

Clinical Study Data Reviewer's Guide

SDRG, Inc.

Study SDRG-002A

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Contents

1. Introduction.....	3
1.1 Purpose.....	3
1.2 Acronyms	3
1.3 Study Data Standards and Dictionary Inventory.....	3
2. Protocol Description	3
2.1 Protocol Number and Title.....	3
2.2 Protocol Design.....	4
2.3 Trial Design Datasets	5
2.3.1. TA – Trial Arms.....	5
2.3.2. TI – Trial Inclusion/Exclusion Criteria.....	5
2.3.3. TS – Trial Summary.....	5
3. Subject Data Description	5
3.1 Overview.....	5
3.2 Traceability Flow Diagram	6
3.3 Annotated CRFs.....	6
3.4 SDTM Subject Domains	7
3.3.1. AE – Adverse Events	8
3.3.2. CM – Concomitant Medications	8
3.3.3. DS – Disposition	8
3.3.4. EX – Exposure	9
3.3.5. LB – Laboratory Test Results	9
3.3.6. MH – Medical History	9
3.3.7. RS – Response	9
3.3.8. SC – Subject Characteristics	9
3.3.9. TR – Tumor Results.....	9
3.3.10. XL – Laboratory Test Results CN	9
3.3.11. XP – Surgeries and Procedures.....	10
3.3.12. ZA – Clinical Assessments	10
4. Data Conformance Summary.....	11
4.1 Conformance Inputs.....	11
4.2 Issues Summary	11
4.3 Additional Conformance Details	12

1. Introduction

1.1 Purpose

This document provides context for tabulation datasets and terminology that benefit from additional explanation beyond the Data Definitions document (define.xml). In addition, this document provides a summary of SDTM conformance findings.

1.2 Acronyms

Acronym	Translation
aCRF	Annotated Case Report Form
DLBCL	Diffuse Large B-Cell Lymphoma
eCRF	Electronic Case Report Form
eDT	Electronic Data Transfer (e.g. central lab data, ECG vendor data, PK data, etc.)
IRC	Independent Review Committee

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	SDTM v1.2/SDTM IG v3.1.2 including SDTM Amendment 1, Oncology domains, TU, TR, and RS, released for public comment in May 2011
Controlled Terminology	2011-07-22
Data Definitions	define.xml v1.0
Medications Dictionary	WHODrug December 2012
Medical Events Dictionary	MedDRA v14.1

2. Protocol Description

2.1 Protocol Number and Title

Protocol Number: SDRG-002A

Protocol Title: A Phase III, Multicenter, Open-Label, Randomized Trial Comparing the Efficacy of SDRG-888 in Combination with Investigator's Chemotherapy Regimen of Choice Versus Pharmab and Investigator's Choice

Protocol Versions: SDRG-002A

1. SDRG-888 or Pharmab in for 8 Cycles in Combination with Chemotherapy for 6 Cycles



2.3 Trial Design Datasets

Are Trial Design datasets included in the submission? Yes

2.3.1. TA – Trial Arms

The primary analysis compares SDRG-888 versus Pharmab. The protocol design in Section 2.2 has been represented using four trial arms in order to differentiate subjects receiving six cycles of chemotherapy from eight cycles of chemotherapy. ARMCD uses the convention randomized treatment underscore number of cycles of chemotherapy (i.e., S_C6, S_C8, P_C6, and P_C8).

2.3.2. TI – Trial Inclusion/Exclusion Criteria

The trial inclusion/exclusion criteria are fully described in the TI domain.

2.3.3. TS – Trial Summary

The TS domain includes the deprecated parameter Adverse Events Dictionary (AEDICT) to support internal processes.

3. Subject Data Description

3.1 Overview

Are the submitted data taken from an ongoing study? No

Were the SDTM datasets used as sources for the analysis datasets? Yes

Do the submission datasets include screen failures? No

Were any domains planned, but not submitted because no data were collected? No

Are the submitted data a subset of collected data? No

Is adjudication data present? No

Additional Content of Interest

The SDTM datasets include both CRF data and electronic data for the study.

