BMT CTN RESOURCE GUIDE

Version 3.0

October 27, 2022

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1. BLOOD AND MARROW TRANSPLANT CLINICAL TRIAL NETWORK (BMT CTN)

The Blood and Marrow Transplant Clinical Trials Network was established in 2001 and renewed in 2006, 2011, and 2017 (through 2024). The purpose of the Network is to conduct large multi-institutional clinical trials to evaluate promising therapeutic approaches for patients facing life-threatening disorders with the goal to improve outcomes of cellular therapies. The Network is funded through the National Heart Lung and Blood Institute (NHLBI) and the National Cancer Institute (NCI), both part of the National Institutes of Health (NIH).

There are 20 Core Clinical Centers (some of which are consortia of two or more centers) with cooperative agreements from the NHLBI and NCI to participate in the BMT CTN (see Section 3).

2. BMT CTN DATA COORDINATING CENTER (DCC)

The NHLBI awarded one grant to the Medical College of Wisconsin (MCW) for the establishment of the Data Coordinating Center (DCC). The DCC's primary role is to provide scientific leadership and overall coordination as well as statistical design and analysis, protocol development and implementation, and medical monitoring services. Additionally, the DCC provides project management, data systems and management, protocol/site monitoring, site training, regulatory support and operational statistical support while also handling the research sample repository, patient advocacy, and contracting for BMT CTN trials.

The BMT CTN DCC is a collaborative partnership of three organizations which provide support to the network. Key personnel are indicated in bold text.

- Medical College of Wisconsin (MCW), Milwaukee WI; PI = **Mary Horowitz, MD**
  - MCW provides scientific leadership and overall coordination for the BMT CTN.
  - MCW and the National Marrow and Donor program (NMDP) collaboratively operate the Center for International Blood and Marrow Transplant Research (CIBMTR)
  - Centers participating in BMT CTN trials must register pre-and post-transplant outcomes of all hematopoietic stem cell transplants done at their institution during their time of participation to the CIBMTR. Registration is done using procedures and forms of the Stem Cell Transplant Outcomes Database (SCTOD). Federal legislation requires submission of these forms for all US allotransplant recipients. Enrollment on a BMT CTN trial must be indicated on the SCTOD pre-transplant registration form. Additionally, CIBMTR pre- and post- transplant Report Forms must also be submitted for all patients enrolled on BMT CTN trials.
- NMDP (National Marrow Donor Program), Minneapolis, MN; PI = **Steve Devine, MD MS** (Project Manager = **Amy Foley, MA**)
  - Protocol oversight and monitoring for select protocols
  - Data capture and management in FormsNet and MediData Rave for select studies
  - Monitoring visits for select protocols
  - Statistical analysis
  - Transplant center contracting: NMDP Budgets and Contracts Associates

- Patient reimbursement: NMDP Budgets and Contracts Associates
- Lab Specimens/Repository: Immunobiology Research Specialists
- Patient advocacy

- Emmes, Rockville, MD; PI = **Adam Mendizabal, PhD** (Project Director = **Iris Gersten**, **MS**)
  - Protocol oversight and monitoring
  - Data capture and management in AdvantageEDC/eClinical
  - Monitoring visits for select protocols
  - Statistical analysis

3. CORE CLINICAL CENTERS

There are 20 Core Clinical Centers (some of which are consortia of two or more centers) with cooperative agreements from the NHLBI and NCI to participate in the BMT CTN (see Appendix 1). Core Center Principal Investigators have voting representation on the Steering Committee (see Section 5) and have responsibility for chairing Protocol Teams, Administrative Committees, and Technical Committees.

Participating Core Clinical Centers are responsible for recruiting, examining, and treating study participants and for collecting all clinical, laboratory, demographic, and other data required by each BMT CTN study. The Principal Investigator for each Core Clinical Center is directly responsible for ensuring that all aspects of BMT CTN protocols are followed. Other key center staff includes other physicians, Co-Investigators, Clinical Research Associates/Coordinators (CRAs/CRCs) and related staff. The Principal Investigator of the Core Clinical Center may designate another individual at his or her center to serve as Lead Investigator for each BMT CTN study.

