelated Donor Heath and Outcome (N Farhadfar/JR Wingard/H Murthy) **Manuscript Prep**

h. **DS18-01** To quantify age-related clonal hematopoiesis in healthy marrow and blood donors that may affect the clinical outcome of recipients following hematopoietic stem cell transplantation (HCT) (T Druley) **Manuscript Prep**

i. **DS18-02** Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections (SR Panch/DF Stroncek/B Savani/NN Shah) **Data File Prep**

5. Future/proposed studies

a. **PROP 1811-132** Effect of Donor Graft Cryopreservation on Allogeneic Transplant Recipient Outcomes (JW Hsu/ N Farhadfar/H Murthy/JR Wingard) (Attachment 4)

b. **PROP 1812-06** The Impact of pre-apheresis Health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome (N Farhadfar/JR Wingard/GE Switzer) (Attachment 5)

6. Other business

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

CIBMTR®
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MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR DONOR HEALTH AND SAFETY
Salt Lake City, UT
Friday, February 23, 2018, 12:15 – 2:15 pm

Co-Chair:	**Galen Switzer, PhD, University of Pittsburgh, Pittsburgh, PA; Telephone: 412-246-6564; E-mail: switzerge@upmc.edu**
Co-Chair:	**Michael Pulsipher, MD, Children's Hospital of Los Angeles, Los Angeles, CA; Telephone: 323-361-2121; E-mail: mpulsipher@chla.usc.edu**
Co-Chair:	**Nirali Shah, MD, MHSc, National Cancer Institute – NIH, Bethesda, MD; Telephone: 301-451-0390; E-mail: nirali.shah@nih.gov**
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Ex Officio Senior Advisor:	**Dennis Confer, CIBMTR Statistical Center, Minneapolis, MN; Telephone: 763-406-3425; E-mail: dconfer@nmdp.org**
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1. Introduction

Nirali Shah welcomed all attendees and called the meeting to order at 12:16 pm. Drs. Switzer, Pulsipher, and Shah chaired the meeting; B Shaw, Scientific Director, D Confer, Ex Officio Senior Advisor, B Logan, Statistical Director, and P Chitphakdithai and D Kiefer, statisticians, where also present.

Dr. Shah introduced and welcomed Dr. Switzer as a returning chair of the committee. Dr. Halter of Universitätsspital Basel and the EBMT Working Party Chair was also introduced

Goals and expectations of the meeting were addressed. A reminder of the voting process, working committee membership and rules of authorship were summarized.

The committee was reminded that it has been recommended that DSWC accept up to one proposal due to limited statistical hours.

2. Accrual summary

The accrual tables were discussed near the end of the meeting. The accrual summaries (NMDP unrelated donors, NMDP related donors, and sample accruals) were noted to be available in the meeting materials.

3. Presentations, published or submitted papers

Nirali Shah provided recognition of the studies that were presented at national conferences and those studies submitted for publication in the past year.

4. Studies in progress

It was noted that for more details regarding studies in progress to please refer to Attachment 3 available in the online meeting materials, however highlights of several studies were given during the meeting:

a. DS05-02a, e, g RDSafe Studies: (M Pulsipher)

Michael Pulsipher was invited to say a few words regarding the RDSafe studies.

Michael noted that DS05-02c was submitted to JAMA and was deferred and will be resubmitted to Journal of Clinical Oncology. The older donor paper (DS05-02a) is looking at the effective age of the related donor experience and will focus on PBSC donation, and will have the manuscript set out for committee review in the upcoming weeks with the goal of submission to Blood. The acute toxicities paper (DS05-02e) is ready to submit as a companion paper to DS05-02a. Analysis for the SAE paper (DS05-02g) has not yet started.

b. DS05-02d HRQoL RDSafe Study (G Switzer)

Galen Switzer was invited to say a few words regarding the RDSafe HRQoL study.

Galen noted that the older adult donor manuscript on the quality of life side of RDSafe was published as well as two manuscripts for pediatric donors. The study looking at unrelated versus related adult donors (DS05-02d) has been analyzed and drafting of a manuscript is underway.

c. DS16-S1 Evaluation of practice guidelines for the assessment and surveillance FU of pediatric HCT donors (L Wiener/G Switzer)

Galen Switzer was invited to say a few words regarding the Evaluation of practice guidelines for the assessment and surveillance FU of pediatric HCT donors study.

Galen noted that the survey was accepted for an oral presentation at EBMT. Galen gave a brief review of the study results and stressed the high response rate to the extensice questionnaire. He noted that this study is still in analysis, but that the manuscript will follow later in the year.

d. **DS17-02** Impact of Collection of Autologous Blood prior to Bone Marrow Harvest on Unrelated Donor Heath and Outcome (N Farhadfar/JR Wingard/H Murthy)

Bronwen Shaw updated the committee on DS17-02, which was discussed at length at last year's meeting. Quality autologous blood collection data is not available for this study, so the aim has changed to examining autologous blood transfusions rather than collections.

Dr. Nosha Farhadfar was invited to say a few words regarding DS17-02. She added that toxicity data is available for analysis for this study. There were no further updates from other stakeholders. This study will shortly be presented at the statistical center meeting.

5. Future/proposed studies

a. **PROP 1710-17** To quantify age-related clonal hematopoiesis in healthy marrow and PBSC donors that may affect the clinical outcome of recipients following hematopoietic stem cell transplantation (HCT) (T Druley)

Mr. Wing Wong from the Druley Lab presented the proposal "To quantify age-related clonal hematopoiesis in healthy marrow and blood donors that may affect the clinical outcome of recipients following hematopoietic stem cell transplantation (HCT)".

As a person ages, they are more likely to develop mutations. The Clonal Hematopoiesis of Indeterminate Potential (CHIP) technique is now commonly recognized in non-diseased individuals to describe somatic mutations above 2% variant allele frequency in individuals. Mutations in leukemic genes have been found in 95% of healthy individuals.

The hypothesis of the study is that healthy donors may transfer abnormal clones that are silent in the donor, but due to the selection imparted by the transplantation process, correlate with particular outcomes in transplant recipients.

The study requests use of donor pre-HCT lab samples corresponding to several transplant patients from their institution. Of the 30 samples (donors) requested, CIBMTR has 25 donor samples available. Additionally, 10 samples from donors aged 18 to 30 and 10 samples from donors aged 31 to 40 were requested (as controls) and we confirmed availability within the CIBMTR repository.

Comments and questions from discussion:

Throughout the discussion Mr. Wing Wong and Dr. Todd Druley both responded to questions.

Question: Can you expand on the ethics of telling donors about mutations and are you linking this data to donor outcomes?
Response: There are no plans to inform the donors as there is no evidence that allelic mutations can positively predict clinical outcomes. The genes being analyzed are a panel of 80 genes, all associated with pediatric or adult myeloid disease.

Question: What is the age range of the donors you requested samples from as that may be a factor in whether mutations are present or not?

Response: This is data that we will need to obtain from the CIBMTR in our matched-pair donors. We are requesting samples from donors of different age groups as well to normalize the donor's differences in age.

Question: What are you looking to bring back to the transplant community as a result of your study?
Response: There will not be any direct recommendations to the transplant community at this time as the sample size is too small. This is a pilot study to see if the transplant process selects for cells with these mutations. If it does, then there are grounds for further studies.

Several other comments included:
Outcomes of the study are interesting whether the hypothesis is shown to be correct or not.

Twenty-eight of the 30 transplants have a 1-year post-transplant sample that can also be compared.

In general, this proposal was very well received as a pilot study addressing the important biological questions of the impact of allelic mutations in the donor throughout the transplantation process.

b. **PROP 1711-107** Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections (SR Panch/DF Stroncek/B Savani/NN Shah) — (Attachment 5)
Dr. Sandhya Panch presented the proposal "Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections".

About 7% of unrelated donors are asked to donate a subsequent time to the same or different participants. Previous publications (Stroncek et al. BBMT 2018) found that levels of pain, donation-related symptoms, and time to symptom resolution at second donation were similar to the first donation. However, the study showed that the second PBSC donations had lower CD34+ cells, CD34+ cells per liter of whole blood processed, and CD34+ cells/kg donor weight.

The hypothesis of the study is that inter-donation time intervals influence CD34+ cell yields at subsequent donations for those donors donating the same product. As a secondary hypothesis, donor demographics and laboratory parameters will be evaluated as they pertain to CD34+ cell yields at subsequent donations.
There were 468 subsequent PBSC donors identified for this study and 39 subsequent BM donors identified.

Comments and questions from discussion:

Throughout the discussion Dr. David Stroncek commented based on the previous publication.

Question: What is the key outcome that will result from this study? Do you think that poor yields from the first donation will mean poor yields for the second donation?

Response: Poor yields at first donation will probably still be associated with poor yields at second donation. However, a shorter time interval between donations may be associated with worse yields than longer time intervals between donations. Subsequent donations with interval time of longer than 9 months may actually help to improve yield based on previously published work.

Question: So by the end of the study do you think you'll have an algorithm that can determine the suitability of a donor based on the last time they donated?
Response: That is an assumption we are making that there is a relationship between first and second donation. Based on previous literature, there is some evidence that there is a relationship, but this needs to be more clearly defined.

Question: Do we know that the donors only received G-CSF and the doses of that G-CSF? Should the second donation be very consistent with the first donation?
Response: Yes.

Question: Have you thought about looking at donors who cross-donate between bone marrow and PBSC?
Response: We decided not to look at patients that were crossing over across source donations. This would be a complicated statistical question to answer. Additionally selection bias may exist based on what the center asked for as far as donor graft source.

