Guide to SDTM Tabulations Data

Study TBTC-022 is a randomized Phase III study titled "Efficacy and Safety of Once-Weekly Rifapentine and Isoniazid Compared to Efficacy and Safety of Once-Weekly Rifapentine and Isoniazid Compared to Twice-Weekly Rifampin and Isoniazid in the Continuation Phase of Therapy for Pulmonary Tuberculosis."

This document provides an introduction to SDTM domains requiring additional explanation beyond what is available in the Data Definitions (define.xml) document.

Contents

Introduction

The TBTC/USPHS Study 22 SDTM database was created to demonstrate and test the use of TB data standards in the CDISC Study Data Tabulation Model (SDTM). An abbreviated study protocol is available at http://clinicaltrials.gov/ct2/show/NCT00023335. This database is available to the public.

This study was started in 1995 and completed in 2001. The design of the forms and procedures predates both CDISC data standards and current data collection conventions. Substantial data manipulation was done in addition to structural and semantic conversion to create conforming SDTM. Appropriate uses for this database are signal detection and hypothesis generation, and as a demonstration of data standards.

Where to Find Key Data

Demographics and Compliance

Basic data on subject demographics and the conduct of the study are in the following domains: DM (Demographics), SE (Subject Elements), and SV (Subject Visits). There were no inclusion or exclusion criteria exceptions recorded and there were no protocol deviations reported, thus neither IE nor DV are in the data package. Note that the draft SDTMIG V3.2.1 addendum standards were implemented in this version of the Study 22 database, thus DM includes new variables for the date of informed consent, the date of first exposure, date of last exposure, date of end of study participation, date of death and death flag.

Exposure to Study Treatment

Exposure data is in the EX domain. All subjects received a study treatment that included either Rifapentine or Rifampin in combination with Isoniazid (INH). Both drugs in the combination are in EX.

Secondary exposure information is included in the XD domain (Study Drug Dose Assigned at Enrollment).

Subject Disposition and Mortality

The DS (Subject Disposition) domain includes the date of enrollment into the study (DSCAT=PROTOCOL MILESTONE) and the date and reason for discontinuation (permanent departure) from the study (DSCAT=DISPOSITION EVENT). The subjects enrolled in this study were all required to complete an induction (intensive) period of clinical care for active TB. This study begins with the continuation phase of their clinical care.

The primary source for deaths in the study population may be found in DM, however these deaths may be traced to two secondary sources in the SDTM database: DS (where DSDECOD=DEATH) and AE (where AEOUT=FATAL). No attempt was made to reconcile

these sources. The deaths in DS are those that were recorded as the reason for permanent departure (Form 8); the deaths in AE are those that were recorded on the mortality report (Form 13) or the adverse event form (Form 9). The Comments domain (CO) includes unstructured information about some of the deaths documented in the mortality report.

Efficacy

Treatment failures and treatment relapses are recorded in CE (Clinical Events). Both suspected and confirmed cases are included. Suspected cases were adjudicated and those that were confirmed are highlighted with CECAT=ADJUDICATED ENDPOINT. The evaluation of the treatment failure and treatment relapse endpoints was similar; however suspected treatment failure was collected while study treatment was ongoing while suspected treatment relapse was collected after study treatment was completed or prematurely terminated. A supplemental qualifier on CE (SUPPCE.QNAM=EVNTOUT) indicates the investigator's final assessment of the information related to a suspected treatment failure or treatment relapse.

Many assessments were made to inform the investigator's judgment of treatment failure and treatment relapse. These are in a variety of domains, including FAMH (Findings about Medical History), LB (Laboratory Tests Results), MB (Microbiology Specimen), MS (Microbiology Susceptibility Test), CM (Concomitant Medications) and ZS (Physical Signs and Symptoms of TB). ZS includes chest x-ray results and signs and symptoms observed in the physical exam.

Safety

Key safety data are found in the standard CDISC domains, including: AE (Adverse Events), LB (Laboratory Test Results), CM (Concomitant Medications), SU (Substance Use), MH (Medical History), and VS (Vital Signs). Laboratory data were standardized and normal ranges were assigned in the process of converting the legacy database to SDTM. The source for the normal ranges is documents at the variable level in define.xml.

Note that in the AE domain, adverse event-like data scattered among several fields was collected into one variable to produce the verbatim terms in AETERM.

HIV status at study start is recorded in MH (where MHCAT=COINFECTION), however laboratory indicators of HIV/AIDS are in LB. These include baseline Western Blot/EIA test results and ongoing CD4 counts.

CM includes summary information about INH administered during the induction phase of clinical care for the study population. Supplemental qualifiers in SUPPCM include the frequency and total number of observed and unobserved doses in the induction phase regimen. Note that this information is only available in summarized form because the study did not start until after the induction phase.

Disease-Specific Information

Key baseline characteristics are in QS (Karnofsky Scale score), SC (social history, including place of birth and education level), and SU (Substance Use). MH (Medical History) includes the TB Diagnosis at study entry, i.e., either Pulmonary TB or Pulmonary and Extra-pulmonary TB. FAMH (Findings about Medical History) includes the results for questions about pre-specified risk factors for TB.

ZS (Clinical Signs and Symptoms of TB) includes chest x-ray and observed signs and symptoms.

Comments

Comments related to adverse events (AE) and treatment failure and treatment relapse (CE) are found in the CO (Comments) domain.

Trial Design Model Datasets

Trial-level information is found in the SDTM special-purpose datasets TI (Trial Inclusion/Exclusion Criteria), TS (Trial Summary), TA (Trial Arms), TE (Trial Elements), and TV (Trial Visits).

TI contains a complete list of the study Inclusion and Exclusion criteria.

TS contains a list of CDISC standard data elements used to describe the study population, intervention, and design.

TA, TE, and TV all contain information about data elements used to describe the planned time periods of the study, including Arm, Element, and Visit. The organization of Epoch within Arm is in TA. This study includes only three epochs: Screening, Continuation, and Follow-up. Screening observations were taken at the end of the Induction Phase of Clinical Care and study treatment picks up at the Continuation Phase of Clinical Care.

Overview of Custom Domains

XD – Study Drug Dose Assigned at Enrollment

Observation class: Interventions

XD is used to report the dose and frequency of study drugs prescribed for the treatment continuation after induction, including INH and either Rifapentine or Rifampin, depending on the treatment assignment. This information is collected at the time of randomization, thus it is planned dosing. See EX for data collected on actual dose administration, which differed from the planned for many subjects.

ZH – Directed Medical History

Observation class: Findings

ZH is used to store summary data that is administrative in nature and not likely to be used in analysis. Examples of secondary sources are yes/no prompts such as “Any major illnesses reported?” and “Other anti-tuberculosis drugs taken?” These are routed to ZH because they are too general for AE and CM but could be of interest to some reviewers. .

ZS – Physical Signs and Symptoms of TB

Observation class: Findings

ZS contains chest x-ray results and signs and symptoms of TB collected repeatedly over the course of the study.

Standard Domains Not Submitted

The were no eligibility exceptions reported for Study 22, nor were there any protocol deviations, thus neither IE nor DV is included in the data submission. This does not guarantee that the population was free of eligibility exceptions and protocol violations.