

Deconstructing ADRS: Tumor Response Analysis Data Set

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ABSTRACT

From the perspective of someone new to both the oncology therapy area and working with ADaM, this paper describes the process of designing a data set to support the analysis of tumor response data. Rather than focus on the programmatic implementation of particular response criteria (e.g., RECIST, Cheson, etc.), we instead concentrate on the structural features of the ADaM data set. Starting from a simple description of a study's primary analysis needs, we explore the design impact of additional protocol features such as multiple response criteria algorithms, multiple medical evaluators, and adjudication. With an understanding of the necessary derived parameters to support our analyses, we have a better conceptual link between the collected SDTM RS data and our ADRS analysis data set -- regardless of response criteria being used (the implementation of which is beyond the scope here). We will also touch on some other practical considerations around missing data, interim analyses, further variations in response criteria, and alternate summary table formats which can have an impact on the design of the data set.

INTRODUCTION

Efficacy analyses of oncology clinical trials usually involve either responder or time-to-event endpoints, depending on the phase and design of the study. Most of the analyses of interest take into account disease status, evaluating subjects' tumors and their change since the start of treatment. There are three SDTM domains designed specifically to collect tumor-related data:

- Tumor Identification (TU): unique identification of the subjects' pre-existing tumors to be followed through the course of the study or new tumors which develop during that time;
- Tumor Response (TR): measurements and assessments of the tumors recorded in the TU domain;
- Disease Response (RS): responder assessments of disease status based on the TR results, as defined by particular response criteria.

These domains were first defined in a disease-specific therapy area supplement before being incorporated into the SDTM Implementation Guide since version 3.1.3 (see SDTMIG). A number of papers have been written describing these domains in greater detail and how they are linked (see Kadeerbai 2014, Eban 2014, etc.).

Various time-to-event (TTE) analyses might be of interest in oncology studies, such as overall survival, time to progression, progression-free survival, etc. (FDA 2007). These are naturally supported by an ADaM BDS data set which implements specific TTE variables (see ADaMIG).

The purpose of this paper is to describe the features needed of an ADaM data set which supports the responder type of analysis. There are various algorithms used to determine whether a subject is a "responder" to treatment, such as RECIST for solid tumors (v1.0 Therasse 2000, v1.1 Eisenhauer 2009), modified RECIST for hepatocellular carcinoma (mRECIST; Lencioni 2010), and Cheson for disease in lymph nodes (Cheson 2007) being among the most common. Although the details and implementation of these criteria are not presented here, they usually assess whether reduction in tumor burden has reached specific thresholds and classify the subject accordingly.

An appropriate ADaM data set design will be described which accommodates analysis needs, regardless of the specific response criteria in use (of which there might be more than one). The types and quantity of observations can grow into a large analysis data set which might be difficult to interpret once completed. The goal of this paper is to deconstruct these complexities by illustrating why they are needed and how they relate back to the source SDTM data. Since the analysis endpoints are derived most directly from the RS domain, the resulting data set is named ADRS.

The motivating examples will start with a simple protocol statement of a primary analysis which is then further expanded with more specific qualifiers. Data set features are described and added to accordingly.

BASIC ANALYSIS NEEDS

A simple example of the primary analysis from an oncology protocol might be stated as "objective tumor response rate (ORR)." Even without knowing the context of ORR (e.g., someone new to the oncology therapy area), the concept of response rates is straightforward and a corresponding summary table can be visualized. For example, Figure 1 shows a table with the number and percentage of subjects, for two treatment groups, who have been

classified as Responders and Non Responders according to some algorithm; 95% confidence intervals (CIs) are reasonably included.

	Treatment A (N=XX)		Treatment B (N=XX)	
	n (%)	[95% CI]	n (%)	[95% CI]
Objective Tumor Response Rate				
Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Non Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]

Figure 1. Summary of Objective Response Rate

An underlying data set for such a table requires one observation per subject and few variables: subject identifier (SUBJID), treatment group (TRTP), and responder category (AVALC). A selection of observations is shown in Figure 2.