Question: Do second donations occur for a patient event, and how can we account for the time interval if that is the case?
Response: Sometimes a donation occurs for a patient event and sometimes it's not. Less than half of second donations were to the same donor in the previous study. There is a fairly common graft pattern of bone marrow first and PBSC second so when you're giving the same product the probability of the product going to the same recipient is lower.

Question: How do you account for lab values and count variability between centers?
Response: A large sample size will help limit this variation. Additionally, the data we have is collected from the same source (ie consistent centers provide the data).

Other comments:

Thirty-nine bone marrow donors is not enough to effectively answer this question. Additionally, CD34+ cell counts were not added to the forms until recently as an optional field, so there will not be that much data available. Since in bone marrow TNC is the target, looking at CD34+ for bone marrow may be inappropriate.

Eliminating the cross-source donors may bias the sample time interval since if the time interval is small, a separate source may be considered instead of the same original source.

The committee was very interested in this study, particularly to follow-up on the previous (unexpected) findings from the recent Stoncek publication.

At the conclusion of the proposals being presented the co-chairs reminded members to vote on a scale of 1 (high scientific impact) to 9 (low scientific impact) and to turn in both their ballets and evaluation forms.

6. Other business

a. Prospective Study. Identifying Predictors of Poor Health-Related Quality-of-life among Pediatric Hematopoietic Stem Cell Donors (G Switzer)

Galen Switzer was invited to say a few words regarding his recently R01 funded prospective study.

The study will interview related donors, recipients, and their families. This study builds on the findings of the quality of life surveys performed in children during RDSafe, which found that a third of donors were below the cut-off for ill-health in their self-reported QOL. The goal of this study it to determine the source of poor donor quality of life by comparing related donor families and the recipients, unrelated recipient families, and healthy matched normative samples. Once completed, the study will be able to be used as a tool to develop intervention studies or guideline recommendations pertaining to related donations.

Comments and questions from discussion:

Question: Will all the siblings be from the same household?
Response: Right now, our working definition will be that the siblings are all living in the same household. We aim to be overly inclusive and adjust for differences on the analytic side.

Question: Will you address ethnic background?
Response: We will collect relatively detailed ethnic background information. For RDSafe we had a diverse population, and we hope to have that in this study as well.

Question: How do you assess whether a center has a donor advocate or not?
Response: Donor advocates will be an individual variable rather than a center-level variable, as programs at a center over time can change drastically. Additionally, one of the outcomes could be the benefits of having a donor advocate and could inform guideline changes.

Question: What do you do if you have different levels of anxiety among parents for example?

Response: What we have done in the past is one of two things. Either we chose a parent that is more responsible or present for the family, or create a composite variable that combines parent's anxiety levels. In addition to that, we have several measures of overall family function.

Question: How do you account for reporting of pain, etc. in younger children?
Response: We use the Ped-QL which has been validated for 5 to 7 year olds. In this survey, response categories are collapsed and visual cues accompany the responses. Additionally, the interviewers are highly qualified.

b. Additional business items

Committee members were encouraged to use the accrual tables available in the meeting materials to formulate new donor-related questions for future studies.

The meeting lasted one hour and eleven minutes.

Working Committee Overview Plan for 2017-2018

DS05-02a RDSafe-a: Older adult related donors compared to adult related donors (M Pulsipher)
This study is currently in manuscript preparation. We anticipate this study to be submitted by July 2018.

DS05-02c RDSafe-a: Older adult related donors compared to adult related donors (M Pulsipher)
This study is currently in submission. We anticipate this study to be accepted by July 2018.

DS05-02d RDSafe-d: QoL for related adult donors compared to unrelated adult donors (G Switzer/M Pulsipher)
This study is currently in manuscript preparation. We anticipate this study to be submitted to by July 2018.

DS05-02e RDSafe-e: Acute toxicities for pediatric donors compared to adult related donors (M Pulsipher) - This study is currently in manuscript preparation. We anticipate this study to be submitted to by July 2018.

DS05-02g RDSafe-g: Late toxicities and SAE for related donors (M Pulsipher) - This study is currently in analysis. We anticipate this study to be in manuscript preparation by July 2018.

DS13-01 Retrospective examination of the role quantity of bone marrow harvests performed by a harvest center has on the overall quality of the harvested product: Assessment of the potential impacts bone marrow product quality has on utilization of bone marrow as a cell source for transplant (N Prokopishyn) - This study is currently in analysis. We anticipate this study to be submitted by July 2018.

DS13-02 A retrospective analysis to understand the potential mechanisms underlying the clinical impact of ABO incompatibility on allogeneic transplant outcomes (B Shaw) - This study is currently in protocol development. We anticipate this study to be in data file preparation by April 2018, analysis by May 2018, and manuscript preparation by July 2018.

DS16-01 One vs two-day apheresis in URD (J Hsu/J Wingard) - This study is currently in protocol development. We anticipate this study will be in analysis by July 2018.

DS16-S1 Evaluation of practice guidelines for the assessment and surveillance FU of pediatric HCT donors (L Wiener/G Switzer) - This study is a collaboration between University of Pittsburgh and the NIH, with statistical analysis done at University of Pittsburgh. We anticipate this study to be submitted by July 2018.

DS16-S2 Survey of the screening and management for clonal disorders of hematopoiesis in related ALLO donors (M Seftel) - This study is currently in manuscript preparation. It will be presented at EBMT in March 2018. We anticipate this study to be submitted by July 2018.

DS17-01 The impact of donor body mass index on collection of Filgrastim (G-CSF) mobilized peripheral blood progenitor cells from unrelated donors (N Farhadfar) - This study is currently in protocol development. We anticipate this study will be in data file preparation by May 2018, and analysis by July 2018.

DS17-02 Impact of Collection of Autologous Blood prior to Bone Marrow Harvest on Unrelated Donor Heath and Outcome (N Farhadfar) - This study is currently in protocol development. We anticipate this study will be in data file preparation by July 2018.

DS18-01 To quantify age-related clonal hematopoiesis in healthy marrow and blood donors that may affect the clinical outcome of recipients following hematopoietic stem cell transplantation (HCT) (T Druley) - This study is a collaboration with Washington University. Statistical analysis will be done at Washington University. This study is currently in protocol development. We anticipate this study will be in manuscript preparation by July 2019.

DS18-02 Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections (SR Panch/DF Stroncek/B Savani/NN Shah) - This study is currently in protocol development. We anticipate this study will be in data file preparation by July 2018.

Oversight Assignments for Working Committee Leadership (March 2018)

Bronwen Shaw	**DS13-02** Clinical impact of ABO incompatibility on alloHCT [Statistical Center Study]
Dennis Confer	**DS05-02a-DS05-02h** RDSafe
Galen Switzer	**DS05-02 d, h** RDSafe **DS16-S2** Evaluation of practice guidelines for the assessment and surveillance FU of pediatric HCT donors
Michael Pulsipher	**DS05-02a, c, e, g** RDSafe **DS09-03** Effects of second donation on marrow/PBSC donors **DS16-S1** Survey of the screening and management for clonal disorders of hematopoiesis in related ALLO donors **DS17-01** The impact of donor body mass index on collection of G-CSF mobilized peripheral blood progenitor cells from unrelated donors **DS18-02** Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections
Nirali Shah	**DS13-01** Assessment of the potential impacts BM product quality on HCT **DS16-01** One vs two day apheresis in URD **DS17-02** The Impact of Pre-Operative Collection of Autologous Blood for Bone Marrow Harvest on Donor Health and Outcome [Statistical Center Study] **DS18-01** To quantify age-related clonal hematopoiesis in healthy marrow and blood donors that may affect the clinical outcome of recipients following hematopoietic stem cell transplantation (HCT)

Accrual Summary for the Donor Health and Safety Working Committee

Characteristics of domestic unrelated NMDP donors donating between 1987 and September 2018[a]

	Bone marrow	PBSC	Total
Number of donors	23781	31652	55433
Donor age at time of donation			
Median (range)	8279 (35)	14155 (45)	22434 (40)
18 to 29	8056 (34)	8704 (27)	16760 (30)
30 to 39	5793 (24)	6193 (20)	11986 (22)
40 to 49	1653 (7)	2600 (8)	4253 (8)
≥50	35 (18-61)	32 (18-62)	33 (18-62)
Donor race / ethnicity			
Caucasian	17370 (73)	23221 (73)	40591 (73)
Hispanic	2280 (10)	2832 (9)	5112 (9)
Black / African American	1371 (6)	1275 (4)	2646 (5)
Asian / Pacific Islander	1124 (5)	1671 (5)	2795 (5)
American Indian / Alaska Native	283 (1)	269 (1)	552 (1)
Other / multiple race	1098 (5)	2142 (7)	3240 (6)
Decline / unknown	255 (1)	242 (1)	497 (1)
Donor sex			
Male	9437 (40)	11434 (36)	20871 (38)
Female	14344 (60)	20218 (64)	34562 (62)
Number of donations			
1	21401 (90)	28886 (91)	50287 (91)
2	2233 (9)	2664 (8)	4897 (9)
3	147 (1)	102 (<1)	249 (<1)
Donor CMV status			
Positive	160 (1)	154 (<1)	314 (1)
Negative	14178 (60)	18745 (59)	32923 (59)
Unknown / inconclusive	9443 (40)	12753 (40)	22196 (40)
Year of donation			
1987	2 (<1)	0	2 (<1)
1988	80 (<1)	0	80 (<1)
1989	176 (1)	0	176 (<1)
1990	280 (1)	0	280 (1)
1991	433 (2)	0	433 (1)
1992	541 (2)	0	541 (1)

