MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR DONOR HEALTH AND SAFETY
Orlando, Florida
Saturday, February 22, 2020, 2:45 – 4:45 pm

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1. Introduction

a. Minutes and Overview Plan from February 2019 meeting
The CIBMTR Donor Health and Safety Working Committee meeting was called to order by Dr. Nirali Shah at 2:49pm on Saturday, February 22nd. The CIBMTR COI policy along with individual leadership COI. Each member of the working committee leadership was introduced, and Dr. Nina Worel, the EBMTR Donor Outcomes Committee Chairperson was welcomed. The processes of participating in the working committee, voting guidance, and rules of authorship were outlined. The advisory committee dashboard indicated that the working committee is in good standing for all metrics. She mentioned that the Donor Health and Safety Working Committee will accept a maximum of 1 proposal this year.

2. Accrual summary

3. Presentations, published or submitted papers

Dr. Jack Hsu reviewed the presentations, publications and submitted papers over the last year.

a. **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. **Biology of Blood and Marrow Transplantation: Journal of the American**

Society for Blood and Marrow Transplantation. 2019 Jul 1; 25(7):1325-1330. doi:10.1016/j.bbmt.2019.01.034. Epub 2019 Feb 2. PMC6615955.

b. **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 donors. **Bone Marrow Transplantation. doi:10.1038/s41409-019-0515-3. Epub 2019 Apr 10.**
c. **DS17-01** Farhadfar N, Hsu JW, Logan BR, Sees JA, Chitphakdithai P, Sugrue MW, Abdel-Azim H, Anderlini PN, Bredeson C, Chhabra S, Diaz MA, Ganguly S, Hematti H, Kamble RT, Kasow KA, Lazarus HM, Lynch DK, Murthy HS, Olsson RF, Papari M, Przepiorka D, Savani BN, Schears R, Seo S, Solh MM, Spitzer T, Yared JA, Pulsipher MA, Shah NN, Switzer GE, Confer DL, Shaw BE, Wingard JR. Weighty choices: selecting optimal G-CSF doses for stem cell mobilization to optimize yield. ***In press Blood Advances.***
d. **DS18-01** Wong WH, Bhatt S, Trinkaus K, Pusic I, Elliott K, Mahajan N, Wan F, Switzer GE, Confer DL, Dipersio J, Pulsipher MA, Shah NN, Sees J, Bystry A, Blundell JR, Shaw BE, Druley TE. Engraftment of rare, pathogenic donor hematopoietic clones with mutations in unrelated hematopoietic stem cell transplantation. **In press *Science Translational Medicine.***
e. **DS16-S2** Seftel MD, Kuxhausen M, Burns L, Chitphakdithai P, Confer D, Kiefer D, Lee S, Logan B, O'Donnell P, Pulsipher M, Shah NN, Switzer G, Shaw BE. Clonal Hematopoiesis in Related Allogeneic Transplant Donors: Implications for Screening and Management. ***Submitted.***
f. **DS16-01** Hsu JW, Shaw BE, Kim S, Logan BR, Sees JA, Confer DL, Pulsipher MA, Shah N, Switzer GE, Abidi MH, Ahmed IA, Anderlini PN, Bredseon C, Chhabra S, Dandoy CE, Diaz MA, Farhadfar N, Ganguly S, Gergis U, Hale GA, Hematti P, Kamble RT, Kasow KA, Lazarus HM, Liesveld JL, Murthy HS, Olsson RF, Savani BN, Schears R, Seo S, Solh M, Spitzer T, Steinberg A, Sugrue M, Warkentin P, Wingard JR. Peripheral Blood Stem Cell Collection in One Day is Preferable to Two Days in Unrelated Donors. ***Submitted.***
g. **DS17-02** Farhadfar N, Murthy HS, Logan BR, Sees JA, Mouhab A, Battiwalla M, Beitinjaneh AM, Chhabra S, Diaz MA, Engles K, Frangoul H, Ganguly S, Gergis U, Kamani NR, Kamble RT, Kasow KA, Lazarus HM, Liesveld JL, Norkin M, O'Donnell PV, Olsson RF, Rossman SN, Savani BN, Schears R, Seo S, Solh MM, Spitzer T, Sugrue M, Yared JA, Linenberger M, Schwartz J, Pulsipher MA, Shah NN, Switzer GE, Confer DL, Shaw BE, Wingard JR. Impact of Autologous Blood Transfusion after Bone Marrow Harvest on Unrelated Donor's Health and Outcome: A CIBMTR Analysis. ***Submitted.***
h. **DS18-01** Wong WH, Young A, Druley T. Detection of rare, deleterious clonal mutations during unrelated allogeneic hematopoietic stem cell transplants using an error correction pipeline for NGS. ***Presented at AACR Annual Meeting 2019.***
i. **DS18-02** Panch SR, Logan BR, Sees JA, Savani BN, Shah NN, Hsu JW, Pulsipher MA, Switzer GE, Shaw BE, Stroncek DF. Lower Hematopoietic Progenitor Cell Counts and Yields at Subsequent Donations Is Influenced By a Shorter Inter-Donation Interval between the First and Subsequent Mobilizations. ***Presented at 62nd ASH Annual Meeting and Exposition.***

4. Studies in progress

Dr. Jack Hsu introduced Dr. Nirali Shah to give a study update on DS18-02.

