

**ADVISORY COUNCIL ON
BLOOD STEM CELL TRANSPLANTATION (ACBSCT)**

US Department of Health and Human Services (HHS)

August 22, 2024

2:00–6:00 p.m.

MEETING MINUTES

Voting Members Present: Navneet Majhail, M.D., M.S., M.B.B.S., Chair; Juliet Barker, M.B.B.S.; Ann Richardson Berkey; Marcie Finney, M.S., M.B.A.; Eapen K. Jacob, M.D.; John Levine, M.D., M.S.; Richard Maziarz, M.D.; and Filippo Milano, M.D., Ph.D

Nonvoting Members Present: *Nancy L. DiFronzo, Ph.D.*, National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH); *Max Grogl, BSc, MSc, PhD*, Naval Medical Research Center, United States Navy, Department of Defense (DOD); *Frank Holloman*, Division of Transplantation, Health Resources and Services Administration (HRSA); *Mark McGinnis, JD*, Office of the General Counsel, Department of Health and Human Services (HHS)

Presenters: *Jeffery Auletta, M.D.*, Center for International Blood and Marrow Transplant Research (CIBMTR) and National Marrow Donor Program (NMDP); *Juliet Barker, MBBS*, Bone Marrow Transplantation and Cell Therapy Program, Weill Cornell-New York Presbyterian Hospital; *Steven Devine, M.D.*, Center for International Blood and Marrow Transplant Research (CIBMTR); *Mike Hearne*, Experience Strategy and Engagement NMDP; *Marcie Finney, M.S., M.B.A.*, Cleveland Cord Blood Center; *Filippo Milano, M.D., Ph.D.*, Cord Blood Transplantation Program, Fred Hutchison Cancer Research Center; *Elizabeth Shpall, M.D.*, Cell Therapy Laboratory and Cord Blood Bank University of Texas MD Anderson Cord Blood Bank; *Heather Stefanski, M.D., Ph.D.*, CIBMTR and NMDP

Designated Federal Officer (DFO): Shelley Tims Grant, Executive Secretary, ACBSCT

WELCOME AND OPENING REMARKS

Shelley Tims Grant, ACBSCT, Executive Secretary

Dr. Navneet Majhail, MD, MS, FASTCT, Chair, ACBSCT

Ms. Grant called the meeting to order at 2:06 p.m. (The meeting was held virtually and open to the public.) Dr. Majhail welcomed the participants and reminded them that the ACBSCT provides advice and recommendations to the Secretary of the Department of Health and Human Services

via the HRSA Administrator on the activities of the C.W. Bill Young Cell Transplantation Program (CWBYCTP) and the National Cord Blood Inventory (NCBI). The main focus of the ACBSCT is to advise HRSA on improving access and outcomes for people who need blood stem cell transplants and cellular therapies, particularly for the medically underserved.

Dr. Majhail opened the meeting by expressing his honor in leading the advisory council and serving the Health Resources and Services Administration (HRSA) and the HHS. He introduced himself as the physician and chief of blood cancers at the Sarah Cannon Cancer Network. He welcomed attendees to the first meeting of the year. He noted that two subcommittees had been formed since the previous meeting in October 2023—one focused on cord blood and the other on drug shortages in blood stem cell transplant and cellular therapy. He acknowledged the efforts of those involved in these subcommittees, particularly the team led by Dr. Shpall, whose findings would be presented during the meeting.

Dr. Majhail highlighted the role of the ACBSCT in advising the Secretary of HHS through HRSA, specifically on the activities of the CW Bill Young Cell Transplantation Program (CWBYCTP) and the National Cord Blood Inventory (NCBI) program. He noted that the council provided a platform to share the latest advances in blood stem cell transplantation, with a focus on increasing access to transplantation, particularly for underserved populations. He recapped the October 2023 meeting, where topics such as the need for blood stem cell transplants and donor recruitment and retention challenges were discussed. Experts such as Dr. Auletta and Ms. Ericka Jensen presented the estimated need for over 18,500 transplants and strategies to improve donor participation and reduce attrition.