4. AFFILIATE CENTERS

Participation in Network trials may be open to qualified centers other than Core Clinical Centers through subcontracts with the DCC. The DCC will actively recruit appropriate Affiliate Centers for Network protocols within the limits of financial resources and in accordance with accrual needs of each protocol. An affiliate center must complete an Affiliate Application (available by navigating to public BMT CTN website: https://bmtctn.net. Select the menu option 'Investigator and Research Staff Resources', 'Center Membership & Study Participation', and then select the 'Affiliate Centers' drop-down) for each protocol of interest and submit it to bmtctnac@emmes.com. Affiliate Centers will be subject to the same quality assurance procedures as Core Centers. BMT CTN protocols may be open to Affiliate Centers who:

- Meet the center qualifications required for the protocol and are approved by the Protocol Team
- Are either FACT-accredited (or pending), or an NMDP/Be The Match participant, or an approved transplant center in an NCI-funded National Clinical Trials Network (NCTN) Group
- Agree to register all transplant recipients (both on and off protocol) through the CIBMTR Statistical Center for the duration of the protocol
- Meet quality assurance standards of the Network

5. BMT CTN STEERING COMMITTEE (SC)

The BMT CTN Steering Committee (SC) is responsible for the design, execution, and analysis of all Network studies. The committee members implement all policy decisions. Members include:

- The Principal Investigator from each of the 20 Core Clinical Centers
- Representatives of Affiliate Centers selected by the Steering Committee for exemplary performance:
  - University of Alabama – Birmingham
  - University of Chicago
  - University of Oklahoma
  - University of South Carolina
  - University of Utah
  - University of Wisconsin
  - Wake Forest University
- NHLBI Project Officer: Nancy DiFronzo, PhD
- NCI Project Officers: Lori Henderson, MD and Rich Little, MD
- The three DCC Principal Investigators: Mary Horowitz, MD, MS (PI, CIBMTR), Steve Devine, MD (Co-PI, NMDP/Be The Match) and Adam Mendizabal, PhD (Co-PI, Emmes)

The SC selects a Committee Chair who first serves a two-year term as Vice-Chair, then a one-year term as Chair-Elect, followed by a two-year term as Chair, and finally a one-year term as Immediate Past Chair.

- Chair: Edward Stadtmauer, MD (University of Pennsylvania)
- Chair Elect: John Levine, MD, MS (Mt. Sinai Medical Center)
- Vice Chair: Dr. Stephanie Lee, MD, MPH (Fred Hutch Cancer Center)
- Past Chair: Helen Heslop, MD, DSc (Hon), Baylor College of Medicine

6. BMT CTN PROTOCOLS

Below is information about BMT CTN Protocols that must remain open with the study's IRB of record as of the date of this Resource Guide. Please see the BMT CTN public website for updates and the NCT number for each trial.

Protocol #	Protocol Short Name	Study Database	GlobalTrace Required?[2]	Protocol Contact Info
1102	RIC vs SOC MDS	AdvantageEDC	YES	bmtctn1102@emmes.com
1301	1301 CNI-free GVHD	AdvantageEDC	YES	bmtctn1301@emmes.com
1302	Allo Myeloma	AdvantageEDC	YES	bmtctn1302@emmes.com
1401	Myeloma Vaccine	AdvantageEDC	YES	bmtctn1401@emmes.com
1502	CHAMP	AdvantageEDC	YES	bmtctn1502@emmes.com
1503	STRIDE2	AdvantageEDC	YES	bmtctn1503@emmes.com
1506	Allo FLT3 Maintenance Therapy	eClinical[1]	YES	1506dcc@emmes.com
1507	Haplo SCD	AdvantageEDC	YES	bmtctn1507@emmes.com
1702	Donor Source Cohort	CIBMTR FormsNet	NO	bmtctn1702@nmdp.org
1703/ 1801	PTCy vs. TAC/MTX Mi-Immune	eClinical	YES	bmtctn1703@emmes.com
1704	CHARM	Medidata Rave	NO	bmtctn1704@nmdp.org
1705	HR aGVHD AAT	eClinical[1]	YES	bmtctn1705@emmes.com
1902	Car T MM	eClinical[1]	YES	bmtctn1902@emmes.com
1903	HIV T Cell	eClinical	YES	bmtctn1903@emmes.com
1904	Treosulfan	eClinical	YES	bmtctn1904@emmes.com
2001	GRASP	eClinical[1]	YES	bmtctn2001@emmes.com
2002	SR aGVHD	eClinical[1]	YES	2002dcc@emmes.com
2101	COVID Vaccine Observational	eClinical and CIBMTR FormsNet	YES	bmtctn2101@emmes.com

[1] Study-specific database training is required.
[2] The GlobalTrace System is used for electronic shipping of protocol-specific research samples.

