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MINUTES AND OVERVIEW PLAN
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**
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Co-Chair:	**Nirali Shah, MD, MHSc, National Cancer Institute – NIH, Bethesda, MD; Telephone: 240-760-6199; E-mail: nirali.shah@nih.gov**
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1. Introduction

Galen Switzer welcomed all attendees and called the meeting to order at 12:17 pm. Drs. Pulsipher, and Shah chaired the meeting; B Shaw, Scientific Director, D Confer, Ex Officio Senior Advisor, B Logan, Statistical Director, and P Chitphakdithai and J Sees, statisticians, where also present.

Dr. Switzer introduced and welcomed Dr. Hsu as a new chair of the committee, replacing Dr. Pulsipher who he thanked for this extensive input to the DSWC over the years since it first started. He also mentioned that the advisory metrics were not included in the slides, but that the working committee is in good standing and progressing in all studies. The Working Committee Leadership had no relevant conflicts of interest to disclose. 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 two proposals due to limited statistical hours. Minutes from Tandem 2018 were approved.

2. Accrual summary

Galen Switzer noted the accrual summaries (NMDP unrelated donors, NMDP related donors, RDSafe donors, and sample accruals) were available in the meeting materials found online.

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, noting the great progress completed in all studies.

4. Studies in progress

Nirali Shah gave a brief overview of study statuses of active studies.
One study update was given during the meeting:

d. 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)

Mr. Wing Hing Wong presented slides showing the results of their study, DS18-01. The manuscript has also been submitted.

As a person ages, they are more likely to develop mutations. Clonal Hematopoiesis of Indeterminate Potential (CHIP) can detect somatic mutations above 2% variant allele frequency in individuals. Mutations in leukemic genes have been found in 95% of healthy individuals.

Using 25 CIBMTR donor samples and Washington University recipients, somatic mutations were tracked from the donor to the recipient at multiple time-points post-transplant to (1) quantify and characterize the mutation burden and spectrum in healthy donors and, (2) examine engraftment dynamics of donor-derived somatic mutations in recipients.

The study found that 64% (N=16) of donors harbor at least 1 somatic mutation. DNMT3A and TET2 were the most commonly mutated genes, as observed in previous literature.

Mutated genes were evaluated as deleterious or not based on a CADD score above 15. In this study, deleterious mutations were more likely to engraft relative to non-deleterious mutations. Additionally, donor-derived DNMT3A is most commonly mutated in the recipient.

In this population, somatic mutations were not associated significantly with donor age.

The number of mutations in recipients that are in donor cells were found to be significantly higher in 30 days and 100 days post transplant when compared to the mutation burden in donor before transplant. This indicates either an increased rate of mutation, or a presence of positive selective force that drive some of these mutations to proliferate.

Finally, the somatic mutations in the donor were correlated with a higher rate of chronic Graft versus Host Disease (GVHD), however these were not significant due to small sample size.

The audience were interested in the turn around time for such testing. There was also a query about whether any of the subjects in the study had a donor-derived leukemia (there was not).

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)

Dr. Jack Hsu presented the proposal "Effect of Donor Graft Cryopreservation on Allogeneic Transplant Recipient Outcomes".

Minimal information is available in the literature on the effect of cryopreservation on allogeneic donor grafts. Utilization of cryopreserved donors grafts could lower logistical issues associated with unrelated donors and expand the unrelated donor pool for quicker utilization. The hypothesis of the study is that there are no significant differences in transplant outcomes between cryopreserved and fresh grafts in donors. The primary transplant outcome to be explored is neutrophil and platelet engraftment. Secondary outcomes includes acute and chronic GVHD, relapse-free and overall survival, transplant related mortality, primary graft failure, and if available graft viability and alterations in cellular content.

The presentation was followed by a lively discussion from the audience. Throughout the discussion Dr. Jack Hsu and the Working Committee Leadership responded to questions.

In general there was enthusiasm for this study. It was noted that a similar proposal has been submitted a few years ago to this committee but had not proceeded due to low numbers of cryopreservation cases available. This number has increased in the intervening years, although the number of BM grafts which are cryopreserved remains low. It was suggested that this study would be a good pilot study on which to base further studies on the mechanisms involved in cryopreservation. There was interest in linking the infusion of the product with any reports of Adverse events (such as allergic reactions). Limitations to the study were raised for example whether data was available on the duration of cryopreservation (no) or the time from harvest to freezing (no). Also of interested was the reason for cryopreservation, but this is not captured.

In general, this proposal was very well received, and believed to be very timely, and would potentially alter practice. It was recognized that CIBMTR was the best mechanism to address this due to the rarity of cryopreservation at individual centers.

