BMT CTN
Blood & Marrow Transplant
Clinical Trials Network

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

May 2021 – April 2022

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 **25,000** uses of cellular therapy for cancer are reported to the 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

60 trials launched

47 trials completed accrual; 13 ongoing

>16,200 patients from >100 centers

~531,000 biospecimens in the Research Sample Repository

154 ancillary and correlative studies launched

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

92 ancillary and correlative studies completed

141 manuscripts published

137 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)**, the **National Marrow Donor Program® (NMDP)/Be The Match®**, and the **Emmes Company**.

The **MCW** is the **3rd** largest private medical school in the nation with **$1.6 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.

The **NMDP/Be The Match** 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 the **CIBMTR,** an international research program with a network of **>350** centers in **>30** countries that submit cellular therapy outcomes data for patients, resulting in a research database with information from **>600,000** patients and **>1,600** publications.

The **Emmes Company** is a contract research organization that has managed **>2,000** Phase I-IV trials and registries involving **>25,000** research sites in **>75** 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. This year, the DCC managed **639** conference calls (mostly videoconferences), updated the Administrative Manual of Procedures, and continued the website redesign project.

BIOSPECIMEN REPOSITORY

Each BMT CTN protocol creates an important opportunity for the scientific community to collect baseline and post-transplant / treatment biologic specimens for clinical research. For most protocols, biologic samples are collected for use in protocol-defined research. Collection of supplementary samples is also incorporated into most protocols for use in future research. These samples and the associated clinical data are made available as a valuable resource for investigators at large. BMT CTN research sample inventories continue to be regularly updated on the Network's public website to help investigators better utilize this resource.

Storing Samples. As of April 30, 2021, a total of **530,910** available research specimens, provided by **7,897** subjects, were stored by the BMT CTN Network: National Heart, Lung, and Blood Institute Repository; BMT CTN Sample Repository operated by NMDP/Be The Match; and the AIDS and Cancer Specimen Resource Repository.

Distributing Samples. This year, the BMT CTN shipped **6,731** frozen sample aliquots from its Sample Repository to project laboratories for protocol-defined and ancillary studies.

Processing Samples. The BMT CTN processing laboratory received and processed samples from **3,127** Network shipments this year. In January - April 2022, the laboratory received approximately **176** shipments per month. Biorepository activity remained high this year due to the opening and high accrual rate of BMT CTN 2101 in conjunction with the BMT CTN 1703 trial reaching later follow-up time points.

DATA COLLECTION AND REVIEW

BMT CTN clinical data are captured through either the Emmes proprietary eClinical system (or previous version, AdvantageEDC) or the CIBMTR Medidata Rave system. This year, participating centers submitted **32,232** forms in the Advantage EDC and eClinical systems and **5,060** forms in Medidata Rave.

The CIBMTR 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, the CIBMTR Research Database is used as the primary study database. This year, participating centers submitted **5,765** forms in FormsNet for BMT CTN 1702. The CIBMTR Research Database is also used for supplemental data collection, especially long-term follow-up data.

After data collection is complete, most studies undergo endpoint review. Each protocol's Endpoint Review Committee provides an independent review of submitted data, in a blinded manner for randomized studies. This year, an Endpoint Review was completed for BMT CTN 1502, increasing the total number to **26** completed reviews.

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. The CIBMTR Survey Research Group completed patient-reported outcomes data collection for BMT CTN 1102 this year and continues to collect surveys for **5** other studies. As of April 30, 2021, the Survey Research Group has collected data for **5,414** patient-reported outcomes time points from **2,038** participants of BMT CTN studies.

NETWORK MANAGEMENT HIGHLIGHTS

NEW WEBSITE AND LOGO

In June 2022, the BMT CTN released the new and improved BMT CTN website (https://bmtctn.net) and the updated BMT CTN logo. The new website consolidates information from the previous public BMT CTN website and the private BMT CTN SharePoint website.

