BMT CTN
Blood & Marrow Transplant Clinical Trials Network®

Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Annual Report

September 2024 – March 2025

www.bmtctn.net

ABOUT THE BMT CTN

The BMT CTN conducts large, multi-institutional clinical trials to improve outcomes of cellular therapies, such as hematopoietic cell transplantation (HCT), for patients facing life-threatening disorders. Established in 2001, the BMT CTN infrastructure facilitates effective communication and cooperation among participating centers and collaborators to conduct multi-institutional trials available to patients in all regions of the United States (US).

OUR SIGNIFICANCE

Approximately **30,000** uses of cellular therapy for cancer are reported to CIBMTR annually, and the number increases by about **5%** per year. Cellular therapy is a rapidly evolving field, and clinical trials face unique challenges, including the relatively small number of treatments performed at any single center, diverse indications for cellular therapy, complexities of the intervention, and multiple post-treatment complications.

BMT CTN Achievements

67 trials launched

59 trials completed accrual; 8 ongoing

>17,300 patients from >100 centers

>513,000 biospecimens in the Research Sample Repository

188 ancillary and correlative studies launched

- **101 used cryopreserved specimens from the Repository or samples shipped directly to a project laboratory**

126 ancillary and correlative studies published

194 manuscripts published

181 abstracts presented

DATA AND COORDINATING CENTER (DCC)

The BMT CTN DCC is managed by **3** organizations with extensive cellular therapy research experience: the **Medical College of Wisconsin (MCW)**, **NMDP**, and the **Emmes Company**.

MCW is the **3rd** largest private medical school in the nation with **$424 million** invested in research and training this year. It is the original home of the International Bone Marrow Transplant Registry [now the **Center for International Blood and Marrow Transplant Research (CIBMTR)**, see below] and has a long history of research and clinical care related to HCT and other cellular therapies.

NMDP is the world leader in HCT donor registry and graft procurement management, and it operates the world's largest HCT-related research sample repository.

Together, **MCW** and **NMDP** operate **CIBMTR,** an international research program with a network of **>310** centers in **>25** countries that submit cellular therapy outcomes data for patients, resulting in a research database with information from **>700,000** patients and **>1,900** publications.

The **Emmes Company** is a contract research organization that has managed **>2,150** Phase I-IV trials and registries involving **32,000** research sites in **>75** countries and has **>2,300** publications in scientific journals.

The DCC manages the efficient development, implementation, and completion of high-quality Phase II and III clinical trials for the Network.

NETWORK MANAGEMENT HIGHLIGHTS

The DCC coordinates and supports all BMT CTN activities to enhance Network effectiveness. During this reporting period, the DCC posted **4** plain language summaries of BMT CTN manuscripts and improved the new section of the public website for patients and caregivers. The DCC also held a study coordinator training session at the 2025 Tandem Meetings that **153** in-person participants attended, and the organization hosted virtual study coordinator meetings in November 2024 and March 2025.

BIOSPECIMEN REPOSITORY

Each BMT CTN protocol creates an important new opportunity for the scientific community to collect baseline and post-treatment biologic specimens for clinical research. For most protocols, biologic samples are collected for use in protocol-defined research aimed at answering specific questions for that patient population and its transplantation outcomes. Collection of supplementary samples for future unspecified research is incorporated into most protocols. These samples and the associated clinical data are made available as a valuable resource for investigators at large. Available BMT CTN research sample inventories are regularly updated in the Investigator & Research Staff Resources section of the Network's public website to help investigators plan correlative studies.

Storing Samples. As of March 31, 2025, **513,880** research sample aliquots, provided by **8,359** subjects, were stored by the BMT CTN Network: National Heart, Lung, and Blood Institute Repository; BMT CTN Sample Repository operated by NMDP; and the AIDS and Cancer Specimen Resource Repository.

Distributing Samples. During this reporting period, the BMT CTN shipped **142** frozen sample aliquots from its Sample Repository to **3** project laboratories for protocol-defined and ancillary studies.

Processing Samples. The BMT CTN processing laboratory received and processed samples from **36** Network shipments during this reporting period, averaging **5** shipments per month.

DATA COLLECTION AND REVIEW

BMT CTN clinical data are captured through the Emmes proprietary eClinical system (or previous version, AdvantageEDC) or CIBMTR's Medidata Rave system. During this reporting period, participating centers submitted **2,342** forms in the AdvantageEDC and eClinical systems.

CIBMTR's Research Database also captures clinical data via FormsNet3. For protocols that require only a limited amount of protocol-specific data, such as BMT CTN 1702, CIBMTR's Research Database is used as the primary study database. During this reporting period, participating centers submitted **8,876** forms in FormsNet for patients enrolled on BMT CTN studies. CIBMTR's Research Database is also used for supplemental data collection, especially long-term follow-up.

After data collection is complete, the protocol's Endpoint Review Committee provides an independent review of submitted data in a blinded manner. During this reporting period, endpoint review was completed for BMT CTN 1801, increasing the total number of completed reviews to **30**.

PATIENT-REPORTED OUTCOMES

The capability to centrally collect patient-reported outcomes data creates an important opportunity for the scientific community. These data are linked to clinical and specimen data using patient IDs and are made available as a valuable resource for investigators at large. During this reporting period, the Survey Research Group collected **106** patient-reported outcomes surveys.

