BMT CTN
Blood & Marrow Transplant Clinical Trials Network®

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

May 2023 – August 2024

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

65 trials launched

55 trials completed accrual; 10 ongoing

>17,000 patients from >100 centers

~513,000 biospecimens in the Research Sample Repository

186 ancillary and correlative studies launched

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

115 ancillary and correlative studies published

181 manuscripts published

170 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 **$1.96 billion** in research funding over the last 10 years. 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, the **MCW** and **NMDP** operate **CIBMTR,** an international research program with a network of **>360** centers in **>35** countries that submit cellular therapy outcomes data for patients, resulting in a research database with information from **>675,000** patients and **>1,800** publications.

The **Emmes Company** is a contract research organization that has managed **>2,000** Phase I-IV trials and registries involving **>30,000** research sites in **>115** countries on **6** continents.

The Data and Coordinating Center 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 **5** plain language summaries of BMT CTN manuscripts and created a new section of the public website for patients and caregivers. The DCC also held a study coordinator training session at the 2024 Tandem Meetings that was attended by **351** in-person participants and had **1,222** total views on the meeting virtual platform.

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 August 31, 2024, a total of **513,132** research sample aliquots, provided by **7,665** 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 **23,369** frozen sample aliquots from its Sample Repository to **15** project laboratories for protocol-defined and ancillary studies.

Processing Samples. The BMT CTN processing laboratory received and processed samples from **384** Network shipments during this reporting period, averaging **32** 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 **9,923** forms in the Advantage EDC and eClinical systems and **201** in Medidata Rave.

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 **7,106** 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 Reviews were conducted for BMT CTN 1801 and completed for BMT CTN 1507, increasing the total number of completed reviews to **29**.

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 **242** 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. In 2019, the BMT CTN launched an Evidence into Practice Task Force to evaluate translation of BMT CTN study results into clinical practice. In 2022, Task Force members presented to the BMT CTN Steering Committee their summary, which included the recommendation to form a standing BMT CTN Dissemination and Implementation Committee. The Steering Committee agreed, and the new standing committee comprises members from across the Network, an implementation scientist (Dr. Todd Molfentor), DCC ex officio members, and ad hoc representation from the BMT CTN Patient and Caregiver Advocacy Committee.

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

Assess protocol finding implementation on healthcare inequities

Define evaluation metrics for dissemination and implementation strategies

The purpose of the Dissemination and Implementation Committee is to incorporate the principles of implementation science into the scientific agenda of the BMT CTN 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.

This reporting period, the committee continued to convene monthly to focus 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 once results are known. Responses are incoming.

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 and plans to deploy it early in the next reporting period.

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 continued to review and support laboratory study proposals submitted in response to the BMT CTN DCC's Network-wide calls for proposals utilizing BMT CTN 1202 biospecimens. **3** studies previously assessed by the Biomarkers Committee as having significant merit were approved by the BMT CTN Executive Committee this year.

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 published a manuscript in Cancer that analyzed the addition of PRO data from several BMT CTN studies into an established CIBMTR survival calculator, and they assisted in 2 quality of life analyses that were published: BMT CTN 0702 published in the British Journal of Haematology and BMT CTN 1506 published in Blood Advances. Committee members also developed a module of standardized sociodemographics / social determinants of health items, which researchers can readily select from, for all BMT CTN clinical trials and initiated discussions to collaborate with ASTCT on a manuscript that would summarize quality of life and PRO data and provide recommendations in the field. Finally, during this reporting period, committee members initiated drafting an updated manuscript to the 2012 publication "Collection of Patient-Reported Outcomes in Blood and Marrow Transplant Clinical Trials Network Studies." The updated manuscript 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 2 new BMT CTN protocols (2203 and 2207) and a proposed BMT CTN Consent Form Template. The committee also reviewed and provided content and logistical feedback for a template Patient Information Card that was developed by the BMT CTN Patient and Caregiver Advocacy Committee. This card will be implemented on future BMT CTN protocols.

