

BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK PROTOCOL #0302 ACUTE GVHD

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1. Introduction

This documents the final study data files delivered to the Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) of the National Heart, Lung and Blood Institute (NHLBI) for the **Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Protocol 0302 Acute GVHD** study conducted from 2003 to 2009 and coordinated by the Emmes Corporation. The study is titled “Initial Systemic Treatment of Acute GVHD: A Phase II Randomized Trial Evaluating Etanercept, Mycophenolate Mofetil (MMF), Denileukin Diftitox (ONTAK), and Pentostatin in Combination with Corticosteroids” and is registered at www.clinicaltrials.gov under NCT00224874. The study is fully documented by the BMT CTN Protocol and by the BMT CTN Manual of Procedures (MOP). The MOP documents detailed procedures and materials for data collection in the study. The present files contain the data files from the BMT CTN Data and Coordinating Center (DCC) data system. The data and all of its accompanying documentation, including this specification document are uploaded to the specified website per NHLBI.

2. Specifications of Final Data Sets

- BMT CTN0302_Final Data Submission to NHLBI BioLINCC_ Documentation.doc
This document serves as a readme file to describe the data submission package.

a. Reference to necessary study documents

- BMTCTN0302_Protocol_FinalVersion.pdf
This is the Version 7.0 of the protocol, which was the final official version of the study protocol.
- BMTCTN0302_Protocol_FirstVersion_SummaryofChanges.pdf
This includes the first version of the protocol along with summary of changes for each version.
- BioLINCC BMT 0302 Redaction Overview.docx
This contains a description of additional modifications to the data by BioLINCC
- BMTCTN0302_CaseReportForms_FinalVersion.pdf
This is the final version of the annotated Case Report Forms that were used to collect data.
- BMTCTN0302_PrimaryPublication.pdf
This is the primary manuscript officially published for the study.

- Documentation for Outcomes Dataset.doc

This is the documentation for the outcome dataset. Since the outcome dataset has no corresponding annotated Case Report Form, this serves as the detailed description for each variable in this outcome dataset, which may include data coding conventions, algorithms to calculate outcome variables, adjudications by the study Endpoint Review Committee and some data variables that may be retrieved from CIBMTR data source.

- BMT CTN Admin Manual of Procedures.pdf

This is the most recent version, version 11.0 of the BMT CTN Admin MOP.

- BMT CTN Technical Manual of Procedures.pdf

This is the most recent version, version 3.0 of the BMT CTN Technical MOP.

- BMT-0302_BioLINCC_Publication_Review.docx

This is an analysis done by BioLINCC of the replicability of the tables in the Primary Outcome Paper based on the publication data included in this submission. The results section includes feedback from the DCC.

b. List of final datasets delivered

- Set 1 – data lock for the primary publication

This set 1 includes all data at the data lock for the primary publication. A complete list of all the SAS data files are in the below table. The .sas file includes all the formats that can be applied to all the related data variables in the alphabetical order to the SAS data files. The Data Dictionary gives the labels/format assignments for the variables within each SAS data file.

- 16 datasets in BMTCTN0302_SASdata_PrimaryPublication
- Format for SASdata_PrimaryPublication.sas
- PrimaryPublication_Data_Dictionary.pdf

- Set 2 – final data lock for study close-out

This set 2 follows the similar structure as set 1, and includes all data at the data lock for the final data lock for study close-out. There may be minor difference between the data in this set and set 1, mainly due to data updates after the primary publication (e.g. data for some secondary endpoints may not be available at the data lock for the primary publication, some data may be corrected after an on-site

data audit etc.) For future analysis, we recommend set 2 data files should be used. Set 1 can be referred to re-generate the results as published in the primary paper.

