

**Health Resources and Services Administration (HRSA)  
Advisory Committee on Blood Stem Cell Transplantation (ACBSCT)**

**U.S. Department of Health and Human Services (HHS)**  
Virtual Meeting, April 27, 2020

**Present Members**

*Voting Members*

Manish Gandhi, MD; Staci Arnold, MD; Michael Bishop, MD, FACP; Arthur W. Bracey, MD; Colleen Delaney, MD, MSc; Sergio Giralt, MD, FACP; Mary Laughlin, MD; Amanda Salazar

*Non-voting (Ex Officio) Members*

Frank Holloman, Health Resources and Services Administration (HRSA); Nancy L. DiFronzo, PhD, National Institutes of Health (NIH); Sridhar Basavaraju, MD, Centers for Disease Control and Prevention (CDC); Safa Karandish, Food and Drug Administration (FDA)

*Executive Secretary*

Robert Walsh

*General Counsel Staff*

Rina Hakimian, JD, MPH

**Welcome and Opening Remarks**

*Robert Walsh, ACBSCT Executive Secretary*  
*Manish Gandhi, MD, ACBSCT Chair*

Mr. Walsh opened the meeting at 10:10 a.m. and then turned the meeting over to Dr. Manish Gandhi for opening remarks.

Dr. Gandhi welcomed all the meeting participants and provided a brief explanation of the Advisory Committee's role and principal purpose: to make blood stem cells from other donors and cord blood units available for patients who need a transplant to treat life-threatening conditions. He stated that the discussions during the meeting would be related to the utilization of cord blood for transplant and utilization of blood stem cells in similar therapies with a heavy focus on the effects surrounding COVID-19 within the community.

**HRSA Division of Transplantation Blood Stem Cell Transplantation Program Update**

*Frank Holloman, Acting Division Director, Division of Transplantation (DoT), Health Resources and Services Administration*

Mr. Holloman provided background on DoT's statutory framework for the operation of the CWBYCTP and NCBI. He highlighted the goals of these programs to increase the number of

bone marrow and cord blood transplants for recipients suitably matched to biologically unrelated donors and to build a public inventory of at least 150,000 new, high quality, and genetically diverse cord blood units (CBUs).

He reported HRSA's progress toward these goals noting that as of September 30, 2019:

- Registry included over 22 million adult volunteer donors with approximately 18% self-identified as belonging to a specific underrepresented racial or ethnic population
- NCBI inventory includes more than 100,000 CBUs with over 60 percent of the contracted cord blood units from underrepresented racial or ethnic populations.

Mr. Holloman also reported that the Program facilitated 6,426 transplants in fiscal year 2019 a 5% increase over fiscal year 2018. Among these 6426 transplants 5,329 of the transplant served domestic patients and 1004 of these transplants served members of underrepresented racial and ethnic populations. 848 CBUs (NCBI and non-NCBI) were released for transplantation in FY 2019 an 11% decrease from fiscal year 2018.

Finally, Mr. Holloman noted that HRSA awarded four new NCBI contracts in 2019 to the Cleveland Cord Blood Center (Cleveland, OH); LifeSouth Community Blood Centers (Gainesville, FL); New York Blood Center (New York City, NY); and the University of Texas – MD Anderson Cancer Center (Houston, TX). He also noted that HRSA expects to award one more NCBI contract in 2020 to Carolinas Cord Blood Bank at Duke University (Durham, NC).

### ***Discussion***

ACBSCT Members expressed concern about recent decreases in funding for the NCBI and the possibility of further diminishing access to transplant for under-represented and hard to match minority populations. They did, however, note that the Patient Access to Cellular Therapy (PACT) Act (discussed later in this summary) is expected to help address some barriers to utilization of cord blood units. Council members also inquired about efforts by the National Marrow Donor Program (NMDP) to increase awareness in the transplant community of all available sources of blood stem cells for transplant.

### **COVID-19: Impact on Unrelated Blood Stem Cell Transplantation**

*Steven Devine, MD, Chief Medical Officer, National Marrow Donor Program Associate Scientific Director, Center for International Blood and Marrow Transplant Research (CIBMTR)*

*John Miller, MD, PhD, Vice President, Medical & Quality Services, National Marrow Donor Program*

*Kristin Naruko, Vice President, Provider Services Operations, National Marrow Donor Program*

Dr. Devine provided an update on the NMDP policies and practices during the COVID-19 pandemic and its impact on the provision of unrelated stem cell transplants and the challenges faced by NMDP and other registries during the COVID-19 pandemic.

