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Design and Construct Efficacy Analysis Datasets in Late Phase Oncology Studies

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ABSTRACT

Under the CDISC frames, the Therapeutic Area Standards (TA Standards) have already been the hotspot. The Coalition for Accelerating Standards and Therapies (CFAST) TA Standards Program was launched to accelerate clinical research and medical product development by facilitating the establishment and maintenance of data standards, tools and methods for conducting research in therapeutic areas important to public health. The Oncology TA is the pioneer of this effort. The SDTM Oncology domain models for Tumor Identification (TU), Tumor Results (TR) and Disease Response (RS) are available in SDTMIG v3.1.3. However, the Oncology TA ADaM has not achieved any standardization. This paper will demonstrate how to design and construct standard efficacy analysis datasets in late phase Oncology studies according to the SDTM Oncology domain models.

Key word: SDTM Oncology domain models, Oncology TA, ADaM

INTRODUCTION

The SDTM standard was designed to support submission to regulatory agencies such as the FDA. Under the CDISC/SDTM frames, the Therapeutic Area Standards (TA Standards) have already been the new focus of many discussions. The CFAST, a joint initiative of CDISC and the Critical Path Institute (C-Path), was launched to accelerate clinical research and medical product development by facilitating the establishment and maintenance of data standards, tools and methods for conducting research in therapeutic areas important to public health. CFAST partners include Trans Celerate Bio Pharma Inc. (TCB), the FDA, and the National Cancer Institute – Enterprise Vocabulary Service (NCI-EVS), with participation and input from many other organizations [1]. The CFAST Program Steering Committee has released a priority list of therapeutic areas data standards project, including Virology, Tuberculosis, Parkinson's Disease, Pain, Multiple Sclerosis, and so on.

The ADaM standard has been developed to meet the needs of agencies and industries. As it has been more widely adopted, ADaM will support more efficient data-sharing among pharmaceutical sponsors, contract research organizations (CROs), and any partner involved in licensing-in, licensing-out or mergers.

As we know, the oncology therapeutic area is the major focus for many pharmaceutical companies and is also the largest area in clinical trials. Many pharmaceutical companies are accelerating their candidate drug development to the market, e.g., Merck's PD-1. From the statistics and programming perspective, good preparations and practices can significantly improve the quality and efficiency in submissions.

The Oncology TA is the pioneer of TA standards programs and the SDTM Oncology domain models for Tumor Identification (TU), Tumor Results (TR) and Disease Response (RS) are available in the SDTMIG v3.1.3. However, the Oncology TA ADaM has not achieved any standardization.

Based on the TA standard concepts from CFAST Program, this paper will demonstrate how to design and construct standard efficacy analysis datasets in late phase Oncology studies:

1) Introduce the general endpoints and related statistical methodologies in late phase oncology studies
2) The SDTM Oncology domain models
3) Propose a template on how to build efficacy analysis datasets in oncology studies based on the type of the endpoints

GENERAL ENDPOINTS AND RELATED STATISTICAL METHODOLOGIES IN LATE PHASE ONCOLOGY STUDIES

In the conventional oncology drug development, endpoints for late phase efficacy studies evaluate whether a drug provides any clinical benefit such as prolongation of survival, or improvement in symptoms, or the change in the tumor burden: both tumor shrinkage (e.g., complete response (CR), objective response rate (ORR)) and disease progression (e.g., PFS, DFS) are useful endpoints. For the advantages and disadvantages of these endpoints, the FDA gives the detailed comparison in the guidance document of "Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics".

In oncology trials, the most universal primary endpoint is the tumor assessment, and the secondary or tertiary endpoint is the overall survival and symptom assessment.

The table below shows a summary for endpoints and common statistical analysis methods used in the oncology efficacy analysis. This summary is the base for us to construct efficacy analysis datasets.