	Bone marrow	PBSC	Total
1993	641 (3)	0	641 (1)
1994	793 (3)	5 (<1)	798 (1)
1995	867 (4)	21 (<1)	888 (2)
1996	1039 (4)	14 (<1)	1053 (2)
1997	1165 (5)	17 (<1)	1182 (2)
1998	1207 (5)	29 (<1)	1236 (2)
1999	1224 (5)	71 (<1)	1295 (2)
2000	1185 (5)	310 (1)	1495 (3)
2001	1056 (4)	454 (1)	1510 (3)
2002	1059 (4)	748 (2)	1807 (3)
2003	878 (4)	989 (3)	1867 (3)
2004	797 (3)	1084 (3)	1881 (3)
2005	645 (3)	1253 (4)	1898 (3)
2006	659 (3)	1374 (4)	2033 (4)
2007	641 (3)	1461 (5)	2102 (4)
2008	662 (3)	1693 (5)	2355 (4)
2009	661 (3)	1822 (6)	2483 (4)
2010	707 (3)	1926 (6)	2633 (5)
2011	748 (3)	2083 (7)	2831 (5)
2012	919 (4)	2470 (8)	3389 (6)
2013	900 (4)	2686 (8)	3586 (6)
2014	871 (4)	2590 (8)	3461 (6)
2015	796 (3)	2475 (8)	3271 (6)
2016	807 (3)	2255 (7)	3062 (6)
2017	810 (3)	2158 (7)	2968 (5)
2018	532 (2)	1664 (5)	2196 (4)
Baseline form[b, c]			
700	11041 (46)	28822 (91)	-
Day of collection, marrow donors[b, d]			
732	11045 (46)	0	-
Day 1 of collection, PBSC donors[b, e]			
730	0	28843 (91)	-
Product form, marrow donors[b, f]			
772	11052 (46)	0	-
First product form, PBSC donors[b, g]			
770	0	28497 (90)	

[a] There have been 4976 bone marrow and 14854 PBSC international donors during this time frame.
[b] Completed with FormsNet1 or FormsNet2 (approximately 2004 and forward).
[c] Form 700 collects information related to vital signs, hematology, MTC, infection, pain, and venous access.
[d] Form 732 collects information related to MTC, infection, pain, vital signs, pre-collection hematology, post-collection hematology, and ABO typing.
[e] Form 730 collects information related to MTC, infection, pain, vital signs, pre-apheresis hematology, post-apheresis hematology, and ABO typing.
[f] Form 772 collects information related to marrow product analysis.
[g] 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.

Characteristics of domestic related NMDP donors donating between 1987 and September 2018[a]

	Bone marrow	PBSC	Total
Number of donors	28	99	127
Donor age at time of donation			
Median (range)	7 (25)	7 (7)	14 (11)
18 to 29	8 (29)	17 (17)	25 (20)
30 to 39	7 (25)	21 (21)	28 (22)
40 to 49	6 (21)	54 (55)	60 (47)
≥50	40 (19-59)	51 (22-61)	49 (19-61)
Donor race / ethnicity			
Caucasian	12 (43)	65 (66)	77 (61)
Hispanic	4 (14)	10 (10)	14 (11)
Black / African American	9 (32)	10 (10)	19 (15)
Asian / Pacific Islander	2 (7)	6 (6)	8 (6)
Other / multiple race	1 (4)	7 (7)	8 (6)
Decline / unknown	0	1 (1)	1 (1)
Donor sex			
Male	13 (46)	47 (47)	60 (47)
Female	15 (54)	52 (53)	67 (53)
Number of donations			
1	28 (100)	97 (98)	125 (98)
2	0	2 (2)	2 (2)
Donor CMV status			
Positive	15 (54)	50 (51)	65 (51)
Negative	13 (46)	48 (48)	61 (48)
Unknown / inconclusive	0	1 (1)	1 (1)
Year of donation			
2009	0	1 (1)	1 (1)
2012	0	1 (1)	1 (1)
2013	0	5 (5)	5 (4)
2014	1 (4)	2 (2)	3 (2)
2015	1 (4)	6 (6)	7 (6)
2016	4 (14)	11 (11)	15 (12)
2017	15 (54)	34 (34)	49 (39)
2018	7 (25)	39 (39)	46 (36)

	Bone marrow	PBSC	Total
Baseline form[b, c]			
700	28 (100)	99 (100)	-
Day of collection, marrow donors[b, d]			
732	28 (100)	0	-
Day 1 of collection, PBSC donors[b, e]			
730	0	99 (100)	-
Product form, marrow donors[b, f]			
772	28 (100)	0	-
First product form, PBSC donors[b, g]	0	98 (>99)	
770			-

[a] There have been 0 bone marrow and 6 PBSC international donors during this time frame.

[b] Completed with FormsNet1 or FormsNet2 (approximately 2004 and forward).

[c] Form 700 collects information related to vital signs, hematology, MTC, infection, pain, and venous access.

[d] Form 732 collects information related to MTC, infection, pain, vital signs, pre-collection hematology, post-collection hematology, and ABO typing.

[e] Form 730 collects information related to MTC, infection, pain, vital signs, pre-apheresis hematology, post-apheresis hematology, and ABO typing.

[f] Form 772 collects information related to marrow product analysis.

[g] 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.

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

	GMARROW[a]	MARROW	PBSC	Total
Variable	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)