COMMUNICATING TRIAL RESULTS

In August 2019, the BMT CTN launched a Task Force to promote translation of evidence into practice. This year, the Task Force published a companion manuscript to the BMT CTN 1102 primary results manuscript in August 2021; made multiple presentations to patient advocacy groups, state oncology societies, and transplant teams; and collaborated on written materials, including a plain language summary of the results and newsletter articles. From a policy perspective, the Task Force reached out to the National Comprehensive Care Network and American Society for Transplantation and Cellular Therapy to request an update to their practice guidelines and to collaborate with the CIBMTR and NMDP/Be The Match team that will submit the BMT CTN 1102 results and other data to the Centers for Medicare & Medicaid Services requesting the organization issue a National Coverage Determination to cover transplantation for these patients. In March 2022, the Task Force also submitted a companion manuscript to the BMT CTN 1301 primary results manuscript.

RECRUITMENT OF PATIENTS FROM UNDER-REPRESENTED GROUPS

The BMT CTN is committed to the ethical conduct of research involving all eligible patients, including women, racial and ethnic minorities, and children. In 2019 and 2020, the BMT CTN tasked two different committees with considering diversity, equity, and inclusion issues specific to the Network and making recommendations for improvement. The first was the standing Special Populations Committee, whose purpose and achievements this year are described on the next page. The BMT CTN also added a Committee on Disparities and Access to its State of the Science Symposium (SOSS, page 8).

SOSS Disparities and Access Committee Recommendations

Engage with other BMT CTN committees to increase considerations of diversity and access issues during study development

Understand the performance of BMT CTN studies to date with respect to diversity and access

Identify and prioritize opportunities to increase accrual diversity and access to BMT CTN studies through partnerships with the community and Network

All of these recommendations are being implemented. Disparities and Access Committee members are appointed to other Network committees to ensure diversity is being addressed in study development. The BMT CTN analyzed diversity and access data, and Dr. Anita D'Souza (MCW) is leading a project to extend the analysis. Opportunities to increase accrual diversity are being identified by the Patient Advocacy Task Force (page 7).

COMMITTEE ACTIVITIES

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. The Biomarkers Committee also endorsed **2** additional studies that were submitted to the Executive Committee for approval.

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. In early 2020, the Special Populations Committee was charged with evaluating the diversity of the BMT CTN Steering Committee participants and site investigators. This year, the BMT CTN revised its communication plan to encourage broader participation in the Network, primarily by expanding the list of people who receive routine Network communications and invitations to Steering Committee. This initiative was informed by the BMT CTN Special Populations Diversity, Equity, and Inclusion project recommendations as well as discussion at the October 2021 Steering Committee Meeting. The Special Populations Committee assisted the DCC in sending out a survey to a broad group of investigators, including site principal investigators (PIs), who have been involved with BMT CTN studies but not included in broad BMT CTN communications.

This resulted in the addition of **>175** new investigators to the BMT CTN distribution list for invitations to participate in Steering Committee calls and meetings. On the survey, the DCC requested demographic information from respondents; these data are now available as a baseline and will aid the Nominating Committee in increasing diversity of Network committees. Of the **325** respondents, **79%** were willing to provide demographic data.

Special Populations Committee Diversity, Equity, and Inclusion (DEI) Project Recommendations

- **Leverage virtual BMT CTN meetings to allow for diverse faculty to attend**
- **Invite diverse faculty to fill leadership roles**
- **Invite early career faculty to fill committee roles**
- **In-state regional representation to provide a facilitator in each location**
- **Conduct a DEI survey at regular intervals**
- **Share and/or collaborate with other societies on DEI initiatives**

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. This year, the Clinical Research Associates Committee reviewed a survey to be distributed to clinical research staff at Network sites regarding optimizing trial operations.

COMMITTEE ACTIVITIES

PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS COMMITTEE

The Publications, Abstracts, and Presentations Committee develops publication and presentation policies. It also 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. This year, the Committee reviewed **13** abstracts and **18** manuscripts.

The Publications Committee also evaluated the BMT CTN's authorship criteria this year, and in March 2022, Committee members presented their recommendations to the Steering Committee. The Committee advised increasing the number of site PIs who merit authorship to improve BMT CTN's commitment to equity and inclusion, and to advance opportunities for junior investigators or smaller sites. The Committee also suggested that opening studies and enrolling patients can demand equal effort as participating on the Protocol Team.