Table 1 Endpoints and Statistical Methods in Oncology Studies

Endpoints	Data Type	Analysis Method
Progression-free Survival (PFS)	Time-to-event	Non-parametric Kaplan-Meier/log-rank test/Cox proportional hazards model
Overall Survival (OS)	Time-to-event	Non-parametric Kaplan-Meier/log-rank test/Cox proportional hazards model
Symptom Endpoints (patient-reported outcomes)	Quantitative	LDA
Objective Response Rate	Qualitative	Categorical Analysis (Miettinen and Nurminen's method)
Complete Response	Qualitative	Categorical Analysis (Miettinen and Nurminen's method)

THE SDTM ONCOLOGY DOMAIN MODELS

Based on the common data structure using tumor assessment as the primary endpoint, there are three SDTM finding domains supporting assessment criteria such as RECIST, which are the three components of the SDTM Oncology domain models. These components are: TU, TR and RS.

TU: The TU domain represents data that uniquely identifies tumors. The tumors are identified and classified according to the disease assessment criteria. The RECIST terms are equivalent to the identification of Target, Non-Target or New tumors. A record in the TU domain contains the following information: a unique tumor ID value; anatomical location of the tumor; method used to identify the tumor; role of the individual identifying the tumor; and timing information.

The following is an example of TU domain from SDTM IG 3.1.3. This domain contains data that uniquely identifies tumors which will be continually tracked during the course of a study and will contribute to the assessment of the response to a therapy.

TULNKID	TUTESTCD	TUTEST	TUORRES	VISIT
T01	TUMIDENT	Tumor Identification	TARGET	SCREEN
T02	TUMIDENT	Tumor Identification	TARGET	SCREEN
T03	TUMIDENT	Tumor Identification	TARGET	SCREEN
T04	TUMIDENT	Tumor Identification	TARGET	SCREEN
NT01	TUMIDENT	Tumor Identification	NON-TARGET	SCREEN
NT02	TUMIDENT	Tumor Identification	NON-TARGET	SCREEN
T04.1	TUSPLIT	Tumor Split	TARGET	WEEK 16
T04.2	TUSPLIT	Tumor Split	TARGET	WEEK 16
T02/T03	TUMERGE	Tumor Merged	TARGET	WEEK 24
NEW01	TUMIDENT	Tumor Identification	NEW	WEEK 32

TR: The TR domain represents quantitative and/or qualitative assessments of the tumors identified in the TU domain. These measurements are usually taken at baseline and then at each subsequent assessment to support response evaluations. A record in the TR domain contains the following information: a unique tumor ID value; test and result; method used; role of the individual assessing the tumor; and timing.

RS: The RS domain represents the response evaluation(s) based on the data in TR. Data from other domains might also be used in the assessment of response. Here is an example of RS.

DOMAIN	RSTESTCD	RSTEST	RSCAT	RSORRES	RSORRESU	RSSTRESC	RSSTRESN	RSSTRESU
RS	SUMVOL	Sum of Volume	TARGET	101.14	mL	101.14	.	mL
RS	SUMVOL	Sum of Volume	TARGET	101.14	mL	101.14	.	mL
RS	BESTRESP	Best Overall Response	RECIST	SD		SD	.	
RS	BESTVOL	Best Response Volume	ENHANCED RECIST	PD		PD	.	
RS	NTRGRESP	Non-target Response	NON-TARGET	PD		PD	.	
RS	OVRLRESP	Overall Response	RECIST	PD		PD	.	
RS	SUMVOL	Sum of Volume	TARGET	152.532	mL	152.532	.	mL
RS	TRGRESP	Target Response	TARGET	SD		SD	.	
RS	SUMVOL	Sum of Volume	TARGET	12.853	mL	12.853	.	mL
RS	SUMVOL	Sum of Volume	TARGET	23.96	mL	23.96	.	mL

Currently, almost all solid tumor oncology studies implement three SDTM oncology domains, therefore, we can standardize the analysis part. In the next section, details will be provided on how to design and construct standard efficacy analysis datasets.

