

ABSTRACT

Information regarding tumor lesions and disease response is key in oncology clinical trials to evaluate if the primary or secondary endpoint, usually being defined as a time to event endpoint, has been achieved. Specific oncology domains described in Study Data Tabulation Model Implementation Guide (SDTMIG) 3.2 and SDTM v1.4, are representing the data collection of tumor lesions and the evaluation of response(s). Identification information of the lesion is collected in the tumor identification domain (TU). Each identified lesion is repeatedly measured or assessed at subsequent time points. The follow up of each of these lesions, lesions that are split up or merged, and new lesions is captured in the tumor results domain (TR). Using all of this information the investigator evaluates the disease response, captured in the disease response domain (RS). Often in parallel with the investigator, multiple independent reviewers are evaluating the lesions and the disease response to better assess patient outcomes and provide standardized endpoint classification.

ONCOLOGY SPECIFIC SDTM DOMAINS

Each of the figures used on this poster is an illustration of data coming from one patient. In order to simplify the figures and make them easier to understand it was decided not to include all variables nor do they contain all the required variables. This poster demonstrates a possible way of implementing of what is described in SDTMIG v3.2.

TU DOMAIN

GENERAL INFORMATION

THE TU DOMAIN REPRESENTS DATA THAT UNIQUELY IDENTIFY TUMORS.

FIGURE 1: EXAMPLE OF TU DOMAIN DATA COLLECTED FOR ONE PATIENT

TUGRPID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	VISIT	TUDTC
A1	A1	TUMIDENT	Tumor Identification	ASSESSABLE TUMOR LESION	ADENOPATHY CERVICAL	SPIRAL CT	SCREENING	2012-11-01
M1	M1	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY INGUINAL	SPIRAL CT	SCREENING	2012-11-01
M2	M2	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	SCREENING	2012-11-01
N1	N1	TUMIDENT	Tumor Identification	NEW	ADENOPATHY MESENTERIC	SPIRAL CT	VISIT 3	2013-06-11

TUMETHOD: The identification is usually done at a baseline visit by using certain methods of assessments, e.g. MRI, CT, PET, or physical examination, as recommended by the Standardized Response Criteria being used.

TULOC: The anatomic location characterizes the TU domain. Additional anatomical location qualifiers (TULAT, TUDIR, TUPORTOT) might also be used in the database and are permissible fields.

TUTESTCD, TUTEST: Each record in TU corresponds to the identification of one lesion (in this example: TUTESTCD = TUMIDENT).

TUORRES: The result of the identification corresponding to the classification of the identified tumor.

TUDTC: The date on which the image/scan/physical exam was done. Remark: TUDTC is not the date that the image was read by the radiologist to identify tumors and thus does not necessarily represent the date of VISIT.

NEW, SPLIT AND MERGED LESIONS

THERE ARE SOME CASES FOR WHICH POST-BASELINE INFORMATION MIGHT BE INCLUDED IN THE TU DOMAIN.

- New lesions represent progressive disease and the identification information is collected in the TU domain for the post-baseline visit on which the lesion was diagnosed.
- Split or Merged Lesions: A tumor lesion which was identified at baseline, might split into one or more distinct tumor lesions during trial conduct or two or more tumor lesions might merge to form one single tumor lesion. Depending on the set up of the trial, different approaches can be followed to collect this information in the datasets. However, to collect information of each distinct tumor lesion the eCRF will need to be set up in a way that allows measurements of each distinct tumor lesion to be captured individually.

FIGURE 2: EXAMPLE OF SPLIT LESION IN THE TU DOMAIN

TUGRPID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	VISIT	TUDTC
M2	M2	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	SCREENING	2012-11-01
M2	M2.1	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	VISIT 2	2013-04-15
M2	M2.2	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	VISIT 2	2013-04-15

TULNKID: Reflects the split of a tumor lesion on visit 2 by adding '1' and '2' to the original TULNKID (see red circle).

TUGRPID: Variable used to link together a block of related records within a subject in a domain. In this case the split tumor lesion and the originally identified tumor lesion are grouped by using TUGRPID = M2 (measurable lesion 2). A similar principle can be applied for merged lesions. TULNKID will then be a concatenation of the original TULNKID so it reflects the original TULNKID values assigned at the screening visit. For example if M1 and M3 merge, TULNKID might become M1/M3.