Publications Committee Recommendations

Site PIs at the top 10 accruing centers should be included in the authorship list for the primary manuscript

With meaningful contributions, the top 2 accruing Affiliate Centers should be included, too

Protocol / writing committees should consider prioritizing junior and mid-career investigators for participation

Site PIs, particularly junior and mid-career investigators, should be given the opportunity to lead protocol-specified ancillary analyses

The Steering Committee approved all **3** recommendations, which will be incorporated in the next BMT CTN Administrative Manual of Procedures amendment slated for June 2022.

PATIENT-REPORTED OUTCOMES WORKING GROUP

In May 2020, a group of BMT CTN investigators with expertise in health-related quality of life met to discuss BMT CTN patient-reported outcomes data available for analyses, potential funding opportunities, and analysis plans for BMT CTN studies that were still accruing or recently completed. They continued to meet quarterly to discuss these issues and agreed it would be useful to formalize the group. The group drafted a charter and presented it to the Steering Committee in April 2022. The purpose of the new Patient-Reported Outcomes Working Group is to ensure that patient-reported outcomes are appropriately selected, collected, and analyzed, not only for the particular study in which they are collected but in consideration of analyses of patient-reported outcomes across the BMT CTN suite of studies. The charter was approved, and the group will be incorporated into the Administrative Manual of Procedures amendment slated for June 2022.

As part of the initiatives undertaken this year, the Patient-Reported Outcomes Working Group led the BMT CTN 1102 quality of life analysis, which was presented at the 2021 American Society of Hematology (ASH) Annual Meeting. The manuscript will be submitted for publication in June 2022. The group also drafted a Patient-Reported Outcomes Technical Document outlining the processes for inclusion of quality of life analyses in BMT CTN trials.

COMMITTEE ACTIVITIES

BMT CTN MYELOMA INTERGROUP

The BMT CTN Myeloma Intergroup develops a national scientific agenda for multiple myeloma transplant studies. This year the Intergroup provided input on study design and ancillary studies for two potential upcoming BMT CTN CAR-T studies for multiple myeloma patients (BMT CTN 1901 and a State of the Science proposal under consideration) and a SWOG-led study for amyloidosis patients to be considered for BMT CTN endorsement next year. The Intergroup also holds an annual workshop on immune profiling and minimal residual disease in multiple myeloma. In January 2022, approximately **250** individuals attended. A summary of the workshop was submitted for publication. The scope of topics for the 2023 meeting will focus on application of bioinformatics to myeloma, development of non-cellular immunotherapies, interrogation of resistance mechanisms, and development of novel cellular approaches to therapy.

PATIENT ADVOCACY TASK FORCE

In April 2021, the DCC formed a Patient Advocacy Task Force to evaluate the role patients and advocates should play in determining the BMT CTN's scientific agenda, how patients should be engaged in developing and implementing trials, how the Network should communicate trials results to patients, and how the BMT CTN should interface with other disease-specific patient advocacy organizations that utilize transplant and cell therapies.

Dr. Sumithira Vasu (The Ohio State University) chaired the Patient Advocacy Task Force, and members included patient and caregiver representatives, NHLBI representatives, members of the CIBMTR Consumer Advocacy Committee, NMDP/Be The Match Patient Services representatives, BMT CTN investigators, ASH Sickle Cell Engagement members, and members of the DCC.

Patient Advocacy Task Force Recommendations

Create a standing BMT CTN Patient Engagement Committee with a dedicated project manager

Assign a patient advocate to each Protocol Team

Simplify the informed consent process

Work with the patient advocacy group, BMT InfoNet, to identify areas of greatest concern for patients

Present BMT CTN trials at grass roots forums at later stages of protocol development and periodically regarding progress

Leverage existing resources at the CIBMTR and NMDP/Be The Match to allow patient engagement in BMT CTN trials

The Task Force presented their recommendations to the Steering Committee in October 2021; a manuscript is being drafted. The Steering Committee agreed that all recommendations should be considered, and the priority is to form a BMT CTN Patient and Caregiver Advocacy Committee to further evaluate and lead the other initiatives. After the meeting, the Patient Advocacy Task Force drafted the Committee charter. Nominations for the Patient and Caregiver Advocacy Committee will be solicited in May 2022.