NMDP has addressed numerous logistical and patient and donor safety issues resulting from the COVID-19 pandemic. Travel disruptions and restrictions posed a significant potential barrier, especially those units shipped internationally. However, the NMDP obtained a waiver to the international travel restrictions and adopted a “hub and spoke” process to facilitate shipment of blood stem cell products from Europe to US. NMDP also issued a “strong recommendation” for that blood stem cell products be cryopreserved prior to initiation of conditioning the intended recipient for transplant. This is intended to ensure that the product will be available for the intended recipient, but questions remain on how this practice may influence recipient outcomes. This NMDP recommendation is consistent with guidance recently developed by the American Society of Transplantation and Cellular Therapy (ASTCT).

NMDP is also addressing barriers to blood stem cell donation from unrelated donors due to donor safety and travel concerns. Most donation activity is now occurring in stand-alone donor centers to minimizing potential for COVID-19 exposure. It is important to note that the NMDP practice for COVID-19 testing of donors is consistent with recent FDA guidance (April 1, 2020), which stated that at this time, FDA does not recommend laboratory tests to screen asymptomatic blood stem cell donors.

The NMDP reported that the COVID-19 pandemic has resulted in an approximately 30% reduction in the procurement of bone marrow for transplant. In the interest of donor safety, the NMDP issued restriction on “bone marrow only” orders. Bone marrow only procurements are limited to situations where recipient survival was clearly better indicated with bone marrow rather than other blood stem cell products (e.g. recipients with non-malignant conditions).

The NMDP also reported that searches for donors and blood stem cell products is down approximately 30-40% and donor workup requests and donor collections are down approximately 10-15%. NMDP noted that searches for CBUs have increased during the pandemic, but that resulting orders and shipments of cord blood products have not significantly increased. Finally, NMDP reported that anecdotally blood stem cell transplant volumes have declined approximately 50-70% during the pandemic though this is not yet verified in the data due to lagging data. Overall, NMDP is projecting April 2020 volumes to be approximately 50% lower than March 2020.

### ***Discussion***

Dr. Arnold asked whether the limited availability of PCR testing may play a role in electing to not screen donors. Dr. Devine responded that even if the PCR testing was widely available, the current recommendations would still apply.

Dr. Bracey expressed concern about the need to test asymptomatic patients for COVID-19 in areas with a high prevalence of infection. Dr. Giralt added that in most cases in high prevalence areas testing is being done by default before any procedure and that any related donor is also tested.

### **COVID-19: Impact on HTC Outcomes Data**

*J. Douglas Rizzo, MD, MS, Senior Scientific Director, CIBMTR Milwaukee, Cancer Service Line Director, Froedtert & the Medical College of Wisconsin*

Dr. Rizzo discussed the expected impacts of the COVID-19 pandemic on the data collected and reported by the Stem Cell Therapeutic Outcomes Database (SCTOD), which is operated under contract with HRSA. He also addressed how the Center for International Blood and Marrow Transplant Research (CIBMTR) is responding to these challenges and plans for analyzing the impacts of COVID-19 on blood stem cell transplant outcomes.

He began by noting that much is unknown about the incidence of COVID-19 in patients with cancer, or hematopoietic cell transplantation (HCT) or the morbidity and mortality in these patients. However, preliminary, small sample studies from China indicate that risk of COVID-19 infection and severe complications resulting from infection are significantly higher among this population in comparison to the general population.

Dr. Rizzo noted the significant impacts of COVID-19 on data submission and research with observational research deemed non-essential and concerns about COVID-19 leading many clinical research staff and data professionals working off-site often without access to systems necessary to accurately and completely conduct data submission and research activities. These challenges have led to a substantial decline in data submission to the SCTOD. Dr. Rizzo also noted that all on-site data audits conducted by the SCTOD have been suspended for the time being but remote audits are occurring at some centers and other audits will be rescheduled.