7. FREQUENTLY ASKED QUESTIONS (FAQS)

1. **How do I inform the BMT CTN of new staff working on a BMT CTN protocol?**
   - Please complete the BMT CTN Site Staff Change Form (located on the BMT CTN website https://bmtctn.net) under 'Investigator & Research Staff Resources' select 'Resources for Research Coordinators' and then select the 'Site Staff Change Form') and send the completed form to the applicable protocol-specific email address(es) indicated on the form.

2. **How can I obtain accrual information for BMT CTN studies?**
   - This information can be found on the BMT CTN website: https://bmtctn.net. From the main page, click the Login link and enter your username and password, then click on the link that says 'Data Reports' in the purple bar in the middle of the page. If you do not have one, please follow the steps above on requesting access through the Site Staff Change Form. On the next page, you will see a table listing BMT CTN studies along the left-hand side. Find the protocol number in question and click the link in the column under 'Accrual by Site' to see the number of patients enrolled at each site as well as the total number of patients enrolled on the study.
   - Note that information for studies with biopharma funding are not listed on this page. Contact the Protocol Coordinator (PC) of the biopharma-funded study to learn how to access accrual information.

3. **Why does data need to be collected for every patient including those that end up being ineligible, refuse study treatment etc.?**
   - Most BMT CTN studies are designed as "intention to treat," which requires that all data be required from every patient randomized on the trial - including those patients that did not complete any study-specific study procedures or were deemed ineligible. An intention to treat (ITT) analysis is an analysis based on the initial treatment intent, not on the treatment eventually administered. ITT analysis is intended to avoid various misleading artifacts that can arise in intervention research. For example, people who have a more refractory or serious problem tend to drop out at a higher rate. Even a completely ineffective treatment may appear to be providing benefits if one merely compares the condition before and after the treatment for only those who finish the treatment (ignoring those who were enrolled originally but have since been excluded or dropped out).
   - For the purpose of ITT analysis, everyone who is assigned a study treatment is considered part of the trial, whether they finish it or not.

4. **Why do we have to report data to both the CIBMTR and the BMT CTN for study participants?**
   - All transplant centers in the US, including BMT CTN centers, are required by law to report pre-and post-transplantation clinical data on allogeneic HCT recipients to the Stem Cell Transplant Outcomes Database, which is a component of the C.W. Bill Young Cell Transplantation Program and is managed by the CIBMTR. The Network stipulates that Core and Affiliate Centers must also report similar data for autologous transplant recipients.

- Some pre-and post-HCT information collected by the CIBMTR is deliberately not captured by the BMT CTN Data capture system (Emmes AdvantageEDC/eClinical), but rather is transferred from the CIBMTR Research Database to the Emmes database for incorporation into study files. Some data such as death, graft failure, GVHD, and relapse need to be captured in real time in AdvantageEDC/eClinical to assist with safety monitoring of the trial. All long-term follow-up for Network studies (beyond the primary and secondary endpoints) is captured through CIBMTR report forms to avoid a duplicative long-term follow-up program.

5. **I am trying to enroll a patient in AdvantageEDC or eClinical but am getting error messages. What should I do?**
   - Send an email to bmtctndm@emmes.com with URGENT in the subject line and someone will assist you.
     - If you receive a message noting that the patient is ineligible and/or a value that you entered is out-of-range, contact the email address above immediately. Do NOT enter an incorrect value on the enrollment form.

6. **Who should I contact if I have a question about AE/SAE reporting?**
   - Many studies have protocol-specific AE/SAE reporting requirements and have a protocol-specific email address for AE/SAE questions; however, if you are unsure of the specific email address, contact bmtctn_ae@emmes.com.
   - Chapter 4 of BMT CTN protocols details AE/SAE reporting.

7. **How do I get supplies for protocol-specific research samples?**
   - Details are provided in the protocol-specific Research Sample Information Guide that is posted on the private side of the BMT CTN website under the Protocols drop down, select the relevant protocol, then navigate to the Protocol Supporting Documents Section.
   - To request sample labels, send an email to bmtctnac@emmes.com with your address, phone number, and protocol number. You will typically receive them in 5 business days. If you need labels sooner, please indicate URGENT in the subject line of the request.
   - To request shipping kits, please use the shipping kit order form located at the end of the protocol-specific Research Sample Information Guide.