In outlining the agenda for the current meeting, Dr. Majhail explained that the focus would remain on increasing access to transplantation. Updates from the American Society of Transplantation and Cellular Therapy (ASTCT) and the National Marrow Donor Program (NMDP) would address efforts to increase access to transplantation and reduce barriers. The subcommittee on cord blood would present its findings, and various experts would discuss transplant outcomes using different donor sources and progress in cord blood transplantation in both clinical trials and standard care. He also mentioned that public comments had been submitted and would be heard before concluding the meeting.

ACBSCT SUBCOMMITTEE ON CORD BLOOD

Elizabeth Shpall, MD, Lead Consultant for ACBSCT Subcommittee, Director, Cell Therapy Laboratory and Cord Blood Bank University of Texas MD Anderson Cord Blood Bank, Houston, TX

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

Juliet Barker, MBBS, Director of Transplantation and Cell Therapy, Weill Cornell-New York Presbyterian Hospital, New York, NY

Filippo Milano, MD, PhD, Director, Cord Blood Transplantation Program, Fred Hutchinson Cancer Research Center, Seattle, WA

Dr. Shpall began the talk by thanking her colleagues Navneet and Shelley and expressed her honor in leading the subcommittee. She outlined the subcommittee's mission, formed after the last ACBS CT meeting, where members requested HRSA to establish a subcommittee focusing on increasing the utilization of cord blood in transplantation and defining a high-quality blood unit for banking specifications. Dr. Shpall introduced the subcommittee's members and consultants, mentioning their work in defining a high-quality unit, promoting more cord blood-focused research, and exploring demonstration projects to increase health equity and access to life-saving transplants. She highlighted that their first objective was to define a high-quality cord blood unit, essential for meeting the statutory goal of adding at least 150,000 genetically diverse units to the National Cord Blood Inventory (NCBI).

Ms. Finney explained how the subcommittee worked to define a high-quality cord blood unit. She referred to FDA guidance, which specifies the safety, purity, potency, and identity requirements for cord blood units. Ms. Finney elaborated on how maternal infectious disease tests, sterility, and hemoglobinopathies are part of the safety criteria. At the same time, total nucleated cells, viable nucleated cells, and CD34 cells are considered under purity and potency. For identity, HLA typing and confirmatory tests are required before release. Ms. Finney concluded by emphasizing that all cord blood banks must follow this table of standards, which would be the recommendation presented to the advisory board.

Dr. Milano addressed the challenges related to cord blood transplantation, particularly the reduced utilization in many transplant centers, where less than 50% perform cord blood transplants. He explained that the increased preference for other types of transplants, like haploidentical and mismatched unrelated donors, has led to a decline in expertise and interest in cord blood transplants. He acknowledged that even centers with more expertise, including his own, had issues with collaboration, which hampered progress. Dr. Milano stressed the need for increased expertise, better education, and collaboration between transplant centers, suggesting that niche areas, such as patients with high-risk diseases or second transplants, could benefit from cord blood. He emphasized the importance of research and collaboration to reverse the declining trend in cord blood transplants. He called for more funding and explored novel therapies to enhance its usage.

Dr. Barker introduced the National Cord Blood Network, a collaborative consortium of transplant centers to increase cord blood transplant activity and utilize the federally funded domestic inventory to treat life-threatening diseases. She explained that the network includes a steering

committee and administrative oversight, with participation from eight centers and ten transplant programs across the U.S. Dr. Barker emphasized the importance of disseminating guidelines and protocols to transplant centers nationwide. She also mentioned efforts to address the challenge of cord blood searches, with a dedicated search coordinator consortium and a focus on promoting health equity initiatives. Additionally, Dr. Barker stressed the need for collaboration with stakeholders, such as HRSA, the Cord Blood Association, and international organizations, to create the infrastructure necessary for advancing cord blood transplants and related research.