STATE OF THE SCIENCE SYMPOSIUM 2021

The purpose of the 2021 Symposium was to identify clinical trial concepts that represent the most important issues facing the field, have the potential to change practice in a significant way, and require a multicenter network to be done effectively. **13** committees, involving **167** individuals, were convened to review the landscape.

Committee Chairs and BMT CTN leadership team prioritized **18** high priority concepts (below), which will serve as guidance for planning future studies.

A manuscript describing the proceedings was published in August 2021:

Heslop HE, Stadtmauer EA, Levine JE, et al. BMT CTN State of the Science Symposium 2021: Looking forward as the Network celebrates its 20th year. Transplantation and Cellular Therapy. 2021 Nov 1; 27(11):885-907. Epub 2021 Aug 27.

Given that the current BMT CTN grant cycle ends in 2024, most of the concepts will be considered for development by the Network only if the Network is renewed or external funding is identified.

Studies Prioritized at the 2021 State of the Science Symposium		
INTERVENTION TREATMENT TRIALS		
Committee	**Concept**	**Status**
GVHD	#1: Treatment of high-risk GVHD by protecting gastrointestinal epithelium	TBD
GVHD	#2: Phase II trial of nonsteroid treatment versus rapid steroid taper for low-risk GVHD	TBD
GVHD	#3: Pre-emption of moderate to severe chronic GVHD	An industry-supported concept was drafted and will be considered for protocol development next year.
Infection and Immune Reconstitution	#1: Antimicrobial deescalation following initial fever in patients receiving allogeneic HCT or CAR-T cell infusion	TBD
Late Effects, Quality of Life, and Economics	#1: Reducing distress-related biology and improving clinical outcomes using propranolol in patients undergoing autologous HCT	TBD
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

Studies Prioritized at the 2021 State of the Science Symposium		
INTERVENTION TREATMENT TRIALS (continued)		
Committee	**Concept**	**Status**
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	This trial is being developed by ECOG-ACRIN; Dr. Jacob Svoboda, a member of the State of the Science Lymphoma Committee, will represent the BMT CTN on the ECOG-ACRIN Protocol Team.
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	During Symposium discussions, it was agreed that SWOG should take the lead on developing this study; Dr. Mehdi Hamadani will represent the BMT CTN on the SWOG Protocol Team, and protocol development is underway (SWOG S2114 / BMT CTN 2201).
Myeloid Malignancies	#1: Molecular evaluation of acute myeloid leukemia patients after stem cell transplantation to understand relapse events (MEASURE)	TBD
Non-Malignant Disorders	#1: Hematopoietic reconstitution for adults with treatment-naïve severe aplastic anemia	An industry-supported concept was drafted and will be considered for protocol development next year.
Optimal Donor and Graft Sources	#1: Haploidentical versus unrelated donor transplantation with PT-Cy and PBSCs	TBD
Pediatric Malignant Disease	#1: A risk-based approach to optimize remission duration following CD19-targeted CAR-T cell therapy	TBD
Pediatric Malignant Disease	#2A: Cytokine-induced memory-like natural killer cells to treat post-HCT myeloid relapse	TBD
Plasma Cell Disorders	#1: Upfront BCMA CAR-T cell consolidation and T cell engagers after autoHCT in patients with newly diagnosed high-risk multiple myeloma	An industry-supported concept was drafted and will be considered for protocol development next year.

