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Practice and Discussions on TAUGs implementations for oncology studies

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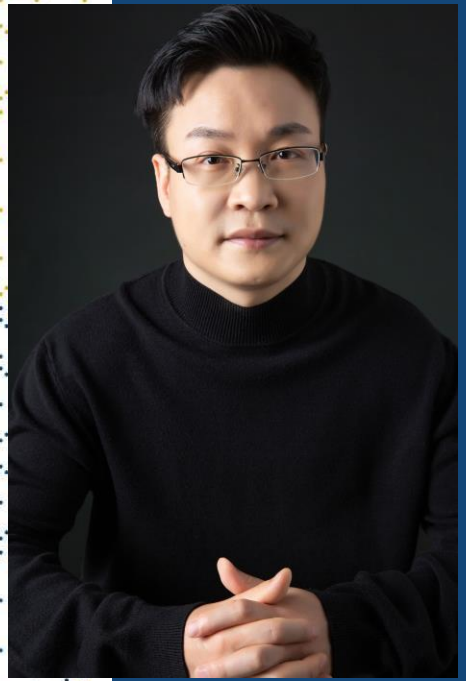

Meet the Speaker

Sen Fan（樊森）

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Sen Fan is senior statistical programming manager from CSPC.

He obtained bachelor's degree from Huazhong University of Science and Technology, and master's degree from Peking Union Medical College.

He used to work in Sanofi and Innoventbio. He has 7 years' experience of CDISC data standards implementations and clinical trial data analysis.

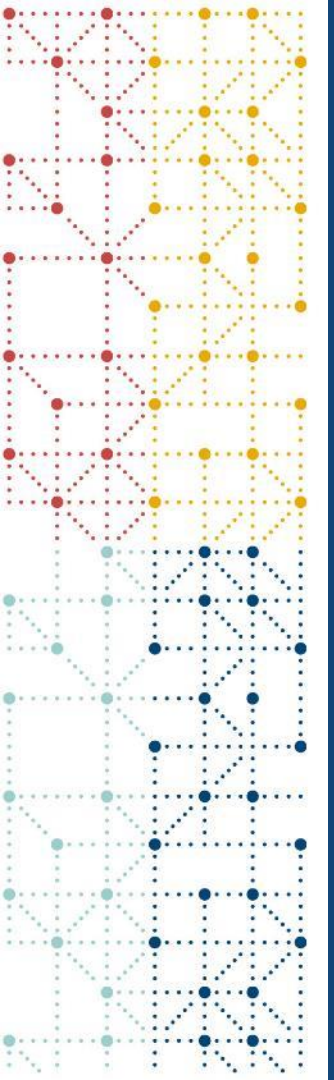
Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC and CSPC.*

- *The author(s) have no real or apparent conflicts of interest to report.*

Agenda

1. Background
2. Practice and Discussions on oncology TAUGs implementations
3. Conclusion



Background

5 oncology Therapeutic Area User Guides (TAUGs) have been successively developed by CDISC

These oncology TAUGs provide advice and examples for the use of CDASH, SDTM and ADaM

- ***Sample CRFs*** *compliant with CDASH, annotated with CDASH and SDTM variables;*
- *Guidance on which domain models and datasets from the SDTMIG to use in representing collected data;*
- *Examples of* ***SDTM datasets****, with text describing the situational context and pointing out records of note;*
- *Cross-implementation variable definition metadata for non-standard (supplemental qualifier) variables used in example SDTM datasets and/or* ***CRF mapping annotations****;*
- *Analysis datasets compliant with* ***ADaM****, with dataset- and variable-level* ***metadata****;*
- ***Table shells*** *illustrating some kinds of statistical analysis that can be represented in the ADaM datasets.*

Similarities and differences of these 5 oncology TAUGs

- Focus on different specific cancer types
- Address some common topics, for example, tumor identifications and response assessments.
- Implementations on a same data point may be inconsistent across these 5 TAUGs.