- 16 datasets in BMTCTN0302_SASdata_FinalDataLock
- Format for SASdata_FinalDataLock.sas
- FinalDataLock_Data_Dictionary.pdf

Dataset Name	Case Report Form or Data Source	Notes/Comments	
		Fields Removed (due to no data, text response or other reasons)	Fields Recoded, adjudication, or other notes
Clinical Forms (in alphabetical order)			
ADM	Re-Admission/ Hospitalization Form	ADM1SPEC ADM2SPEC ADM4SPEC Comments: ADMCOMM1	
AE	Adverse Event Form AE1, AE2, AE3, AE4, AE5, AE6	AE1 form AESPEC1 Comments: AE1COMM AE2 form AVSTAT_A SEMEDHX SESUMM SEISUBBY SEISUBDT SEASUBBY SEASUBDT AE3 form AVSTAT_B All variables related to Study Product 2-5 All variables related to Concomitant Medications 4-25. Comments: AE3COMM AE4 form AVSTAT_C All Variables Related to Lab Tests 2-10 All Variables Related to Diagnostic Tests 2-10 Comments: AE4COMM AE5 form AVSTAT_D AEREVIEW ARFREVBY ARFREVDT ARCM1DIS ARCM2ALL AE6 form AVSTAT_E AMREVINP Comments: AE6COMM	The series of AE forms are combined in one dataset.
BL1	Baseline Form	Comments: B0302COM	
CGV	Follow Up GVHD Form	All Variables Related to Biopsy 3-6. Comments: CGVCOMM	

Dataset Name	Case Report Form or Data Source	Notes/Comments	
		Fields Removed (due to no data, text response or other reasons)	Fields Recoded, adjudication, or other notes
DEM	Demographics Form	NAMECODE IUBMID CRIDNUM RACESP RACE2SP Comments: DEMCOMM1	
DTH	Death Form	DTHSPEC1 DTHSPEC2 SCNDCZ2 DTHSPEC3 SCNDCZ3 DTHSPEC4 SCNDCZ4 DTHSPEC5 Comments: DTCMMNTS	
ENROLL	Enrollment Form	Comments: COMMENTS	
FUS	Follow Up Status Form	Comments: FUS1COMM	
GVH	Acute GVHD Form	Comments: GVHCOMM	
INF	Infection Form	CERTNTY1 ORGN02 INFSPEC2 CERTNTY2 ORGN03 INFSPEC3 CERTNTY3 SVRTY03 INFSPEC4 Comments: INFCOM	
IRC	Immune Reconstitution Form	Comments: IRCCOMMT	
LAF	Laboratory Assessment Form	Comments: LBCMNTS	
MD2	Medication Form	Comments: MD2COMM	
TX4	Toxicity Form	Comments: TX4COMM	
SGF	Secondary Graft Failure Form	Comments: SGFCOMM	

Dataset Name	Case Report Form or Data Source	Notes/Comments	
		Fields Removed (due to no data, text response or other reasons)	Fields Recoded, adjudication, or other notes
Analysis Dataset			
OUTCOMES	This dataset does not a corresponding Case Report Form and it includes the Endpoint Review Committee (ERC) adjudicated outcomes, the computed variables and selected data retrieved from Center for International Blood and Marrow Transplant Research (CIBMTR) if applicable.	<ul style="list-style-type: none"> • This OUTCOMES dataset includes the most important data fields for the primary analysis and is made up of 2 parts: (1) All the ERC data, which means the ERC adjudicated the study outcomes for the patients e.g. the acute GVHD response at Day 28. (2) All the coded variables, which means they are not the directly-collected data by CRFs, e.g. computed days for survival analysis, computed age, etc. • The original data submitted by the transplant centers in CRFs (such as DEM, DTH, GVH, CGV etc.) are still included in this data submission (as listed above individually) for reference and completeness, but analyses should use this outcome data that were adjudicated by ERC if the data fields in OUTCOMES is different from the site-reported raw data. The primary manuscript used this OUTCOMES data to publish the study results. • A detailed documentation is provided with this data submission to add more specifics for each variable in this OUTCOMES database. Please refer as needed. 	