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
Hemoglobinopathies	#1: Late effects after HCT for sickle cell disease registries	TBD
Infection and Immune Reconstitution	#2B: 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 the CIBMTR; of the 516 targeted patients, 456 are enrolled, and enrollment is anticipated to end in June 2022.
Myeloid Malignancies	#2: Phase II platform trial to test multiple maintenance therapies after allogeneic HCT for high-risk acute myeloid leukemia	TBD

STUDIES IN PROGRESS

RARE AND NON-MALIGNANT DISEASES

BMT CTN 1507

Reduced intensity conditioning for haploidentical bone marrow transplantation in patients with symptomatic sickle cell disease

Chairs: Robert Brodsky, Michael DeBaun, Adetola Kassim, Mark Walters

Primary Objective: Estimate event-free survival at 2 years after a reduced intensity conditioning regimen and HLA-haploidentical bone marrow transplantation in children with sickle cell disease and adults with severe sickle cell disease

Accrual: **69** of 80 projected patients enrolled (**42** of 40 adults and **27** of 40 children)

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: **1** 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: **18** of 156 projected patients enrolled

GVHD PREVENTION, TREATMENT, AND DISEASE BIOLOGY

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: **73** of 122 projected patients enrolled

BMT CTN 2002

A Phase 3, randomized, open-label, multicenter study, to compare T-Guard to ruxolitinib for the treatment of patients with grade III or IV steroid-refractory acute graft-versus-host disease

Chairs: John Levine, Gabrielle Meyers, Gérard Socié

Primary Objective: Assess the rate of complete response in grades III and IV steroid refractory acute GVHD participants on day 28 post-randomization

Accrual: **0** of 246 projected patients enrolled

STUDIES IN PROGRESS

CONDITIONING REGIMENS / MAINTENANCE THERAPY

Alliance A051301 / BMT CTN 1201

(Lead group: The Alliance for Clinical Trials in Oncology)

A randomized double-blind Phase III study of ibrutinib during and following autologous stem cell transplantation versus placebo in patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL) of the activated B cell subtype

Chairs: Charalambos Babis Andreadis, Timothy Fenske

Primary Objective: Compare progression-free survival at 2 years in patients with non-germinal cell B-cell-like DLBCL between patients who receive ibrutinib during and following autologous HCT versus those who receive placebo during and following autologous HCT

Accrual: **93** of 166 projected patients enrolled

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: **486** 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: **750** of 1,100 projected patients enrolled

GRAFT SOURCES

BMT CTN 1702 CTRL-ALT-D

Clinical transplant-related long-term outcomes of alternative donor allogeneic transplantation

Chairs: Stefan Ciurea, Stephanie Lee

Primary Objective: Estimate and compare overall survival between the 2 arms: Patients who are very likely to find a matched unrelated donor versus those who are very unlikely to find one

Accrual: **1,726** of 1,732 projected patients enrolled

STUDIES IN PROGRESS

CELLULAR AND GENE THERAPY

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: **2** of 40 projected patients enrolled

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 1 week of autologous HCT and the efficacy of HST-NEETs in reducing the HIV intact proviral reservoir at 6 months after autologous HCT

Accrual: **4** of 12 projected patients enrolled

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+ HSC 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: **25** patients

DISEASE BIOLOGY

BMT CTN 2101 / CIBMTR SC21-07

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

Chairs: Joshua Hill, Miguel-Angel Perales, Marcie Riches

Primary Objective: Compare the immunogenicity of SARS-CoV-2 vaccines at 7-35 days after the second vaccine dose (or 14-35 days after a single dose vaccine) in patients starting their vaccination course less than 6 months after HCT or CAR-T cell therapy versus those starting their vaccination course 6-12 months after therapy in 3 strata defined by type of therapy: Autologous HCT recipients, allogeneic HCT recipients, and CAR T-cell recipients

Accrual: **456** of 516 projected patients enrolled

STUDIES CLOSED TO ACCRUAL THIS YEAR

BMT CTN 1703 PROGRESS III

A randomized, multicenter, 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

Chairs: Javier Bolanos-Meade, Shernan Holtan

Primary Objective: Compare one-year GVHD-free, relapse-free survival as a time to event outcome between the 2 GVHD prophylaxis regimens

Accrual: **431** of 428 projected patients enrolled

Key Highlights: The study was approved by the Protocol Review Committee in October 2018, Data and Safety Monitoring Board in December 2018, and NMDP Single IRB in February 2019. The study was activated in June 2019. Accrual to both studies was temporarily suspended due to the COVID-19 pandemic on March 24, 2020, but re-opened on May 15, 2020. Accrual completed one year ahead of projections when the final patient was enrolled in June 2021.