SPECIAL POPULATIONS COMMITTEE

The Special Populations Committee ensures that children, women, and under-represented minority groups are considered for inclusion in all appropriate investigational protocols developed by the Network and makes recommendations to increase their participation.

During the previous reporting period, the Special Populations Committee carefully reviewed their committee charge and process for reviewing new BMT CTN protocols. The committee determined it should provide guidance to protocol teams on ways to increase access to clinical trials for patients who are traditionally underserved. Committee members drafted a tip sheet for parameters to consider. The tip sheet outlines barriers to special populations (e.g., under-represented minorities, children, geographically restricted populations) and includes examples for building in 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 inclusive. The Special Populations Committee presented their recommendations and tip sheet to the Steering Committee at its June 2023 meeting, and the Steering Committee approved them. The tip sheet was provided to the 2207 protocol team in September 2023 and will be provided to all new protocol teams.

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. The committee worked this reporting period on the BMT CTN Executive Committee-approved project to provide recommendations on a uniform approach for defining cause of death, with the goal of publishing the guidance. Committee members developed a draft recategorization for Cause of Death, and they plan to work with CIBMTR and other groups in areas such as solid organ transplantation to assess how they have collected these complicated data.

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 reviewed the 2203 and 2207 consent forms and key protocol sections. Committee representatives serving on these protocol teams then presented the committee's feedback to the protocol teams. Committee members also created new materials for these studies, including a protocol summary with QR codes, complementary study information on the BMT CTN website, and a patient ID card.

The Patient and Caregiver Advocacy Committee also reviewed and ranked the submitted Access to Clinical Trials proposals and provided their feedback to the Steering Committee. Two projects were selected to be conducted, and committee members (one per team) have been participating in their project teams. Finally, the committee drafted content for a new Patients and Caregivers section of the public BMT CTN website.

Pages in New Patient and Caregiver Section of BMT CTN Website

- **Welcome**
- **Questions to Ask**
- **Enrolling in BMT CTN studies**
- **Find BMT CTN Study Results**
- **Submit Feedback**
- **About Us**

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 **28** abstracts and **27** manuscripts. The committee also recommended authorship guideline updates be amended in the Administrative Manual of Procedures. These updates were approved by the Steering Committee, and the updated Manual of Procedures will be released in October 2024.

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.

The Myeloma Intergroup hosted its annual meeting at the BMT Tandem Meetings in February 2024. Attended by **>100** in-person and virtual attendees, the meeting focused on a landscape assessment of upcoming, accruing studies and study results as well as general topics, such as initiatives to improve access to trials, imaging to include in clinical trials, scalability of mass spectrometry on serum, and evaluation of circulating tumor DNA to bring the solid tumor experience to the myeloma field.

In February 2024, the Myeloma Intergroup leadership team invited the National Clinical Trials Network (NCTN) Myeloma Committee Chairs from Alliance, ECOG-ACRIN, and SWOG to discuss the intergroup's structure. The group determined the leadership team should include NCTN Myeloma Committee representatives, and the full intergroup should meet more frequently. In August 2024, the revised charter was drafted, including transition of the leadership team to a Senior Advisory Committee. Invite letters were sent to NCTN Myeloma Committee Chairs to select representatives for this committee, and an updated call cadence was developed with the plan to hold **4** full Myeloma Intergroup calls per year, including the annual Tandem Meetings hybrid meeting, and **4** Senior Advisory Committee calls per year. The updated charter and structure will be instituted in October 2024.

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 will be 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 anticipated to initiate drafting a manuscript to summarize the data gathered 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 develop a Network-wide approach to increase patient access to transplant clinical trials for underrepresented minorities. 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.

The Proactive Financial Navigation project will provide additional support in accessing financial resources to patients offered participation on the BMT CTN 2207 aplastic anemia study. This project is anticipated to be activated in November 2024.