Despite these challenges, the CIBMTR has added voluntary forms to the data collection to help collect information on the impacts of COVID-19. As of April 16, 2020 there were reports of 37 COVID -19 infections among blood stem cell transplant recipients from 19 reporting centers (4 of these centers were outside of the U.S.) and 7 deaths among those infected.

### ***Discussion***

Dr. Laughlin asked what steps the transplant community can take to mitigate risks of patients and donors given the likelihood of a potential surge of COVID cases over the next several months. Dr. Rizzo responded that programs should continue to encourage potential recipients and donors to maintain social distance and be as smart as they can to avoid risk. Transplant centers can provide virtual visits and virtual checks of patient vital signs as much as possible. Dr. Devine added that there is an awareness of the potential for a surge in the potential number of transplants over the summer and early fall and the potential risk of a second wave in the winter and potentially repeating what is currently being done as a response

Dr. Giralt asked if data is being collected on the investigational agents being used, particularly remdesivir and convalescent plasma, and if that data will be included in with the SCTOD report. Dr. Rizzo replied that it is currently being collected within the comprehensive report but the access to remdesivir or convalescent serum is not currently collected with post-transplant data.

### **Patient Access to Cellular Therapy (PACT) Act Overview: Potential Impact on Blood Stem Cell Transplantation**

*Ellie Beaver, Manager, Health Policy, National Marrow Donor Program*

*Jessica Knuston, Government Affairs Director, National Marrow Donor Program*

The PACT Act, which was first introduced in 2018 and signed into law in December 2019, represents a significant restructuring of how Medicare reimburses transplant programs for costs related to the identification matching blood stem cell donors and the costs related to acquisition of the blood stem cell product for transplant. The new law requires Medicare reimburse donor search and cell acquisition on a reasonable cost basis, separate from the payment for the inpatient transplant stay. The new payment model will be modeled after solid organ payment policy and is widely supported by the blood stem cell transplant community.

Ms. Beaver and Ms. Knutson provided the Council with an update on the PACT Act and NMDP's plans to support the transplant community through the transition to the new model. They reported that it is expected the Centers for Medicare and Medicaid Services (CMS) will include details on the implementation of this new payment model in the FY 2021 Inpatient Prospective Payment System (IPPS) Proposed Rule consistent with the effective date required by the law. NMDP expects that CMS will propose a phased implementation through fiscal years 2021 and 2022.

The NMDP is preparing to provide guidance and education on the new reimbursement model throughout the implementation to ensure accurate coding and reporting of costs, which is very important to maximize the benefits.

## **Discussion**

Dr. Giralt expressed his appreciation to everyone who worked on these reimbursement issues as it has been a top concern for the transplant centers for more than ten years.

### **Ossium Health Overview: Deceased Bone Marrow for Advanced Cellular Therapies and Emergency Medicine**

*Kevin Caldwell II, Esq, Co-Founder, President, CEO, Ossium Health, Inc.*

*Erik Woods, PhD, HCLD(ABB), Co-Founder, CSO, Ossium Health, Inc.*

*Brian Johnstone, PhD, FORS, Vice President, Research and Development, Ossium Health, Inc.*

*Matthew Metz, PhD, PMP, Director, Strategic Partnerships, Ossium Health, Inc.*

Mr. Caldwell provided the Council with information on a new model for acquiring bone marrow as a source of blood stem cells for transplant. Ossium Health has entered into partnerships with 27 of the 58 organ procurement organizations in the U.S. for the purpose of procuring bone marrow from deceased donors already donating solid organs. Bone marrow for use in blood stem cell transplant is generally procured from living donors once the intended recipient is identified. Ossium is proposing a model to procure bone marrow from deceased donors to be cryopreserved and stored for later use when an appropriately matched donor is identified.

Mr. Caldwell suggested that outcomes for transplants using cryopreserved bone marrow are equivalent to transplants utilizing bone marrow for a living donor. He further suggested that the deceased donation model allows for larger volumes of bone marrow to the potential benefit of transplant patients by making matched products more readily available for transplant. Mr.

Caldwell also highlighted interest from the HHS Biomedical Advanced Research and Development Authority benefit of stockpiling cryopreserved bone marrow for use in emergencies such as radiologic or nuclear events that may necessitate blood stem cell transplant on a large scale.