BMT CTN 1801 MI-IMMUNE COMPANION STUDY

Microbiome and immune reconstitution in cellular therapies and HCT

Chairs: Ami Bhatt, Leslie Kean, Miguel-Angel Perales

Primary Objective: Test whether the engraftment stool microbiome diversity predicts one-year non-relapse mortality in patients undergoing reduced-intensity allogeneic HCT

Accrual: **323** of 300 projected patients enrolled

Key Highlights: See above. The lessons involving biospecimen collection for prospective microbiome and immune profiling were presented as a poster abstract at the 2021 ASH Annual Meeting in December.

BMT CTN 1704 CHARM

Composite health assessment risk model for older adults: Applying pre-transplant comorbidity, geriatric assessment, and biomarkers to predict non-relapse mortality after allogeneic transplantation

Chairs: Andrew Artz, Mohamed Sorror

Primary Objective: Determine the set of assessments and biomarkers that could together constitute a robust and valid composite health risk model for accurate personalized estimation of one-year non-relapse mortality

Accrual: **1,227** of 1,221 projected patients enrolled

Key Highlights: The Protocol Team was formed in March 2018. The study was approved by the Protocol Review Committee in December 2018 and Data and Safety Monitoring Board in January 2019. The first subject was enrolled in July 2019. Accrual was temporarily suspended in response to the COVID-19 pandemic in March 2020 but resumed June 1, 2020. Accrual was suspended for a second time when the original accrual goal of 1,100 subjects was met on July 14, 2021. After review and approval by the Data and Safety Monitoring Board, the accrual goal was expanded to 1,221 subjects to mitigate missing data for the evaluable subject population. The study reopened to accrual on October 1, 2021. Subject accrual completed on December 20, 2021, one month ahead of projections. Follow-up of enrolled patients continues with an anticipated date for follow-up completion of March 2023.

RESEARCH FINDINGS THIS YEAR

BMT CTN investigators have published **141** manuscripts, including **35** primary study results papers, from **46** trials and the DCC / Network.

This year investigators published **15** manuscripts, **4** of which were primary results manuscripts for the trials described below.

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 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 considering 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. The BMT CTN Evidence into Practice Task Force worked with the study team this year on various dissemination activities, including a companion publication on challenges and opportunities in implementing the study results. An application to the Centers for Medicare & Medicaid Services (CMS) to consider a change in it National Coverage Determination (which currently only allows coverage for patients on CMS-designated clinical trials) was also initiated this reporting period.
Publications:	Primary manuscript: Nakamura R, Saber W, Martens MJ, et al. 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. doi: 10.1200/JCO.20.03380. Epub 2021 Jun 9. PMC8791814. Warlick ED, Ustun C, Andreescu A, et al. BMT CTN study 1102 heralds a new era in HCT in high-risk MDS: Challenges and opportunities in implementation. Cancer. 2021 Dec 1; 127(23):4339-4347. doi: 10.1002/cncr.33826. Epub 2021 Aug 10. PMC8578257.
GVHD BIOLOGY, PREVENTION, TREATMENT, AND BIOMARKERS	
1301: A randomized, multi-center, Phase II trial of **calcineurin inhibitor-free interventions** for prevention of graft-versus-host disease (PROGRESS II)	
Results:	Showed that CNI-free approaches using donor T cell depletion, either by ex vivo CD34 selection or in vivo PTCy as a single agent **did not result in superior chronic GVHD-free, relapse-free survival** compared with standard Tac / MTX prophylaxis.
Impact:	The trial did not demonstrate a superior approach compared to Tac / MTX in part because the outcomes of the control arm were better than anticipated. This highlights several challenges in determining the best and most relevant approaches to clinical trial design, particularly in the context of current and ongoing changes in real world practices. However, it should be emphasized that HLA-matched HCT with contemporary myeloablative