The Education for Patients and Investigators project is developing multimedia materials for patients and investigators for the upcoming BMT CTN 2203 and 2207 studies. Project team members will also conduct focus groups in October-November 2024 with patients and caregivers as well as BMT and referring physicians to obtain feedback on the materials.

ACTIVATION TASK FORCE

In June 2023, Stephanie Lee presented to the BMT CTN Steering Committee the proposal for the network to conduct a time and motion study of BMT CTN processes to prospectively observe centers open a study and collect real-time procedural data. A task force to initiate the project was established in August 2023. As the project evolved, a formal quality assurance protocol was created, and the task force was later transformed into the BMT CTN 2302 (FAST) Protocol Team.

HIGH RISK MULTIPLE MYELOMA CAR-T PROTOCOL TASK FORCE

In June 2023, Marcelo Pasquini presented a potential study concept of chimeric antigen receptor T-cell therapy (CAR-T) consolidation for patients with newly diagnosed multiple myeloma. The study concept was not ready for protocol development but would require 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 underway with the industry partner, Janssen, and it is anticipated protocol development will start in early 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.

The 2021 priority concepts will serve as guidance for planning future studies. Work on several studies has already begun, and the other studies will be reconsidered for development later in 2024 after the next BMT CTN grant cycle has started. Study concepts included in the Core Center grant applications will also be evaluated for development.

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 Mount Sinai Acute GVHD International Consortium (MAGIC) and opened to accrual during this reporting period.	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 and opened to accrual during this reporting period.	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 peripheral blood stem cell (PBSC) transplantation. The protocol will be released to centers in October 2024. It is funded by Incyte.	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	TBD	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, which is in development. Dr. Jacob Svoboda, a member of the State of the Science Symposium 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. It is slated to activate by the end of 2024.	N/A
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 (FDA) 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. Fourteen patients are randomized, 12 of which are patients from BMT CTN sites.	BMT CTN 2201 / SWOG S2114
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

Studies Prioritized at the 2021 State of the Science Symposium		
INTERVENTION TREATMENT TRIALS (continued)		
Committee	**Concept**	**Status**
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 will be released to sites in October 2024.	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 2024.	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 an 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

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: **35** of 40 projected patients enrolled

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: **67** 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: **29** of 234 projected patients enrolled

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: **2** of 338 projected patients enrolled

STUDIES IN PROGRESS

CONDITIONING REGIMENS / MAINTENANCE THERAPY

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: **658** of 689 projected patients enrolled

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: **1,207** of 1,420 projected patients enrolled

CELLULAR AND GENE THERAPY

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

Target Accrual: **26** of 29 projected patients enrolled; **13** of 25 patients confirmed evaluable

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: **14** of 396 projected patients enrolled

STUDIES CLOSED TO ACCRUAL THIS YEAR

BMT CTN 1705

A randomized, double-blind, placebo-controlled multicenter Phase III trial of alpha 1 - antitrypsin (AAT) combined with corticosteroids vs corticosteroids alone for the treatment of high risk acute graft-versus-host disease following allogeneic hematopoietic stem cell transplant

Chairs: Amin Alousi, John Magenau

Primary Objective: Compare the rate of complete response and partial response on day 28 post-randomization between AAT and corticosteroids versus placebo to match and corticosteroids in patients with high-risk acute GVHD

Accrual: **136** of 136 projected patients enrolled

Key Highlights: The Protocol Team was formed in October 2018. The study was approved by the Protocol Review Committee in May 2019 and the Data and Safety Monitoring Board in August 2019. Version 1.0 of the protocol was released to BMT CTN centers in September 2019. The study was activated and first patient enrolled in January 2020. Due to the COVID-19 pandemic, accrual was put on hold in March 2020 and re-opened on June 1, 2020. All 25 participating centers were activated by January 2021. Due to a voluntary drug recall by CSL Behring, the study was put on a second hold on January 13, 2021, and accrual re-opened on May 26, 2021. The study was closed to accrual on August 15, 2023, with 136 of 136 participants enrolled. The primary endpoint is Day 28 complete / partial remission with one-year follow-up period. The database lock is slated for September 2024.