Note: All the data files can be linked by the randomized subject ID (RANDID).

Below is the forms submission schedule for reference. For example, some forms such as GVHD, toxicity are assessed at multiple times per protocol schedule so each data point will have a record in the data set for each patient; while some forms are event-driven forms such as death, which means, only those with event will have a corresponding record in the dataset.

BMT CTN PROTOCOL #0302 Forms Submission Schedule

FORM	Prior to Enrollment	Day 0	Days Post Randomization											
			7	14	21	28	35	42	49	56	90	120	180	270
Eligibility	X													
Baseline		X												
Acute GVHD		X	X	X	X	X	X	X	X	X				
Follow-up GVHD											X	X	X	X
Laboratory¹		X	X	X	X	X				X	X			
Toxicity		X				X				X	X			
Follow-up Status Form						X				X	X		X	X
Medication Form						X				X ²				
Immune Reconstitution Form		X		X		X								
Infection			Submit after each infectious event										X ³	X ³
Unexpected, Grades 3-5 Adverse Event			Submit after each unexpected, Grades 3-5 adverse event											
Readmission / Hospitalization			Submit after each hospitalization											
Death			Submit in the event of the participant's death											
CIBMTR Day 100 Report⁴			Submit at Day 100 post-transplant ⁵											
CIBMTR Follow-up⁶			Submit yearly post-transplant											

Notes:

- ¹ Includes Karnofsky/Lansky performance status, CBC with differential and platelet count, creatinine, and LFTs.
- ² This form is only required if the patient is randomized to receive MMF.
- ³ If a severe, life-threatening, or fatal infection is reported on the Day 180 or Day 270 Follow-up Status Form, then an Infection Form must be submitted documenting the infection.
- ⁴ Includes Core, Disease, and Graft Inserts.
- ⁵ If patient is not already 100 days post transplant at time of enrollment.
- ⁶ Includes Core and Disease Follow-up Forms.

3. List of Major Publications

Primary publication

- Alousi A, Weisdorf D, Logan B, Bolaños-Meade J, Carter S, DiFronzo N, Pasquini M, Goldstein S, Ho V, Hayes-Lattin B, Wingard J, Horowitz M, and Levine J. Etanercept, mycophenolate, denileukin or pentostatin plus corticosteroids for acute graft vs. host disease: a randomized phase II trial from the BMT CTN. *Blood First Edition Paper*, Blood. 2009;114(3):511–517.

Secondary publication

- Mycophenolate Pharmacokinetics and Association with Response to Acute Graft vs Host Disease (GVHD) Treatment From the Blood and Marrow Transplant Clinical Trials Network. *Biology of Blood Marrow Transplant*. 2010
- Optimal two-stage randomized Phase II clinical trials. *Clinical Trials*. 2005 Feb 1; 2(1):5-12.
- Graft-versus-host disease treatment: predictors of survival. *Biology of Blood and Marrow Transplantation*. 2010 Dec 1; 16(12):1693-1699. Epub 2010 Jun 10.
- Acute graft-versus-host disease biomarkers measured during therapy can predict treatment outcomes: a BMT CTN study. *Blood*. 2012 Apr 19; 119(16):3854-3860. Epub 2012 Mar 1.
- Lymphocyte phenotype during therapy for acute graft versus host disease: a brief report from BMT-CTN 0302. *Biology of Blood and Marrow Transplantation*. 2013 Mar 1; 19(3):481-485. Epub 2012 Dec 11.
- A prognostic score for acute graft-versus-host disease based on biomarkers: a multicentre study. *Lancet Haematology*. 2015 Jan 1; 2(1):e21-e29.
- Circulating Angiogenic Factors Associated with Response and Survival in Patients with Acute Graft-Versus-Host Disease: Results from BMT CTN 0302 and 0802, *Biology of Blood and Marrow Transplantation*. 2015 Jun; 21(6) 1029-36., Epub 2015 Mar 3