TECHNICAL COMMITTEE ACTIVITIES

DISSEMINATION AND IMPLEMENTATION COMMITTEE

Dissemination and implementation science is an emerging field in medicine requiring knowledge and skills beyond the scope of most Network protocol teams. It focuses on barriers to the translation of research findings to clinical practice. The purpose of the Dissemination and Implementation Committee is to incorporate the principles of implementation science into the scientific agenda of the Network to promote the uptake of evidence-based findings from BMT CTN studies into routine practice to amplify the Network's impact on patient care.

Dissemination and Implementation Committee Responsibilities

Educate BMT CTN stakeholders

Help develop and review protocols to incorporate implementation outcomes in study design and target stakeholders for dissemination

Identify potential challenges to and assessment of implementation

Support dissemination and implementation strategies, particularly to address healthcare inequalities

Define evaluation metrics for dissemination and implementation strategies

During this reporting period, the committee continued to convene monthly to refine their processes to disseminate and implement the information learned from Network trials and to continue their work on **2** priority projects.

The first project developed and deployed a survey to understand the status of uptake of the BMT CTN 1703 Graft-versus-Host Disease (GVHD) Prevention PROGRESS III study and potential barriers for activation of the upcoming BMT CTN 2203 PROGRESS IV study, with a plan to understand barriers that might also exist for widespread implementation of study therapies from the latter trial once results are known. Committee members analyzed responses and will present a poster at the EBMT Annual Meeting.

The second project reviewed BMT CTN 1502 aplastic anemia study results dissemination and the incorporation of dissemination and implementation concepts into the upcoming BMT CTN 2207 aplastic anemia study. The committee developed a survey of practice patterns in aplastic anemia and plans to deploy it early in the next reporting period. In collaboration with the BMT CTN 2207 Protocol Chair, committee members submitted a commentary to Blood Advances that will be published during the next reporting period.

The Dissemination and Implementation Committee is exploring opportunities for the upcoming year, including projects to assess implementation of BMT CTN 1102 results into clinical practice and whether recent studies regarding mismatched donor use are translating to changes in donor selection practices. The committee is also planning projects reviewing the implementation of findings from BMT CTN 1702 and 1704.

BIOMARKERS COMMITTEE

The Biomarkers Committee informs the Network's scientific agenda with a focus on questions involving analysis of biologic specimens for genomic and proteomic markers, and it advises Network protocol teams in their review of ancillary study proposals that request the use of BMT CTN research samples. This year, the Biomarkers Committee met quarterly to discuss an approach to standardize sample collection scheduled across protocols and to prepare for the upcoming non-malignant disease biorepository protocol. The committee also discussed and proposed ways to maximize sample utilization.

TECHNICAL COMMITTEE ACTIVITIES

PATIENT-REPORTED OUTCOMES (PRO) COMMITTEE

The PRO Committee ensures that PRO are appropriately selected, collected, and analyzed, not only for the particular study in which they are collected but in consideration of analyses of PRO across the BMT CTN suite of studies.

During this reporting period, PRO Committee members assisted in the BMT CTN 1703 PRO analysis that was published in the Journal of Clinical Oncology in January 2025. Committee members also drafted an updated manuscript to the 2012 publication "Collection of Patient-Reported Outcomes in Blood and Marrow Transplant Clinical Trials Network Studies" that is anticipated to be completed in the next reporting period.

CLINICAL RESEARCH ASSOCIATES COMMITTEE

The Clinical Research Associates Committee reviews each BMT CTN protocol before it is distributed to centers, focusing on reviewing and resolving logistical issues; assists in developing and reviewing Case Report Forms; reviews education materials for use at participating clinical centers; and provides input for the annual BMT CTN Coordinators' meeting. During this reporting period, the Clinical Research Associates Committee reviewed the BMT CTN 2303 protocol.

PHARMACY COMMITTEE

The Pharmacy Committee reviews BMT CTN protocols for appropriate use and administration of pharmaceuticals, and it helps develop draft template chemotherapy and other medication risk language to include in upcoming BMT CTN study protocol and informed consent document. The Pharmacy Committee is also available for ad hoc assistance in answering medication-related questions, such as those related to the Network's approach to chemotherapy shortages and investigational product handling issues.

SPECIAL POPULATIONS COMMITTEE

The Special Populations Committee consists of pediatric and adult transplant physicians from Core and Affiliate Centers. It ensures that all patient groups are considered for participation in all appropriate investigational protocols developed by the Network, and it makes recommendations to increase participation of patients who are less likely to enroll. For example, the Committee ensures that, for studies involving pediatric participants, appropriate modifications are addressed in informed consent, patient care, and monitoring documents. It also reviews eligibility criteria to ensure they do not unnecessarily restrict access to the broad range of transplant recipients considered eligible for standard of care cellular therapies.

The committee provides guidance to protocol teams on ways to increase access to clinical trials for patients who are less likely to participate. Committee members drafted a tip sheet for parameters to consider. The tip sheet outlines barriers to special populations (e.g., children, geographically restricted populations) and includes examples for building feasibility and flexibility into the study design (e.g., broadening inclusion criteria, allowing for longer windows for follow-up assessments, including virtual visit options) so that the protocol is more accessible. The committee presented their recommendations and tip sheet to the Steering Committee at its June 2023 meeting, and the Steering Committee approved them. This tip sheet is now available to all protocol teams to consider.

