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BDS Dataset with PARQUAL and PARQTYP Variables for Time-to-Safety Events Analysis

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ABSTRACT

An analysis of adverse events can use the ADaM datasets, specifically ADAE or ADTTE. ADAE is OCCDS data structure, and ADTTE, structured in the BDS with additional time-to-event (TTE) variables, specifically supports survival analysis related to censoring factors, making CNSR a required variable.

This paper describes an approach to creating a BDS Dataset named ADSTOI (a name given by the author), which is designed for the analysis of time to various events related to safety topics of interest (STOI) by grade level and treatment cycle within the oncology therapeutic area across four scenarios that do not involve censoring factors. The ADSTOI design aims to provide clarity and traceability in the calculation process of time to various events. Additionally, this paper introduces two variables, the parameter qualifier type (PARQTYP) and the parameter qualifier (PARQUAL), and demonstrates how these variables are used in the analysis of time to various events of STOI, supporting decision-making regarding the standard criteria for PARQTYP and PARQUAL in ADaM.

INTRODUCTION

This paper describes the creation of the BDS ADSTOI dataset, which is used for the analysis of the time to various events of STOI across four distinct scenarios.

The four scenarios are:

- **Scenario 1:** Explores the time to onset of STOI by treatment cycle.
- **Scenario 2:** Investigates the time to onset of STOI by grade level and treatment cycle.
- **Scenario 3:** Examines the time to resolution of STOI by treatment cycle.
- **Scenario 4:** Analyzes the use of specific medications for treating STOI by grade level and treatment cycle.

Additionally, it discusses the use of PARQTYP and PARQUAL, which helps in effectively linking specific STOI to parameters, simplifying the analysis process when multiple STOIs are involved.

DETAILS OF ADSTOI DATASET DESIGN ACROSS FOUR SCENARIOS

SCENARIO 1: TIME TO ONSET OF STOI BY TREATMENT CYCLE

The scenario 1 is for the time to onset of STOI by treatment cycle. Figure 1 displays a table showing an example of the analysis results for this scenario.

Figure 1: Example of Analysis Result of Time to Onset of Serious Infection by Treatment Cycle

	TRT1 (N=xx) n (%)	TRT2 (N=xx) n (%)	Total (N=xx) n (%)
Time to Onset of Serious Infection (days)			
Cycle x			
Number of Subjects, n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Events	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx.x	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Cycle x+1			
.....			

Figure 2 shows the key variables in ADSTOI Dataset used for the analysis of scenario 1 (Row is not a variable, and it is simply used for explanation purpose). PARAM is assigned as "Time to STOI Onset in Cycle (days)". PARQTYP and PARQUAL are used to identify the specific STOI Serious Infection associated with PARAM. PARQTYP and PARQUAL will be explained in more detail in their respective section later. AVAL, representing the time to onset of Serious Infection, is computed through AVAL= ASTDT– ACYSTDT, where ASTDT is the analysis start date of Serious Infection, and ACYSTDT refers to the most recent dose date associated with this ASTDT. AVISIT/AVISITN identifies the dose interval. ANL01FL flags the records selected for the analysis of time to Serious Infection onset. For instance, Cycle 1 has 2 records (displayed in rows 1 and 2), only the initial record in row 1 is used for the analysis of scenario 1, as denoted by the analysis flag ANL01FL = Y.

For scenario 1, AVAL is calculated as AVAL = ASTDT – ACYSTDT. Both ASTDT and ACYSTDT are included in the ADSTOI dataset, clearly demonstrating how the time difference is calculated between the Serious Infection analysis start date (ASTDT) and the most recent dose date linked to that analysis start date (ACYSTDT). This ensures clarity and traceability in the calculation of the time to onset of STOI.

Figure 2: Example of Time to Onset of Serious Infection by Treatment Cycle in BDS ADSTOI

ROW	USUBJID	TRT01A	ACYSTDT	ASTDT	AVISIT	AVISITN	PARQTYP	PARQUAL	PARAM	PARAMCD	AVAL	ANL01FL
1	101	TRT1	1/4/2024	1/6/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	2	Y
2	101	TRT1	1/4/2024	1/10/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	6	
3	101	TRT1	2/4/2024	2/7/2024	Cycle 2	2	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	3	Y
4	101	TRT1	3/4/2024	3/8/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	4	Y
5	101	TRT1	3/4/2024	3/14/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	10	

SCENARIO 2: TIME TO ONSET OF STOI BY GRADE LEVEL AND TREATMENT CYCLE

The scenario 2 is for the time to onset of STOI, categorized by grade level and treatment cycle. Figure 3 displays a table that illustrates an example of the analysis results for this scenario.