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)

Dr. Nosha Farhadfar presented the proposal "The Impact of pre-apheresis Health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome". This proposal aims to examine the association between greater emotional distress and poorer post procedural outcomes including longer hospital stays, more postoperative pain perception, and higher rates of re-hospitalization using RDSafe and BMT CTN 0201 data. Results of this proposal may help to identify donors at risk for poorer outcomes and delayed recovery. The findings of this proposal may also help guide interventions to minimize

donation associated toxicities and improve PBSC collection yield. The hypothesis of the study is that pre-donation HRQoL significantly influences donation associated toxicities, donor recovery time and PBSC collection yield.

The presentation was followed by a lively discussion from the audience. Throughout the discussion Dr. Nosha Farhadfar and Working Committee Leadership both responded to questions.

A major strength of this study is that it leverages not only clinical data but also patient-reported data which is available from previous studies. All felt this was a very good use of the resources and data available to us to answer an interesting and provocative question.

The link between stress and inflammation is well established, although not in this setting. The proposal includes only PBSC donors, however a suggestion was made to include BM donors too (data are available), analyses should be done separately to account t for different donor stressors. Relevant confounders were discussed – these are available (central line data, dose of GCSF). GCSF-primed procedures are available though these are very few. Donor medications that may also impact cell yield were raised and this data is likely to be available for some donors. A question about addressing donor mental health at registration or work up was raised, but these data appear to be differently collected.

In general, this proposal was very enthusiastically received as an examination of donor's mental and physical health on their own well-being as well as the viability of the product they produce. It was recognized that CIBMTR was the best mechanism to address this, due to the previously existing clinical and PRO data.

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

No other business was discussed
The meeting lasted fifty-eight minutes, concluding at 1:15pm.

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Working Committee Overview Plan for 2019-2020

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2018	Hours allocated 7/1/2018-6/30/2019	Total Hours allocated
DS05-02d RDSafe-d: QoL for related adult donors compared to unrelated adult donors	Manuscript Preparation	Submission – July 2019	N/A	N/A	N/A	N/A	N/A
DS05-02g RDSafe-g: Late toxicities and SAE for related donors	Analysis	Submission – July 2019	N/A	N/A	N/A	N/A	N/A
DS13-02 A retrospective analysis to understand the potential mechanisms underlying the clinical impact of ABO incompatibility on allogeneic transplant outcomes	Protocol Development	Submission – July 2019	N/A	N/A	N/A	N/A	N/A
DS16-01 Comparison between one and two day apheresis in unrelated donors	Manuscript Preparation	Submission – July 2019	70	**70**	210	140	**70**
DS16-S2 Survey of the screening and management for clonal disorders of hematopoiesis in related ALLO donors	Submitted	Accepted – July 2019	5	**5**	5	5	**5**
DS17-01 The impact of donor body mass index on collection of Filgrastim (G-CSF) mobilized peripheral blood progenitor cells from unrelated donors	Manuscript Preparation	Submission – July 2019	30	**30**	30	30	**30**

DS17-02 Impact of Collection of Autologous Blood prior to Bone Marrow Harvest on Unrelated Donor Heath and Outcome	Manuscript Preparation	Submission – July 2019	N/A	N/A	N/A	N/A	N/A
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)	Submitted	Accepted – July 2019	10	**10**	0	10	**10**
DS18-02 Factors Affecting CD34+ Cell Yields at Subsequent Marrow/PBSC Collections	Analysis	Submission – July 2019	150	**150**	0	150	**150**
DS19-01 Effect of Donor Graft Cryopreservation on Allogeneic Transplant Recipient Outcomes	Draft Protocol	Manuscript Preparation – July 2020	330	**330**	0	0	**0**
DS19-02 The Impact of pre-apheresis Health related quality of life on peripheral blood progenitor cells yield and donor's health and outcome	Draft Protocol	Analysis – July 2020	270	**270**	0	0	**0**

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Oversight Assignments for Working Committee Leadership (March 2019)

Bronwen Shaw	**DS13-02** Clinical impact of ABO incompatibility on alloHCT [Statistical Center Study]
Dennis Confer	**DS05-02 d, g** RDSafe
Galen Switzer	**DS05-02d** 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	**DS16-01** One vs two day apheresis in URD **DS17-01** The impact of donor body mass index on collection of G-CSF mobilized peripheral blood progenitor cells from unrelated donors **DS17-02** The Impact of Pre-Operative Collection of Autologous Blood for Bone Marrow Harvest on Donor Health and Outcome [Statistical Center Study]