TECHNICAL AND EXECUTIVE COMMITTEE ACTIVITIES

TOXICITY AND SUPPORTIVE CARE COMMITTEE

The Toxicity and Supportive Care Committee works with the DCC to define methods for evaluating adverse events and toxicities post-transplantation, reviews toxicity evaluation and monitoring requirements on Network protocols, and designs and approves forms and procedures for collecting toxicity data. During this reporting period, the Toxicity and Supportive Care Committee facilitated a review of the BMT CTN 2303 protocol via email. Committee members also inquired about submitting a correlative study proposal to facilitate a reconciliation review of the cause of death forms for BMT CTN studies and recent CIBMTR studies, such as BMT CTN 1703 and 1704. This study would meet the objectives of the BMT CTN Executive Committee-approved project to provide recommendations for a uniform approach for defining cause of death, with the goal of publishing the guidance.

PATIENT AND CAREGIVER ADVOCACY COMMITTEE

The purpose of the Patient and Caregiver Advocacy Committee is to ensure that patient and caregiver perspectives are reflected in the BMT CTN research portfolio and trial conduct. The committee's scope includes providing input on evaluation and prioritization of study concepts; interfacing with patient advocacy and community organizations; protocol team patient and caregiver engagement plans; patient, caregiver, and family-facing materials; and website and social media content and communication plans.

During this reporting period, the Patient and Caregiver Advocacy Committee continued to draft content for the Patients and Caregivers section of the public BMT CTN website. Sections that were incorporated during this reporting period include additional layperson summaries on the Study Results page.

Committee members also reviewed and provided feedback on the patient consent forms for BMT CTN-led studies in development (2203 and 2207) and on the infographics created by an Access to Clinical trials project team. The committee created study-specific patient materials, including a protocol summary with QR codes linking to complementary study information on the BMT CTN website and a patient ID card.

Committee members participated as representatives of BMT CTN-led trials and the Access to Clinical Trials Projects to provide their feedback during team calls and then relay information to the Patient and Caregiver Advocacy Committee, and members presented at Steering Committee meetings and the annual BMT CTN Coordinators Track.

In February 2025, Patient and Caregiver Advocacy Committee members were invited to attend BMT CTN activities and host their own committee meeting at the annual Tandem Meetings. The meeting agenda included reviewing the history of the committee and considering future projects and initiatives.

PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS COMMITTEE

The Publications, Abstracts, and Presentations Committee develops publication and presentation policies, and it reviews publications and presentations to ensure confidentiality of study participants and proprietary information as well as to ensure appropriate acknowledgements of contributions, sponsorship, and authorship. During this reporting period, the committee reviewed **12** abstracts and **7** manuscripts.

OTHER COMMITTEE ACTIVITIES

BMT CTN MYELOMA INTERGROUP

The BMT CTN Myeloma Intergroup develops a national scientific agenda for multiple myeloma transplant studies. During this reporting period, the Intergroup provided input to various stakeholders on study design and ancillary studies for **2** potential upcoming studies for multiple myeloma patients: A BMT CTN chimeric antigen receptor T-cell (CAR-T) study proposal for patients with high-risk disease, which is still under consideration, and a National Clinical Trials Network (NCTN)-led study for patients with standard-risk disease at time of diagnosis.

The Myeloma Intergroup hosted its annual meeting at the Tandem Meetings in February 2025. The agenda focused on a landscape assessment of upcoming, accruing studies and study results, and it described initiatives to incorporate health-related quality of life studies into trials, consideration of Duffy Null neutrophil count into trials, and consideration of other ancillary studies that may address important questions in the myeloma field.

As of October 2024, the structure of the Myeloma Intergroup meetings was revised:

BMT CTN Myeloma Intergroup Senior Advisory Committee

These representatives from the BMT CTN and the NCTN Myeloma Committees convene meetings **4** times per year to provide guidance and oversight of the responsibilities of the full Myeloma Intergroup.

BMT CTN Myeloma Intergroup

Member criteria were reviewed and redefined. BMT CTN Myeloma Intergroup meetings are held **4** times per year, including at the annual Tandem Meetings. The BMT CTN Myeloma Intergroup develops the BMT CTN scientific agenda for multiple myeloma transplant and cell therapy studies.

SCIENTIFIC ADVISORY COMMITTEES

As part of its State of the Science Symposia, the BMT CTN created **12** Scientific Advisory Committees to address specific areas pertinent to HCT trials. These committees convene before each symposium and as needed for the Network's scientific agenda.

Infection / Immune Reconstitution

Reconvened to update BMT CTN technical documents on infectious diseases, this committee finalized a guidelines manuscript, which was published in Transplantation and Cellular Therapy in March 2024. Due to recommendations from the journal's peer review, the committee updated the BMT CTN Infectious Disease Technical Document to provide clarification in the Infections Grading System. The second version of the Technical Document was finalized and implemented in September 2024.

Cellular Therapy for Solid Tumors

The BMT CTN Executive Committee convened this ad hoc committee to review recent advances in the field to identify the most compelling opportunities for multicenter clinical research studies within the next **5** years. Members for the committee were selected in June 2023, and the first committee meeting was held in August 2023. The committee provided recommendations for the Network to consider exploring in the field to the BMT CTN Steering Committee in February 2024. The committee is expected to submit a manuscript summarizing the data regarding cellular therapies in solid tumor malignancies during the next reporting period.