[a] GCSF-primed marrow

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	37744	10623	6882
Source of data			
CRF	21889 (58)	5634 (53)	4225 (61)
TED	15855 (42)	4989 (47)	2657 (39)
Number of centers	249	218	316
Disease at transplant			
AML	12782 (34)	3782 (36)	2223 (32)
ALL	5581 (15)	1464 (14)	1153 (17)
Other leukemia	1312 (3)	328 (3)	227 (3)
CML	3217 (9)	856 (8)	715 (10)
MDS	6063 (16)	1873 (18)	915 (13)
Other acute leukemia	388 (1)	119 (1)	72 (1)
NHL	3579 (9)	951 (9)	559 (8)
Hodgkins Lymphoma	800 (2)	162 (2)	120 (2)
Plasma Cell Disorders, MM	766 (2)	228 (2)	108 (2)
Other malignancies	54 (<1)	13 (<1)	17 (<1)
Breast cancer	7 (<1)	3 (<1)	1 (<1)
SAA	1191 (3)	297 (3)	280 (4)
Inherited abnormalities erythrocyte diff fxn	665 (2)	184 (2)	127 (2)
SCIDs	648 (2)	186 (2)	182 (3)
Inherited abnormalities of platelets	38 (<1)	9 (<1)	9 (<1)
Inherited disorders of metabolism	261 (1)	63 (1)	80 (1)
Histiocytic disorders	332 (1)	83 (1)	71 (1)
Autoimmune disorders	16 (<1)	7 (<1)	4 (<1)
Other	44 (<1)	15 (<1)	19 (<1)
AML Disease status at transplant			
CR1	6446 (50)	1924 (51)	970 (44)
CR2	2591 (20)	762 (20)	469 (21)
CR3+	257 (2)	70 (2)	50 (2)
Advanced or active disease	3341 (26)	989 (26)	687 (31)
Missing	143 (1)	37 (1)	43 (2)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
ALL Disease status at transplant			
CR1	2643 (47)	730 (50)	464 (40)
CR2	1641 (29)	402 (27)	344 (30)
CR3+	466 (8)	120 (8)	111 (10)
Advanced or active disease	787 (14)	198 (14)	202 (18)
Missing	44 (1)	14 (1)	31 (3)
MDS Disease status at transplant			
Early	1233 (20)	327 (18)	212 (23)
Advanced	4332 (72)	1419 (76)	568 (63)
Missing	457 (8)	114 (6)	124 (14)
NHL Disease status at transplant			
CR1	446 (13)	158 (17)	58 (10)
CR2	664 (19)	166 (18)	93 (17)
CR3+	302 (9)	82 (9)	47 (8)
PR	431 (12)	108 (11)	78 (14)
Advanced	1655 (47)	419 (44)	271 (49)
Missing	50 (1)	9 (1)	9 (2)
Recipient age at transplant			
0-9 years	3381 (9)	833 (8)	898 (13)
10-19 years	3499 (9)	871 (8)	820 (12)
20-29 years	4018 (11)	1092 (10)	855 (12)
30-39 years	4481 (12)	1152 (11)	887 (13)
40-49 years	5945 (16)	1647 (16)	1104 (16)
50-59 years	7884 (21)	2177 (20)	1205 (18)
60-69 years	7285 (19)	2369 (22)	975 (14)
70+ years	1251 (3)	482 (5)	138 (2)
Median (Range)	46 (0-84)	49 (0-79)	40 (0-79)
Recipient race/ethnicity			
Caucasian, non-Hispanic	31488 (85)	8851 (85)	5200 (83)
African-American, non-Hispanic	1728 (5)	446 (4)	296 (5)
Asian, non-Hispanic	809 (2)	351 (3)	233 (4)
Pacific islander, non-Hispanic	49 (<1)	17 (<1)	12 (<1)
Native American, non-Hispanic	143 (<1)	47 (<1)	23 (<1)
Hispanic	2619 (7)	655 (6)	452 (7)
Other	44 (<1)	25 (<1)	21 (<1)
Unknown	864 (N/A)	231 (N/A)	645 (N/A)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Recipient sex			
Male	22065 (58)	6269 (59)	4075 (59)
Female	15679 (42)	4354 (41)	2807 (41)
Karnofsky score			
10-80	12440 (33)	3698 (35)	2071 (30)
90-100	23812 (63)	6374 (60)	4287 (62)
Missing	1492 (4)	551 (5)	524 (8)
HLA-A B DRB1 groups - low resolution			
<=3/6	21 (<1)	25 (<1)	1 (<1)
4/6	204 (1)	75 (1)	29 (<1)
5/6	5329 (14)	1325 (14)	977 (15)
6/6	31770 (85)	7921 (85)	5383 (84)
Unknown	420 (N/A)	1277 (N/A)	492 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	834 (2)	66 (1)	27 (1)
6/8	1639 (4)	105 (2)	117 (3)
7/8	7450 (20)	1297 (19)	934 (23)
8/8	26608 (73)	5482 (79)	3001 (74)
Unknown	1213 (N/A)	3673 (N/A)	2803 (N/A)
HLA-DPB1 Match			
Double allele mismatch	8931 (30)	536 (25)	298 (28)
Single allele mismatch	16049 (54)	1101 (51)	549 (52)
Full allele matched	4646 (16)	522 (24)	206 (20)
Unknown	8118 (N/A)	8464 (N/A)	5829 (N/A)
High resolution release score			
No	397 (1)	156 (43)	362 (67)
Yes	28516 (99)	207 (57)	178 (33)
Unknown	8831 (N/A)	10260 (N/A)	6342 (N/A)
KIR typing available			
No	24082 (64)	10499 (99)	6842 (99)
Yes	13662 (36)	124 (1)	40 (1)
Graft type			
Marrow	14336 (38)	3792 (36)	3234 (47)
PBSC	23388 (62)	6730 (63)	3645 (53)
BM+PBSC	8 (<1)	6 (<1)	2 (<1)
BM+UCB	0	1 (<1)	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
PBSC+UCB	12 (<1)	94 (1)	1 (<1)
Number of cord units			
1	5 (100)	0	1 (100)
Conditioning regimen			
Myeloablative	24422 (65)	6581 (62)	4710 (68)
RIC/Nonmyeloablative	13151 (35)	4000 (38)	2093 (30)
TBD	171 (<1)	42 (<1)	79 (1)
Donor age at donation			
To Be Determined/NA	180 (<1)	1269 (12)	57 (1)
0-9 years	11 (<1)	15 (<1)	0
10-19 years	1043 (3)	307 (3)	145 (2)
20-29 years	16285 (43)	4188 (39)	2531 (37)
30-39 years	10995 (29)	2720 (26)	2168 (32)
40-49 years	7072 (19)	1608 (15)	1499 (22)
50+ years	2158 (6)	516 (5)	482 (7)
Median (Range)	31 (0-69)	30 (0-109)	33 (18-67)
Donor/Recipient CMV serostatus			
+/+	9249 (25)	2887 (28)	1677 (26)
+/-	4528 (12)	1376 (13)	860 (13)
-/+	12323 (33)	3133 (31)	2128 (33)
-/-	11116 (30)	2822 (28)	1874 (29)
CB - recipient +	0	4 (<1)	0
CB - recipient -	0	2 (<1)	0
CB - recipient CMV unknown	0	1 (<1)	0
Unknown	528 (N/A)	398 (N/A)	343 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	1089 (3)	271 (3)	300 (4)
CD34 selection	665 (2)	282 (3)	105 (2)
Tacrolimus + MMF +- others	4514 (12)	1101 (10)	572 (8)
Tacrolimus + MTX +- others (except MMF)	16190 (43)	4697 (44)	1910 (28)
Tacrolimus + others (except MTX, MMF)	1971 (5)	682 (6)	273 (4)
Tacrolimus alone	919 (2)	285 (3)	117 (2)
CSA + MMF +- others (except Tacrolimus)	2583 (7)	581 (5)	566 (8)
CSA + MTX +- others (except Tacrolimus, MMF)	6473 (17)	1656 (16)	2128 (31)
CSA + others (except Tacrolimus, MTX, MMF)	985 (3)	297 (3)	283 (4)
CSA alone	462 (1)	115 (1)	267 (4)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Other GVHD prophylaxis	687 (2)	202 (2)	116 (2)
Missing	1206 (3)	454 (4)	245 (4)
Donor/Recipient sex match			
Male-Male	15602 (42)	4222 (40)	2727 (40)
Male-Female	9473 (25)	2543 (24)	1586 (23)
Female-Male	6359 (17)	1927 (18)	1323 (19)
Female-Female	6134 (16)	1702 (16)	1201 (18)
CB - recipient M	5 (<1)	53 (1)	0
CB - recipient F	7 (<1)	42 (<1)	1 (<1)
Unknown	164 (N/A)	134 (N/A)	44 (N/A)
Year of transplant			
1986-1990	349 (1)	45 (<1)	85 (1)
1991-1995	1795 (5)	448 (4)	610 (9)
1996-2000	3148 (8)	1113 (10)	894 (13)
2001-2005	5002 (13)	987 (9)	1433 (21)
2006-2010	9213 (24)	1853 (17)	1391 (20)
2011-2015	12850 (34)	3618 (34)	1714 (25)
2016-2019	5387 (14)	2559 (24)	755 (11)
Follow-up among survivors, Months			
N Eval	16177	4874	2672
Median (Range)	53 (0-344)	37 (0-325)	51 (0-337)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	5199	1233	1179
Source of data			
CRF	3988 (77)	952 (77)	795 (67)
TED	1211 (23)	281 (23)	384 (33)
Number of centers	144	127	188
Disease at transplant			
AML	1937 (37)	411 (33)	381 (32)
ALL	1060 (20)	259 (21)	268 (23)
Other leukemia	91 (2)	25 (2)	23 (2)
CML	112 (2)	29 (2)	28 (2)
MDS	502 (10)	123 (10)	100 (8)
Other acute leukemia	80 (2)	19 (2)	21 (2)
NHL	367 (7)	81 (7)	80 (7)
Hodgkins Lymphoma	93 (2)	25 (2)	21 (2)
Plasma Cell Disorders, MM	34 (1)	10 (1)	5 (<1)
Other malignancies	10 (<1)	0	0
SAA	89 (2)	28 (2)	21 (2)
Inherited abnormalities erythrocyte diff fxn	149 (3)	46 (4)	30 (3)
SCIDs	235 (5)	67 (5)	83 (7)
Inherited abnormalities of platelets	15 (<1)	3 (<1)	4 (<1)
Inherited disorders of metabolism	308 (6)	80 (6)	76 (6)
Histiocytic disorders	97 (2)	25 (2)	31 (3)
Autoimmune disorders	9 (<1)	0	1 (<1)
Other	11 (<1)	2 (<1)	6 (1)
AML Disease status at transplant			
CR1	966 (50)	219 (53)	192 (50)
CR2	548 (28)	104 (25)	104 (27)
CR3+	51 (3)	6 (1)	11 (3)
Advanced or active disease	364 (19)	80 (20)	72 (19)
Missing	8 (<1)	1 (<1)	2 (1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
ALL Disease status at transplant			
CR1	477 (45)	108 (42)	122 (46)
CR2	397 (37)	100 (39)	95 (35)
CR3+	118 (11)	35 (14)	28 (10)
Advanced or active disease	68 (6)	16 (6)	23 (9)
MDS Disease status at transplant			
Early	161 (32)	30 (25)	46 (46)
Advanced	306 (61)	86 (71)	43 (43)
Missing	34 (7)	5 (4)	10 (10)
NHL Disease status at transplant			
CR1	56 (15)	5 (6)	17 (22)
CR2	68 (19)	17 (21)	20 (25)
CR3+	42 (12)	10 (12)	9 (11)
PR	65 (18)	12 (15)	10 (13)
Advanced	133 (37)	36 (44)	22 (28)
Missing	0	1 (1)	1 (1)
Recipient age at transplant			
0-9 years	1562 (30)	456 (37)	440 (37)
10-19 years	681 (13)	143 (12)	160 (14)
20-29 years	490 (9)	86 (7)	91 (8)
30-39 years	507 (10)	104 (8)	113 (10)
40-49 years	546 (11)	123 (10)	108 (9)
50-59 years	731 (14)	149 (12)	141 (12)
60-69 years	599 (12)	151 (12)	117 (10)
70+ years	83 (2)	21 (2)	9 (1)
Median (Range)	27 (0-81)	22 (0-75)	19 (0-78)