PROPOSE A TEMPLATE ON HOW TO BUILD EFFICACY ANALYSIS DATASETS

Our proposed standard oncology efficacy analysis datasets will have the characters below:

1) Cover most statistical analyses for efficacy endpoints, including sensitivity analysis
2) ADaM-Compliant BDS for Time to Event analyses
3) Clear traceability and derivation rules between the SDTM oncology domains and analysis datasets

A). EFFICACY ANALYSES IN LATE ONCOLOGY STUDIES

In most late oncology studies, the endpoints based on tumor assessments (e.g., Progress-free Survival (PFS)) are used as the primary endpoints, overall survival (OS) and objective response rate (ORR) are the second endpoints to support the efficacy analysis. In this circumstance, the PFS generally should be verified by central reviewers blinded to study treatments. i.e. both data from investigators and radiologists' tumor measurements will be stored in the data base, and our statistical analysis will be based on these two types of source data.

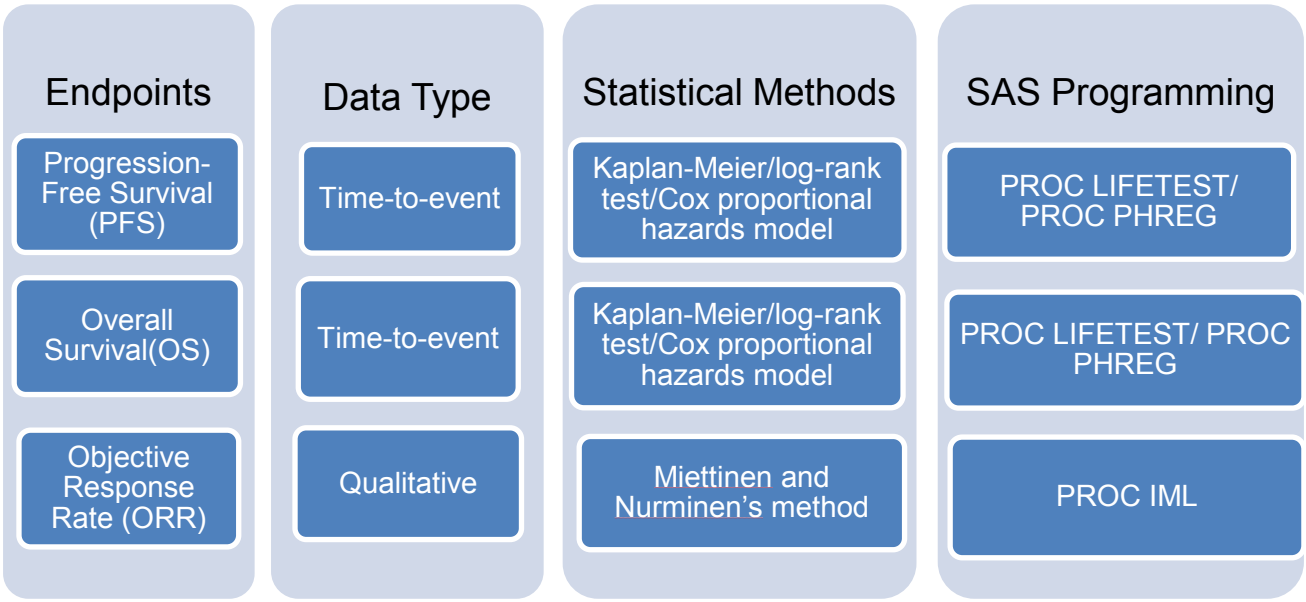
PFS is defined as the time from randomization until objective tumor progression or death. If PFS is the primary endpoint, missing data can complicate the analysis of PFS. The SAP should provide very detailed analysis of PFS, e.g. the date of documented progression, incomplete and/or missing follow-up visits and censoring methods, primary

analysis and one or more sensitivity analyses to evaluate the robustness of the results. All the analyses may complicate the construction of analysis datasets.

Overall survival (OS) is defined as the time from randomization until death from any cause. This endpoint is precise and easy to measure, documented by the date of death. Comparing to PFS, OS is easier to build.

Overall Response Rate (ORR) is defined as the proportion of patients whose best response is PR or CR per RECIST 1.1. It is different from PFS and OS, as it is proportional.

This picture shows how to analyze the endpoints based on tumor assessments. When we build analysis datasets, we should consider the data type and statistical methods.