TASK FORCE ACTIVITIES

ACCESS TO CLINICAL TRIALS TASK FORCE

In 2023, the BMT CTN decided to initiate a Network-wide approach to increase patient access to transplant clinical trials. During the October 2023 BMT CTN Steering Committee, **11** project proposals were presented, and **2** projects were approved (described below). Teams were solicited for the projects, and both projects are underway.

Proactive Financial Navigation

This project will provide additional support in accessing financial resources to patients offered participation on the BMT CTN 2207 aplastic anemia study. Since BMT CTN 2207 was activated during this reporting period, the project team anticipates the financial navigation services will be utilized during the next reporting period after patient screening starts.

Multimedia Education for Patients and Investigators

This project is developing patient and investigator materials for the upcoming BMT CTN 2203 and 2207 studies. Project team members drafted infographics for the **2** trials and presented them to the Steering Committee in February 2025. Team members continue to refine the infographics based on feedback from the protocol teams, focus groups, the Patient and Caregiver Advocacy Committee, and the Steering Committee. Project team members are also creating scripts for educational videos.

HIGH-RISK MULTIPLE MYELOMA CAR-T PROTOCOL TASK FORCE

In June 2023, Marcelo Pasquini presented a study concept of CAR-T consolidation for patients with newly diagnosed multiple myeloma. The study concept was not ready for protocol development but required further discussion among volunteer BMT CTN investigators to provide advice for the potential project.

A task force was formed in August 2023 and met several times to refine the study concept proposal. Contract negotiations are now underway with the industry partner, Janssen, and it is anticipated that a protocol team will be formed and protocol development will start during the next reporting period.

SCIENTIFIC LANDSCAPE REVIEW TASK FORCES

In October 2024, with the new grant period, the BMT CTN Steering Committee reviewed **12** clinical trial concepts to consider for the Network's future scientific agenda. From those concepts, it became evident there are **2** areas in the field that require a landscape review. Task forces were created for experts to review and provide recommendations to the Steering Committee:

GVHD

This task force's charge was to evaluate the landscape for acute GVHD prevention studies in the myeloablative setting. The task force held their first meeting in November 2024, and after **3** meetings, task force members presented their review and recommendations to the Steering Committee in February 2025.

CAR-T

This task force's charge is to assess how to improve CAR-T therapy by reducing toxicity and increasing efficacy with particular focus on cytokine release syndrome / immune effector cell-associated neurotoxicity syndrome and lymphodepleting chemotherapy. The task force held their first meeting in January 2025 and continues to meet, with the plan to provide their recommendations to the Steering Committee in June 2025.

STATE OF THE SCIENCE SYMPOSIUM 2021

The BMT CTN has held **4** State of the Science Symposia – in 2001, 2007, 2014, and 2021 – to survey the HCT landscape and identify areas in greatest need of multicenter trials. In 2021, **13** committees involving **167** individuals convened to identify clinical trial concepts that represent the most important issues facing the field and have the potential to change practice in a significant way.

During this reporting period, **1** study completed accrual [GVHD studies conducted by the Mount Sinai Acute GVHD International Consortium (MAGIC)] and **3** studies were activated (BMT CTN 2203, 2207, and 2208). Additionally, **3** other studies remain open to accrual, **4** studies are in development, and **2** are under consideration.

Studies Prioritized at the 2021 State of the Science Symposium		
INTERVENTION TREATMENT TRIALS		
Committee and Concept	**Status**	**BMT CTN Protocol Number**
GVHD #1: Treatment of high-risk GVHD by protecting gastrointestinal epithelium	A trial of receptor-interacting serine / threonine-protein kinase 1 (RIPK1) for patients with Minnesota high-risk acute GVHD was activated by MAGIC.	N/A
GVHD #2: Phase II trial of nonsteroid treatment versus rapid steroid taper for low-risk GVHD	This study, a serial biomarker-guided steroid taper for Minnesota standard-risk / Ann Arbor 1 GVHD in pediatric patients, is also being conducted by MAGIC. This study opened to accrual in October 2022 and completed accrual in March 2025.	N/A
GVHD #3: Pre-emption of moderate to severe chronic GVHD	Protocol development for this study started in October 2022 as the next BMT CTN acute GVHD prevention study. It is a Phase III study of tacrolimus / methotrexate / ruxolitinib vs. post-transplant cyclophosphamide / tacrolimus / mycophenolate mofetil in non-myeloablative / reduced intensity conditioning allogeneic PBSC transplantation. This study is funded by Incyte, and the protocol was released to centers in October 2024. The study was activated as of February 2025.	BMT CTN 2203
Infection and Immune Reconstitution #1: Antimicrobial de-escalation following initial fever in patients receiving allogeneic HCT or CAR-T cell infusion	TBD	N/A