Recipient race/ethnicity			
Caucasian, non-Hispanic	2908 (59)	739 (63)	650 (62)
African-American, non-Hispanic	743 (15)	167 (14)	136 (13)
Asian, non-Hispanic	300 (6)	70 (6)	74 (7)
Pacific islander, non-Hispanic	23 (<1)	2 (<1)	12 (1)
Native American, non-Hispanic	34 (1)	6 (1)	13 (1)
Hispanic	945 (19)	189 (16)	169 (16)
Other	0	1 (<1)	1 (<1)
Unknown	246 (N/A)	59 (N/A)	124 (N/A)
Recipient sex			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Male	2858 (55)	712 (58)	675 (57)
Female	2341 (45)	521 (42)	504 (43)
Karnofsky score			
10-80	1330 (26)	297 (24)	281 (24)
90-100	3728 (72)	851 (69)	829 (70)
Missing	141 (3)	85 (7)	69 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	70 (1)	27 (3)	5 (<1)
4/6	2051 (41)	393 (41)	411 (38)
5/6	2231 (45)	401 (42)	522 (48)
6/6	630 (13)	136 (14)	158 (14)
Unknown	217 (N/A)	276 (N/A)	83 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2478 (56)	405 (58)	474 (54)
6/8	1066 (24)	160 (23)	212 (24)
7/8	594 (13)	89 (13)	127 (14)
8/8	294 (7)	49 (7)	66 (8)
Unknown	767 (N/A)	530 (N/A)	300 (N/A)
HLA-DPB1 Match			
Double allele mismatch	682 (40)	42 (45)	39 (38)
Single allele mismatch	858 (50)	41 (44)	51 (50)
Full allele matched	160 (9)	10 (11)	12 (12)
Unknown	3499 (N/A)	1140 (N/A)	1077 (N/A)
High resolution release score			
No	156 (9)	32 (39)	31 (79)
Yes	1499 (91)	50 (61)	8 (21)
Unknown	3544 (N/A)	1151 (N/A)	1140 (N/A)
KIR typing available			
No	3935 (76)	1227 (>99)	1171 (99)
Yes	1264 (24)	6 (<1)	8 (1)
Cord blood number of units			
1	3609 (69)	0	913 (77)
2	1588 (31)	0	266 (23)
3	2 (<1)	0	0
Unknown	0 (N/A)	1233 (N/A)	0 (N/A)
Graft type			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
UCB	4951 (95)	1138 (92)	1127 (96)
BM+UCB	1 (<1)	1 (<1)	0
PBSC+UCB	247 (5)	94 (8)	52 (4)
Conditioning regimen			
Myeloablative	3433 (66)	805 (65)	773 (66)
RIC/Nonmyeloablative	1756 (34)	426 (35)	403 (34)
TBD	10 (<1)	2 (<1)	3 (<1)
Donor age at donation			
To Be Determined/NA	137 (3)	76 (6)	65 (6)
0-9 years	4642 (89)	976 (79)	1029 (87)
10-19 years	273 (5)	104 (8)	52 (4)
20-29 years	44 (1)	21 (2)	7 (1)
30-39 years	43 (1)	27 (2)	12 (1)
40-49 years	24 (<1)	11 (1)	4 (<1)
50+ years	36 (1)	18 (1)	10 (1)
Median (Range)	4 (0-72)	4 (0-73)	3 (0-67)
Donor/Recipient CMV serostatus			
+/+	1204 (23)	251 (20)	245 (21)
+/-	532 (10)	119 (10)	113 (10)
-/+	966 (19)	223 (18)	217 (18)
-/-	655 (13)	153 (12)	165 (14)
CB - recipient +	1045 (20)	252 (20)	218 (18)
CB - recipient -	714 (14)	187 (15)	178 (15)
CB - recipient CMV unknown	83 (2)	48 (4)	43 (4)
GvHD Prophylaxis			
Ex vivo T-cell depletion	23 (<1)	9 (1)	4 (<1)
CD34 selection	182 (4)	70 (6)	39 (3)
Tacrolimus + MMF +- others	1379 (27)	309 (25)	182 (15)
Tacrolimus + MTX +- others (except MMF)	200 (4)	55 (4)	54 (5)
Tacrolimus + others (except MTX, MMF)	214 (4)	54 (4)	47 (4)
Tacrolimus alone	131 (3)	43 (3)	23 (2)
CSA + MMF +- others (except Tacrolimus)	2453 (47)	518 (42)	586 (50)
CSA + MTX +- others (except Tacrolimus, MMF)	92 (2)	27 (2)	39 (3)
CSA + others (except Tacrolimus, MTX, MMF)	311 (6)	104 (8)	134 (11)
CSA alone	57 (1)	15 (1)	44 (4)
Other GVHD prophylaxis	125 (2)	17 (1)	15 (1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	32 (1)	12 (1)	12 (1)
Donor/Recipient sex match			
CB - recipient M	2858 (55)	712 (58)	674 (57)
CB - recipient F	2341 (45)	521 (42)	504 (43)
CB - recipient sex unknown	0	0	1 (<1)
Year of transplant			
1996-2000	0	2 (<1)	4 (<1)
2001-2005	113 (2)	82 (7)	22 (2)
2006-2010	1783 (34)	406 (33)	425 (36)
2011-2015	2567 (49)	491 (40)	569 (48)
2016-2019	736 (14)	252 (20)	159 (13)
Follow-up among survivors, Months			
N Eval	2515	664	606
Median (Range)	52 (1-176)	37 (2-191)	49 (1-217)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	6033	890	403
Source of data			
CRF	2317 (38)	276 (31)	161 (40)
TED	3716 (62)	614 (69)	242 (60)
Number of centers	82	63	51
Disease at transplant			
AML	1980 (33)	297 (33)	118 (29)
ALL	946 (16)	170 (19)	60 (15)
Other leukemia	141 (2)	26 (3)	19 (5)
CML	206 (3)	20 (2)	14 (3)
MDS	994 (16)	137 (15)	59 (15)
Other acute leukemia	81 (1)	14 (2)	3 (1)
NHL	631 (10)	84 (9)	58 (14)
Hodgkins Lymphoma	134 (2)	18 (2)	17 (4)
Plasma Cell Disorders, MM	182 (3)	30 (3)	15 (4)
Other malignancies	16 (<1)	0	0
Breast cancer	1 (<1)	0	0
SAA	261 (4)	31 (3)	12 (3)
Inherited abnormalities erythrocyte diff fxn	289 (5)	41 (5)	16 (4)
SCIDs	109 (2)	18 (2)	8 (2)
Inherited abnormalities of platelets	9 (<1)	0	0
Inherited disorders of metabolism	8 (<1)	0	0
Histiocytic disorders	31 (1)	2 (<1)	2 (<1)
Autoimmune disorders	5 (<1)	0	0
Other	9 (<1)	2 (<1)	2 (<1)
AML Disease status at transplant			
CR1	1215 (61)	189 (64)	72 (61)
CR2	312 (16)	33 (11)	12 (10)
CR3+	23 (1)	4 (1)	0
Advanced or active disease	423 (21)	69 (23)	32 (27)
Missing	7 (<1)	2 (1)	2 (2)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
ALL Disease status at transplant			
CR1	597 (63)	112 (66)	43 (72)
CR2	257 (27)	35 (21)	10 (17)
CR3+	39 (4)	5 (3)	2 (3)
Advanced or active disease	53 (6)	18 (11)	5 (8)
MDS Disease status at transplant			
Early	175 (18)	19 (14)	6 (10)
Advanced	789 (79)	114 (83)	51 (86)
Missing	30 (3)	4 (3)	2 (3)
NHL Disease status at transplant			
CR1	103 (16)	19 (23)	8 (14)
CR2	124 (20)	14 (17)	11 (19)
CR3+	70 (11)	6 (7)	2 (3)
PR	58 (9)	11 (13)	6 (10)
Advanced	270 (43)	32 (39)	31 (53)
Missing	2 (<1)	1 (1)	0
Recipient age at transplant			
0-9 years	556 (9)	70 (8)	29 (7)
10-19 years	629 (10)	65 (7)	25 (6)
20-29 years	484 (8)	93 (10)	37 (9)
30-39 years	470 (8)	79 (9)	33 (8)
40-49 years	844 (14)	121 (14)	57 (14)
50-59 years	1450 (24)	208 (23)	102 (25)
60-69 years	1402 (23)	225 (25)	109 (27)
70+ years	198 (3)	29 (3)	11 (3)
Median (Range)	50 (0-78)	51 (0-76)	52 (0-74)
Recipient race/ethnicity			
Caucasian, non-Hispanic	3899 (67)	485 (58)	264 (68)
African-American, non-Hispanic	690 (12)	89 (11)	43 (11)
Asian, non-Hispanic	269 (5)	73 (9)	22 (6)
Pacific islander, non-Hispanic	22 (<1)	3 (<1)	0
Native American, non-Hispanic	23 (<1)	1 (<1)	0
Hispanic	909 (16)	184 (22)	60 (15)
Unknown	221 (N/A)	55 (N/A)	14 (N/A)
Recipient sex			
Male	3540 (59)	533 (60)	235 (58)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Female	2493 (41)	357 (40)	168 (42)
Karnofsky score			
10-80	2091 (35)	367 (41)	164 (41)
90-100	3801 (63)	502 (56)	221 (55)
Missing	141 (2)	21 (2)	18 (4)
Graft type			
Marrow	1660 (28)	209 (23)	115 (29)
PBSC	4348 (72)	673 (76)	284 (70)
BM+PBSC	6 (<1)	3 (<1)	0
BM+UCB	19 (<1)	5 (1)	1 (<1)
PBSC+UCB	0	0	3 (1)
Conditioning regimen			
Myeloablative	3530 (59)	518 (58)	217 (54)
RIC/Nonmyeloablative	2469 (41)	367 (41)	179 (44)
TBD	34 (1)	5 (1)	7 (2)
Donor age at donation			
To Be Determined/NA	34 (1)	4 (<1)	2 (<1)
0-9 years	406 (7)	43 (5)	19 (5)
10-19 years	571 (9)	75 (8)	28 (7)
20-29 years	731 (12)	116 (13)	46 (11)
30-39 years	738 (12)	130 (15)	66 (16)
40-49 years	1004 (17)	148 (17)	57 (14)
50+ years	2549 (42)	374 (42)	185 (46)
Median (Range)	46 (0-81)	45 (0-79)	47 (0-76)
Donor/Recipient CMV serostatus			
+/+	2457 (41)	431 (49)	177 (45)
+/-	650 (11)	62 (7)	49 (13)
-/+	1490 (25)	202 (23)	87 (22)
-/-	1347 (23)	178 (20)	77 (20)
Unknown	89 (N/A)	17 (N/A)	13 (N/A)
GvHD Prophylaxis			
Ex-vivo T-cell depletion	65 (1)	19 (2)	3 (1)
CD34 selection	80 (1)	26 (3)	7 (2)
Post-CY + other(s)	1057 (18)	148 (17)	70 (17)
Post-CY alone	32 (1)	8 (1)	3 (1)
TAC + MMF +- other(s) (except post-CY)	698 (12)	59 (7)	25 (6)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
TAC + MTX +- other(s) (except MMF, post-CY)	2520 (42)	331 (37)	196 (49)
TAC + other(s) (except MMF, MTX, post-CY)	557 (9)	195 (22)	45 (11)
TAC alone	51 (1)	7 (1)	2 (<1)
CSA + MMF +- other(s) (except post-CY)	157 (3)	11 (1)	4 (1)
CSA + MTX +- other(s) (except MMF, post-CY)	497 (8)	52 (6)	26 (6)
CSA + other(s) (except MMF, MTX, post-CY)	57 (1)	9 (1)	2 (<1)
CSA alone	53 (1)	8 (1)	2 (<1)
Other(s)	90 (1)	7 (1)	6 (1)
Missing	119 (2)	10 (1)	12 (3)
Donor/Recipient sex match			
Male-Male	1954 (32)	329 (37)	140 (35)
Male-Female	1305 (22)	168 (19)	83 (21)
Female-Male	1569 (26)	199 (22)	94 (23)
Female-Female	1184 (20)	188 (21)	82 (20)
CB - recipient M	15 (<1)	4 (<1)	1 (<1)
CB - recipient F	4 (<1)	1 (<1)	3 (1)
Unknown	2 (N/A)	1 (N/A)	0 (N/A)
Year of transplant			
2006-2010	511 (8)	48 (5)	38 (9)
2011-2015	3239 (54)	455 (51)	206 (51)
2016-2019	2283 (38)	387 (43)	159 (39)
Follow-up among survivors, Months			
N Eval	3825	575	258
Median (Range)	25 (1-126)	23 (2-121)	25 (2-109)