In oncology late phase studies, we perform sensitivity analysis to determine whether the PFS analysis is robust. However, these sensitivity analyses are only exploratory and supportive of the primary analysis, and efficacy may not be claimed based on sensitivity analysis alone. This is a point that we need to consider when we design analysis dataset for analysis of PFS. Here is an example for primary analysis and two sensitivity analysis for PFS.

Table 2 Primary and Sensitivity Analysis of PFS

Situation	Primary analysis	Sensitivity analysis 1	Sensitivity analysis 2
No PD and no death	Censored at last disease assessment	Censored at last disease assessment	Progressed at date of treatment discontinuation or initiation of new anticancer treatment, whichever occurs later
PD or death documented after ≤ 1 missed disease assessment	Progressed at date of documented PD or death	Progressed at date of documented PD or death	Progressed at date of documented PD or death
PD or death documented after ≥ 2 missed disease assessments	Progressed at date of documented PD or death	Censored at last disease assessment prior to the ≥ 2 missed disease assessment	Progressed at date of documented PD or death

B). ADaM-COMPLIANT BDS FOR TIME TO EVENT ANALYSES

From the last section, we know that there are two types of data collected for analysis. PFS and OS is for Time to Event (TTE), and ORR is for the categorical data. Time to PFS and OS are different from continuous data and the basic ADaM BDS structure can't support the survival analysis for TTE analysis. A new ADaM BDS structure, ADaM TTE analysis dataset structure is designed to support commonly employed time-to-event analysis methods, such as the Kaplan-Meier curve, log-rank tests (stratified or trend), and Cox proportional hazards models.

Besides the basic ADaM BDS structure, ADaM-TTE adds more variables to support time to event data analysis. The following table shows the additional variables for ADaM-TTE.

Table 3 Additional Variables to Support Time to Event Data Analysis Adhere to ADaM BDS

Variable Name	Variable Label	CDISC Notes
AVAL	Analysis Value	AVAL is the elapsed time to the event of interest from the origin. For example, if AVAL is measured in days, AVAL would be ADT – STARTDT or ADT – STARTDT + 1.
ADT	Analysis Date	Analysis date of event or censoring associated with AVAL in numeric format.
STARTDT	Time to Event Origin Date for Subject	The original date of risk for the time-to-event analysis. This is generally the time at which a subject is first at risk for the event of interest evaluation (as defined in the Protocol or Statistical Analysis Plan). For example, this may be the randomization date or the date of first study therapy exposure.
CNSR	Censor	CNSR is a required variable for a time-to-event analysis dataset, though it is a conditionally required variable with respect to the ADaM BDS. For example, CNSR = 0 for event and CNSR > 0 for censored records.
EVNTDESC	Event or Censoring Description	Describe the event of interest or an event that warrants censoring. Values for EVNTDESC will be defined in the metadata as sponsor-defined controlled terminology
CNSDTDSC	Censor Date Description	Describe the circumstance represented by the censoring date if different from the event date that warrants censoring

C). BUILD STANDARD EFFICACY ANALYSIS DATASETS FOR ONCOLOGY STUDIES – AN EXAMPLE

Per the analysis specified in protocol or SAP, how many efficacy datasets will be sufficient? As stated in ADaM, one goal in creating analysis datasets is to have the optimum number of analysis datasets needed to perform the various analyses.

We propose four analysis datasets (Table 4) to support most statistical analyses, including multiple datasets to support same type of data (PFS vs OS). Although PFS and OS are the same type of data, it's clearer to split PFS and OS into two analysis datasets since the two endpoints belong to different types stated in the FDA guidance.