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

Dr. Nirali Shah presented this update on behalf of Dr. Sandhya Panch and Dr. David Stroncek. This study was presented at ASH and is currently in manuscript development. The goal of the study is to evaluate factors contributory to CD34+ yield for second collection. Conclusions are that a longer inter-donation interval was associated with better PBSC mobilization and collection; yields may be improved marginally by increasing G-CSF dose within permissible limits; and in most instances sub-optimal mobilizers at first donation appear to donate suboptimal numbers of HSC at their subsequent donation. The study also included a much smaller number of bone marrow donors and was not included in this presentation. It was suggested that reviewers may be interested in knowing more about donors that failed the second donation. The committee members asked questions and there was time for discussion.

e. **DS19-01** Effect of Donor Graft Cryopreservation on Allogeneic Transplant Recipient Outcomes (J Hsu/N Farhadfar/H Murthy/J Wingard) **Data file prep**

f. **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) **Draft protocol received**

5. Future/proposed studies

Dr. Galen Switzer invited Dr. Nosha Farhadfar to present proposal 1911-16.

a. **PROP 1911-16** Acute Toxicities of Bone Marrow or Peripheral Blood Stem Cell Donation in Donors with Sickle Cell Trait (N Farhadfar/J Wingard) (Attachment 4)

Dr. Nosha Farhadfar presented this proposal. The hypothesis is that bone marrow donors with sickle cell trait experience more peri-collection pain, toxicities and a slower recovery compared to donors without sickle cell trait. Initial population selection identified 95 donors with the sickle cell trait that would be matched to donors without the trait from a pool of 7476. Generally, members of the working committee felt this was an important study that needed to be done. A question was raised about the impact of the study; if these donors do experience more pain and toxicity, haplodonors would likely tolerate the increase in pain and toxicity as they are donating for a relative.

Other factors may significantly impact pain such as race/ethnicity and other genetic polymorphisms. Race/ethnicity can be taken into account, but further genetic analyses should be considered. Matching for race/ethnicity could be considered when selecting the control cohort (more than one control group could be selected as there is a large pool available)

Pain data is collected at baseline to know whether donors were already experiencing pain prior to donation. An attendee questioned whether the study is interested in whether there is more pain or a higher degree of pain – the data are all collected so this can be addressed.

PBSC donors were not included in the proposal since there were so few (n=13).

Dropped proposed studies

a. **PROP 1911-238** Improving Donor Education and Safety Programs by a Comprehensive Review of Donor Deferrals Based on Infection Risk identified in National Marrow Donor Program. *Dropped due to feasibility.*

6. Other business

a. **Review/guideline papers** L Gowda

Dr. Lohith Gowda presented his idea of developing a formal process for the Donor Health and Safety Working Committee to write guidelines or literature reviews. He aims to develop guidelines that will enable transplant workforce to incorporate newer developments into their clinical practice and identify future areas of research to enhance donor safety and education. The committee members had interest in pursuing this and had suggested collaborating with different groups such as WMDA and ASFA. One noted that it will be important to consider what has already been done well so the committee can focus energy on topics that will be most impactful to donors.

b. **Biobank update** S Devine

Dr. Steven Devine, Chief Medical Officer of NMDP/Be The Match, presented an update on the biobank initiative. The idea of biobanking is to expedite the path to transplant by reducing lag time in identifying and procuring a graft from a volunteer donor, and theoretically leading to better recipient outcomes. Biobanking means the donor can donate when it is most convenient for them, but also means there may not ever be a recipient waiting to receive their product; This raises ethical issues. Another potential benefit is that the product has already been characterized, so the transplant center would have key information such as CD34 and TNC ahead of time. There have been 6 products collected to date, and the plan is to add 2-3 per month and work towards 5-10 per month, considering capacity. In order to understand whether cryopreserved cells are associated with equivalent patient outcomes, the recipients will be enrolled on a prospective study to understand if this approach will reduce time to transplant and whether transplant physician will prioritize bio banked cells over living cells.

There are implications of creating a bank representing the most common HLA types – does this just increase disparities in donor availability since less of the biobank grafts are likely to be distributed to ethnically diverse patients.

From the donor side there are questions including: what are the implications of collecting BMT instead of peripheral blood, what are ethical issues of harvesting but not using stem cells, implications of consent statement that these could be used for research, what if a donor experienced a complication while donating for the bank rather than for a patient, etc?

The recommendation from the Donor Health and Safety Working Committee (to the DPSM) was that these biobank donors are considered research participants, data should be collected from these donors such as symptoms and longitudinal health related quality of life.

There was a lively discussion, with members of the committee voicing several comments for consideration on this topic.