Key analysis data points include:

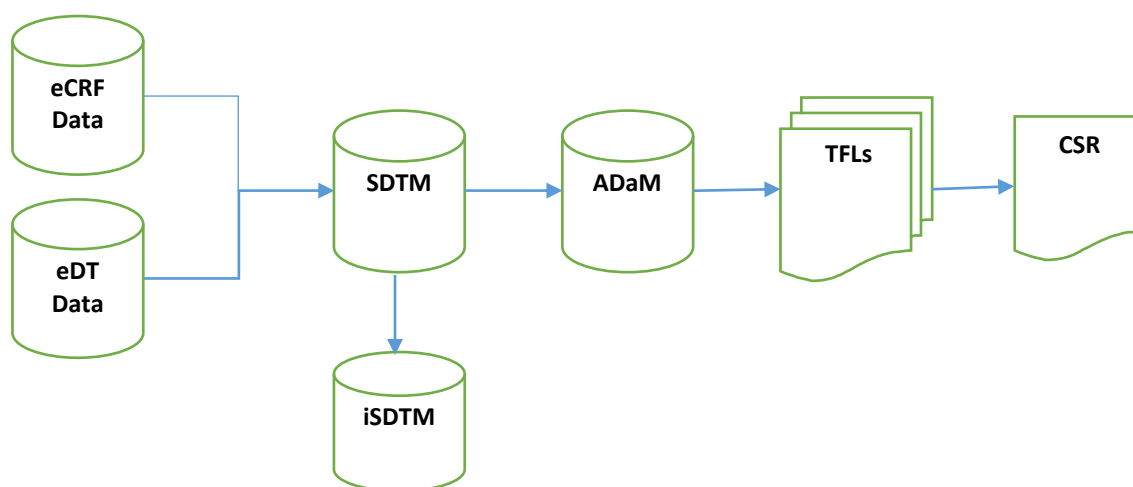
- Disease response endpoints: RS domain where RSEVAL = INVESTIGATOR
- Non-protocol-specified anti-lymphoma therapy: CM and XP domains where --CAT = ANTI-LYMPHOMA THERAPY
- Euro-Quality of Life 5-Dimensions: QS domain where QSCAT = EQ-5D
- Safety analysis: AE domain
- Subject deaths: AE domain where AEOUT = FATAL, DS domain where DSSCAT = STUDY DISCONTINUATION and DSDECOD = DEATH

Per protocol, an Independent Review Committee assessed disease response. IRC assessments are located in the TU, TR, and RS domains and identified by --EVAL equal to INDEPENDENT ASSESSOR. The RS domain includes the IRC adjudicated disease response. These observations can be identified by RSEVAL equal to INDEPENDENT ASSESSOR and RSACPTFL equal to Y.

Reference start date was assigned as the date of first randomized treatment for subjects that received at least one dose of randomized treatment. If a subject was randomized, but not dosed, the reference start date was assigned to the date of randomization

A CRF collected pregnancy event information; however, no pregnancy events were reported.

3.2 Traceability Flow Diagram



3.3 Annotated CRFs

Collected fields that have not been tabulated have been annotated as “Not Mapped”. SDRG Inc. collects certain data elements to facilitate operational processes including data cleaning and dynamically creating additional forms in the electronic data capture system. All fields that have been annotated as “Not Mapped” meet this criterion.

Explanation of data fields [Not Submitted]

aCRF page Number(s)	Data Collection Field	Explanation of why [NOT SUBMITTED]
5	Were there any product complaints?	For internal use only.
30	PI Signature Date	Not needed for analysis.

3.4 SDTM Subject Domains

Controlled terminology codelist for LBTEST and LBTESTCD is extensible. One additional code exists in LB and XL:

- LBTESTCD/XLTESTCD BIOTINIDASE
- LBTEST/XLTEST Biotinidase

This test allows for detection of disease-causing mutations in affected patients which will have an impact on treatment regimen selected.

Dataset – Dataset Label	Efficacy	Safety	Other	Custom	SUPP-	Related Using RELREC
AE – Adverse Events		X			X	CM
CM – Concomitant Medications	X	X				AE
DM – Demographics			X			
DS – Disposition			X			
EG – ECG Test Results			X			
EX – Exposure			X			FAEX
FA – Findings About		X				
FAEX – Findings About Exposure			X			EX
FAMH – Findings About Medical History			X			MH
LB – Laboratory Test Results		X			X	
MH – Medical History			X			FAMH
QS – Questionnaires	X					
RS – Response	X					
SC – Subject Characteristics			X			
SE – Subject Elements			X			
SV – Subject Visits			X			
TR – Tumor Results	X					TU

Dataset – Dataset Label	Efficacy	Safety	Other	Custom	SUPP-	Related Using RELREC
TU – Tumor Identification	X					TR
VS – Vital Signs		X				
XL – Laboratory Results CN				X	X	
XP – Surgeries and Procedures	X	X				
ZA – Clinical Assessments			X			

3.3.1. AE – Adverse Events

As the subject receives multiple study medications, AEACN has been assigned to MULTIPLE and the action taken for each study medication has been represented in SUPPAE. Additionally, AEREL represents the causality of both study medications. The causality for each study medication has been represented in SUPPAE.