Table 4 Efficacy Analysis Datasets Metadata

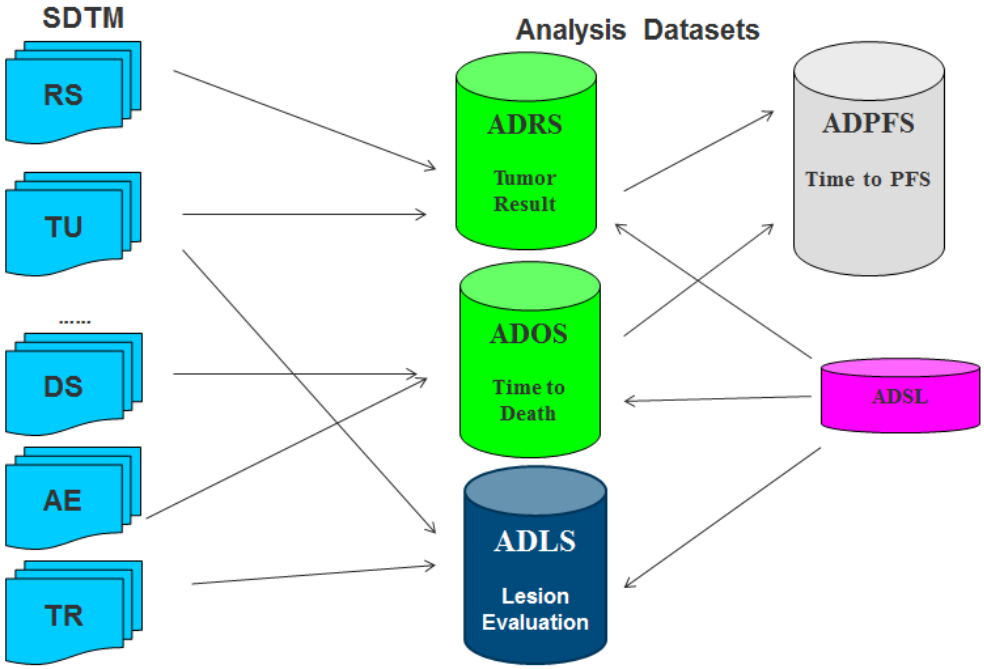
Dataset Name	Dataset Description	Dataset Location	Dataset Structure	Key Variables of Dataset	Class of Dataset

ADRS	Data for Disease Responses	adrs.xpt	one record per subject per parameter per timepoint	USUBJID, PARCAT1, PARCAT2, PARAMCD	BDS
ADPFS	Data for time to PFS	adpfs.xpt	one record per subject per parameter	USUBJID, PARCAT1, PARCAT2, PARAMCD	BDS-TTE
ADOS	Data for time to Overall Survival	ados.xpt	one record per subject per parameter	USUBJID, PARAMCD	BDS-TTE
ADLS	Data for Lesion Size Evaluation	adls.xpt	one record per subject per parameter per timepoint	USUBJID, PARCAT1, PARCAT2, PARAMCD	BDS

The ADRS captures disease assessment per RECIST, such as documented PD, CR. And we also derive some PARAMCD, such as Best Overall Response, Objective Response in ADRS. The ADPFS is built based on ADRS records as well.

This picture below shows the traceability between SDTM and ADaM. First, we create ADRS based on data source RS and TU. ADPFS can be created based on analysis datasets ADRS and ADOS.

Figure 1 Traceability between SDTM and ADaM



When we develop programs to generate ADRS and ADPFS, as there are multiple assessors (e.g. RADIOLOGIST 1, RADIOLOGIST 2, ADJUDICATOR) and multiple analysis (Primary and Sensitivity analyses) , we need to specify complicated logic for each PARAMCD or same PARAMCD with different PARCAT1 and PARCAT2. For the

complicated analysis datasets, we recommend to define detailed derivation rule for each PARAMCD by using parameter value-level metadata.

Here is an example on how to construct parameter value-level metadata for ADPFS. In the ADPFS datasets, Investigators and Radiologists provide the tumor assessments based on the same image and per the SAP, we have primary analysis and two types of sensitivity analyses. We also have complicated logic for some censoring rules. It is recommended to have separate documents to document the logic for different scenarios.