8. **What are Numbered Memoranda?**
   - Numbered Memoranda are distributed to staff at participating transplant centers to communicate important information regarding the BMT CTN. There are three types of memos: (1) General, CTN-, (2) Study-specific, Protocol ####-, and (3) COVID-. The distribution lists may include the study PIs, sub-Investigators, pharmacists, regulatory, data, clinic, and laboratory coordinators listed on protocol rosters provided by each center. The memos are posted on the private side of the BMT CTN Website. The General and COVID Numbered Memos are located under the 'Committees and Resources' drop-down menu, and the study specific memos are posted under their respective protocol links.

9. **What do I need to know about the NMDP single IRB?**
    - The NMDP IRB serves as the single IRB (sIRB) for all BMT CTN studies released after July 1, 2017 (see Memo CTN-147). These studies include protocols BMT CTN 1702 and beyond. Note some centers piloted the use of the NMDP sIRB for the BMT CTN 1503 study.
    - Effective 8/14/2021, a maximum of 60 days is allowed from release of a new version of a NMDP IRB-approved Informed Consent Form (ICF) to Site Implementation (see Memo CTN-185).
    - It is the BMT CTN's recommendation that only expedited reviews by site IRBs and scientific review committees should be conducted for protocols under the purview of the NMDP sIRB. This recommendation is in agreement with the final NIH Policy on Use of a Single IRB for Multi-Site Research which, although it does not prohibit duplicate review, states that such reviews are counter to the intent and goal of this policy (see Memo CTN-172).

APPENDIX 1: BMT CTN CORE AND CONSORTIA PI LIST AS OF 01SEP2022

Center	Consortia Center	PI
Baylor College of Medicine (Consortium)	Baylor College of Medicine/ Houston Methodist Hospital	Helen Heslop
		Cath Bollard
	Baylor College/Texas Children's Hospital	Carl Allen
	Children's National Medical Center	Cath Bollard
City of Hope		Ryo Nakamura
Dana Farber Cancer Institute (Consortium)	Dana Farber/Brigham & Women's Hospital	Joseph Antin
	Massachusetts General Hospital	Yi-Bin Chen
Duke University (Consortium)	Duke University Medical Center	Joanne Kurtzberg
	University of Virginia	Karen Ballen
Fred Hutchinson Cancer Research Center		Fred Appelbaum Stephanie Lee (cc)
H. Lee Moffitt Cancer Center (Consortium)	H. Lee Moffitt Cancer Center	Joseph Pidala
	Moffitt at Memorial Healthcare System	Hugo Fernandez
Johns Hopkins		Richard Jones
Medical College of Wisconsin		Saurabh Chhabra
Memorial Sloan-Kettering		Miguel Perales
Mount Sinai (Consortium)	Mount Sinai Medical Center	John Levine
	Mayo Clinic--Minnesota	William Hogan
	Vanderbilt University	Adetola Kassim
Northside Hospital (Consortium)	Northside Hospital Atlanta	Asad Bashey
	Levine Cancer Institute	Edward Copelan
	University of Miami	Krishna Komanduri
Ohio State (Consortium)	Ohio State	Sumithira Vasu
	Roswell Park	Phil McCarthy
		Theresa Hahn
	UCSF	Lloyd Damon
	University of North Carolina	Bill Wood
	VCU/Medical College of Virginia	John McCarty
Oregon Health and Science University (Consortium)	Oregon Health and Science University	Richard Maziarz
	Case Western Reserve University	Brenda Cooper
	Cleveland Clinic	Betty Hamilton
	Loyola University	Patrick Stiff
PTCTC (Consortium)	Boston Children's Hospital	Leslie Kean
PTCTC (Consortium)	University of Utah	Mike Pulsipher
PTCTC (Consortium)	Children's Healthcare of Atlanta	Muna Qayed
Stanford Hospitals and Clinics		Robert Lowsky
University of Florida (Consortium)	University of Florida	John Wingard
	Emory University	Edmund Waller
University of Michigan (Consortium)	University of Michigan	Greg Yanik
	Indiana University	Sherif Farag
	Karmanos Cancer Center	Joseph Uberti
University of Minnesota		Dan Weisdorf
University of Pennsylvania		Edward Stadtmauer
Washington University		Peter Westervelt