Studies Prioritized at the 2021 State of the Science Symposium		
INTERVENTION TREATMENT TRIALS (continued)		
Committee	**Concept**	**Status**
Late Effects, Quality of Life, and Economics #1: Reducing distress-related biology and improving clinical outcomes using propranolol in patients undergoing autologous HCT	TBD	N/A
Lymphoid Malignancies #1: A Phase II trial of CD19-targeted CAR-T cell therapy after novel BTKi-based lead-in as frontline therapy for ultra-high-risk mantle cell lymphoma	During the October 2024 Steering Committee meeting, a study concept was proposed for a Phase II multicenter study of MB-CART2019.1 therapy as frontline consolidation for high-risk mantle cell lymphoma. The concept was highly rated among the Steering Committee; therefore, the Network is exploring potential funding support from Miltenyi.	N/A
Lymphoid Malignancies #2: A Phase III randomized trial of observation versus consolidative autologous HCT after brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone (BV + CHP) induction in CD30+ peripheral T cell lymphoma	BMT CTN endorsed this ECOG-ACRIN trial. Dr. Jacob Svoboda, a member of the SOSS Lymphoma Committee, represents the BMT CTN on the ECOG-ACRIN Protocol Team. The protocol was approved by the National Cancer Institute (NCI) Steering Committee in December 2023 and the NCI Cancer Therapy Evaluation Program (CTEP) in August 2024. The study was activated and opened to accrual in February 2025.	BMT CTN 2208 / ECOG-ACRIN EA4232
Lymphoid Malignancies #3: A Phase II trial evaluating immunotherapy consolidation in diffuse large B-cell lymphoma with stable disease or partial remission on first imaging after CD19-targeted CAR-T cell therapy	BMT CTN endorsed this SWOG-led study. Dr. Mehdi Hamadani represents the BMT CTN on the SWOG Protocol Team. Protocol development started in September 2021. The protocol was approved by the US Food and Drug Administration in November 2022, the NCI Central Institutional Review Board (IRB) in January 2023, and CTEP in February 2023. The protocol was released to sites / activated in February 2023, and 27 patients are randomized, 22 of which are patients from BMT CTN sites.	BMT CTN 2201 / SWOG S2114

Studies Prioritized at the 2021 State of the Science Symposium		
INTERVENTION TREATMENT TRIALS (continued)		
Committee	**Concept**	**Status**
Myeloid Malignancies #1: Molecular evaluation of acute myeloid leukemia patients after stem cell transplantation to understand relapse events (MEASURE)	BMT CTN endorsed this Alliance study in development. Dr. Nelli Bejanyan represents the BMT CTN on the Alliance protocol team. This trial is a part of the NCI's MyeloMATCH umbrella trial. The study was approved by the NCI Leukemia Steering Committee in July 2024 for further development.	BMT CTN 2206 / Alliance A161901
Non-Malignant Disorders #1: Hematopoietic reconstitution for adults with treatment-naïve severe aplastic anemia	A concept for a Phase 2 study of haploidentical and unrelated donor transplantation for aplastic anemia concept was developed and presented to Sanofi, which has agreed to support the study. Protocol development began in June 2023. The study was approved by the Protocol Review Committee and NMDP IRB in February 2024 and the Data and Safety Monitoring Board in April 2024. The protocol was released to sites in June 2024. A subsequent protocol amendment was approved by the NMDP IRB in August 2024. The updated protocol was released to sites in October 2024, and the study was activated in January 2025.	BMT CTN 2207
Optimal Donor and Graft Sources #1: Haploidentical versus unrelated donor transplantation with post-transplant cyclophosphamide and PBSCs	TBD	N/A
Pediatric Malignant Disease #1: A risk-based approach to optimize remission duration following CD19-targeted CAR-T cell therapy	The Pediatric Transplantation and Cellular Therapy Consortium (PTCTC) is developing a study (CAR-CURE).	N/A
Pediatric Malignant Disease #2: Cytokine-induced memory-like natural killer cells to treat post-HCT myeloid relapse	TBD	N/A
Plasma Cell Disorders #1: Upfront BCMA CAR-T cell consolidation and T cell engagers after autologous HCT in patients with newly diagnosed high-risk multiple myeloma	A concept was drafted and presented to Janssen, which has tentatively agreed to support this study; pending contract execution, protocol development will begin during the next reporting period.	N/A

Studies Prioritized at the 2021 State of the Science Symposium		
OBSERVATIONAL TRIALS		
Committee	**Concept**	**Status**
Comorbidity and Regimen-Related Toxicity #1: Corticosteroids with or without a second agent for immune effector cell-associated neurotoxicity syndrome (ICANS)	TBD	N/A
Hemoglobinopathies #1: Late effects after HCT for sickle cell disease registries	A study in collaboration with the National Heart, Lung, and Blood Institute's (NHLBI's) Cure Sickle Cell Initiative will be funded by NHLBI under the MCW Cure Sickle Cell grant. The protocol team will be selected and convened by the end of 2025.	N/A
Infection and Immune Reconstitution #2: Prospective observational study of the immunogenicity of the available mRNA vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine after HCT and CAR-T cell therapy	The study was activated in April 2021, an accelerated timeline made feasible because of collaboration with CIBMTR. Of 516 targeted patients, 523 were enrolled, and enrollment closed in June 2022. A manuscript on the allogeneic HCT cohort was published in April 2023. A manuscript on the full cohort (allogeneic and autologous HCT and CAR-T therapy) was published in May 2024.	BMT CTN 2101 / CIBMTR SC21-07
Myeloid Malignancies #2: Phase II platform trial to test multiple maintenance therapies after allogeneic HCT for high-risk acute myeloid leukemia	The Molecular Evaluation of AML Patients After Stem Cell Transplant to Understand Relapse Events (MEASURE) study was proposed by a National Institutes of Health (NIH) investigator who served on the State of the Science Symposium Committee. CIBMTR opened this study in August 2022 with sponsorship from NMDP.	N/A