Figure 2 Analysis Parameter Variables for ADPFS Datasets

	Variable Name	Variable Label	Type	Length	Codelist / Controlled Terms or Formats	Derivation
2	STARTDT	Time to Event Origin Date for Subject	Num	8	IS8601DA.	ADSL.RANDDT
3	ADT	Analysis Date	Num	8	IS8601DA.	Refer to for ADPFS-PARAM-SHEET
4	PARAM	Parameter	Char	50	Progression Free Survival (days)	
5	PARAMCD	Parameter Code	Char	8	PFS	
6	PARAMN	Parameter (N)	Num	8	111	
7	PARCAT1	Parameter Category 1	Char	20	INVESTIGATOR RADIOLOGY	
8	PARCAT2	Parameter Category 2	Char	20	PRIMARY=Primary Analysis SENSITIVITY1=Sensitivity Analysis 1 SENSITIVITY2=Sensitivity Analysis 2	
9	AVAL	Analysis Value (N)	Num	8		ADT-STARTDT+ (ADT>=STARTDT)
10	AVALC	Analysis Value (C)	Char	20		ADT-STARTDT+ (ADT>=STARTDT)
11	CNSR	Censor	Num	8	0=Event 1=Censor	Refer to for ADPFS-PARAM-SHEET
12	EVNTDESC	Event or Censoring Description	Char	100		Refer to for ADPFS-PARAM-SHEET
13	CNSDTDSC	Censor Date Description	Char	100		Refer to for ADPFS-PARAM-SHEET
14	SRCDOM	Source Domain	Char	6	ADORR or ADOS or ADSL or CM (for New Treament Initiation) or DS (for Discontinuation)	
15	SRCVAR	Source Variable	Char	8	ADORR.SRCVAR or ADOS.SRCVAR or CM.CMSTDTC(for New Treament Initiation) or DS.DSSTDTC (for Discontinuation)	
16	SRCSEQ	Sequence Number	Num	8	ADORR.SRCSEQ or ADOS.SRCSEQ or CM.CMSEQ(for New Treament Initiation) or DS.DSSEQ (for Discontinuation)	

Figure 3 Parameter value-level metadata

	A	B	C	D	E	F	G	H
1	PARAMCD	PARAM	PARCAT1	PARCAT2	ADT	EVNTDESC	CNSR	CNSDTDSC
2	T2PFS	Time to Progression Free Survival (days)	INVESTIGATOR	PRIMARY	Need to do three steps: 1). ADT = min(ADORR.ADT where PARAMN=1 and PARCAT1='INVESTIGATOR' and AVALC= ('PROGRESSIVE DISEASE') (for Investigator, PD), ADOS.ADT where PARAMN=1 and cnsr=0 (for death))) 2).If ADT obtained above is missing, then ADT = Last	If ADT is non-mssing from step 1 in Column E: - if ADT=ADOS.ADT, then EVNTDESC='DEATH' - else EVNTDESC='PROGRESSED AT DATE OF DOCUMENTED PD'	If ADT is non-mssing from step 1 in Column E, then CNSR=0 else CNSR=1	If CNSR=1: - if ADT = 'Last Assessment Date' then CNSDTDSC='LAST ASSESSMENT DATE' - if ADT=ADSL.RANDDT then
3	T2PFS	Time to Progression Free Survival (days)	RADIOLOGY	PRIMARY	Need to do three steps: 1). ADT = min(ADORR.ADT where PARAMN=1 and PARCAT1='RADIOLOGY' and AVALC= ('PROGRESSIVE DISEASE') (for Radiology, PD) and adjfl='Y', ADOS.ADT where PARAMN=1 and cnsr=0 (for death)) 2).If ADT obtained above is missing, then ADT = Last	If ADT is non-mssing from step 1 in Column E: - if ADT=ADOS.ADT, then EVNTDESC='DEATH' - else EVNTDESC='PROGRESSED AT DATE OF DOCUMENTED PD'	If ADT is non-mssing from step 1 in Column E, then CNSR=0 else CNSR=1	If CNSR=1: - if ADT = 'Last Assessment Date' then CNSDTDSC='LAST ASSESSMENT DATE' - if ADT=ADSL.RANDDT then
4	T2PFS	Time to Progression Free Survival (days)	INVESTIGATOR	SENSITIVITY1	Need to do four steps: 1). ADT = min(ADORR.ADT where PARAMN=1 and PARCAT1='INVESTIGATOR' and AVALC= ('PROGRESSIVE DISEASE') (for Investigator, PD), ADOS.ADT where PARAMN=1 and cnsr=0 (for death)). 2).If ADT obtained above is non-missing, then find the tumor	If ADT is non-mssing from step 1 in Column E: - if ADT=ADOS.ADT, then EVNTDESC='DEATH' - else if ADT=ADORR.ADT where PARAMN=1 and	If ADT is non-mssing from step 1 in Column E: - if ADT=ADOS.ADT, then CNSR=0	If using TDATE and adt=ADOS.ADT (for death), then CNSDTDSC='LAST ASSESSMENT PRIOR TO DEATH'
5	T2PFS	Time to Progression Free Survival (days)	RADIOLOGY	SENSITIVITY1	Need to do four steps: 1). ADT = min(ADORR.ADT where PARAMN=1 and PARCAT1='RADIOLOGY' and AVALC= ('PROGRESSIVE DISEASE')(for Radiology, PD) and adjfl='Y', ADOS.ADT where PARAMN=1 and cnsr=0 (for death)). 2).If ADT obtained above is non-missing, then find the tumor	If ADT is non-mssing from step 1 in Column E: - if ADT=ADOS.ADT, then EVNTDESC='DEATH' - else if ADT=ADORR.ADT where PARAMN=1 aand	If ADT is non-mssing from step 1 in Column E: - if ADT=ADOS.ADT, then CNSR=0	If using TDATE and adt=ADOS.ADT (for death), then CNSDTDSC='LAST ASSESSMENT PRIOR TO DEATH'