SUBJID	TRTP	AVALC
1	Treatment A	Responder
2	Treatment A	Non Responder
3	Treatment B	Responder
4	Treatment B	Non Responder
⋮	⋮	⋮

Figure 2. Analysis Data Set for Simple Summary

OBJECTIVE RESPONSE EXPLAINED

In the introductory example, we have summarized the “objective response” assigned to each subject for the study. This is derived from another categorization, best overall response (BOR), which considers individual timepoint “overall response” assessments during the course of the study for a subject and keeps the best of these. Further details of overall response will be shown later, but we note for now that results might come from an ordered set of possibilities such as:

1. Complete response (CR)
2. Partial response (PR)
3. Stable disease (SD)
4. Progressive disease (PD)

An assessment might also be categorized as ‘Not evaluable’ (NE). These categories and the tumor measurement criteria that define them will depend on the response algorithm being used for the study.

For our example, a subject is considered to be a Responder for objective response if their best overall response is either CR or PR. If not (i.e., SD, PD, or NE) then the subject is a Non Responder. It is natural that a summary of ORR be accompanied by a summary of BOR, as shown in Figure 3. The link between the categories of these two endpoints is illustrated.

	Treatment A (N=XX)		Treatment B (N=XX)	
Objective Tumor Response Rate				
Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Non Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Best Overall Response				
Complete Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Partial Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Stable Disease	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Progressive Disease	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Not Evaluable	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]

Figure 3. Summaries of ORR and BOR

We can expand our earlier data set to accommodate both summaries by using PARAMCD / PARAM variables in an ADaM BDS structure. One parameter code, 'OBJRESP', represents the categorization for Objective Response and the 'BESTRESP' code corresponds to BOR. Additional values for AVALC are associated with the BOR observations. This updated data set, named ADRS, is shown in Figure 4 and now has two observations per subject – one for each value of PARAMCD. We also include the numeric variable AVAL for convenience as a one-to-one code of AVALC, which can be used for sorting purposes in the summary table. Not shown are other required ADaM variables (STUDYID, USUBJID).

SUBJID	PARAMCD	PARAM	AVAL	AVALC
1	OBJRESP	Objective Response	9	Responder
1	BESTRESP	Best Overall Response	1	Partial Response
2	OBJRESP	Objective Response	9	Responder
2	BESTRESP	Best Overall Response	0	Complete Response
3	OBJRESP	Objective Response	10	Non Responder
3	BESTRESP	Best Overall Response	2	Stable Disease
4	OBJRESP	Objective Response	10	Non Responder
4	BESTRESP	Best Overall Response	3	Progressive Disease
⋮	⋮	⋮	⋮	⋮

Figure 4. Incorporating PARAMCD / PARAM Variables for ADRS Data Set

MORE SPECIFIC ANALYSIS

We now consider some additional qualifications used to specify the primary analysis and how we accommodate these in the ADRS data set.

DIFFERENT RESPONSE CRITERIA

As previously mentioned, there are various response criteria algorithms which have been developed and a protocol might specify the use of more than one. For example, a study of hepatocellular carcinoma might state the primary analysis as “objective tumor response rate *according to mRECIST*” while also assessing response with RECIST v1.1; the latter might be used a secondary endpoint to check consistency with the primary analysis or for comparison purposes with other studies using the RECIST v1.1 criteria.

The summary table for the primary analysis remains as before, with the added notation to specify the mRECIST response criteria being used; a similar table is produced for the secondary analysis using RECIST v1.1 (Figure 5).

Response with respect to mRECIST		Treatment A (N=XX)		Treatment B (N=XX)	
Objective Tumor Response Rate					
Responder					
Response with respect to RECIST 1.1		Treatment A (N=XX)		Treatment B (N=XX)	
Objective Tumor Response Rate					
Responder					
Non Responder					
Best Overall Response					
Complete Response					
Partial Response					
Stable Disease					
Progressive Disease					
Not Evaluable					

Figure 5. Summary Tables for Different Response Criteria

To accommodate both types of response criteria in the ADRS data set, additional qualifying information is included. Strictly speaking, ADaM implementation guidelines require that such information be included within PARAM, which can be problematic with the 8-character limit of the paired PARAMCD variable. Our approach is to use the PARCAT1N / PARCAT1 variables to record the response criteria type, as shown in Figure 6 (variable PARAM has now been omitted for space). The resulting data set now includes four observations per subject to support the tables of Figure 5.