BMT CTN 1902

Phase II multicenter trial of anti-B cell maturation antigen (BCMA) chimeric antigen receptor T cell therapy for multiple myeloma patients with sub-optimal response after autologous HCT and maintenance lenalidomide

Chairs: Alfred Garfall, Sergio Giralt

Primary Objective: Evaluate the efficacy of BCMA CAR-T cell therapy to improve the response in patients who received an upfront autologous HCT and lenalidomide maintenance

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

Key Highlights: The study was approved by the Data and Safety Monitoring Board in January 2021 and NMDP IRB in February 2021. Site qualification and selection activities began in September 2020 with 15 sites selected to participate in the study (13 Core / Consortium and 2 Affiliate). The first of 3 patients in the staggered safety run-in phase was enrolled in December 2021. The protocol-specified follow-up and corresponding data review of the safety run-in phase was completed in October 2022. The BMT CTN Medical Monitor noted no safety signals, and the trial was opened for the continuing enrollment phase on October 14, 2022. As of July 2023, 14 of 15 participating sites were activated. The final site was activated in October 2023. The trial met accrual projections with the final participant enrolled on December 26, 2023. The final CAR-T infusion occurred in February 2024, and the final 6-month post-CAR-T infusion follow-up visit occurred in August 2024. As the primary endpoint is assessed at 6 months post-CAR-T infusion, the data freeze for the primary endpoint analysis will take place in September 2024. The protocol-specified 12-month follow-up will continue through February 2025.

STUDIES CLOSED TO ACCRUAL THIS YEAR

BMT CTN 1903 AUTO-RESIST

Administration of HIV-specific T cells to HIV+ patients receiving high dose chemotherapy followed by autologous stem cell rescue

Chairs: Richard Ambinder, Kieron Dunleavy

Primary Objective: Determine the proportion of participants who can be treated with HIV antigen-specific T-cells targeting conserved epitopes (HST-NEETs) within one week of autologous HCT and the efficacy of HST-NEETs in reducing the HIV intact proviral reservoir at 6 months after autologous HCT

Accrual: **12** of 12 projected patients enrolled

Key Highlights: The Protocol Team was formed in September 2019. The study was approved by the Protocol Review Committee in May 2020 and Data and Safety Monitoring Board in January 2021. The protocol opened for accrual on October 26, 2021. Activation was initially delayed because of the requirement for a contract between each center and Children's National Medical Center, which manufactured the cell product. Accrual was completed and the study closed to enrollment on July 5, 2024, with a total of 12 participants. Eight of the 11 activated sites enrolled at least one participant. The estimated primary completion date is predicted to occur in the first quarter of 2026.

RESEARCH FINDINGS THIS REPORTING PERIOD

BMT CTN investigators have published **181** manuscripts, including **44** primary study results papers, from **46** trials and the DCC / Network.

During this reporting period, investigators published **22** manuscripts, **5** of which were primary results manuscripts.