Figure 4 The ADPFS dataset (key variables only)

	USUBJID	STARTDT	ADT	PARAM	PARAMCD	PARAMN	PARCAT1	PARCAT2
1	1001-01-0000001	2013-04-24	2014-01-23	Time to Progression Free Survival (days)	T2PFS	111	INVESTIGATOR	PRIMARY
2	1001-01-0000001	2013-04-24	2014-01-23	Time to Progression Free Survival (days)	T2PFS	111	INVESTIGATOR	SENSITIVITY1
3	1001-01-0000001	2013-04-24	2014-01-23	Time to Progression Free Survival (days)	T2PFS	111	INVESTIGATOR	SENSITIVITY2
4	1001-01-0000001	2013-04-24	2014-01-23	Time to Progression Free Survival (days)	T2PFS	111	RADIOLOGY	PRIMARY
5	1001-01-0000001	2013-04-24	2014-01-23	Time to Progression Free Survival (days)	T2PFS	111	RADIOLOGY	SENSITIVITY1
6	1001-01-0000001	2013-04-24	2014-01-23	Time to Progression Free Survival (days)	T2PFS	111	RADIOLOGY	SENSITIVITY2

	USUBJID	AVAL	CNSR	EVNTDESC	CNSDTDSC
1	1001-01-0000001	275	0	PROGRESSED AT DATE OF DOCUMENTED PD	
2	1001-01-0000001	275	0	PROGRESSED AT DATE OF DOCUMENTED PD	
3	1001-01-0000001	275	0	PROGRESSED AT DATE OF DOCUMENTED PD	
4	1001-01-0000001	275	1	DISCONTINUED	LAST ASSESSMENT DATE
5	1001-01-0000001	275	1	DISCONTINUED	LAST ASSESSMENT DATE
6	1001-01-0000001	275	0	PROGRESSED AT DATE OF TREATMENT DISCONTINUATION	

The data on the progression in PFS is from ADRS. The subject's tumor assessments per RECIST from Investigators and Radiologists are in ADRS, displayed below:

Figure 5 The ADRS dataset (key variables only)