SUBJID	PARCAT1N	PARCAT1	PARAMCD	AVAL	AVALC
1	15	mRECIST HCC	OBJRESP	9	Responder
1	15	mRECIST HCC	BESTRESP	1	Partial Response
1	12	RECIST 1.1	OBJRESP	10	Non Responder
1	12	RECIST 1.1	BESTRESP	2	Stable Disease
2	15	mRECIST HCC	OBJRESP	9	Responder
2	15	mRECIST HCC	BESTRESP	0	Complete Response
2	15	RECIST 1.1	OBJRESP	9	Responder
2	15	RECIST 1.1	BESTRESP	1	Partial Response
3	15	mRECIST HCC	OBJRESP	10	Non Responder
3	15	mRECIST HCC	BESTRESP	2	Stable Disease
3	15	RECIST 1.1	OBJRESP	10	Non Responder
3	15	RECIST 1.1	BESTRESP	2	Stable Disease
4	15	mRECIST HCC	OBJRESP	10	Non Responder
4	15	mRECIST HCC	BESTRESP	3	Progressive Disease
4	15	RECIST 1.1	OBJRESP	10	Non Responder
4	15	RECIST 1.1	BESTRESP	2	Stable Disease
⋮	⋮	⋮	⋮	⋮	⋮

Figure 6. Incorporating PARCAT1N / PARCAT1 Variables for ADRS Data Set
 Note: OBJRESP = Objective Response; BESTRESP = Best Overall Response for PARAMCD / PARAM.

DIFFERENT ASSESSORS

The evaluation of tumor response can be made by various types of reviewers, e.g., by site investigators themselves or by independent (i.e., external and blinded) assessors. In a study where multiple types of evaluators are used, the primary analysis might be focused on “objective tumor response rate according to mRECIST *by independent*

SUMMARY OF DERIVED PARAMETERS

Thus far we have discussed objective response and best overall response. Another related endpoint which might be analyzed is “Disease Control” response, where a Responder is defined as having best overall response of CR or PR or SD (see earlier definitions). Including this endpoint (with PARAMCD='DISCTRL'), for both mRECIST and RECIST 1.1 criteria and for independent and investigator assessors, the ADRS data set now includes 12 observations per subject, as illustrated in Figure 9.

Note that each of these endpoints has been derived; hence the data set will also include variable PARAMTYP with value 'DERIVED' for these observations.



Figure 9. Combinations of Evaluator Type, Response Criteria and Analysis Endpoints

MISSING DATA

Implicit in the above counting of ADRS observations is that a subject will have data for each parameter. While the ‘Not Evaluable’ category of BOR accounts for a tumor assessment which was conducted and a result could not be determined, it is also possible that a subject does not have any available on-treatment assessments (e.g., early lost to follow-up). To explicitly include this in the analysis data set, a dummy observation for PARAMCD='BESTRESP' with AVALC='Missing' can be created. Then following the earlier definitions, it follows that the subject is a Non Responder for both objective response and disease control endpoints. The summary table in Figure 10 displays the additional BOR category that results from this consideration.

	Treatment A (N=XX)		Treatment B (N=XX)	
Objective Tumor Response Rate				
Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Non Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Best Overall Response				
Complete Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Partial Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Stable Disease	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Progressive Disease	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Not Evaluable	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Missing	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]

Figure 10. Summary Table Including BOR Category of 'Missing'

OVERVIEW OF SDTM DATA TO DERIVED ADAM PARAMETERS

At the start of a study, a subject’s tumors are assigned into “target” and “non-target” groups as per the criteria of the algorithm(s) being used. At each subsequent time of assessment, these groups are evaluated separately for response according to the algorithm’s rules and then a composite result of “overall response” is determined for that

timepoint. These three results from each visit are represented as distinct observations in the SDTM RS domain, differentiated by RESTSTCD / RSTEST pairs:

- TRGRES P / Target Response
- NTRGRES P / Non-target Response
- OVRLRES P / Overall Response

These timepoint-specific Overall Response results are used by the response algorithms to determine the Best Overall Response discussed throughout this paper, which is subsequently used to derive the objective and disease control responses as previously described. This process is repeated for each algorithm type and evaluator type used in the study. In Figure 11, for a subject with n tumor assessment timepoints, the relationship between the source SDTM RS parameters (TRGRES P, NTRGRES P, OVRLRES P) and the derived ADRS parameters (BESTRES P, OBJRES P, DISCTRL) is illustrated.

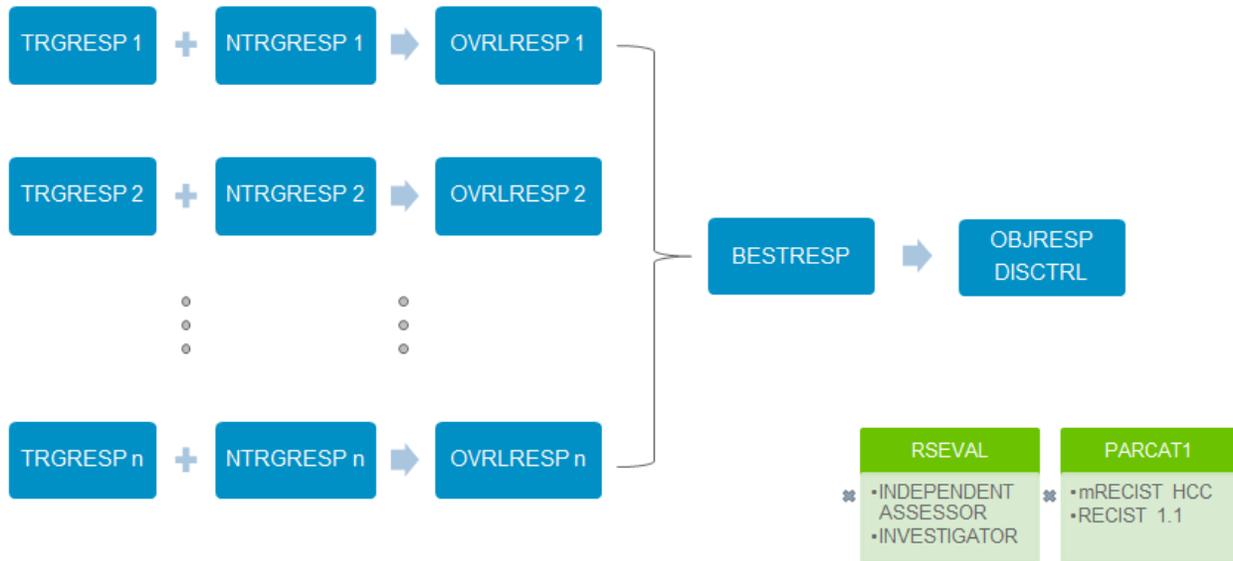


Figure 11. Relationship between SDTM RS and Derived ADRS Parameters

Combining the source RS parameters into ADRS, for traceability purposes, leads to a large accumulation of observations. The example shown in Figure 12 (with some variables omitted for space) is for a single subject with three assessment timepoints given by the VISIT variable; with the combinations of three parameters (mapping RS.RSTESTCD/RSTEST to ADRS.PARAMCD/PARAM), two evaluators and two response criteria, this gives 36 collected observations in addition to the 12 derived ones.