Significant Findings and Impact of BMT CTN Studies	
RARE AND NON-MALIGNANT DISEASES	
0601: Unrelated donor reduced intensity bone marrow transplant for children with **severe sickle cell disease**	
Results:	Determined that a **reduced-intensity conditioning regimen** of alemtuzumab, fludarabine, and melphalan, followed by a bone marrow transplant resulted in low rates of regimen-related organ toxicity and a one-year event-free survival of 76% but unacceptably high rates of GVHD. Also found that this regimen, although effective for engraftment of bone marrow, was **associated with unacceptably high levels of graft failure after cord blood transplantation; this led to early closure of the cord blood cohort.**
Impact / Future Outlook:	This finding confirmed that using a reduced-intensity regimen followed by bone marrow HCT results in acceptable rates of engraftment and survival but also showed high risks of chronic GVHD, underscoring the need for future trials to explore more effective GVHD prophylaxis. Additionally, early in the study, there was a **disappointing finding that using cord blood as a stem cell source with this regimen resulted in unacceptably high levels of graft failure, indicating the need for novel transplant strategies for the large number of sickle cell disease patients who cannot find a human leukocyte antigen (HLA)-matched adult donor.** During this reporting period, a follow-up report was published; the extended follow-up confirmed engraftment and cure were achievable with the reduced-intensity regimen and unrelated bone marrow HCT, but GVHD prophylaxis was inadequate. Since the completion of 0601 and recognition of the GVHD-related complications, successful application of novel GVHD prophylaxis has been reported with this conditioning regimen in HLA-matched and minimally mismatched unrelated transplants. This progress is in conjunction with the successful use of reduced-intensity conditioning regimens in haploidentical transplantation with post-transplantation cyclophosphamide to offset chronic GVHD, thus helping advance alternate donor transplantation for patients with severe sickle cell disease. These efforts are parallel to new gene therapy studies.
Selected Publications:	Primary results: A BMT CTN Phase II trial of unrelated donor marrow transplantation for children with severe sickle cell disease. Blood. 2016 Nov 24; 128(21): 2561-2567. Epub 2016 Sept 13. Long-term outcomes after unrelated donor transplantation for severe sickle cell disease on the BMT CTN 0601 trial. American Journal of Hematology. 2024 Apr 1; 99(4):785-788. Epub 2024 Feb 11.

Significant Findings and Impact of BMT CTN Studies	
COMPARISON OF HCT AND NON-HCT THERAPY	
1102: A multi-center biologic assignment trial **comparing reduced intensity allogeneic hematopoietic cell transplant to hypomethylating therapy or best supportive care** in patients aged 50-75 with intermediate-2 and **high risk myelodysplastic syndrome**	
Results:	Demonstrated **a significant survival advantage** for older patients with higher-risk myelodysplastic syndrome (MDS) who underwent a matched donor reduced-intensity HCT versus those receiving non-HCT therapy, using a donor versus no-donor approach.
Impact / Future Outlook:	The study **results support early consideration of HCT for older patients with higher risk MDS**. Disseminating the study results is key to ensuring a change in practice and better access to HCT for these patients. As a part of these efforts, BMT CTN investigators initiated an application to the Centers for Medicare & Medicaid Services (CMS) to consider a change in its National Coverage Determination, which currently only allows coverage for patients on CMS-designated clinical trials. CMS released its National Coverage Determination for allogeneic HCT for patients with MDS on March 6, 2024. Patients receiving allogeneic HCT with Medicare insurance and meeting the above criteria outlined by CMS after this date should receive coverage based on the National Coverage Determination. During this reporting period, the cost-effectiveness companion study was published, showing for patients ≥65 years old with high-risk MDS, reduced-intensity HCT is a high-value strategy; for patients aged 50-64 years old, HCT is a lower-value strategy but has similar cost-effectiveness to other therapies commonly used in oncology. Additionally, a genetic analysis was published, showing that the benefit of HCT in patients with IPSS intermediate-2 and high-risk MDS extends to high-risk genetic subgroups.
Selected Publications:	Primary results: Biologic assignment trial of reduced-intensity HCT based on donor availability in patients 50-75 years of age with advanced MDS. Clinical Oncology. 2021 Oct 20; 39(30):3328-3339. Epub 2021 Jun 9. Cost-effectiveness of reduced-intensity allogeneic HCT for older patients with high-risk MDS: Analysis of BMT CTN 1102. JCO Oncology Practice. 2024 Apr 1; 20(4):572-580. Epub 2024 Jan 23. Allogeneic HCT improves outcome in MDS across high-risk genetic subgroups: Genetic analysis of the BMT CTN 1102 study. Journal of Clinical Oncology. 2023 Oct 1; 41(28):4497-4510. Epub 2023 Aug 22.