Summary information for these 5 oncology TAUGs

Indication	Version Date	CDASH	CDASHIG	SDTM	SDTMIG	ADAM	ADAMIG	Tumor Response Evaluation Criteria
Breast Cancer	2016/05/16	V1.1	-	V1.4	V3.2	V2.1	V1.0	RECIST
Prostate Cancer	2017/07/10	V1.1	-	V1.4	V3.2	V2.1	V1.0	RECIST; PCWG
Colorectal Cancer	2018/11/15	V1.1	V1.0	V1.4	V3.2	V2.1	V1.1	irRC
Lung Cancer	2019/05/06	V1.0	V2.0	V1.7	V3.3	V2.1	V1.1	RECIST; iRECIST
Pancreatic Cancer	2021/10/05	V1.1	V2.1	V1.7	V3.3	V2.1	V1.2	-

Practice and Discussions on oncology TAUGs implementations

1. Is it necessary to represent the tumor imaging information in the SDTM PR domain?

pr.xpt

Row	STUDYID	DOMAIN	USUBJID	PRSEQ	PRREFID	PRSPID	PRTRT	PRPRESP	PROCCUR	PRLOC	VISITNUM	VISIT	PRSTDTC
1	ABC123	PR	ABC123-1234	1	0124578	1	X-RAY	Y	Y	CHEST	10	SCREENING	2014-04-15
2	ABC123	PR	ABC123-2345	1	6587466_1		CT SCAN			CHEST	10	SCREENING	2014-05-30
3	ABC123	PR	ABC123-2345	2	6587466_2		CT SCAN			ABDOMINAL CAVITY	10	SCREENING	2014-05-30
4	ABC123	PR	ABC123-2345	3	6587466_3		CT SCAN			PELVIS	10	SCREENING	2014-05-30

tu.xpt

Row	STUDYID	DOMAIN	USUBJID	TUSEQ	TUREFID	TULNKID	TUTESTCD	TUTEST	TUORRES	TUSTRESC	TULOC	TULAT
1	ABC123	TU	ABC123-1234	1	0124578	T01	TUMIDENT	Tumor Identification	TARGET	TARGET	BREAST	RIGHT
2	ABC123	TU	ABC123-2345	1	6587466_1	T01	TUMIDENT	Tumor Identification	TARGET	TARGET	BREAST	LEFT
3	ABC123	TU	ABC123-2345	2	6587466_1	NT01	TUMIDENT	Tumor Identification	NON-TARGET	NON-TARGET	PLEURAL CAVITY	
4	ABC123	TU	ABC123-2345	3	6587466_1	NT02	TUMIDENT	Tumor Identification	NON-TARGET	NON-TARGET	BREAST	RIGHT

Row	TUMETHOD	TUEVAL	TUEVALID	VISITNUM	VISIT	TUDTC
1 (cont)	X-RAY	INDEPENDENT ASSESSOR	RADIOLOGIST	10	SCREENING	2014-04-15
2 (cont)	CT SCAN	INDEPENDENT ASSESSOR	RADIOLOGIST	10	SCREENING	2014-05-30
3 (cont)	CT SCAN	INDEPENDENT ASSESSOR	RADIOLOGIST	10	SCREENING	2014-05-30
4 (cont)	CT SCAN	INDEPENDENT ASSESSOR	RADIOLOGIST	10	SCREENING	2014-05-30

PRTYP
EFFUSION

relrec.xpt

Row	STUDYID	DOMAIN	USUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
1	ABC123	PR		PRREFID		ONE	A
2	ABC123	TU		TUREFID		MANY	A