SUBJID	RSEVAL	PARCAT1	VISIT	PARAMCD	PARAMTYP	AVALC
1	INDEPENDENT ASSESSOR	mRECIST HCC		OBJRESP	DERIVED	Responder
1	INDEPENDENT ASSESSOR	mRECIST HCC		BESTRESP	DERIVED	Partial Response
1	INDEPENDENT ASSESSOR	mRECIST HCC		DISCTRL	DERIVED	Responder
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 2	TRGRES		SD
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 2	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 2	OVLRESP		SD
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 4	TRGRES		PR
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 4	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 4	OVLRESP		PR
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 6	TRGRES		PR
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 6	NTRGRES		PD
1	INDEPENDENT ASSESSOR	mRECIST HCC	CYCLE 6	OVLRESP		PD
1	INDEPENDENT ASSESSOR	RECIST 1.1		OBJRESP	DERIVED	Non Responder
1	INDEPENDENT ASSESSOR	RECIST 1.1		BESTRESP	DERIVED	Stable Disease
1	INDEPENDENT ASSESSOR	RECIST 1.1		DISCTRL	DERIVED	Responder
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 2	TRGRES		SD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 2	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 2	OVLRESP		SD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 4	TRGRES		SD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 4	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 4	OVLRESP		SD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 6	TRGRES		SD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 6	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	RECIST 1.1	CYCLE 6	OVLRESP		SD
1	INVESTIGATOR	mRECIST HCC		OBJRESP	DERIVED	Non Responder
1	INVESTIGATOR	mRECIST HCC		BESTRESP	DERIVED	Stable Disease
1	INVESTIGATOR	mRECIST HCC		DISCTRL	DERIVED	Responder
1	INVESTIGATOR	mRECIST HCC	CYCLE 2	TRGRES		SD
1	INVESTIGATOR	mRECIST HCC	CYCLE 2	NTRGRES		NonCR/NonPD
1	INVESTIGATOR	mRECIST HCC	CYCLE 2	OVLRESP		SD
1	INVESTIGATOR	mRECIST HCC	CYCLE 4	TRGRES		PD
1	INVESTIGATOR	mRECIST HCC	CYCLE 4	NTRGRES		PD
1	INVESTIGATOR	mRECIST HCC	CYCLE 4	OVLRESP		PD
1	INVESTIGATOR	mRECIST HCC	CYCLE 6	TRGRES		PD
1	INVESTIGATOR	mRECIST HCC	CYCLE 6	NTRGRES		PD
1	INVESTIGATOR	mRECIST HCC	CYCLE 6	OVLRESP		PD
1	INVESTIGATOR	RECIST 1.1		OBJRESP	DERIVED	Non Responder
1	INVESTIGATOR	RECIST 1.1		BESTRESP	DERIVED	Stable Disease
1	INVESTIGATOR	RECIST 1.1		DISCTRL	DERIVED	Responder
1	INVESTIGATOR	RECIST 1.1	CYCLE 2	TRGRES		SD
1	INVESTIGATOR	RECIST 1.1	CYCLE 2	NTRGRES		NonCR/NonPD
1	INVESTIGATOR	RECIST 1.1	CYCLE 2	OVLRESP		SD
1	INVESTIGATOR	RECIST 1.1	CYCLE 4	TRGRES		SD
1	INVESTIGATOR	RECIST 1.1	CYCLE 4	NTRGRES		NonCR/NonPD
1	INVESTIGATOR	RECIST 1.1	CYCLE 4	OVLRESP		SD
1	INVESTIGATOR	RECIST 1.1	CYCLE 6	TRGRES		PD
1	INVESTIGATOR	RECIST 1.1	CYCLE 6	NTRGRES		NonCR/NonPD
1	INVESTIGATOR	RECIST 1.1	CYCLE 6	OVLRESP		PD

Figure 12. ADRS Including Source Data from RS Domain

OTHER CONSIDERATIONS

MULTIPLE INDEPENDENT ASSESSORS

When independent evaluation is used for a study, the protocol might plan for a subject's tumor scans to be read by multiple assessors at each timepoint. In case of disagreement between the assessors, adjudication is performed to select the most acceptable outcome for each subject. The RS domain has a variable (RSEVALID) to distinguish between the independent assessors; example values could be 'READER 1' and 'READER 2'. When adjudication has been performed, the corresponding observations have a variable RSACPTFL populated with either 'Y' or 'N' depending on which is considered to be the acceptable outcome.