Another approach would be to not collect data of each split lesion or merged lesion as newly identified tumor lesions. In these cases the information of the split/merged tumor will only be represented in the TR domain. For example the clinical trial study team can decide that if two or more measurable lesions merge, the measurement of the first measurable tumor lesion is put on 0 mm x 0 mm, while the measurement of the other lesion will contain the total diameters of the merged lesion.

TR DOMAIN

GENERAL INFORMATION

THE TR DOMAIN REPRESENTS QUANTITATIVE MEASUREMENTS AND/OR QUALITATIVE ASSESSMENTS OF EACH TIME POINT FOR EACH TUMOR IDENTIFIED IN THE TU DOMAIN.

- For assessable lesions the assessment is qualitative and thus the tumor results, collected in TR, can only be collected on post-baseline visits. In the example tumor lesion, A1, identified at screening, did not change on visit 1, while on visit 3 the tumor lesion decreased in size compared to baseline.

FIGURE 3: EXAMPLE OF TR DOMAIN DATA COLLECTED FOR 1 PATIENT WITH REGARDS TO ASSESSABLE TUMOR LESION A1 IDENTIFIED AT SCREENING. THE UPPER TABLE IS PART OF THE TU- DOMAIN AND IS LINKED WITH THE TR DOMAIN (AS SHOWN IN THE LOWER TABLE) VIA THE -LNKID VARIABLE

TUGRPID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	VISIT	TUDTC
A1	A1	TUMIDENT	Tumor Identification	ASSESSABLE TUMOR LESION	ADENOPATHY CERVICAL	SPIRAL CT	SCREENING	2012-11-01

TRLNKID	TRTESTCD	TRTEST	TRORRES	TRMETHOD	VISIT	TRDTC
A1	LESSTAT	Lesion Status	NO CHANGE	SPIRAL CT	VISIT 1	2013-01-25
A1	LESSTAT	Lesion Status	NOT EVALUABLE	SPIRAL CT	VISIT 2	2013-03-26
A1	LESSTAT	Lesion Status	DECREASED	SPIRAL CT	VISIT 3	2013-05-13

- For measurable lesions the measurement is quantitative and results for baseline and post-baseline measurements will be collected in TR. Depending on the Standardized Response Criteria being used, it may be necessary to collect more than one measurement per visit.

TRTESTCD and TRTEST: In Figure 4 the tumor lesion was measured in 2 perpendicular dimensions reported per VISIT in TR. The bi-dimensional measurement is reflected in TRTESTCD and TRTEST. For the assessable tumor lesion TRTEST = Lesion Status (see Figure 3).

TRORES and TRORESU: The result of the bi-dimensional measurement / assessment.

TRDTC: Reflects the date of measurement or assessment and not the date on which the investigator/radiologist read the image.

FIGURE 4: EXAMPLE OF TR DOMAIN DATA COLLECTED FOR 1 PATIENT WITH REGARDS TO MEASURABLE TUMOR LESION M2 IDENTIFIED AT SCREENING. THE UPPER TABLE IS A PART OF THE TU- DOMAIN AND SHOWS THE LINK WITH TR DOMAIN (AS SHOWN IN THE LOWER TABLE) VIA -LNKID VARIABLE

TUGRPID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	VISIT	TUDTC
M2	M2	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	SCREENING	2012-11-01
M2	M2.1	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	VISIT 2	2013-04-15
M2	M2.2	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	VISIT 2	2013-04-15

TRLNKID	TRTESTCD	TRTEST	TRORRES	TRORRESU	TRMETHOD	VISIT	TRDTC
M2	BIDMEAS1	Bidimensional Measurement 1	55.0	mm	SPIRAL CT	SCREENING	2012-10-11
M2	BIDMEAS2	Bidimensional Measurement 2	27.0	mm	SPIRAL CT	SCREENING	2012-10-11
M2	BIDMEAS1	Bidimensional Measurement 1	53.0	mm	SPIRAL CT	VISIT 1	2013-01-16
M2	BIDMEAS2	Bidimensional Measurement 2	24.0	mm	SPIRAL CT	VISIT 1	2013-01-16
M.2.1	BIDMEAS1	Bidimensional Measurement 1	30.0	mm	SPIRAL CT	VISIT 2	2013-04-15
M.2.1	BIDMEAS2	Bidimensional Measurement 2	7.0	mm	SPIRAL CT	VISIT 2	2013-04-15
M.2.2	BIDMEAS1	Bidimensional Measurement 1	12.0	mm	SPIRAL CT	VISIT 2	2013-04-15
M.2.2	BIDMEAS2	Bidimensional Measurement 2	6.0	mm	SPIRAL CT	VISIT 2	2013-04-15