Significant Findings and Impact of BMT CTN Studies	
GVHD BIOLOGY, PREVENTION, TREATMENT, AND BIOMARKERS	
1703 (PROGRESS III): Randomized, Phase III trial of **tacrolimus / methotrexate versus post-transplant cyclophosphamide / tacrolimus / mycophenolate mofetil** in non-myeloablative / reduced intensity conditioning allogeneic peripheral blood stem cell transplantation	
Results:	Demonstrated **significantly higher one-year GVHD-free, relapse / progression-free survival (GRFS) with post-transplant cyclophosphamide (PTCy) / tacrolimus (Tac) / mycophenolate mofetil (MMF)** compared to Tac / MTX after allogeneic HLA-matched HCT using reduced intensity conditioning.
Impact / Future Outlook:	The substantial improvement in GRFS survival supports **PTCy / Tac / MMF as the new standard for GVHD prevention** following well-matched allogeneic HCT with reduced intensity conditioning in adults. The anticipated change in practice will be assessed by a planned review of CIBMTR data, comparing use of GVHD prophylaxis regimens before and after this study. Initiatives to disseminate the results and assess the study impact are underway by the Dissemination and Implementation Committee. During this reporting period, the committee developed and deployed a survey to understand the status of uptake of the 1703 study results 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 once results are known. Review of responses and presentation of the results are planned in the next reporting period.
Publication:	Primary results: Post-transplantation cyclophosphamide-based GVHD prophylaxis. New England Journal of Medicine. 2023 Jun 22; 388(25):2338-2348.
2002: Randomized, open-label, multicenter study **comparing T-Guard to ruxolitinib for the treatment of patients with grade III or IV steroid-refractory acute GVHD**	
Results:	Found that **patient mortality rates precluded further study of the T-Guard agent** for patients with severe steroid refractory acute GVHD
Impact / Future Outlook:	The study was halted prior to target enrollment due to meeting a stopping rule in December 2022 with 12 participants enrolled; 7 patients were randomized to the T-Guard arm and 5 to the ruxolitinib arm. The primary endpoint of Day 28 complete remission was met in 2 of 7 T-Guard treated patients but none of the 5 ruxolitinib treated patients. Despite these responses, 4 of 7 patients in the T-Guard arm died before Day 60, compared to 0 of 5 deaths by Day 60 on the ruxolitinib arm. **The outcomes of this study were disappointing and further underscore the lack of treatment options for these seriously ill patients.**
Publication:	Primary results: Anti-CD3/CD7 immunoconjugate (T-Guard) for severe, steroid-refractory GVHD: Final report of BMT CTN 2002. Bone Marrow Transplantation. 2023 Dec 1; 58(12):1416-1418. Epub 2023 Sep 25.