Dr. Shpall summarized the committee's three key recommendations. First, according to FDA specifications, HHS should define a high-quality cord blood unit. Second, the National Cancer Institute and NIH should be encouraged to support research on cord blood transplantation and cellular therapy. Finally, HHS should support demonstration projects to increase cord blood utilization, particularly for underserved racial and ethnic minority populations.

INCREASING ACCESS TO BLOOD STEM CELL TRANSPLANTATION

Update on Access Initiative to Address and Sustain Equal Outcomes for All Transplant Recipients

Jeffery Auletta, MD, Co-Chair, Access Initiative, Senior Vice President, NMDP, Chief Scientific Director, Center for International Blood and Marrow Transplant Research (CIBMTR), Minneapolis, MN

Dr. Auletta focused on the American Society for Transplantation and Cellular Therapy (ASTCT) initiative and the National Marrow Donor Program (NMDP) to improve access to stem cell transplants for ethnically diverse populations. He highlighted stark disparities in transplant access, noting that while 36% of non-Hispanic white patients successfully navigate the system to receive transplants, only 17% of ethnically diverse patients do. While factors like disease type play a role, Dr. Auletta emphasized that social and systemic barriers, such as poverty and racial inequity, create a “spider web” of challenges that prevent diverse patients from receiving necessary treatments.

The initiative addresses these barriers through four pillars: education, community engagement, research, and system change. Efforts include physician education programs, facilitating HLA typing in community settings, and improving caregiver support systems. Ongoing projects such as the Medicaid scan examine disparities in state policies regarding transplant eligibility, and the junior faculty immersion program promotes diversity in the transplant workforce. Advocacy is a key component, with the initiative pushing for policies like the Life-Saving Leave Act to protect donors’ jobs and improve Medicaid reciprocity for patients needing transplants across state lines.

Dr. Auletta stressed the importance of partnerships to dismantle the social determinants of health that limit transplant access. Collaborations with nonprofit organizations, corporate sponsors, and

government entities are crucial to overcoming these entrenched issues. Through the ACCESS Initiative, ASTCT and NMDP aim to increase awareness, reduce barriers, and ultimately ensure that more patients from diverse backgrounds receive life-saving transplants. Looking ahead, the ACCESS Initiative plans to continue its efforts through future workshops and broader engagement across the transplant ecosystem.

Discussion

- Dr. John Levine asked for elaboration on the caregiver initiative, noting that more details could help advance access to transplants. Dr. Auletta responded by saying he would send a link for more details and explained that the initiative explores using technology to support caregivers and reconsidering the traditional mandate of having a single caregiver, recognizing the role of a broader social unit.
- Dr. Juliet Barker emphasized that the lack of caregivers is a significant issue for transplant patients in New York City, sometimes leading to denial of transplants due to insufficient social support rather than medical or insurance factors.
- Dr. Richard Maziarz commented that his team had worked on caregiver availability for 20 years, noting that the age of both transplant recipients and caregivers impacts outcomes and that educational support systems should be tailored accordingly. He also mentioned that payers may deny transplants without a strong caregiver plan, combining institutional and financial factors. Dr. Juliet Barker added that some institutions are unsympathetic to admitting patients with compromised support, as their length of stay could be longer than those with adequate resources, making it a challenging issue for transplant physicians.

Strategies to Improve Adult Donor Retention

Mike Hearne, Director, Experience Strategy and Engagement NMDP, Minneapolis, MN

Mr. Hearne focused on strategies to improve donor retention within the NMDP (formerly known as the National Marrow Donor Program). As the Director of Experience Strategy and Engagement, he emphasized the need to enhance the donor experience from the initial awareness phase to the donation process. His team, part of a broader group of 600 people, ensures that life-saving therapies are available when patients need them, highlighting the importance of timing. Mr. Hearne explained how the donor experience is interconnected, much like a web, and how it involves keeping potential donors engaged for extended periods—sometimes years or even decades—before they are called to donate.