AESER

QNAM	Description
AEACN1	Action Taken with SDRG-888 or Pharmab
AEACN2	Action Taken with Chemotherapy
AEREL1	Relationship/causality to SDRG-888 or Pharmab
AEREL2	Relationship/causality to Chemotherapy

3.3.2. CM – Concomitant Medications

Concomitant medications taken due to an adverse event were collected with the corresponding AE. The relationship between these medications and the AE is defined in RELREC. Non-protocol-specified anti-lymphoma medications can be identified by CMCAT = ANTI-LYMPHOMA THERAPY.

3.3.3. DS – Disposition

Subjects have two observations with DSCAT equal to DISPOSITION EVENT. DSCAT equal to STUDY DISCONTINUATION indicates the subject's completion status at study exit. DSSCAT equal to the randomized treatment, SDRG-888 or PHARMAB, indicates the subject's treatment completion status.

3.3.4. EX – Exposure

Each SDRG-888 or Pharmab infusion is represented as one observation. If the infusion is interrupted, EXENDTC is the end date/time of the last interruption and the start and end date/times of each segment are in the FAEX dataset. A relationship between the single observation in EX and interruption segments in FAEX has been defined in RELREC. Chemotherapy regimens have been tabulated in the EX domain.

3.3.5. LB – Laboratory Test Results

QNAM	Description
LBCVRESC	Character result in conventional units
LBCVRESU	Conventional unit
LBCVNRLO	Reference range lower limit in conventional units
LBCVNRHI	Reference ranges upper limit in conventional units

3.3.6. MH – Medical History

Historical DLBCL characteristics collected at study entry including the histopathological diagnosis and Ann Arbor stage have been tabulated in FAMH. A relationship between the DLBCL condition in the MH domain and additional DLBCL characteristics in FAMH has been defined in RELREC.

3.3.7. RS – Response

The investigator's assessment of disease response is identified by RSEVAL equal to INVESTIGATOR. The IRC's assessment of disease response is identified by RSEVAL equal to INDEPENDENT ASSESSOR and RSACPTFL equal to Y.

3.3.8. SC – Subject Characteristics

Stratification factors entered by the investigator into IVRS have been tabulated in the SC domain. SCTESTCD for stratification factors is STRATn, n=1-N. Please refer to define.xml for the corresponding values of SCTEST.

3.3.9. TR – Tumor Results

Tumor measurements and qualitative properties performed by the investigator are identified by TREVAL equal to INVESTIGATOR. Tumor measurements and qualitative properties performed by the IRC are identified by TREVAL equal to INDEPENDENT ASSESSOR. A relationship between the measurements and properties in TR and the tumor descriptors in the TU domain has been defined in RELREC.

3.3.10. XL – Laboratory Test Results CN

XL is a custom domain that contains laboratory test results. The data is a mirror image of the LB domain data except the standard variables are represented in conventional units rather than SI units.

3.3.11. XP – Surgeries and Procedures

XP is a sponsor-defined domain that tabulates historical and coincident surgeries and procedures. Spontaneously reported surgeries and procedures are coded with MedDRA v14.1. Non-protocol-specified anti-lymphoma surgeries and procedures can be identified by XPCAT = ANTI-LYMPHOMA THERAPY.

3.3.12. ZA – Clinical Assessments

ZA is a sponsor-defined domain that tabulates the Eastern Cooperative Oncology Group (ECOG) score

4. Data Conformance Summary

4.1 Conformance Inputs

Was a validator used to evaluate conformance? Yes

If yes, specify the versions of OpenCDISC and the OpenCDISC validation rules:

Pinnacle 21 Enterprise 3.4 (FDA), SDTM v3.1.3 rules

Were sponsor-defined validation rules used to evaluate conformance? Yes

If yes, describe any significant sponsor-defined validation rules:

SDRG Inc. executes a sponsor-defined conformance rule to confirm variable values that are 200 characters have not been truncated.

Were the SDTM datasets evaluated in relation to define.xml? Yes

Was define.xml evaluated? Yes

4.2 Issues Summary

Dataset	Diagnostic Message	Severity	Count	Explanation
LB	Missing Units on Value	Error	22	Not an error: Lab results for pH and Specific Gravity have no units

4.3 Additional Conformance Details

Dataset	Diagnostic Message	Severity	Count	Explanation
AE	The length of Reported Term for the Adverse Event (AETERM) is 200 characters. Please confirm the value has not been truncated.	Warning	3	SDRG Inc. clinical data management confirmed the reported adverse event term was not truncated. In all cases, the reported term was split for clinical coding per MedDRA. Please refer to Modified Reported Term (AEMODIFY) for the specific term to which Dictionary Derived Term (AEDECOD) applies.