The RSACPTFL flag is most relevant for actually implementing a response criteria algorithm; when creating the derived parameters corresponding to independent assessment, the RSACPTFL='Y' observations will be used. For traceability, all of the observations from multiple assessors along with these newly discussed variables are included in the ADRS data set. Figure 13 provides an example; note that RSEVALID and RSACPTFL are only populated for non-derived parameters with RSEVAL='INDEPENDENT ASSESSOR'.

SUBJID	RSEVAL	RSEVALID	RSACPTFL	PARCAT1	VISIT	PARAMCD	PARAMTYP	AVALC
1	INDEPENDENT ASSESSOR			mRECIST HCC		OBJRESP	DERIVED	Responder
1	INDEPENDENT ASSESSOR			mRECIST HCC		BESTRESP	DERIVED	Partial Response
1	INDEPENDENT ASSESSOR			mRECIST HCC		DISCTRL	DERIVED	Responder
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 2	TRGRES		SD
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 2	TRGRES		SD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 2	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 2	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 2	OVLRES		SD
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 2	OVLRES		SD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 4	TRGRES		PR
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 4	TRGRES		SD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 4	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 4	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 4	OVLRES		PR
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 4	OVLRES		SD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 6	TRGRES		PR
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 6	TRGRES		SD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 6	NTRGRES		PD
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 6	NTRGRES		NonCR/NonPD
1	INDEPENDENT ASSESSOR	READER 1	Y	mRECIST HCC	CYCLE 6	OVLRES		PD
1	INDEPENDENT ASSESSOR	READER 2	N	mRECIST HCC	CYCLE 6	OVLRES		SD
:	:	:	:	:	:	:	:	:
1	INVESTIGATOR			RECIST 1.1	CYCLE 6	OVLRES		PD
:	:	:	:	:	:	:	:	:

Figure 13. ADRS with Variables RSEVALID and RSACPTFL

INTERIM ANALYSES

While a subject is ongoing in a trial, adjudication of differing independent assessments might only be performed under certain circumstances (e.g., when disease progression, which necessitates withdrawal, is in question); otherwise, this activity occurs once the subject has completed the study. This can be problematic if there is an interim analysis to be performed and there are unresolved, conflicting assessments. The statistical analysis plan should describe how to handle such cases (e.g., use the “worst case” independent assessment).

With respect to ADRS, it would be advisable to include a flag variable that indicates when such a scenario has been encountered and which set of assessments has been used in the response algorithm. Once adjudication is later performed, it might be that the acceptable results differ from those chosen for use in the interim analysis. The presence of this flag can be used to identify affected subjects and make note of them in the study report.

VARIATIONS IN RESPONSE CRITERIA

Not only are there various response algorithms to consider (RECIST v1.0, RECIST v1.1, mRECIST, Cheson, etc.), the exact implementation might be further modified depending on the needs of the analysis or protocol. For example, BOR might require confirmation (i.e., consecutive assessments of CR in order for BOR to be set as CR). This is mainly a concern of programming details of the algorithm, but the controlled terminology of ADRS might need to be expanded to also include ‘unconfirmed’ categories which might be of clinical interest for the summary table. See Figure 14 for illustration of additional categories.

	Treatment A (N=XX)		Treatment B (N=XX)	
Objective Tumor Response Rate				
Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Non Responder	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Best Overall Response				
Complete Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Unconfirmed Complete Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Partial Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Unconfirmed Partial Response	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Stable Disease	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Progressive Disease	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Not Evaluable	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]
Missing	xx (xx.x%)	[xx.x%,xx.x%]	xx (xx.x%)	[xx.x%,xx.x%]

Figure 14. Summary Including Unconfirmed Responses

CONCLUSION

Although a responder-type summary is relatively straightforward, the primary analysis for an oncology trial might involve numerous qualifiers on the endpoint being used. As a result, the underlying data set might contain a great many observations which are used for similar, supporting analyses in addition to those representing the originally collected data. While the qualifying variables usually follow from the structure of the source SDTM data set, it is important to understand the relationship between the RS domain records and the derived ADRS parameters. By carefully considering our analysis needs, we can focus on the key elements needed from the ADRS data set and expand from there to incorporate the other aspects of the study design and response criteria being used.

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