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TO: Donor Health and Safety Working Committee Members

FROM: Bronwen Shaw, MD, PhD; Scientific Director and Dennis Confer, MD; Ex Officio Senior Advisor for the Donor Health and Safety Working Committee

RE: Studies in Progress Summary

DS05-02: Related Donor Safety Study (RDSafe) (M Pulsipher/G Switzer) The goals of this prospective, funded study include comparing the incidence of adverse events, and the quality of life, of related donors to unrelated donors. Pediatric, adult, and older adult (60+ year olds) related donors were enrolled. Enrollment was completed for adult donors on May 31, 2013 and on July 25, 2014 for pediatric donors. The study has been broken down into eight discrete areas reflecting specific analyses, studies not yet completed are listed below. No updates.

DS05-02d: RDSafe-d: HRQoL for related adult donors compared to unrelated adult donors (G Switzer/M Pulsipher) This study seeks to compare health related quality of life differences between related and unrelated adult donors. Currently this study is in manuscript preparation with a goal of submission by July 2019.

DS05-02g: RDSafe-g: Late toxicities and SAE for related donors (M Pulsipher) This analysis will describe any late toxicities or severe adverse events for the related donors followed in RDSafe. This study completed data collection in September 2015 and is in analysis with a goal of submission by July 2019.

DS13-02: Clinical impact of ABO incompatibility on alloHCT (G Murthy/B Shaw) The primary aim of this this study is to examine the impact of ABO mismatching (match, major mismatch, minor mismatch, bidirectional mismatch) on overall survival; secondary effects to examine are the association of ABO matching on graft manipulation method (none vs plasma removal/depletion vs red cell depletion method vs other) and the impact of graft manipulation on infused cell count (CD34/TNC) and transplant outcome. This study is currently in protocol development with a goal of submission by July 2019. No update.

DS16-01: One vs two day apheresis in URD (J Hsu/J Wingard) This study proposes to analyze the outcomes of PBSC donors by one-day vs. two-day collections. This study is currently in manuscript preparation with the goal of submission by July 2019. Poster presented at TCT 2019.

DS16-S2: Survey of the screening and management for clonal disorders of hematopoiesis in related ALLO donors (M Seftel) The primary aims of this survey are to 1) establish whether HCT centers that evaluate related allogeneic donors screen for CDH; 2) understand, if CDH is detected, whether the donor is deferred; 3) understand what other steps donor centers take in order to manage the donor with a CDH. The data has been analyzed and an abstract submitted to EBMT. The survey is currently in manuscript prep. The goal is to submit the study by July 2019. No update.

DS17-01 The impact of donor body mass index on collection of Filgrastim (G-CSF) mobilized peripheral blood progenitor cells from unrelated donors (N Farhadfar/J Hsu/JR Wingard) The primary aim of this study is to evaluate the impact of donor BMI on G-CSF mobilized peripheral blood progenitor cells yield in healthy volunteer donors. The secondary objective of this study is (1) to evaluate whether overweight and obese healthy unrelated donors elicit an appropriate marrow response with a lower G-CSF dose than current standard, and (2) to examine whether there is an 'upper limit' G-CSF dose above which overweight or obese donors have already provided sufficient cells, but experience more side effects. The study is in manuscript preparation with the goal of submission by July 2019. No update.

DS17-02 Impact of Collection of Autologous Blood prior to Bone Marrow Harvest on Unrelated Donor Heath and Outcome (N Farhadfar/JR Wingard/H Murthy) The aim of this study is to assess the impact of autologous blood transfusion on donor outcomes. This study is currently in manuscript preparation with the goal of submission by July 2019. Poster presented at TCT 2019.

DS18-01 To quantify age-related clonal hematopoiesis in healthy marrow and blood donors that may affect the clinical outcome of recipients following hematopoietic stem cell transplantation (HCT) (T Druley) This sample-based study uses donor whole blood, recipient blood/marrow pre-HCT, and recipient's blood/marrow post-HCT following engraftment to determine whether genetic alterations found in the donor are transmitted to the recipient' post-HCT. This study is in collaboration with the Druley lab at Washington University School of Medicine. This study is currently in manuscript prep with the goal of submission by July 2019. (Update by Mr. Wing Hing Wong).

DS18-02 Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections (SR Panch/DF Stroncek/B Savani/NN Shah) This study examines the impact of inter-donation intervals on CD34+ cell and mononuclear cell (PBSC) or TNC (BM) yields of unrelated NMDP donors making two PBSC donations, or two BM donations. This study is currently in data file prep with the goal of analysis by July 2019. No update.

Proposal: 1811-132

Title:
Effect of Donor Graft Cryopreservation on Allogeneic Transplant Recipient Outcomes.

Jack W. Hsu, MD, University of Florida
Nosha Farhadfar, MD, University of Florida
Hemant Murthy, MD, University of Florida
John R. Wingard, MD, University of Florida

Specific aims:
This is a descriptive study that will examine the effect of donor graft cryopreservation on transplant outcomes in allogeneic transplant recipients.
Primary endpoints:

- Time to neutrophil engraftment.
- Time to platelet engraftment.

Secondary endpoints:

- Incidence of acute and Chronic GVHD
- Relapse free and overall survival
- Transplant related mortality
- Primary graft failure
- For cryopreserved grafts (if information is available)
    - Viability
    - Alterations in cellular content of the grafts which can be attributed to the freeze and thaw processes (TNC, lymphocyte content, MNC, CD34+ pre-freeze and post-thaw).

Additionally, if the information is available, this study will investigate the effect of the following time intervals on the above study endpoints:

- between collection of the stem cell product and cryopreservation
- between cryopreservation and thawing/infusion of the stem cell product.

Scientific justification:
Stem cell transplantation has emerged as an acceptable treatment for many hematologic malignancies. An increase in numbers of volunteers registered in the National Donor Registry has improved the chances of finding a match for recipients of allogeneic transplants. The current standard practice is to infuse the graft from the matched donor within 48 hours of collection. However, multiple factors may prevent the rapid infusion of donor graft, requiring that it be cryopreserved for future use.
There is considerable experience with utilization of cryopreserved grafts in the autologous transplant setting, however, not much information is available in the allogeneic setting. Most of the available information on cryopreservation exists in the setting of matched related PBSC donor grafts. A study of 105 patients who were transplanted using cryopreserved PBSC grafts from related donors found no significant difference in rates of engraftment of neutrophils and

platelets.[1] Additionally, there were no statistically significant differences found in recurrence, non-relapse mortality, GVHD, and overall survival. In contrast, a smaller study of 76 patients who underwent allogeneic transplant with cryopreserved PBSC from either related (n=57) or unrelated (n=19) donors found a significant delay in neutrophil and platelet engraftment in cryopreserved grafts as well as an increased risk of extensive chronic GVHD at 1-year post transplant.[2] No differences in 2 year relapse free and overall survival were seen. A retrospective study by the EBMT compared the outcomes of 224 cryopreserved matched related sibling donor PBSC grafts to 107 fresh matched sibling PBSC grafts.[3] That study found more rapid neutrophil engraftment and a higher incidence of acute GVHD in the frozen donor group. No statistically significant differences in disease free survival, overall survival, and chronic GVHD were seen. Considerably less information is available in the setting of bone marrow grafts. A small study of 19 cryopreserved matched related donor bone marrow graft recipients was compared with 19 fresh related donor marrow graft recipients, found no differences in engraftment or incidence of GVHD between the two groups.[4] In contrast, another small study of 10 frozen related donor marrow grafts found no statistically significant differences in engraftment or 100 day survival.[5] However, there was a statistically significant increase in acute graft vs. host disease in the cryopreserved cohort. In the unrelated donor setting, a descriptive study of 10 unrelated cryopreserved bone marrow graft recipients found a time to ANC >500 cells/μL of 22.6 days with 5 of 9 evaluable patients alive at 100 days.[6] In the study by Medd, et al., no statistically significant differences were found in neutrophil or platelet engraftment between cryopreserved and fresh matched PBSC grafts.[2] Unfortunately, due to the very small sample size of these studies no definitive conclusions can be reached.
This study will attempt to determine if there is an impact on recipient outcomes with the use of cryopreserved versus fresh allogeneic donor grafts. The primary endpoint will be neutrophil and platelet engraftment. Secondary endpoints include incidence of acute and chronic GVHD, relapse free survival, and overall survival.