1. Is it necessary to represent the tumor imaging information in the SDTM PR domain?

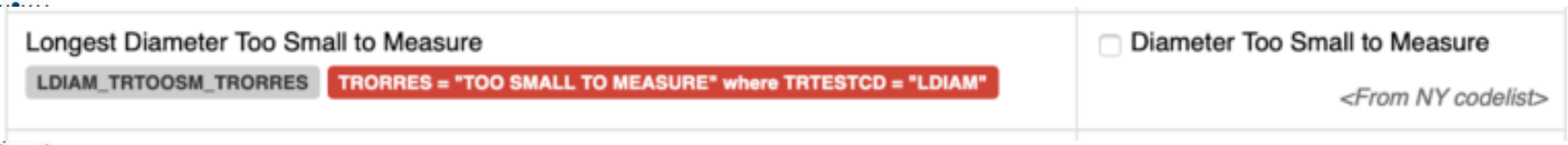
- **It's stated in the TAUG-PrCa that,**

"If only the findings from a procedure are collected, then --METHOD in the Findings domain(s) may be sufficient to reflect the procedure; a related PR record is optional. It is at the sponsor's discretion whether to represent the procedure as both a test method and related PR record. "

2. How to capture baseline and post-baseline tumor information, respectively?

- As per the RECISIT 1.1, target/non-target lesions are selected at baseline and measured repeatedly during follow-up.
- The oncology TAUGs provide sample CDASH CRFs, in which a single form was used to capture both baseline and post-baseline tumor information.
- The sample CRFs use a dynamics option according to different visits in the database. The tumor identification information (e.g., tumor location, location detail, laterality and directionality), is only collected once at the baseline visit and the database will automatically move identification information gathered at baseline into the proper post-baseline results forms.
- Accordingly, when constructing SDTM datasets, we need to keep in mind: 1.TU domain should contain only one record for each unique tumor identified by an assessor, must not be repeated for every visit; 2.TR domain contains repeated quantitative measurements and/or qualitative assessments of the tumors.

3. How to collect the target lesion measurement information when its diameter was too small to measure?



- As per RECISIT 1.1, when target lesion becomes too small to measure, it's important that a quantitative value should still be recorded on the CRF.
- If it is the opinion of the radiologist that the lesion has likely disappeared, the measurement should be recorded as 0 mm. If the lesion is believed to be present and is faintly seen but too small to measure, a default value of 5 mm should be assigned.

4. How to collect the diameter of target lesions?

What was the diameter of tumor? **TRDIAM** **TRORRES where TRTESTCD = "DIAMETER"**	.__.__
Diameter Unit **TRDIAMU** **TRORRESU** *Pre-specified*	mm *<From UNIT codelist>*

What was the longest diameter of the tumor? **LDIAM_TRORRES** **TRORRES where TRTESTCD = "LDIAM"**	.
Longest Diameter Unit **LDIAM_TRORRESU** **TRORRESU where TRTESTCD = "LDIAM"** *Pre-populated*	mr *<From UNIT codelist>*
What was the perpendicular diameter of the tumor? **PDIAM_TRORESS** **TRORRES where TRTESTCD = "LPERP"**	.
Perpendicular Diameter Unit **PDIAM_TRORRESU** **TRORRESU where TRTESTCD = "LPERP"** *Pre-populated*	mr *<From UNIT codelist>*

5. How to collect the date of non-target/target/overall response (RSDAT) in CRF?

- **Some sponsors collect RSDAT by using an ambiguous question (e.g., "assessment date") without any supplemental instructions, which may lead to unexpected data collected.**

- We should know that RSDAT should be the procedure date (e.g., scan date) associated with the response instead of the date when investigator gives the response judgement.
- However, the exact date of a response may not always be straightforward, since scanning/imaging on different organs may be performed on separate dates.

5. How to collect the date of non-target/target/overall response (RSDAT) in CRF?

- Our practice is to provide a detailed explanation text pre-printed besides the field on the CRF: “Assessment may be performed on separate days. If response is PD, then use the earliest date of any assessment contributing to PD. If response is CR/PR/SD/NE, then use the latest date of all corresponding assessments.”

- Another option is to derive RSDTC in SDTM by programming instead of collecting it in CRF.