## **Discussion**

Dr. Laughlin inquired if Ossium is a for-profit entity. Mr. Caldwell explained that it is a Delaware public benefit corporation, which is a for-profit company with an explicit public purpose and mission to improve human health using innovation and biotechnology driven by the bone marrow bank. Dr. Laughlin questioned if the process of informed consent from the families of the individuals donating the organs and bone marrow allow donation to the for-profit company? Mr. Caldwell explained that their donors are typically consented twice. At the time of death, procurement agents interacting with the donor's family requests specific consent and explicitly ask if they are comfortable donating to both for-profit and non-profit organizations. Mr. Caldwell indicated that they do not accept donations from a donor that has not been fully consented.

Dr. Giralt asked about the ethnic diversity of the Ossium donors? Mr. Caldwell explained that the diversity is consistent with of organ donors in general and could follow up with specific numbers.

Dr. Horowitz asked about the differences between deceased and live bone marrow donation. Specifically, she asked how often and when the procured blood stem cells were tested after procurement. Dr. Woods explained that one study compared a set of three live donors to a set of three deceased donors. He indicated that there is ongoing collection of data across all the units received and post-thaw analysis is done on every donor. He also noted that Ossium has three clinical trials currently pending and have completed mirroring transplants, including re-transplants, and have seen very good engraftment comparable to local cord blood in the mirroring model. Dr. Horowitz asked if Ossium would share the post-thaw data and Dr. Woods and Mr. Caldwell agreed to do so.

Dr. Arnold asked about the interface with existing registries and does the consent process include the consent to participation in research and the length of storage? Mr. Caldwell explained that the procurement organizations provide detailed consent. The family then signs the consent documents which are provided to Ossium. The documentation of consent for research versus clinical is required to accept the donor. Mr. Caldwell also indicated that the interface with existing registries would be similar to cord blood bank registries.

Dr. Bracey asked if Ossium's efforts could be considered redundant with the cord blood procurement and indicated that procuring bone marrow from deceased donors seems to require a great deal of funding. Mr. Caldwell answered that the company has been successful with fund raising and that in his opinion the main advantage bone marrow over cord blood is cell volume and the likelihood and speed of engraftment. He concluded that their goal is to provide bone marrow that can be used for a broad range of purposes and not be redundant with cord blood collection.

## **COVID-19: Impact on Cord Blood Banking**

*Marcie Finney, MS, MBA, Executive Director, Cleveland Cord Blood Center*

*David Lin, MD, MHA, Medical Director and Executive Director of the WA Center for Apheresis Therapy*

*Joanne Kurtzberg, MD, Co-Chair NMDP Cord Blood Advisory Group, Director, Carolinas Cord Blood Bank*

Ms. Finney and Drs. Lin and Kurtzberg provided the Council with information on the impact of the COVID-19 pandemic on the collection and utilization of cord blood as a source of blood stem cells for transplant. The presenters also provided insight on how cord blood banks have acted to mitigate risk of COVID-19 infection among cord blood bank staff when collecting and processing cord blood units.

In response to the COVID-19 pandemic cord blood banks are limiting non-essential travel; limiting the number of cord blood collection sites, and reducing staffing to minimum essential staff. Banks have also initiated contingency plans due to disruptions to options for shipping CBUs, potential disruptions to supply chains for materials necessary to process CBUs, and the possibility that cord blood collection could cease at certain banks or collection sites due to infection risk.

The presenters highlighted that the current public cord blood inventory is at extremely low risk of transmitting COVID-19 to a blood stem cell transplant recipient as most CBUs in storage were collected prior to the onset of the COVID-19 pandemic. Dr. Kurtzberg also presented some preliminary data indicating that COVID-19 does not appear to be transmitted from mother to fetus through the placenta nor is the virus. In 75 cases mothers with confirmed COVID-19 infection delivered babies with no documented infection in the babies.

Despite these findings, cord blood banks are screening mothers for risk factors for COVID-19 infection consistent with recent FDA guidance. Overall, clear data are not yet available on the level of disruption of cord blood collection due to the pandemic, but individual banks are reporting significant decreases in the volume of cord blood collections. The presenters also noted that while there has been an increase in transplant centers searching for cord blood units during the pandemic as a possible source for blood stem cell transplants there is not yet evidence of a significant increase in utilization of cord blood at this time.