NEW LESIONS

NEW LESIONS INFORMATION SHOULD BE INCLUDED IN BOTH TU AND TR DOMAINS, LINKED VIA -LNKID (EVEN IF NO ASSESSMENTS OR MEASUREMENTS ARE REQUIRED PER PROTOCOL).

The occurrence of a new tumor lesion is a sign of disease progression and often means that the endpoint of the trial has been reached. The level of detail being collected about this newly identified lesion might be different within each trial. For some clinical trials it is decided to collect limited information as no further details are needed to determine progressive disease. For other clinical trials it might be necessary to also collect the measurements and assessments of this lesion.

FIGURE 5: EXAMPLE OF NEW LESION FOR WHICH MEASUREMENTS ARE DONE, REPRESENTED IN THE TU (UPPER TABLE) AND TR DOMAINS (LOWER TABLE)

TUGRPID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	VISIT	TUDTC
N1	N1	TUMIDENT	Tumor Identification	NEW	ADENOPATHY MESENTERIC	SPIRAL CT	VISIT 3	2013-06-11

TRLNKID	TRTESTCD	TRTEST	TRORRES	TRORRESU	TRMETHOD	VISIT	TRDTC
N1	BIDMEAS1	Bidimensional Measurement 1	17.0	mm	SPIRAL CT	VISIT 3	2013-06-11
N1	BIDMEAS2	Bidimensional Measurement 2	10.0	mm	SPIRAL CT	VISIT 3	2013-06-11

RESULTS OF THE INVESTIGATOR AND INDEPENDENT ASSESSOR(S)

GENERAL INFORMATION

DEPENDING ON THE PRIMARY OBJECTIVE OF THE TRIAL, IT MAY BE DECIDED TO SHARE THE IMAGES AND ASSESSMENTS WITH AN INDEPENDENT REVIEW COMMITTEE.

Independent radiologists and oncologists will review the images and assessments and their evaluation will also be captured in the clinical database.

FIGURE 6: EXAMPLE OF THE TU DOMAIN CONTAINING DATA FROM THE ECRF AND DATA FROM AN INDEPENDENT ASSESSOR

TUGRPID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	TUEVAL	VISIT
A1	A1	TUMIDENT	Tumor Identification	ASSESSABLE TUMOR LESION	ADENOPATHY CERVICAL	SPIRAL CT	INVESTIGATOR	SCREENING
M2	M2	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY PARATRACHEAL	SPIRAL CT	INVESTIGATOR	SCREENING
R1-101	R1-101	TUMIDENT	Tumor Identification	MEASURABLE TUMOR LESION	ADENOPATHY INGUINAL	PET	RADIOLOGIST	SCREENING
R1-501	R1-501	TUMIDENT	Tumor Identification	ASSESSABLE TUMOR LESION	ADENOPATHY INGUINAL	PET	RADIOLOGIST	SCREENING

TUEVAL, TREVAL, RSEVAL: Allows the reader to distinguish between the results from the investigator / radiologist at the site and the independent assessor. If only eCRF data is collected, the -EVAL variable can be left empty.

-EVALID: Can be used to provide additional detail of who is providing measurements or assessments. This variable should always be used in conjunction with the -EVAL variable. In Figure 7 the data from two radiologists (TUEVALID = RADIOLOGIST 1 and TUEVALID = RADIOLOGIST 2) are displayed.

TUREFID, TRREFID: Each image has its own identifying reference number. The red circles in Figure 7 indicate the tumor lesions that were read on image 27595 by each radiologist.

TULNKID, TRLNKID: In Figure 7, this consists of an indication of the assessor and an identification number of the tumor lesion: R1-101 is lesion 101 identified by Radiologist 1. Despite the fact that the identification number 101 is used twice, once for a tumor lesion identified by radiologist 1 and once for a tumor lesion identified by radiologist 2, it doesn't mean that it concerns the same tumor. Radiologist 1 and 2 are reading the images independently of each other.