He discussed NMDP's challenges, particularly the decline in global donor availability since the pandemic. Three key factors were driving this issue: the emotional and mental health stress among donors, the shift toward younger donors (who are often less available), and the need to improve access and equity, especially for ethnically diverse donors, who show lower availability and

retention. Hearne outlined how the current social context, including distractions and an attention economy, complicates donor engagement and stressed the importance of understanding deeper motivations for donors, such as their desire for contentment, purpose, and connection to like-minded communities.

To address these challenges, Mr. Hearne presented several initiatives to boost retention, including digital registration improvements, donor contact information validation, and enhanced engagement strategies targeting specific donor segments. His team is working to implement a loyalty experience, expand communication channels to include social media and Discord platforms and develop a personalized member portal to streamline the donation process. Additionally, they are focused on performance management and better support for donors during the final stages of donation. They use tools like Salesforce to provide tailored communication that addresses barriers specific to ethnically diverse populations.

Discussion

- Dr. Juliet Barker asked about the availability of adult donors for patients of non-European ancestry, particularly those of African ancestry, and whether multiple donors could be worked up simultaneously to address the urgency in cases like acute leukemia. Mr. Hearne responded by explaining that proactive outreach efforts were being made to engage donors and improve donor readiness. He mentioned ongoing pilots with transplant centers to recommend alternative donor sources for patients with poor search prognoses.
- Ms. Ann Berkey asked how often NMDP reaches out to registry members, particularly younger people, and how to keep them engaged and involved. Mr. Hearne responded by explaining that they aim to balance communication to avoid over-communicating. They are actively increasing engagement efforts while making interactions more beneficial for the donors, including encouraging them to advocate and share with their networks.
- Shelley Grant asked about the retention rates by race and ethnicity, noting that they seemed to vary widely. Mr. Hearne confirmed that retention and availability differed significantly, especially regarding who agrees to donate, with ethnically diverse groups showing lower availability than non-ethnically diverse groups by around 20 percentage points.

DONOR SOURCES FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

Update on Transplant Outcomes Using Different Donor Sources

Steven Devine, MD, Chief Medical Officer, NMDP, Senior Scientific Director, Center for International Blood and Marrow Transplant Research (CIBMTR), Minneapolis, MN

Dr. Devine discussed recent advancements in overcoming HLA barriers in transplantation, primarily focusing on adult-related and unrelated donors. He highlighted that over the past 15 to 20 years in

the U.S., there has been a significant decline in the use of matched-related donors, with about 60% of donors now being unrelated to the recipient. Post-transplant cyclophosphamide (PTCy) for GVHD prophylaxis has been a key driver in these changes, especially in mobilized peripheral blood transplants. These advancements have expanded access to transplantation for racially and ethnically diverse patients. The trends showed a growth in the use of mismatched donors since 2012, enabling more diverse patients to receive life-saving transplants.

Dr. Devine also focused on research comparing outcomes of patients receiving transplants from 8/8 matched unrelated donors and 7/8 mismatched donors. Recent studies showed no significant difference in overall survival or GVHD-free relapse-free survival between these groups, thanks to PTCy use. Additionally, there has been a rise in the number of mismatched transplants using peripheral blood, particularly in ethnically diverse populations. While PTCy has improved outcomes, some disparities remain, especially in mismatched related and unrelated donor settings, requiring further research. Overall, access to transplants has increased significantly for patients of all ancestries, partly due to these efforts in research and clinical practice.