STUDIES IN PROGRESS

RARE AND NON-MALIGNANT DISEASES

ITN077AI / BMT CTN 1905

(Lead group: Immune Tolerance Network)

A multicenter randomized controlled trial of best available therapy versus autologous hematopoietic stem cell transplant for treatment-resistant relapsing multiple sclerosis (MS)

Chairs: Jeffrey Cohen, George Georges, Paolo Muraro, Marcelo Pasquini

Primary Objective: Compare the efficacy, safety, immunologic effects, and cost-effectiveness of autologous HCT vs. best available therapy over 72 months in participants with relapsing MS and continued MS disease activity despite treatment with disease modifying therapies. The primary efficacy objective is to compare MS relapse-free survival, analyzed as time until MS relapse or death from any cause

Accrual: **72** of 156 projected patients enrolled

NMD2201 / BMT CTN 2202 TransIT

(Lead group: PTCTC)

A Phase III randomized trial comparing unrelated donor bone marrow transplantation with immune suppressive therapy for newly diagnosed pediatric and young adult patients with severe aplastic anemia

Chairs: Michael A. Pulsipher, Bronwen Shaw, David A. Williams

Primary Objective: Compare time from randomization to treatment failure or death from any cause of immune suppression therapy versus bone marrow transplantation

Accrual: **40** of 234 projected patients enrolled

BMT CTN 2207

A Phase II trial of non-myeloablative conditioning and transplantation of haploidentical related, partially HLA-mismatched, or matched unrelated bone marrow for newly diagnosed patients with severe aplastic anemia

Chairs: Amy Dezern, Sally Arai

Primary Objective: Determine GVHD-free failure-free survival at one year after initiation of conditioning. Events for GVHD-free failure-free survival include Grade III-IV acute GVHD, chronic GVHD requiring immunosuppression, primary or secondary graft failure requiring second definitive therapy, failure to receive an HCT infusion, and death

Accrual: None of 60 projected patients enrolled yet

GVHD BIOLOGY, PREVENTION, TREATMENT, AND BIOMARKERS

BMT CTN 2203

A randomized, multicenter, Phase III trial of tacrolimus / methotrexate / ruxolitinib versus post-transplant cyclophosphamide / tacrolimus / mycophenolate mofetil in non-myeloablative / reduced-intensity conditioning allogeneic peripheral blood stem cell transplantation

Chairs: Zachariah DeFilipp, Elizabeth Hexner

Primary Objective: Compare GVHD-free survival between the 2 GVHD prophylaxis regimens; an event for this time-to-event outcome is defined as Grade III-IV acute GVHD, chronic GVHD requiring systemic immune suppression, or death by any cause

Accrual: **1** of 572 projected patients enrolled

STUDIES IN PROGRESS

COMPARISON OF HCT AND NON-HCT THERAPY

SWOG S2113 / BMT CTN 2205

(Lead group: SWOG)

A Phase III, randomized study of daratumumab, cyclophosphamide, bortezomib, and dexamethasone (Dara-VCD) induction followed by autologous stem cell transplant or Dara-VCD consolidation and daratumumab maintenance in patients with newly diagnosed AL amyloidosis

Chairs: Patrick Hagen, Terri Parker, Surbhi Sidana, Brian Walker

Primary Objective: Compare major organ deterioration progression-free survival between participants randomized to the autologous HCT and non-autologous HCT arms of this study

Accrual: **11** of 338 projected patients enrolled

ECOG-ACRIN EA4232 / BMT CTN 2208

(Lead group: ECOG-ACRIN Cancer Research Group)

A randomized Phase III study to evaluate benefits of autologous stem cell transplant in patients with peripheral T-cell lymphoma that achieved a first complete remission following induction therapy

Chairs: Nora Bennani, Neil Chua, Marc Hoffmann, Jakub Svoboda

Primary Objective: Demonstrate improvement in progression-free survival in the autologous HCT arm compared to the observation arm

Accrual: None of 294 projected patients enrolled yet

CELLULAR AND GENE THERAPY

SWOG S2114 / BMT CTN 2201

(Lead group: SWOG Cancer Research Network)

Randomized Phase II trial of consolidation therapy following CD19 CAR T-cell treatment For relapsed / refractory large B-cell lymphoma or grade IIIB follicular lymphoma

Chairs: Volkan Beylergil, Mehdi Hamadani, Brian Hess, Nasheed Hossain

Primary Objective: Compare progression-free survival in participants with relapsed / refractory diffuse large B-cell lymphoma or follicular lymphoma grade 3B with stable disease or partial remission on first imaging response by central review (day +30 PET/CT scan) after commercial CD19 CAR-T cell therapy who are randomized to receive each consolidation therapy versus those that receive no consolidation therapy (i.e., control)

Accrual: **24** of 396 projected patients enrolled

TIME-AND-MOTION

BMT CTN 2302

Facilitating activation of study trials (FAST)

Chairs: Stephanie Lee, Claudio Brunstein

Primary Objective: Understand the factors that lead to fast vs. slow clinical trial activation

Accrual: N/A

STUDIES CLOSED TO ACCRUAL THIS YEAR

ECOG-ACRIN EA4151 / BMT CTN 1601

(Lead group: ECOG-ACRIN Cancer Research Group)