Figure 3: Example of Analysis Result of Time to Onset of Serious Infection by Grade Level and Treatment Cycle

	TRT1 (N=xx) n (%)	TRT2 (N=xx) n (%)	Total (N=xx) n (%)
Time to Onset of Serious Infection (days)			
Cycle x			
Grade n			
Number of Subjects, n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Events	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx.x	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Grade n+1			
.....			

Figure 4 displays the key variables in ADSTOI dataset used for the analysis of scenario 2. In this dataset, on top of the ADSTOI design for scenario 1, ADSTOI dataset adds 2 new variables - ATOXGR (Analysis Toxicity Grade) and ANL02FL (Analysis Flag 02) - in addition to the variables from scenarios 1.

For scenario 2, the PARAM variable remains the same as in scenario 1, which is "Time to STOI Onset in Cycle (days)." The ATOXGR variable is used to further categorize the analysis by different toxicity grade levels. When a subject experiences multiple specific adverse events during the same dosing period, all events are included, except for subsequent events with the same grade as the earlier one closest to it. For instance, in Cycle 1, two events (in rows 1 and 2) with different grades are both included in the grade-specific analysis, marked by the analysis flag ANL02FL = Y, due to their distinct grades. However, in Cycle 3, since the two events have the same grade (grade 3), only the earlier event (row 4) is included in the analysis, with only this row having ANL02FL = Y in Cycle 3.

Figure 4: Example of Time to Onset of Serious Infection by Grade Level and Treatment Cycle in BDS ADSTOI

ROW	USUBJID	TRT01A	ACYSTDT	ASTDT	AENDT	AVISIT	AVISITN	PARQTYP	PARQUAL	PARAM	PARAMCD	AVAL	ATOXGR	ANL01FL	ANL02FL
1	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	2	2	Y	Y
2	101	TRT1	1/4/2024	1/10/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	6	1		Y
3	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	3	3	Y	Y
4	101	TRT1	3/4/2024	3/8/2024	3/12/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	4	3	Y	Y
5	101	TRT1	3/4/2024	3/14/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	10	3		

SCENARIO 3: TIME TO RESOLUTION OF STOI BY TREATMENT CYCLE

The scenario 3 examines the time to resolution of STOI by treatment cycle. Figure 5 depicts a table that illustrates an example of the analysis results specific to this scenario.

Figure 5: Example of Analysis Result of Time to Resolution of Serious Infection by Treatment Cycle

Time to Resolution of Serious Infection (days)			
Cycle x			
Number of Subjects, n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Events	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx.x	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Cycle x+1			
.....			

Figure 6 shows the key variables in ADSTOI Dataset used for the analysis of scenario 3. In this dataset, two new variables - analysis end date of Serious Infection (AENDT) and derivation type (DTYPE) - are included, in addition to the variables from scenarios 1 and 2.

For scenario 3, the PARAM is assigned the value "Time to STOI Resolution in Cycle (days)". AVAL represents the duration until resolution of a Serious Infection, calculated as AVAL= AENDT– ASTDT. If a subject experiences multiple Serious Infections within a single dose interval, the time to resolution is calculated as the difference between the latest AENDT and the earliest ASTDT across all Serious Infections events with an outcome of 'Recovered/Resolved' in that interval.

In this example, Cycle 1 has 2 Serious Infections, so a new row is added. The ASTDT in the new row is set to the ASTDT of the first row, while the AENDT corresponds to the AENDT of the second row. As a result, the time to resolution for the Serious Infection in Cycle 1 is calculated using the values in the new row, with the DTYPE assigned as "Merged" and ANL01FL set to Y. A similar process is applied to Cycle 3, where a new row is created, and the time to resolution is calculated from its values. In Cycle 2, which has only one Serious Infection, the time to resolution is calculated from that row, with ANL01FL set to Y.

Figure 6: Example of Time to Resolution of Serious Infection by Treatment Cycle in BDS ADSTOI

ROW	USUBJID	TRT01A	ACYSTDT	ASTDT	AENDT	AVISIT	AVISITN	PARQTYP	PARQUAL	PARAM	PARAMCD	AVAL	ATOXGR	DTYPE	ANL01FL
6	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	2	2		
7	101	TRT1	1/4/2024	1/10/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	2	1		
8	101	TRT1	1/4/2024	1/6/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	6		Merged	Y
9	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	1	3		Y
10	101	TRT1	3/4/2024	3/8/2024	3/12/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	4	3		
11	101	TRT1	3/4/2024	3/14/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	2	3		
12	101	TRT1	3/4/2024	3/8/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	8		Merged	Y

SCENARIO 4: MEDICATION USE FOR TREATING STOI BY GRADE LEVEL AND TREATMENT CYCLE

The scenario 4 analyzes the use of medication for treating STOI, broken down by grade level and treatment cycle. Figure 7 presents a table showcasing an example of the analysis results relevant to this scenario.