Patient eligibility:

Entry criteria:

- This study will investigate patients who received their first allogeneic transplant for hematologic malignancy from 2008-2017.
- Related and unrelated bone marrow or PBSC donor grafts.

Exclusion criteria:

- Mismatched donors, umbilical cord blood, haploidentical grafts.
- T-cell depleted grafts
- GCSF stimulated bone marrow grafts
- Transplantation for a non-malignant condition.
- Ex-vivo T-cell depletion, CD34+ selection and post-transplant cyclophosphamide in GVHD prophylaxis
- ABO incompatibility between donor and recipient

Study definitions:

- *Time to cryopreservation*: time interval between collection of stem cell product and freezing (it is assumed that the graft would be frozen immediately upon receipt at the transplant center.

- *Duration of Cryopreservation*: for cryopreserved products, defined as the time between cryopreservation and infusion of product into patient.
- *Time to engraftment:* Defined as time between day of transplantation and recovery of neutrophils (ANC>500/mm^3 x3 days) and platelets (platelets > 20,000/mm^3 unsupported by platelet transfusions).

Donor variables:

- Age
- Type (related/unrelated)
- BMI
- Weight
- Gender (male vs. female)
- Race/ethnicity

Graft variables (if information is available):

- Graft composition
    - Total nucleated cell count
    - Mononuclear cell count
    - Absolute lymphocyte count
    - CD34+ cell count
    - For cryopreserved grafts, the above cell counts will be investigated at pre-freeze and post-thaw.
- For cryopreserved products (if information is available)
    - Method of cryopreservation
        - Concentration of DMSO
        - Other cryoprotectants (albumin, glycol, etc.)
    - Post-thaw viability
    - RBC depletion +/-
    - Time to cryopreservation
    - Duration of Cryopreservation

Recipient variables:

Patient-related:

- Age at HCT, years: cut-point determined statistically
- Gender (male vs female)
- Karnofsky performance score: ≥90% vs. <90%
- HCT comorbidity index at transplant 0-2 vs. ≥ 3
- Disease diagnosis
- Disease-Risk Index (low vs. intermediate vs. high/very high; and low/intermediate vs. high/very high)
- Disease status at transplantation
- CMV status (+/+ vs. +/- vs. -/+ vs. -/-)

Transplant related:

- Conditioning regimen: MAC vs. NMA
- TBI dose in conditioning regimen (none vs. ≤450 cGy vs. >450 cGy)
- Cell dose ($CD34^+$ cells for PBSC, TNC for BM graft)
- Graft source (Bone marrow vs PBSC)
- Year of transplant
- GVHD prophylaxis
    - CNI + MTX ± other except MMF vs. CNI + MMF ± other vs. CNI + other except MMF, MTX
    - ATG/Alemtuzumab (Yes vs No)

Outcome variables:

Primary:

- Time to neutrophil engraftment
- Time to platelet engraftment

Secondary:

- Incidence of acute and chronic GVHD
- Relapse free survival
- Overall survival
- Transplant related mortality
- Primary graft faliure

For cryopreserved grafts:

- Effect of time to cryopreservation on primary and secondary endpoints
- Effect of duration of cryopreservation on primary and secondary endpoints
- Change in cryopreserved graft composition between pre-freeze and post-thaw
- Change in graft viability between pre-freeze and post-thaw

Data requirements:

Patients, disease and transplant related characteristics will be obtained from the CIBMTR database. No additional supplemental data collection is anticipated.

Study design (scientific plan):

The primary endpoint of this study is to investigate the impact of cryopreservation on engraftment. Secondary endopoints include incidence of acute and chronic GVHD, TRM, relapse free and overall survival. If possible, a case control analysis between fresh and cryopreserved donor would allow for a more meaningful comparison between the two groups. Patients would be matched as closely as possible to the variables listed above. Characteristics between the two groups will be analyzed using the chi-squre test for discrete variables and the Kruskai-Wallis test for continuous variables. Kaplan-Meyer and cumulative incidence estimates will be utilized for analysis of the various endpoints. Multivariate analysis will be performed using a Cox proportional hazard model.

If enough information is available, a similar descriptive analysis will be performed investigating factors which may affect the primary and secondary endpoints with cryopreserved grafts. Descriptive analysis of changes in graft composition and viability after cryopreservation will be analyzed in this cohort if the information is available.

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3. Parody R, Caballero D, Márquez-Malaver FJ, et al. To freeze or not to freeze peripheral blood stem cells prior to allogeneic transplantation from matched related donors. Eur J Haematol. 2013;91(5):448-455. doi:10.1111/ejh.12140.
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5. Lasky LC, Van Buren N, Weisdorf DJ, et al. Successful allogeneic cryopreserved marrow transplantation. *Transfusion*. 1989;29(2):182-184.
6. Stockschläder M, Krüger W, tom Dieck A, et al. Use of cryopreserved bone marrow in unrelated allogeneic transplantation. *Bone Marrow Transplant*. 1996;17(2):197-199.

Inclusion/Exclusion

	Excluded	Included
CRF First allogeneic transplants between 2008-2017	---	29904
Malignant diseases	SAA-severe aplastic anemia (N=1591) Inherit.abnorm.erythrocyte diff-funct. (N=1529) SCID & oth immune system disorders (N=1159) Inherit.abnorm. of platelets (N=40) Inherit.disord. of metabolism (N=470) Histiocytic disorders (N=305) Autoimmune diseases (N=21) Other, specify (N=42)	24747
Bone Marrow or PBSC	Umbilical cord blood (N=4463) BM + PB (N=20) BM + UCB (N=12) PB + UCB (N=222) Other (N=1) PB + OTH (N=21) UCB + OTH (N=24) BM + PB + OTH (N=2)	19982
Matched transplants	Twins (not HLA matched) (N=243) Other related (N=3063) Partially-matched unrelated (N=1973) Mis-matched unrelated (N=133) Multi-donor (N=49) Unrelated (matching TBD) (N=362) Missing (N=164)	13995
GVHD prophylaxis methods	Ex-vivo T-cell depletion (N=72) CD34 selection (N=188) Post-CY + other(s) (N=337) Post-CY alone (N=56) Missing (N=425)	12917
ABO compatibility	Minor mismatch (N=2569) Major mismatch (N=2336) Bi-directional (N=719) Missing (N=183)	7110
T-cell depletion grafts	None	7110
Missing forms	100day + baseline – Product (N=35)	7075
Consent for research	N=156	6954
Embargoed centers	N=142	6812

Table 1: Demographics

Variable	No Cryopreserved Product N (%)	Cryopreserved Product N (%)
Number of Recipients	5975	833
Number of centers	225	114
Patient-related		
Recipient age at transplant		
0-9 years	212 (4)	10 (1)
10-19 years	298 (5)	19 (2)
20-29 years	455 (8)	56 (7)
30-39 years	503 (8)	74 (9)
40-49 years	903 (15)	144 (17)
50-59 years	1530 (26)	263 (32)
60 years and older	2074 (35)	267 (32)
Median (Range)	54 (1-81)	55 (1-78)
Recipient race		
Caucasian, non-Hispanic	4861 (84)	622 (77)
African-American, non-Hispanic	214 (4)	53 (7)
Asian, non-Hispanic	260 (5)	35 (4)
Pacific islander, non-Hispanic	27 (<1)	0
Native American, non-Hispanic	29 (1)	1 (<1)
Hispanic, Caucasian	349 (6)	92 (11)
Hispanic, African-American	8 (<1)	3 (<1)
Hispanic, Asian	1 (<1)	2 (<1)
Hispanic, Pacific islander	1 (<1)	1 (<1)
Hispanic, Native American	9 (<1)	1 (<1)
Unknown	216 (N/A)	23 (N/A)
Recipient sex		
Male	3605 (60)	506 (61)
Female	2370 (40)	327 (39)
Recipient Karnofsky score		
90-100%	3622 (62)	511 (63)
< 90%	2264 (38)	304 (37)
Unknown	89 (N/A)	18 (N/A)
Recipient Sorror score		
0	1808 (31)	229 (28)
1	812 (14)	115 (14)
2	817 (14)	111 (13)
3	2424 (41)	372 (45)
Unknown	114 (N/A)	6 (N/A)
Donor type		
HLA-identical sibling	2583 (43)	678 (81)
Well-matched unrelated	3392 (57)	155 (19)
Disease-related		
Disease at transplant		

Variable	No Cryopreserved Product N (%)	Cryopreserved Product N (%)
AML	2410 (40)	323 (39)
ALL	730 (12)	101 (12)
Other leukemia	244 (4)	45 (5)
CML	244 (4)	30 (4)
MDS	1636 (27)	203 (24)
Other acute leukemia	56 (1)	6 (1)
NHL	488 (8)	102 (12)
Hodgkins Lymphoma	72 (1)	8 (1)
Plasma Cell Disorders, MM	92 (2)	12 (1)
Other Malignancies	3 (<1)	3 (<1)
AML Disease stage at transplant		
CR1	1507 (63)	187 (58)
CR2	388 (16)	58 (18)
CR3+	20 (1)	2 (1)
Advanced or active disease	480 (20)	75 (23)
Missing	15 (1)	1 (<1)
Unknown	3565 (N/A)	510 (N/A)
ALL Disease stage at transplant		
CR1	492 (67)	66 (65)
CR2	168 (23)	22 (22)
CR3+	18 (2)	3 (3)
Advanced or active disease	52 (7)	10 (10)
Unknown	5245 (N/A)	732 (N/A)
MDS Disease stage at transplant		
Early	309 (19)	43 (21)
Advanced	1307 (80)	160 (79)
Missing	20 (1)	0
Unknown	4339 (N/A)	630 (N/A)
NHL Disease stage at transplant		
CR1	84 (18)	20 (20)
CR2	95 (20)	13 (13)
CR3+	35 (7)	10 (10)
PR	2 (<1)	0
Advanced	264 (55)	57 (57)
Unknown	5495 (N/A)	733 (N/A)
Transplant-related		
Stem cell source		
Marrow	998 (17)	45 (5)
PBSC	4977 (83)	788 (95)
GvHD Prophylaxis		
No GVHD prophylaxis (forms under review)	88 (1)	12 (1)
Tacrolimus + MMF +- others	929 (16)	129 (15)
Tacrolimus + MTX +- others (except MMF)	3192 (53)	461 (55)