- Concerns about cell lose after thawing marrow, in addition to potential losses with RBC depletion. This can be combatted by collecting more cells up front (comments were made about the acceptability of collecting 2 liters of marrow from healthy donors, even young large donors).

- Consider the scalability and practicality; how fast will products turn over, how many products will be stored? The expense of the bank was raised.
- Optics of having a BioBank with common HLA were discussed. Will this further skew the available for ethnic minorities? The ultimate goal is to include rare HLA types in the BioBank too, but this could take a long time Engaging with formal biomedical ethicist group was suggested.
- If BM is taken from minority donor with non-common HLA to put in the BioBank, this may decrease the availability of peripheral blood (or BM) donors available on the registry.
- Altruistic donors might be discouraged from donating knowing that their product will be frozen and not go directly to a recipient. Questions were raised about whether qualitative work had been done with focus groups in advance to determine the acceptability to donors
- Harm to a donor whose product is never used was raised, including the impact to the worldwide registries
- Donors need to know the likelihood of their product being used to give informed consent – is this known?
- Possibility of separating donations that can be provided to more than one recipient
- Considerations of cost effectiveness and efficiency were raised. One member suggested speeding up delivery of cells from a live donor (and diverting some of the money directed to the BioBank) would negate the need for a costly BioBank. He quoted the success of the FastTrack pilot project.
- Supportive in carrying out prospective study
- The diseases that use bone marrow are not the diseases that need to get to transplant as soon as possible. Diseases that need to get to transplant as soon as possible, such as AML, use PBSC (and may use UCB as a back up)
- Will transplanters really be willing to use frozen marrow? Do we really know cell loss with freeze-thaw marrow? This may be mitigated by knowing the yield of the product in a Biobank (usually not known until the product shows up in their building)
- Storing cadaveric marrow instead of exposing healthy volunteers to harm was proposed
- Dr. Switzer proposed Intermediate solutions to some of the concerns: donors need to be treated as research participants, collect data from donors, and collect data from transplant physicians on their likelihood to use the product to enhance understanding of the landscape.

c. **17-SIBS** Identifying Predictors of Poor Health-Related Quality of Life among Pediatric Hematopoietic Stem Cell Donors. G Switzer

Dr. Galen Switzer gave an update and encouraged pediatric centers to join this NHLBI sponsored R01 study. Conclusions from RDSafe were that there are significant HRQoL deficits among pediatric HSC donors, youngest children were most at risk, and parents overestimated HRQoL of the donor child. Overestimation was largest for donors with the poorest self-reported HRQoL, and pre-donation HRQoL predicted post-donation HRQoL. The goal of the current study is to determine the reason for poor donor HRQoL and to develop interventions or guidelines to assist donors. Data will be collected from the full related donor family, a control sample containing siblings of recipients receiving a donation from an unrelated source, the transplant center, and will again use the healthy matched normative sample from PedsQL.

d. **Additional business items** As needed and as time allows for discussion.
No other business was discussed.

Working Committee Overview Plan for 2020-2021

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2020	Hours allocated 7/1/2020-6/30/2021	Total Hours allocated
DS13-02: A retrospective analysis to understand the potential mechanisms underlying the clinical impact of ABO incompatibility on allogeneic transplant outcomes	Protocol development	Manuscript preparation – July 2021	270	200	140	60	200
DS16-01: Comparison between one and two day apheresis in unrelated donors	Published	Published – July 2020	0	0	0	0	0
DS16-S2: Survey of the screening and management for clonal disorders of hematopoiesis in related ALLO donors	In press	Published – July 2020	0	0	0	0	0
DS17-01: The impact of donor body mass index on collection of Filgrastim (G-CSF) mobilized peripheral blood progenitor cells from unrelated donors	Submitted	Published – July 2020	0	0	0	0	0
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)	Published	Published – July 2020	0	0	0	0	0

DS18-02: Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections	Manuscript preparation	Published – July 2021	20	30	20	10	30
DS19-01: Effect of Donor Graft Cryopreservation on Allogeneic Transplant Recipient Outcomes	Data file preparation	Submitted – July 2021	230	230	100	130	230
DS19-02: The Impact of pre-apheresis Health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome	Protocol development	Manuscript preparation – July 2021	270	200	100	100	200
DS20-01: Acute Toxicities of Bone Marrow Donation in Donors with Sickle Cell Trait	Protocol pending	Data file preparation – July 2021	330	100	0	100	100

Oversight Assignments for Working Committee Leadership (March 2020)

Bronwen Shaw	**DS13-02** Clinical impact of ABO incompatibility on alloHCT [Statistical Center Study]
Dennis Confer	**DS05-02g** RDSafe
Galen Switzer	**DS05-02g** RDSafe **DS19-01** Effect of Donor Graft Cryopreservation on Allogeneic Transplant Recipient Outcomes
Jack Hsu	**DS05-02g** RDSafe **DS18-02** Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections **DS19-02** The Impact of pre-apheresis Health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome
Nirali Shah	**DS20-01** Acute Toxicities of Bone Marrow Donation in Donors with Sickle Cell Trait