FIGURE 7: EXAMPLE OF INDEPENDENT ASSESSOR DATA IN THE TU DOMAIN

TUREFID	TULNKID	TUTESTCD	TUORRES	TULOC	TUMETHOD	TUEVAL	TUEVALID	TUACPT-FL	VISIT
27595	R1-101	TUMIDENT	MEASURABLE TUMOR LESION	ADENOPATHY INGUINAL	PET	RADIOLOGIST	RADIOLOGIST 1	N	SCREENING
27595	R1-102	TUMIDENT	MEASURABLE TUMOR LESION	ADENOPATHY ABDOMINAL	PET	RADIOLOGIST	RADIOLOGIST 1	N	SCREENING
27595	R1-501	TUMIDENT	ASSESSABLE TUMOR LESION	ADENOPATHY INGUINAL	PET	RADIOLOGIST	RADIOLOGIST 1	N	SCREENING
27595	R1-502	TUMIDENT	ASSESSABLE TUMOR LESION	ADENOPATHY COMMON ILLAC	PET	RADIOLOGIST	RADIOLOGIST 1	N	SCREENING
31430	R1-301	TUMIDENT	NEW	OTHER	SPIRAL CT	RADIOLOGIST	RADIOLOGIST 1	N	VISIT 2
27595	R2-101	TUMIDENT	MEASURABLE TUMOR LESION	ADENOPATHY ABDOMINAL	PET	RADIOLOGIST	RADIOLOGIST 2	Y	SCREENING
27595	R2-102	TUMIDENT	MEASURABLE TUMOR LESION	ADENOPATHY MEDIOSTINAL	PET	RADIOLOGIST	RADIOLOGIST 2	Y	SCREENING
27595	R2-501	TUMIDENT	ASSESSABLE TUMOR LESION	ADENOPATHY MEDIOSTINAL	PET	RADIOLOGIST	RADIOLOGIST 2	Y	SCREENING
32693	R2-801	TUMIDENT	NEW	SUBCUTANEOUS MASS	SPIRAL CT	RADIOLOGIST	RADIOLOGIST 2	Y	VISIT 1

ADJUDICATION

IF FOR EXAMPLE THE OVERALL RESPONSE OR TIME TO PROGRESSION OF BOTH INDEPENDENT ASSESSORS DIFFER, ADJUDICATION BY A THIRD INDEPENDENT ASSESSOR NEEDS TO BE DONE.

The third independent assessor will indicate which data should be used for analysis per patient. This information is collected in an acceptance flag variable, -ACPTFL (TUACPTFL, TRACPTFL, RSACPTFL). In Figure 7 the data of radiologist 2 has been accepted for this patient on all time points (TUACPTFL = Y and thus TRACPTFL and RSACPTFL will also be Y for this patient). This means that the new lesion which was identified on VISIT1 by radiologist 2 is also accepted and the patient was diagnosed with progressive disease on VISIT 1.

RS DOMAIN

THE RS DOMAIN COLLECTS THE RESPONSE EVALUATION. THIS EVALUATION IS BASED ON ALL RELEVANT INFORMATION WHICH IS AVAILABLE FROM THE PATIENT AND IS NOT LIMITED TO ONLY THE DATA IN THE TR DOMAIN (E.G. DATA COLLECTED IN THE FOLLOWING SDTM DOMAINS: LB, PE, ...).

Variables like RSEVAL, RSEVALID, RSLNKID are variables that also can be used within the RS domain as explained in the two other domains.

RSLNKGRP: Variable used to link the response assessment to the measurement and assessment records in TR via TRLNKGRP. In Figure 8 the most important response assessment is done on visit level thus -LNKGRP is a variable which groups the measurements and assessments on time point. In this example more than one independent assessor is assessing the response on the same visit and thus information with regards to the assessor should also be included in -LNKGRP e.g. R2-V2 is a concatenation of radiologist 2-Visit 2.

RSTEST, RSTESTCD: Represent the type of response assessment e.g. overall response, response of measurable lesions, response of assessable lesions, and spleen response.

RSORRES: The result of the response assessment as specified in the standardized response criteria.

RSCAT: The standardized response criteria being used within the trial. Within the example Cheson criteria 2007 has been used.