6. Intermediate analysis data set: ADEVENT or ADDATES?

adevent.xpt

Row	STUDYID	USUBJID	ASEQ	ASTDT	ASTDY	*PARQUAL*	PARAMCD	AVALC	ANL01FL
1	ABC-123	ABC-123-001	1	2013DEC29	-4	PROTOCOL	DISPOSIT	RANDOMIZED	
2	ABC-123	ABC-123-001	2	2013DEC30	-2	INVESTIGATOR	ASSESS	PD	Y
3	ABC-123	ABC-123-001	3	2013DEC31	-1	CENTRAL	ASSESS	SD	Y
4	ABC-123	ABC-123-001	4	2014JAN01	1	PROTOCOL	DISPOSIT	TREATMENT	Y
5	ABC-123	ABC-123-001	5	2014JAN21	20	INVESTIGATOR	ASSESS	SD	Y
6	ABC-123	ABC-123-001	6	2014JAN22	22	CENTRAL	ASSESS	SD	Y
7	ABC-123	ABC-123-001	7	2014FEB13	44	INVESTIGATOR	ASSESS	PR	Y
8	ABC-123	ABC-123-001	8	2014FEB14	45	CENTRAL	ASSESS	PR	Y
9	ABC-123	ABC-123-001	9	2014MAR06	65	INVESTIGATOR	ASSESS	PR	Y
10	ABC-123	ABC-123-001	10	2014MAR07	66	CENTRAL	ASSESS	PR	Y
11	ABC-123	ABC-123-001	11	2014MAR28	87	INVESTIGATOR	ASSESS	PD	Y
12	ABC-123	ABC-123-001	12	2014MAR29	88	CENTRAL	ASSESS	PD	Y
13	ABC-123	ABC-123-001	13	2014MAR30	89	PROTOCOL	DISPOSIT	TREATMENT	Y
14	ABC-123	ABC-123-001	14	2014MAR31	90	PROTOCOL	EVENT	PROHIB MED	
15	ABC-123	ABC-123-002	1	2013NOV10	-3	PROTOCOL	DISPOSIT	RANDOMIZED	
16	ABC-123	ABC-123-002	2	2013NOV11	-2	INVESTIGATOR	ASSESS	PD	Y
17	ABC-123	ABC-123-002	3	2013NOV12	-1	CENTRAL	ASSESS	PD	Y
18	ABC-123	ABC-123-002	4	2013NOV13	1	PROTOCOL	DISPOSIT	TREATMENT	Y

6. Intermediate analysis data set: ADEVENT or ADDATES?

addates.xpt

Row	STUDYID	USUBJID	ASEQ	ADT	ADTDESC	ADTDESCD	ADY
1	ABC-123	ABC-123-001	1	03MAR2014	Date of Randomization	RANDDT	1
2	ABC-123	ABC-123-001	2	15OCT2014	Change in Anti-Cancer Therapy	RXCHGDT	227
3	ABC-123	ABC-123-001	3	15SEP2014	Date of Last Tumor Assessment with No PD	LNOPDDT	197
4	ABC-123	ABC-123-001	4	03DEC2014	Date Last Known Alive	LSTALVDT	276
5	ABC-123	ABC-123-001	5	01NOV2014	Date of Analysis Cut-off	CUTOFFDT	244
6	ABC-123	ABC-123-002	1	16MAY2014	Date of Randomization	RANDDT	1
7	ABC-123	ABC-123-002	2	08JUL2014	Date of Last Tumor Assessment with No PD	LNOPDDT	49
8	ABC-123	ABC-123-002	3	03AUG2014	Date of Tumor Assessment with PD	PDDT	85
9	ABC-123	ABC-123-002	4	01NOV2014	Date of Analysis Cut-off	CUTOFFDT	87
10	ABC-123	ABC-123-003	1	16APR2014	Date of Randomization	RANDDT	1
11	ABC-123	ABC-123-003	2	08SEP2014	Date of Last Tumor Assessment with No PD	LNOPDDT	146
12	ABC-123	ABC-123-003	3	08DEC2014	Date of Missing Tumor Assessment	MISEXDT	237
13	ABC-123	ABC-123-003	4	01DEC2014	Date of Toxicity Leading to Discontinuation	TOXICDT	230
14	ABC-123	ABC-123-003	5	09DEC2014	End of Study Date	EOSDT	238
15	ABC-123	ABC-123-003	6	10DEC2015	Date Lost to Follow-Up	LOSTFUDT	604