	USUBJID	ADJFL	ADT	AVISIT	PARAM	PARAMCD	PARAMN	PARCAT1	PARCAT2	AVAL	AVALC	PARAMTYP
1	1001-01-0000001		2013-06-20	Treatment Cycle 3	OVERALL RESPONSE	OVALRESP	1	INVESTIGATOR		3	STABLE DISEASE	
2	1001-01-0000001		2013-08-15	Treatment Cycle 5	OVERALL RESPONSE	OVALRESP	1	INVESTIGATOR		2	PARTIAL RESPONSE	
3	1001-01-0000001		2013-10-08	Treatment Cycle 7	OVERALL RESPONSE	OVALRESP	1	INVESTIGATOR		2	PARTIAL RESPONSE	
4	1001-01-0000001		2013-12-03	Treatment Cycle 9	OVERALL RESPONSE	OVALRESP	1	INVESTIGATOR		3	STABLE DISEASE	
5	1001-01-0000001		2014-01-23	Safety Followup	OVERALL RESPONSE	OVALRESP	1	INVESTIGATOR		4	PROGRESSIVE DISEASE	
6	1001-01-0000001		.		OBJECTIVE RESPONSE	OBJERESP	3	INVESTIGATOR		1	Y	DERIVED
7	1001-01-0000001		2013-06-20	Treatment Cycle 3	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 1	3	STABLE DISEASE	
8	1001-01-0000001	Y	2013-06-20	Treatment Cycle 3	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 2	3	STABLE DISEASE	
9	1001-01-0000001		2013-08-15	Treatment Cycle 5	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 1	2	PARTIAL RESPONSE	
10	1001-01-0000001	Y	2013-08-15	Treatment Cycle 5	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 2	2	PARTIAL RESPONSE	
11	1001-01-0000001		2013-10-08	Treatment Cycle 7	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 1	2	PARTIAL RESPONSE	
12	1001-01-0000001	Y	2013-10-08	Treatment Cycle 7	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 2	2	PARTIAL RESPONSE	
13	1001-01-0000001	Y	2014-01-23	Safety Followup	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 2	2	PARTIAL RESPONSE	
14	1001-01-0000001		2014-01-23	Safety Followup	OVERALL RESPONSE	OVALRESP	1	RADIOLOGY	RADIOLOGIST 1	3	STABLE DISEASE	
15	1001-01-0000001	Y	2013-08-15	Treatment Cycle 5	BEST OVERALL RESPONSE	BESTRESP	2	RADIOLOGY	RADIOLOGIST 2	2	PARTIAL RESPONSE	
16	1001-01-0000001		2013-08-15	Treatment Cycle 5	BEST OVERALL RESPONSE	BESTRESP	2	RADIOLOGY	RADIOLOGIST 1	2	PARTIAL RESPONSE	
17	1001-01-0000001		.		OBJECTIVE RESPONSE	OBJERESP	3	RADIOLOGY		1	Y	DERIVED

Figure 6 The ADOS dataset (key variables only)

	USUBJID	STARTDT	ADT	PARAM	PARAMCD	AVAL	CNSR	EVNTDESC	CNSDTDSC
1	1001-01-0000002	2013-04-24	2014-02-20	Time to Death (days)	T2DTH	303	1	PROGRESSIVE DISEASE	LAST CONTACT
2	1001-01-0000003	2013-02-04	2014-01-02	Time to Death (days)	T2DTH	333	1	PROGRESSIVE DISEASE	LAST CONTACT
3	1001-01-0000004	2013-04-26	2014-04-14	Time to Death (days)	T2DTH	354	1	COMPLETED THE STUDY	LAST CONTACT
4	1001-01-0000005	2013-04-08	2013-10-01	Time to Death (days)	T2DTH	177	1	PROGRESSIVE DISEASE	LAST CONTACT
5	1001-01-0000006	2012-11-13	2014-01-02	Time to Death (days)	T2DTH	416	1	PROGRESSIVE DISEASE	LAST CONTACT
6	1001-01-0000007	2012-11-27	2013-12-05	Time to Death (days)	T2DTH	374	1	PROGRESSIVE DISEASE	LAST CONTACT

CONCLUSION

This paper proposed a way to implement the standard efficacy analysis datasets, based on the CFAST Program TA standard concept. The general endpoints, related statistical methodologies and the SDTM Oncology domain models were introduced, and the detailed examples were demonstrated to show how to design and construct four universal ADaM analysis datasets that can be used among most late oncology studies.

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