FIGURE 8: EXAMPLE OF LINKING BETWEEN TR DOMAIN AND RS DOMAIN

TRLNKGRP	TRLNKID	TRTESTCD	TRTEST	TRORRES	TRORRESU	TRMETHOD	TRACPT-FL	VISIT
R2-V1	R2-101	LDIAM	Longest Diameter	104.49	mm	PET	Y	SCREENING
R2-V1	R2-101	PPD	Product Perpendicular Diameters	7245.34	mm ²	PET	Y	SCREENING
R2-V2	R2-101	LDIAM	Longest Diameter	77.75	mm	SPIRAL CT	Y	VISIT 1
R2-V2	R2-101	PPD	Product Perpendicular Diameters	2506.68	mm ²	SPIRAL CT	Y	VISIT 1
R2-V2	R2-501	TUMSTATE	Tumor State	PRESENT		SPIRAL CT	Y	VISIT 1
R2-V2	R2-801	TUMSTATE	Tumor State	PRESENT		SPIRAL CT	Y	VISIT 1

RSLNKGRP	RSTEST	RSCAT	RSORRES	RSEVAL	RSEVALID	RSACPTFL	VISIT
R1-V2	Overall Response	CHESON 2007	SD	RADIOLOGIST	RADIOLOGIST 1	N	VISIT 1
R2-V2	Overall Response	CHESON 2007	PD	RADIOLOGIST	RADIOLOGIST 2	Y	VISIT 1

For some RSTEST's, RSLNKGRP is empty. Best Overall Response is an evaluation of response determined on patient level and independent of the visit. For this reason RSLNKGRP and VISIT are empty for this RSTEST. For each response grouped on type of tumor RSLNKGRP is also empty in the example as RSLNKGRP is used to link to all of the measurements and assessments in the TR domain per time point.

FIGURE 9: EXAMPLE OF DIFFERENT RSTEST'S WITH AN EMPTY RSLNKGRP VARIABLE

RSLNKGRP	RSTEST	RSCAT	RSORRES	RSSTAT	RSREASND	RSEVAL	VISIT
	Assessable Lesion Response	CHESON 2007	SD			RADIOLOGIST	VISIT 1
	Measurable Lesion Response	CHESON 2007	PR			RADIOLOGIST	VISIT 1
	Liver Response	CHESON 2007	CR			RADIOLOGIST	VISIT 1
	Spleen Response	CHESON 2007	CR			RADIOLOGIST	VISIT 1
	Best Overall Response	CHESON 2007	PR			RADIOLOGIST	VISIT 1

CONCLUSION

With the increase of clinical trials in oncology and the associated collection of complex data, new domains have been developed in 2012 by CDISC to collect the information about tumors in a more structured and standardized way. Three main domains are used to represent this type of data. Each of the domains is unique in its purpose but all three are related and linked to each other in a specific way. This is only the beginning of a structured guidance with regards to oncology related data. More is yet to come as CDISC is actively collaborating with a variety of partners on the development of Therapeutic Area Data Standards (CFast project). One of the initiatives is to develop a Breast Cancer Therapeutic Area Data Standards containing maps, metadata, examples and controlled terminology related to breast cancer. The guidance is not limited to the three SDTM domains described in this paper but will also include information on how to deal with specific biomarker data, relevant family history, treatment history, and more. Using these standards will help to compare data across clinical trials and it will enhance the review and approval process of new agents. With these advantages we can only expect that more specific guidelines for oncology will follow in order to set up clinical databases consistently and with a high standard of quality.

REFERENCES

- Study Data Tabulation Model Implementation Guide: Human Clinical Trials, Version 3.2, CDISC Submission Data Standards Team (November 26, 2013)
- Study Data Tabulation Model, Version 1.4, CDISC Submission Data Standards Team (November 26, 2013)
- www.cdisc.org (August 29, 2014)
- Bruce D. Cheson, et al, Revised Response Criteria for Malignant Lymphoma, Journal of Clinical Oncology (February 10, 2007)

RECOMMENDED READING

- Study Data Tabulation Model Implementation Guide: Human Clinical Trials, Version 3.2, CDISC Submission Data Standards Team (November 26, 2013)
- Study Data Tabulation Model, Version 1.4, CDISC Submission Data Standards Team (November 26, 2013)
- www.cdisc.org

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