Discussion

- Dr. Barker emphasized that while mismatched unrelated donors transplanted with PTCy have been a breakthrough, relying solely on adult donors does not guarantee timely donor availability, especially for patients with acute leukemia. Dr. Devine agreed, clarifying that while donor options have expanded, the time to transplant remains similar across different donor sources. However, urgent cases may face challenges with adult donor availability.
- Dr. Barker highlighted the racial and ethnic disparities in patients who never receive transplants, noting that some of the issues are driven by donor availability. Dr. Milano expressed concerns about the misleading perception of cord blood transplants due to incorrect graft selection in many centers. At the same time, Dr. Majhail emphasized the importance of bridging the knowledge gap through mentorship and experience-sharing to improve cord blood transplant outcomes in less experienced centers.

NMDP's Efforts to Support Cord Blood – Standard of Care and Clinical Trials

Heather Stefanski, MD, PhD, Vice President, Center for International Blood and Marrow Transplant Research (CIBMTR) and Clinical Services NMDP, Minneapolis, MN

Dr. Stefanski began her talk by sharing her background as a pediatric bone marrow transplant physician at the University of Minnesota, where her leukemia patients primarily received either sibling-matched transplants or cord blood. She expressed enthusiasm about discussing the work of the National Marrow Donor Program (NMDP), particularly its focus on supporting cord blood research and use in the transplant community. Dr. Stefanski highlighted NMDP's commitment to educating healthcare providers, providing resources to cell and gene therapy developers, and

ensuring that cord blood remains integral to the future of cell therapy. She then outlined the topics she would cover, including program enhancements, selection guidelines, and future directions, such as the BMT CTN trial, which focuses on cord blood inventory and its importance for ethnically diverse patients.

Dr. Stefanski discussed the cord blood immersion program, which aims to train new faculty and fellows, particularly at transplant centers that perform fewer cord blood transplants. She highlighted the program's success and its role in fostering the next generation of skilled transplant physicians. Dr. Stefanski also touched on the Cord Blood Bank Alliance and its goal to simplify processes for banks working with cell and gene therapy developers. Additionally, she described using search prognosis scores to guide donor selection strategies, especially for patients with a low likelihood of finding a perfect match. This innovative approach aims to expedite transplants by pivoting quickly to alternative donors, including cord blood, to improve patient outcomes.

Discussion

- Dr. Milano commented that it was crucial to establish proper standards for cord blood transplants. Current practices lack consistency compared to other transplant types, and without following these standards, the data may present misleading results.
- Dr. Barker explained that they involved experienced search coordinators from across the country to improve the process of cord blood searches, as many coordinators and doctors were uncomfortable with it. She emphasized the importance of peer-to-peer learning and detailed teaching materials to enhance unit selection and ensure successful transplants.
- Dr. Maziarz commented that establishing and adhering to a standard for cord blood selection would benefit everyone, noting that participation in clinical trials, such as the Amadou vessel studies, may lead institutions to adopt different selection criteria, highlighting the need for universal guidelines.
- Dr. Barker emphasized that while they fully support the immersion program, it is crucial for trainees to have ongoing mentorship over several years and noted that if senior leadership at transplant centers does not support cord blood transplants, the training may not make a significant impact.
 - Dr. Stefanski highlighted that applicants for the immersion program needed a commitment letter from their director to ensure support for future cord blood transplants and shared that Dr. Sanchez Petito was actively discussing the reintroduction of cord blood transplants at OSU, emphasizing the need for institutional commitment.

PUBLIC COMMENTS

Dr. John Wagner reflected on the progress and challenges in hematopoietic stem cell transplants. He emphasized the advances in improving survival rates. However, he noted that more work was needed to address graft-versus-host disease (GVHD) and relapse-free survival. Dr. Wagner highlighted the development of the national hematopoietic stem cell program and its impact, particularly in cord blood transplantation. He discussed the potential of novel immune therapies, such as regulatory T cells (T regs), in preventing GVHD and enhancing cancer treatment. Dr. Wagner stressed the importance of making these therapies more accessible and cost-effective, with hopes for further advancements in the future.

