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Developing ADaM Dataset for Cardiovascular Outcome Studies

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ABSTRACT

CDISC released Therapeutic Area Data Standards User Guide for Cardiovascular Studies (TAUG-CV) Version 1.0 (Provisional) at July 2014. The TAUG-CV describes the most common data needed for ACS or reporting cardiovascular endpoints, and how to store these data in the SDTM datasets. This paper presents a method to create the ADaM dataset following the Basic Data Structure (BDS) for the clinical events reporting following the TAUG-CV.

INTRODUCTION

Other than using ADTTE to analyze time to cardiovascular events, a standard analysis for outcome trials, there is also a need to summarize events information and to create the concordance tables between investigators reported events and adjudicators adjudicated events. These types of the analyses can't be produced using ADTTE, and a standard ADaM dataset is not available from CDISC either. So there is a need to create a dataset which could be used to produce these types of the outputs.

METHODOLOGY

A group of statisticians and programmers carefully evaluated the TAUG-CV and the details of GSK's CV outcome studies and created a set of standard report mockups. Based on these mockups, a standard dataset ADEVENT is proposed following the principles of CDISC BDS structure with the introduction of an additional concept variable called PARQUAL, currently being discussed and will be included in the future releases of ADAM IG. This variable is proposed to be parameter qualifier to distinguish analysis values coming from different evaluators, a typical scenario in CV outcome where both investigator and adjudicator results are collected for the same event.

As in the TAUG-CV, the Cardiovascular Endpoints Section of this TAUG-CV is organized by the seven groupings of endpoints of interest, in the order determined by the Cardiovascular Endpoints Working Group:

1. Death
2. Transient Ischemic Attack and Stroke (Stroke or TIA)
3. Myocardial Infarction
4. Percutaneous Coronary Intervention
5. Peripheral Vascular Intervention
6. Heart Failure Event
7. Unstable Angina Hospitalization Event

The 'Death' and 'Stroke or TIA' are used as examples to explain how ADEVENT is structured.
The two mock-up tables below show why we need to create a specific dataset for the events analysis other than ADTTE.

Table1. Summary of All Adjudicated Stroke Event Details

	Treatment A (N=xxxx)		Treatment B (N=xxxx)	
	# of Subjects	# of Events	# of Subjects	# of Events
Stroke (Fatal/Non-Fatal)				
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Non-Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Type of Stroke				
Ischemic	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
With Hemorrhagic Transformation	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Without Hemorrhagic Transformation	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Hemorrhagic	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Intraparenchymal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Intraventricular	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subarachnoid	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unknown Location	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Undetermined Type of Stroke	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Since types of stroke are not in the ADTTE, the above table can't be generated using the ADTTE dataset.

Table2:.Summary of Concordance Between Investigator Reported and Adjudicated Death Events

		Adjudicated Event Type			
Treatment	**Investigator-Reported Event Type**	**CV death**	**Non-CV death**	**Undetermined**	**Total events**
Total (N=xxxx)	**CV death**	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Non-CV death	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Undetermined	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Total events				

Similar as mock-up table1, the death type is not in the ADTTE.

DATASET ADEVENT

ADEVENT is a dataset following the Basic Data Structure (BDS). Each event has 2 records in the dataset, and the 2 records are linked by variable CEGRPID. The variable PARQUAL is used to separate the adjudicator or investigator results. The PARAM and PARAMCD are the standard eCRF collection forms used for GSK CV outcome studies. AVALC is the clinical endpoints specified for the study and is derived or collected on the endpoint pages. Variables MCRITy, MCRITyMN and MCRITyML are used for the event details. See the value level metadata below. CRITy, CRITyMN and CRITyML are also created

for the event details that contain binary Y/N values.

Table3. ADEVENT value level metadata

Value Level Metadata Name	Where PARAM =	Controlled Term or Formats
ADEVENT.AVALC	'Death'	1. CV Death 2. Non-CV Death 3. Undetermined
ADEVENT.AVALC	'Stroke or TIA'	1. Stroke 2. Transient Ischemic Attack 3. Non-Event
ADEVENT.MCRIT1	'Death'	Death reason detail
ADEVENT.MCRIT1MN	'Death'	
ADEVENT.MCRIT1ML	'Death' and AVALC= 'CV Death'	1. Acute MI 2. Sudden cardiac death 3. Heart failure (HF) 4. Stroke 5. Cardiovascular procedures 6. Cardiovascular 7. hemorrhage 8. Other
ADEVENT.MCRIT1ML	'Death' and AVALC='Non-CV Death'	*Study specific*
ADEVENT.MCRIT1	'Stroke or TIA'	Stroke type
ADEVENT.MCRIT1MN	'Stroke or TIA'	
ADEVENT.MCRIT1ML	'Stroke or TIA' and AVALC='Stroke'	1. Ischemic 2. Hemorrhagic 3. Undetermined
ADEVENT.MCRIT2	'Stroke or TIA'	Stroke type level 2
ADEVENT.MCRIT2MN	'Stroke or TIA'	
ADEVENT.MCRIT2ML	'Stroke or TIA' and AVALC='Stroke' and MCRIT1ML='Ischemic'	1. With Hemorrhagic Transformation 2. Without Hemorrhagic Transformation
ADEVENT.MCRIT2ML	'Stroke or TIA' and AVALC='Stroke' and MCRIT1ML='Hemorrhagic'	1. Intraparenchymal 2. Intraventricular 3. Subarachnoid 4. Unknown Location

Table 4. ADEVENT mock-up dataset

USUBJID	PARAM	AVALC	MCRIT1	MCRIT1ML	MCRIT2M	MCRIT2ML
1	Death	CV Death	Death reason detail	MI		
2	Death	Non-CV Death	Death reason detail	Cancer		
3	Death	Undetermined				
3	Stroke or TIA	Stroke	Stroke type	Hemorrhagic	Stoke type level 2	Subarachnoid
4	Stroke or TIA	TIA				

CONCLUSIONS

The ADEVENT is an efficient dataset closely aligned to BDS principles, providing the capacity to create complex event tables and together with ADTTE could be used for complete CV event analysis.

DISCUSSION

Additionally, one proposal that caught our attention during the review of TAUG-CV is whether the cardiovascular events expected in CV endpoint studies should be recorded as an adverse event or a clinical event in SDTM. The TAUG-CV team recommendation per standard is that they should be clinical events when being evaluated as a CV endpoint, since they are expected to occur in CV endpoint studies(TAUG-CV 1.8). However, in our experience recording the CV event in both adverse event (AE) and clinical event SDTM is easier for collecting the data. There are different CRF pages for AE and events, if the adjudicator negatively adjudicated a CV event, then the event need be reported as an AE/SAE. So following the TAUG-CV would mean that the AE page need be retrospectively filled. It would cause inconvenience and also potential delays in mandatory reporting of SAEs.

REFERENCES

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