A randomized Phase III trial of consolidation with autologous hematopoietic cell transplantation followed by maintenance rituximab vs. maintenance rituximab alone for patients with mantle cell lymphoma in minimal residual disease-negative first complete remission

Chairs: Timothy Fenske, Brad Kahl, Matthew Lunning

Primary Objective: Compare overall survival in mantle cell lymphoma patients in minimal residual disease-negative first complete remission who undergo autologous HCT followed by maintenance rituximab vs. maintenance rituximab alone (without autologous HCT)

Accrual: **663** of 689 projected patients enrolled

Key Highlights: The study concept was approved by the NCI Lymphoma Steering Committee's Mantle Cell Lymphoma Subcommittee and, in June 2016, endorsed by the BMT CTN Steering Committee. The study was approved by the NCI Central IRB and CTEP in January 2017 and activated in August 2017. The ECOG-ACRIN Data Safety and Monitoring Committee conducted a planned interim analysis for efficacy and futility during this reporting period. The analysis showed the overall survival of MRD-negative first complete remission patients treated with high-dose chemotherapy and autologous stem cell transplant, followed by 3 years of maintenance rituximab (Arm A) is not significantly different than that for patients receiving 3 years of maintenance rituximab alone (Arm B). Also, the futility analysis suggests the outcome is not likely to differ when the study reaches the planned analysis at full information. Based on these findings, the study closed to accrual. There were **51** participating BMT CTN sites, which enrolled **610** patients (**92%** of the total accrued patients). The study team is currently in the process of preparing data for analysis.

SWOG S1803 / BMT CTN 1706

(Lead group: SWOG Cancer Research Network)

Phase III study of daratumumab / rHuPH20 (NSC-810307) + lenalidomide or lenalidomide as post-autologous stem cell transplant maintenance therapy in patients with multiple myeloma using minimal residual disease to direct therapy duration

Chairs: Amrita Krishnan, Parameswaran Hari

Primary Objective: Compare overall survival between the 2 treatment arms with lenalidomide as the comparator arm and lenalidomide + daratumumab / rHuPH20 as the experimental arm in post-autologous transplant multiple myeloma patients

Accrual: **1,329** of 1,350 projected patients enrolled in Step 2

Key Highlights: This is a SWOG-led study that the BMT CTN endorsed. The study opened to accrual in June 2019. A protocol revision was submitted to increase sample size to 1,420 registered patients (Step 1) to account for a smaller than expected number of patients eligible for the second randomization. Accrual was put on temporary hold in March 2023 while the amendment underwent review when the target Step 1 accrual of 1,100 was met. The amendment to increase the target accrual was approved, and the study was reopened to accrual in November 2023. In January 2025, the study was closed to accrual because Registration Step 1 was approaching the protocol-specified accrual goal. The study continues to randomize patients (Step 2). There are **56** participating BMT CTN sites, which have enrolled **936** patients into Step 2 (**70%** of the total accrued).

STUDIES CLOSED TO ACCRUAL THIS YEAR

BMT CTN 1904

Hematopoietic cell transplantation using treosulfan-based conditioning for the treatment of bone marrow failure diseases

Chairs: Lauri Burroughs, Margaret MacMillan

Primary Objective: Determine the one-year GVHD-free, event-free survival in patients with bone marrow failure diseases undergoing HCT using treosulfan-based conditioning

Accrual: **40** of 40 projected patients enrolled

Key Highlights: The first Protocol Team call was held in September 2019. The study was approved by the Protocol Review Committee in March 2020. As the investigational new drug (IND) holder, the Fred Hutchinson Cancer Research Center Scientific Review Committee reviewed and approved the protocol next. Then the BMT CTN Data and Safety Monitoring Board reviewed and approved the protocol in April 2021. The NMDP sIRB approved the study in May 2021. Fred Hutchinson Cancer Research Center submitted the protocol as an amendment to the existing IND in June 2021. Protocol accrual completed in the first quarter of 2025; accrual was defined by the transplant date, and the last patient's last visit is anticipated to occur in February 2026 (+/- 28 days). The protocol team determined there will be an endpoint review to adjudicate selected endpoints.

BMT CTN 2001

A multi-center, Phase 2 gene transfer study inducing fetal hemoglobin in sickle cell disease

Chairs: David Williams, Mark Walters

Primary Objective: Determine if treatment with a single infusion of autologous CD34+ hematopoietic stem cells transduced with the lentiviral vector containing shmiR targeting BCL11A will lead to a complete absence of severe vaso-occlusive events in the period from 6-24 months after gene therapy

Accrual: **28** of 29 projected patients enrolled; **20** of 25 patients confirmed evaluable

Key Highlights: This study is funded by NHLBI through the Cure Sickle Cell Initiative (OT3-HL147741 BMT CTN, OT2-HL154815 Boston Children's Hospital), NIH (R01-HL137848 Dr. Williams), and the California Institute of Regenerative Medicine (CLIN2SCD-12031) to be conducted through the BMT CTN infrastructure. The Protocol Team was formed in June 2020. The protocol was approved by the NHLBI Scientific Review Committee (a requirement of the Cure Sickle Cell Initiative) and Protocol Review Committee in November 2020 and by the Data and Safety Monitoring Board in February 2021.