Dr. Alexis Harris, a sociology professor and recipient of a cord blood transplant for MDS in 2016, emphasized the importance of considering racial and economic equity in patient care and access to transplants. She shared her gratitude for the life-saving treatment she received but stressed that such options should not be determined by race or luck. Dr. Harris urged decision-makers to include diverse patient perspectives in their processes, especially regarding policies that impact marginalized groups. She called for greater attention to equity and diversity in the medical field, thanking the audience for their efforts.

- Ms. Shelley Grant asked Dr. Harris to share her journey from diagnosis to discovering cord blood transplant and Dr. Milano's involvement in her care. Alexis explained how it took six months for her to be diagnosed, how she eventually found Dr. Milano, who introduced her to cord blood transplants, and how she successfully underwent the procedure, becoming a strong advocate for cord blood donation.
- Ms. Shelley Grant asked Alexis Harris if she had experienced challenges with graft-versus-host disease after her cord blood transplant. Dr. Harris responded that she did face issues with skin, gut, mouth, and liver complications, which were managed with a drug she disliked but that ultimately saved her life.

Jennifer Jones Austin, a cord blood transplant recipient, shared her experience of being diagnosed with acute myeloid leukemia in 2009 and given a 1% chance of survival. Despite no matches in the bone marrow registry, Dr. Juliet Barker at Memorial Sloan Kettering Cancer Center administered a cord blood transplant in 2010, which saved her life. She faced challenges like graft-versus-host disease but successfully recovered and has remained cancer-free for nearly 15 years. Ms. Jones Austin highlighted the difficulties people of color face in finding matches and emphasized the importance of advancing cord blood transplant options to improve equity in treatment.

- Dr. Richard Maziarz reflected on the impact of grassroots efforts, mentioning the case of Rod Carew's daughter and praising Jennifer Jones Austin's husband's contributions to donor recruitment, emphasizing the importance of such initiatives. Jennifer Jones Austin agreed, sharing that although bone marrow transplant efforts helped others, it was cord blood from

two African American baby boys that ultimately saved her life. This highlights the need to continue investing in cord blood transplantation for those for whom bone marrow is not an option.

- Dr. Juliet Barker highlighted that in Jennifer's case, cord blood was the only option due to her severe illness. Its advantage was its flexibility in adjusting the transplant date, unlike adult donors whose availability might not align with the patient's readiness.

NEW BUSINESS AND DISCUSSIONS

The committee discussed and considered motions to adopt recommendations from the Subcommittee on Cord Blood Transplantation.

Motion: To approve the recommendation by the Subcommittee on Cord Blood Transplantation:
“For the purposes of the National Cord Blood Inventory, HHS should define a high-quality cord blood unit as one meeting the specifications outlined in the FDA Guidance for Industry for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood.”

Motion By: Juliet Barker

Seconded By: Ann Berkey

Carried: The motion was unanimously approved by roll call vote.

Motion: To approve the recommendation by the Subcommittee on Cord Blood Transplantation:
“HHS should strongly encourage the National Institutes of Health (NIH) or other relevant HHS agencies to support research specifically focused on cord blood transplantation and cord blood-derived cellular therapy including the necessary associated infrastructure. The aim of this research funding is to leverage the utilization of NCBI-funded high quality cord blood units to meet the need for treatment of patients with life-threatening cancers and non-malignant diseases.”

Motion By: Ann Berkey

Seconded By: Juliet Barker

Carried: The motion was unanimously approved by roll call vote.

Motion: To approve the recommendation by the Subcommittee on Cord Blood Transplantation:
“HHS should support, fund, and continue additional demonstration projects that have the potential to increase cord blood utilization and thereby extend access to allogeneic hematopoietic transplantation, especially for minority patient groups.”

Motion By: Juliet Barker

Seconded By: Ann Berkey

Carried: The motion was unanimously approved by roll call vote.

ADJOURNMENT

Dr. Majhail thanked the participants for a robust and enlightening meeting. The meeting adjourned at 5:40 p.m.