Variable	No Cryopreserved Product N (%)	Cryopreserved Product N (%)
Tacrolimus + others (except MTX, MMF)	431 (7)	30 (4)
Tacrolimus alone	131 (2)	29 (3)
CSA + MMF +- others (except Tacrolimus)	430 (7)	46 (6)
CSA + MTX +- others (except Tacrolimus, MMF)	587 (10)	95 (11)
CSA + others (except Tacrolimus, MTX, MMF)	41 (1)	9 (1)
CSA alone	75 (1)	14 (2)
Other GVHD prophylaxis	71 (1)	8 (1)
Conditioning regimen		
Myeloablative	3308 (55)	469 (56)
RIC	2037 (34)	267 (32)
Nonmyeloablative	443 (7)	66 (8)
Other	168 (3)	28 (3)
TBD	19 (<1)	3 (<1)
Donor age at donation		
0-9 years	109 (4)	5 (1)
10-19 years	192 (7)	9 (1)
20-29 years	307 (11)	43 (6)
30-39 years	310 (11)	66 (10)
40-49 years	522 (19)	149 (22)
50-59 years	797 (28)	218 (32)
60 years and older	562 (20)	195 (28)
Unknown	3176 (N/A)	148 (N/A)
Median (Range)	49 (0-82)	53 (3-85)
Donor race		
Caucasian, non-Hispanic	3697 (82)	529 (79)
African-American, non-Hispanic	176 (4)	39 (6)
Asian, non-Hispanic	273 (6)	26 (4)
Pacific islander, non-Hispanic	20 (<1)	0
Native American, non-Hispanic	26 (1)	1 (<1)
Hispanic, Caucasian	263 (6)	74 (11)
Hispanic, African-American	7 (<1)	0
Hispanic, Asian	1 (<1)	1 (<1)
Hispanic, Pacific islander	1 (<1)	0
Hispanic, Native American	9 (<1)	1 (<1)
Hispanic, race unknown	27 (1)	0
Other	5 (<1)	0
Unknown	1470 (N/A)	162 (N/A)
Donor/Recipient sex match		
Dnr Male/Rec Male	2446 (41)	295 (35)
Dnr Male/Rec Female	1451 (24)	194 (23)
Dnr Female/Rec Male	1157 (19)	210 (25)
Dnr Female/Rec Female	919 (15)	133 (16)
Unknown	2 (N/A)	1 (N/A)

Variable	No Cryopreserved Product N (%)	Cryopreserved Product N (%)
Donor/Recipient CMV serostatus		
0 +/+	1907 (32)	334 (41)
1 +/-	635 (11)	95 (12)
2 -/+	1718 (29)	219 (27)
3 -/-	1652 (28)	174 (21)
Unknown	63 (N/A)	11 (N/A)
Year of transplant		
2008	759 (13)	121 (15)
2009	689 (12)	114 (14)
2010	472 (8)	70 (8)
2011	309 (5)	50 (6)
2012	329 (6)	37 (4)
2013	636 (11)	86 (10)
2014	864 (14)	141 (17)
2015	758 (13)	91 (11)
2016	652 (11)	73 (9)
2017	507 (8)	50 (6)
Follow-up among survivors, Months		
N Eval	3051	370
Median (Range)	37 (1-126)	48 (1-123)

Proposal: 1812-06

Title:
The Impact of pre-apheresis Health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome

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Hypothesis:
Pre-donation HRQoL have a significant impact on the Peripheral blood stem cell (PBSC) collection yield

Study aims:
Primary aim: Primary aim of this study is to determine the impact of pre-donation HRQoL and psychological distress on peripheral blood stem cell yield Collection yield is defined as CD34+/L of blood processed ($x10^6$/L) on Day 5 filgrastim administration, Day 1 apheresis

Secondary aims:

- to determine the impact of pre-procedural HRQoL on peri-collection pain and acute toxicities experienced in PBSC donors
- To determine the impact of pre-apheresis HRQoL on post-donation complete recovery

Scientific justification:
Emotional distress is accompanied by changes in the associated neural, endocrinological and immunological system. There is an increasing literature linking biobehavioral factors such as chronic and acute stressors and depressed mood to higher levels of inflammatory burden, potentially through physiologic stress mechanisms. Psychological stress in humans induces an inflammatory response through pro-inflammatory cytokines such as interleukin 1beta (IL-1β), interleukin 6 (IL-6) and tumor necrosis factor alpha (TNFα) [1-4]. Psychological factors including stress, anxiety and depression has been shown to influence the onset and course of clinical pain conditions such as headache, migraine and fibromyalgia by modulating the hypothalamic-pituitary-adrenal axis, the core pathway of the human stress system. Substantial evidence from clinical observations has also shown the association between greater emotional distress and depressive symptoms and poorer post procedural outcomes including longer hospital stays, more postoperative complications such as pain perception, higher pain medication requirement, and higher rates of re-hospitalization [4-7]. In a prospective study, *Billen A.* and colleagues [8] examined the impact of pre-donation health related quality of life (HRQoL) on recovery time and toxicities in 275 peripheral blood stem cell (PBSC) and 37 bone marrow unrelated donors from the United Kingdom. Poorer pre-donation mental health was associated with a longer recovery time after BM donation (p=0.03) and pain after PBSC donation (p=0.003). HRQoL factors that might influence donation associated toxicities and recovery are less known in the related donor setting. There is also paucity of data on impact of HRQoL (especially mental health) on stem cell collection yield. Study by *Larijani et al* [9] investigating association between pre-apheresis anxiety level measured by Beck's anxiety inventory and PBSC yield in 111 donors revealed a decrease in collection yield in donor's

experiencing elevated anxiety level. However, this was a single center study focusing on only single domain of HRQoL (anxiety), thus the impact of donor's HRQoL on collection yield still remains unclear.

Scientific impact:
The findings from this study will guide in better understanding potential psychosocial factors influencing collection yield and clinical outcomes of peripheral stem cell donors which may lead to safer and more efficient peripheral blood stem cell mobilization

Study population:
Related peripheral blood stem cell donors prospectively enrolled in RDSafe study between 2010 and 2013. HRQoL was assessed by SF-12v2 among 118 related and 112 unrelated donors.
BMT CTN 0201 sub-study cohort which included 142 PBSC donors. HRQoL was assessed using SF-8.

Variables to be analyzed:
Donor-related:

- Gender (male vs. female)
- Age
- Ethnicity (Caucasian vs. Hispanic/Latino vs. African American vs. Asian/Pacific Island vs. others)
- Marital status
- Donor BMI (kg/m^2): normal vs. overweight vs. obese vs. morbidly obese
- Year of donation
- Presence or absence of central venous catheter (CVC)

Procedure factors:

- Baseline (pre-filgrastim) WBC ($x10^9/L$)
- Baseline (pre-filgrastim) neutrophils ($x10^9/L$)
- Baseline (pre-filgrastim) platelets ($x10^9/L$)
- Baseline (pre-filgrastim) mononuclear cells ($x10^9/L$)
- Pre-Day 5 of filgrastim (day 1 of apheresis) WBC ($x10^9/L$)
- Pre-Day 5 of filgrastim (day 1 of apheresis) neutrophils ($x10^9/L$)
- Pre-Day 5 of filgrastim (day 1 of apheresis) platelet ($x10^9/L$)
- Pre-Day 5 of filgrastim (day 1 apheresis) mononuclear cells ($x10^9/L$)
- Average daily filgrastim dose (μg)
- Average daily filgrastim dose per donor actual body weight (μg/kg)
- Total filgrastim dose (μg)
- Total filgrastim dose per donor actual body weight (μg/kg)
- Volume of blood processed on Day 5 filgrastim administration (day 1 of apheresis) Small <12L vs. Standard 12-18L vs. large ≥18 L vs. unknown
- One day versus two-day collection

Outcomes:

- CD34+/L of blood processed ($x10^6/L$) on Day 5 filgrastim administration, Day 1 apheresis

- Incidence of bone pain grade 2-4 based on average daily dose of filgrastim (mcg/d) at 24 hours after administration of the first dose, highest pain recorded between Day 1 and Day 5 dosage, 2 days post donation and 1week post donation

- Incidence of highest toxicity level grade 2-4 across selected body symptoms based on average daily dose of filgrastim (mcg/d) at 24 hours after administration of the first dose, highest pain recorded between Day 1 and Day 5 dosage, 2 days post donation and 1week post donation

Statistical analysis:

The primary endpoint is collection yield expressed as CD34+ per L of blood processed on Day 5 of G-CSF administration. The secondary endpoints are donation associated pain and toxicities and time to recovery. HRQoL measures (physical and mental health) will be split into 4 groups based on percentiles. The influence of the previously defined demographic and HRQOL factors on individual collection yield and adverse reactions (pain and acute toxicities) will be examined using either a chi square for categorical variables or t-test or mann-Whitney-U test as appropriate for continuous variables. Cell yield will be compared between groups in univariate analysis using Analysis of Variance. Multivariate analysis of collection yields will be performed using linear regression analysis. The probability of complete recovery will be calculated using Kaplan-Meier estimator and groups will be compared using log rank test.

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