In February 2021, bluebird bio, the company who makes the gene therapy vector to be used in this trial, decided to temporarily suspend their Phase 1/2 and Phase 3 studies of LentiGlobin gene therapy for sickle cell disease due to a reported suspected unexpected serious adverse reaction. The BMT CTN 2001 study was subsequently put on pause for 11 months by NHLBI, which issued a hold on all gene therapy sickle cell disease trials. The hold was lifted on December 1, 2021, and the second version of the protocol, which included additional measures to address safety concerns, was released to sites in April 2022.

The first site opened to enrollment in July 2022, and the first infusion of the gene therapy product occurred in March 2023. Nine participating sites are activated; 28 participants enrolled on Segment A of the protocol, and 21 participants have received the gene therapy product to date. The 5 remaining gene therapy infusions are expected to occur by October 2025. One participant who received the gene therapy product was determined to be ineligible after infusion for failure to meet the protocol-defined vaso-occlusive event eligibility criterion. Another patient has reached their 2-year follow-up time point.

RESEARCH FINDINGS THIS REPORTING PERIOD

BMT CTN investigators have published **194** manuscripts, including **47** primary study results papers, from **50** trials and the DCC / Network.

During this reporting period, investigators published **14** manuscripts, **3** of which were primary results manuscripts.

Significant Findings and Impact of BMT CTN Studies	
COMPARISON OF HCT AND NON-HCT THERAPY	
1503: A study to **compare bone marrow transplantation to standard care** in adolescents and young adults with **severe sickle cell disease**	
Results:	This Phase II biologic assignment trial compared HLA-identical related or unrelated donor transplantation with standard care in persons aged 15-40 with severe sickle cell disease. Results showed that **short-term mortality was not excessive after transplant** (11%) when compared with standard care (7%) and that **transplant recipients had fewer pain crises and improved quality of life.**
Impact / Future Outlook:	The results of this trial support the use of HLA-identical related or unrelated donor transplantation in adolescents and young adults with severe sickle cell disease. Further follow-up is required to determine whether it confers a long-term survival advantage. The myeloablative regimens used in the trial generated comparable survival to those reported with reduced intensity regimens and supports the idea that **conditioning regimen intensity may not be a critical determinant of survival among adults with severe sickle cell disease.** More information to support this may come from another BMT CTN trial that assesses the use of haploidentical donors with post-HCT cyclophosphamide (BMT CTN 1507). BMT CTN 1507 has completed enrollment with results from the adult cohort published and results from the pediatric cohort pending.
Selected Publication:	Hematopoietic cell transplant compared with standard care in adolescents and young adults with sickle cell disease. Blood Advances. 2025 Mar 11; 9(5):955-965. Epub 2024 Oct 29.
GRAFT SOURCES	
1507: **Reduced intensity conditioning for haploidentical bone marrow transplantation** in patients with symptomatic sickle cell disease	
Results:	Found that related **HLA-haploidentical bone marrow transplantation is an accessible and potentially curative therapy for adults with sickle cell disease**. The two-year rates of graft failure and event-free and overall survival are comparable to those reported after HLA-matched sibling myeloablative BMT in children.

Significant Findings and Impact of BMT CTN Studies	
1507 (continued)	
Impact / Future Outlook:	**This novel conditioning with related haploidentical donors addressed the most important limiting factors associated with allogeneic BMT in adults with sickle cell disease**: Limited allogeneic donor pool and toxicity associated with a myeloablative conditioning regimen. Since more than 90% of individuals with sickle cell disease are likely to have a suitable related haploidentical donor, most could get a transplant, adding to the potentially curative treatment options for adults with sickle cell disease. Results of the pediatric cohort are anticipated to become available in May 2025. A long-term study is suggested to assess the benefits of early versus later curative therapy to prevent chronic organ damage with all forms of novel treatment.
Selected Publication:	Haploidentical bone marrow transplantation for sickle cell disease. NEJM Evidence. 2025 Mar 1; 4(3):EVIDoa2400192. Epub 2025 Feb 25.
PROGNOSTIC SYSTEMS FOR TREATMENT-RELATED MORTALITY	
1704: Composite health assessment risk model for older adults: Applying pre-transplant comorbidity, geriatric assessment, and biomarkers to **predict non-relapse mortality after allogeneic transplantation** (CHARM)	
Results:	Prospectively designed and validated a composite health risk assessment model inclusive of geriatric assessment, biomarkers, PRO, and comorbidities to better **risk-stratify older patients prior to allogeneic HCT**.
Impact / Future Outlook:	CHARM can **improve decision-making, selection of the best transplant strategy by weighing risks versus benefits, allow calibration of data across trials and institutions, and ensure that appropriate older patients are not excluded from curative intent allogeneic HCT**. Intervention trials focusing on comorbidities, nutritional deficiencies, inflammation, and impaired cognition could further improve transplant outcomes. Future efforts to improve prognostic capacity may require artificial-intelligence modeling integrating broader clinical, sociodemographic, and/or biologic data. Adoption of CHARM in practice should enable future validation, similar to real-world validation of comorbidity by the HCT-Comorbidity Index. Future trials could incorporate modifications based on CHARM score related to conditioning regimens or GVHD prophylaxis.
Selected Publication:	Novel composite health assessment risk model for older allogeneic transplant recipients: BMT-CTN 1704. Blood Advances. 2025 Mar 18: bloodadvances.2025015793. [Epub ahead of print]

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