Significant Findings and Impact of BMT CTN Studies	
CONDITIONING REGIMENS / MAINTENANCE THERAPIES	
1506: Randomized, double-blind, placebo-controlled trial of the **FLT3 inhibitor gilteritinib administered as maintenance therapy following allogeneic transplant for patients with FLT3/ITD AML**	
Results:	Overall improvement in relapse-free survival was not statistically significant; however, **relapse-free survival was improved by gilteritinib in participants with detectable internal tandem duplication of FLT3 (FLT3-ITD) minimum residual disease (MRD) pre- or post-HCT**
Impact / Future Outlook:	The study **did not support the assumption that all patients with FLT3-ITD AML should receive a FLT3 inhibitor post-HCT (p=0.053).** However, the investigators found that post-HCT maintenance with gilteritinib does provide a **significant benefit for patients with peri-HCT FLT3-ITD MRD.** The study **validated the utility of FLT3-ITD mutations as useful markers of MRD with clear implications for intervention.** A quality-of-life analysis was also published this reporting period, showing that gilteritinib maintenance was not associated with any difference in quality of life or patient-reported impact of side effects. Additional 1506 analyses are underway, examining MRD, conditioning regimen, and NPM1 mutation status.
Selected Publications:	Primary results: Gilteritinib as post-transplant maintenance for AML with internal tandem duplication mutation of FLT3. Journal of Clinical Oncology. 2024 May 20;42(15):1766-1775. Epub 2024 Mar 12. Health-related quality of life with gilteritinib versus placebo post-transplant for FLT3-ITD+ acute myeloid Leukemia. Blood Advances. 2024 Aug 21. [Epub ahead of print.]
MULTIPLE MYELOMA TREATMENT	
1401: Phase II trial of single autologous hematopoietic cell transplant followed by lenalidomide maintenance for **multiple myeloma with or without vaccination with dendritic cell / myeloma fusions**	
Results:	Showed that **addition of dendritic cell / myeloma fusion vaccination to post transplant lenalidomide maintenance did not result in a statistically significant increase in complete response rates at one-year** despite being associated with a significant increase in circulating multiple myeloma-reactive lymphocytes indicative of tumor-specific immunity.
Impact / Future Outlook:	Differences in early clinical response between the vaccine and control arms did not meet statistical significance and may require longer follow-up. This study is a **first of its kind,** academically led, collaborative, multicenter, randomized trial of personalized cell therapy with site specific production and centralized assessment of vaccine characterization and immune response. It sets an important **precedent for cell-based therapeutics in an academic framework** that will facilitate evaluation of combined or sequential interventions for immune-based therapy for cancer. Since this study's successful completion, the BMT CTN has launched 3 cellular therapy studies involving CAR-T cell therapy (1902), HIV-specific T cells (1903), and gene transfer (2001).
Publication:	Primary results: Randomized trial of a personalized dendritic cell vaccine after autologous stem cell transplant for multiple myeloma: BMT CTN 1401. Clinical Cancer Research. 2023 Dec 1; 29(23):4784-4796. Epub 2023 Jul 18.

Significant Findings and Impact of BMT CTN Studies	
SUPPORTIVE CARE	
2101: Prospective observational study of the **immunogenicity of vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)** after autologous HCT, allogeneic HCT, and chimeric antigen receptor T-cell therapy	
Results:	Showed that **starting mRNA SARS-CoV-2 vaccination prior to, and reinitiation 3 to 4 months after HCT / CAR-T therapy**, irrespective of concurrent GVHD or use of immunosuppressive medications, is warranted
Impact / Future Outlook:	This is one of the **largest prospective analyses of vaccination for any pathogen within the first year after allogeneic HCT** and supports current guidelines for SARS-CoV-2 vaccination starting 3 months post-allogeneic HCT, per the initial cohort results published in the previous reporting period. Additionally, there are few studies of mRNA vaccine formulations for other pathogens in HCT recipients, and these data provide encouraging proof-of-concept for the utility of early vaccination targeting additional pathogens with mRNA vaccine platforms. The study also found T-cell responses to the vaccine among some patients without a robust antibody response, suggesting there may be protective effects even in the absence of high levels of antibody. Results from the entire study cohort of patients receiving allogeneic HCT, autologous HCT, or CAR-T therapy were published during this reporting period. They confirmed the allogeneic HCT results recommending mRNA SARS-CoV-2 vaccination 3 to 4 months after HCT / CAR-T therapy but also found that pre-cellular therapy SARS-CoV-2 infection or vaccination and baseline B-cell count were key predictors of post-cellular therapy immunity. Therefore, mRNA SARS-CoV-2 vaccination prior to HCT / CAR-T therapy is also supported.
Publications:	SARS-CoV-2 vaccination in the first year after allogeneic hematopoietic cell transplant: A prospective, multicentre, observational study. EClinicalMedicine. 2023 May 1; 59:101983. Epub 2023 Apr 27. Primary results: SARS-CoV-2 vaccination in the first year after HCT or CAR-T cell therapy: A prospective, multicenter, observational study. Clinical Infectious Diseases. 2024 Aug 22; S2666-6367(24)00590-6.

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