Significant Findings and Impact of BMT CTN Studies	
GVHD BIOLOGY, PREVENTION, TREATMENT, AND BIOMARKERS (continued)	
1301 (continued)	
Impact (continued):	conditioning, with either Tac and MTX or PTCy and a bone marrow graft, administered as post-remission therapy, results in two-year survival rates >75% and should be considered the **new benchmark for patients with hematologic malignancies**. The BMT CTN Evidence into Practice Task Force submitted a manuscript in April 2022 reviewing the study results and implications for clinical practice and future clinical trial design. The BMT CTN's subsequent GVHD prophylaxis study, BMT CTN 1703 (PROGRESS III), compares Tac / MTX to PTCy in the setting of reduced intensity conditioning allogeneic HCT using PBSC graft source. It completed accrual in June 2021.
Publication:	Primary manuscript: Luznik L, Pasquini MC, Logan B, et al. Randomized Phase III BMT CTN trial of calcineurin inhibitor-free chronic GVHD interventions in myeloablative HCT for hematologic malignancies. Journal of Clinical Oncology. 2022 Feb 1; 40(4):356-368. Epub 2021 Dec 2. PMC8797487.
1802: Open-label, single-arm, multicenter study of combination **anti-CD3 / CD7 immunotoxin (T-Guard) for steroid-refractory acute graft-versus-host disease**	
Results:	Discovered that **certain patient characteristics may be associated with high mortality** in this challenging disease, leading to early closure of the study.
Impact / Future Outlook:	The first three patients enrolled on the study died within 30 days of treatment. An in-depth analysis was peformed to **identify baseline variables and predictive factors for early mortality among all patients treated with T-Guard**, including those on this study and prior Phase I and II studies. Four factors were identified as potentially associated with high risk of mortality: Obesity (body mass index 36.6 kg/m^2), high lactate dehydrogenase or other evidence of early thrombotic microangiopathy, previous treatment with a checkpoint inhibitor, and active infection. Although a causal relationship could not be definitely established, given the challenge in distinguishing treatment toxcities from effects of steroid-refractory acute GVHD, it was determined that **risks could be mitigated with additional safety measures** and that further study of this therapeutic agent was important, given the urgent need for new treatments for these patients. A revised protocol (BMT CTN 2002) addressing the safety concerns and broadening to a Phase III randomized study design was developed with extensive input from the FDA and European Medicines Agency. BMT CTN 2002 was activated globally in December 2021, and the first participant is anticipated to be enrolled in May 2022.
Publication:	Primary manuscript: Meyers G, Hamadani M, Martens M, et al. Lessons learned from early closure of a clinical trial for steroid-refractory acute GVHD. Bone Marrow Transplantation. 2022 Feb 1; 57(2):302-303. doi:10.1038/s41409-021-01529-x. Epub 2021 Nov 23. PMC8825705.

Significant Findings and Impact of BMT CTN Studies	
QUALITY OF LIFE / PATIENT CONSENT	
1505: A randomized **recruitment intervention** trial (RECRUIT)	
Results:	Showed **implementing trust-based approaches increased minority patient recruitment** in some but not all multicenter trials
Impact / Future Outlook:	This study was funded by a National Institute on Minority Health and Health Disparities grant. It was led by an investigator at University of Texas Health Science Center and conducted among several NIH-funded networks / groups. The findings highlighted the importance of relationships between physician-investigators and minority-serving physicians and their minority patients as well as other trust-based approaches. Perhaps most importantly for the BMT CTN, the study underscored the **need to address minority patient recruitment during protocol development and monitor throughout the course of the study**. A variety of approaches, including those used in this study, have been undertaken by the BMT CTN.
Publication:	Primary manuscript: Tilley BC, Mainous AG 3rd, Amorrortu RP, et al. Using increased trust in medical researchers to increase minority recruitment: The RECRUIT cluster randomized clinical trial. Contemporary Clinical Trials. 2021 Oct 1; 109:106519. Epub 2021 Jul 30. PMC8665835.

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