6. Intermediate analysis data set: ADEVENT or ADDATES?

➢ ADDATES (ADaM Other) is better than ADEVENT (OCCDS Structure)

- These dates are not analysis parameters in the sense that they are summarized in a statistical output.
- It's cumbersome to assign values for PARAMCD/PARAM/AVALC for ADEVENT.
- It's also much easier to creating a transposed dataset from ADDATES for downstream use in ADTTE.

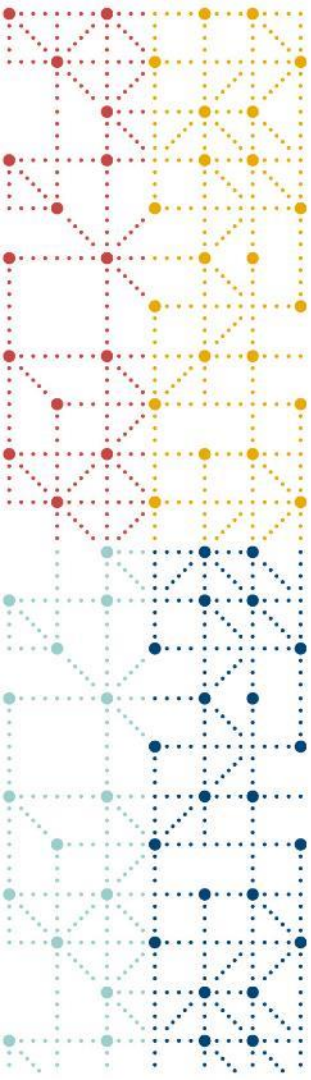
7. How to collect lesions/responses information in clinical trials when both RECIST 1.1 and iRECIST are used as response criteria?

- **In iRECIST, the principles used to establish objective tumor response are largely unchanged from RECIST 1.1. Differences are:**
  - when PD is firstly observed, it should be confirmed by the next scan in iRECIST.
  - new lesions in iRECIST may be assessed quantitatively as “new lesion targets” or qualitatively as “new lesion non-targets”.

- **Sponsor may decide to:**
  - *collect RECIST and iRECIST on separated CRFs, or*
  - *collect RECIST and iRECIST on a single CRF using dynamic navigation.*

7. How to collect lesions/responses information in clinical trials when both RECIST 1.1 and iRECIST are used as response criteria?

Baseline	VISITs before RECIST 1.1 PD	VISIT when RECIST 1.1 PD occurs	VISITs after RECIST 1.1 PD occurs
Target Lesions	Target Lesions	Target Lesions	Target Lesions
Non-target Lesions	Non-target Lesions	Non-target Lesions	Non-target Lesions
	New Lesion (Y/N)	New Lesion (Y/N)	**New Target Lesions**
	Tumor Response - RECIST 1.1	Tumor Response - RECIST 1.1	**New Non-target Lesions**
		New Target Lesions	**Tumor Response - iRECIST**
		New Non-target Lesions	
		Tumor Response - iRECIST	



Conclusion

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- **Implementations on a same concept/data point may be inconsistent across these 5 TAUGs. The reasons can be:**
  - **based on different foundational CDISC standards;**
  - **better option is provided in a TAUG with a latter version date, which means evolvement.**

- **When there are inconsistencies across these 5 TAUGs, if independent of different foundational CDISC standards versions, we recommend to refer to the latest TAUG.**

Thank You!