## **Cord Blood Transplantation: Challenges and Opportunities Perspective from the American Society for Transplantation and Cellular Therapy (ASTCT) – Cord Blood Special Interest Group**

*Juliet Barker, MBBS, Attending Physician, Adult BMT Service and Director, CBT Program, Memorial Sloan Kettering Cancer Center, Professor of Medicine, Weill Cornell Medical College, Chair, ASTCT Cord Blood Special Interest Group*

*Filippo Milano, MD, PhD, Director Cord Blood Program, Fred Hutchinson Cancer Research Center, University of Washington, School of Medicine*

*John Wagner, MD, Professor of Pediatrics and Co-Director, Center for Translational Medicine, University of Minnesota*

Drs. Barker, Milano, and Wagner presented on behalf of the ASTCT Cord Blood Special Interest Group on trends and challenges for the utilization of cord blood for blood stem cell transplant. The presenters then described a proposed demonstration project that could be implemented with coordination between ASTCT and NMDP to support improved utilization of cord blood.

The presenters described the benefits of cord blood as a source of blood stem cells for transplant. CBUs are collected and stored making them readily available for transplant with logistics for receiving the blood stem cells considerably easier than scheduling collection from an identified live donor. They also noted that patient outcomes of transplants utilizing CBUs are comparable to those transplants using blood stem cells from adult donors and that cord blood continues to be an important source of blood stem cells to ensure access to transplant for individuals who are not of European descent. Non-Europeans are significantly less likely to find an adequate match from donor registries and are less likely to identify an eligible donor for a haploidentical transplant. Haploidentical transplants use blood stem cells from a half-matched donors, usually a family member. The practice of haploidentical transplant has recently increased as outcomes have improved.

Despite these benefits the use of CBUs in transplant has declined in recent years due to a variety of factors, including cost, complexity of CBU selection, and complexity of post-CBU transplant care.

Due to the decline in utilization of CBUs for transplant nearly 80% of blood stem cell transplant programs have little or no experience with cord blood transplant. The presenters highlighted that the U.S. population is becoming increasingly diverse that younger more diverse patients are increasingly harder to match to donors. The presenters reported that 54% of patients over 60 are able to identify an ideal matched donor while only 34% of patients under 20 are able to identify an ideal match as younger individuals are more likely to have a unique human leukocyte antigen (HLA) type.

In conclusion, the presenters recommended several strategies to support the availability of cord blood as a source of blood stem cells for transplant. They proposed:

- Continued support of cord blood collections in high quality cord blood banks;
- Consolidation of high quality CBUs in the event of closures of some cord blood banks; and
- Development of a demonstration project to optimize the conduct of cord blood transplant by providing high-quality guidance to transplant centers on how best to utilize cord blood and coordination among entities involved in cord blood collection, selection, logistics, and transplant.

The aim of the proposed demonstration project is to enhance access to cord blood transplant and improve transplant outcomes with a specific focus on serving racial and ethnic minorities and patients with high-risk disease. The Council was very interested in supporting these

recommendations and is planning further detailed discussion and analysis of this possibility at the next ACBSCT meeting in fall 2020.

### ***Discussion***

Dr. Giralt asked how much of the barrier to cord blood is due to the cost of the product and how feasible is it to homogenize the way cord blood transplants are performed and requested? Dr. Wagner responded that the cost itself has been a barrier by transplant centers and insurers. He also noted that there is a perception of higher cost during and post-transplant, but comparatively, the cost of collecting non-hematopoietic stem cells from a sibling or related donor is significantly higher. Dr. Milano added that the effort put forth concerning the guidelines is aimed toward homogenization. Dr. Barker noted the importance of unit selection and highlighted the collaborative initiative to map out the step-by-step selection process to show how it is done.

Dr. Delaney commented that she was particularly struck by the importance of the increasing diversity of the U.S. population. She expressed concern that cord blood transplantation is declining and suggested that the issue of alternative donors or non-fully matched related donors needs to be addressed recognizing all aspects of the issue.

### **Adjournment**

Dr. Gandhi gave his appreciation to the speakers for their efforts for the insightful meeting.

Mr. Walsh echoed Dr. Gandhi's statements and thanked everyone for attending especially in the time of the COVID-19 pandemic. The meeting was adjourned at 3:32 p.m.