Figure 7: Example of Analysis Result of Medication X Use for Treating Serious Infection by Grade Level and Treatment Cycle

	TRT1 (N=xx) n (%)	TRT2 (N=xx) n (%)	Total (N=xx) n (%)
Medication X Use for Treating Serious Infection (Yes)			
Cycle x			
None	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade >=3	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cycle x+1			
.....			

Figure 8 illustrates the key variables in the ADSTOI Dataset used for the analysis of scenario 4. This Dataset introduces a new variable, AVALC (Analysis Value (C)), in addition to the variables from scenarios 1, 2, and 3.

For scenario 4, the value "Med x Use to Treat STOI in Cycle by Grade" is assigned to PARAM. AVALC is used to indicate whether Medication x was utilized for treating a Serious Infection. Within a single dosing interval, if a subject receives Medication x for multiple Serious Infections with the same grade, it is counted only once. Cycle 3 includes two Serious Infections with grade 3, both marked as AVALC=Y. However, only the first occurrence is selected for the analysis of scenario 4, which is identified as ANL01FL=Y.

Figure 8: Example of Med x Use to Treat Serious Infection by Grade Level and Treatment Cycle in BDS ADSTOI

ROW	USUBJID	TRT01A	CYSTDT	ASTDT	AENDT	AVISIT	AVISITN	PARQTYP	PARQUAL	PARAM	PARAMCD	AVALC	ATOXGR	ANL01FL
13	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG		2	
14	101	TRT1	1/4/2024	1/10/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG	Y	1	Y
15	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG	Y	3	Y
16	101	TRT1	3/4/2024	3/8/2024	3/12/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG	Y	3	Y
17	101	TRT1	3/4/2024	3/14/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG	Y	3	

PARQTYP and PARPUAL

PARQTYP is parameter qualifier type variable, while PARQUAL is parameter qualifier variable. Both are aimed at fully describing PARAM.

Currently, neither PARQTYP nor PARQUAL are included as BDS variables in ADaMIG 1.3. However, PARQTYP has been discussed in the CDSIC ADaM teams, and PARQUAL has been utilized in CDSIC ADaM examples and FDA documentation. This paper illustrates the use of PARQTYP and PARQUAL in the ADSTOI dataset, aiding in the decision-making regarding the standard criteria for PARQTYP and PARQUAL in ADaM.

PARQUAL CASES USED IN CDSIC ADAM EXAMPLES AND FDA DOCUMENTATIONS

The following four cases illustrate how PARQUAL is used to identify the source of parameters or to describe the parameters:

Case 1: In the Prostate Cancer Therapeutic Area User Guide v1.0, PARQUAL is assigned as "INVESTIGATOR REVIEW" for investigator-based assessments, "INDEPENDENT REVIEW" for Independent Review assessments, and NULL for Overall Survival (OS) (refer to Figure 9).

Figure 9: PARQUAL Example Sourced from Prostate Cancer Therapeutic Area User Guide v1.0

adtte.xpt

Row	STUDYID	USUBJID	TRTP	PARAM	PARQUAL	PARAMCD	AVAL	CNSR	ADT
1	ABC-123	ABC-123-001	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	10.8090349075975	0	15OCT2014
2	ABC-123	ABC-123-001	A	Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	15.8090349075975	0	20OCT2014

Case 2: In the CDISC Breast Cancer Therapeutic Area User Guide v1.0, PARQUAL assigns "Investigator" for investigator-based assessments, "Central" for central imaging assessments, "Pathologic" for biopsy-based assessments, and "Protocol" for events influencing the assessment (refer to Figure 10).

Figure 10: PARQUAL Example Sourced from CDISC Breast Cancer Therapeutic Area User Guide v1.0

adtte.xpt **Proposed**

Row	STUDYID	USUBJID	*PARQUAL*	PARAMCD	AVAL	CNSR	SRCSEQ
1	ABC-123	ABC-123-001	INVESTIGATOR	PFS	87	0	11
2	ABC-123	ABC-123-001	CENTRAL	PFS	88	0	12
3	ABC-123	ABC-123-002	INVESTIGATOR	PFS	19	1	5
4	ABC-123	ABC-123-002	CENTRAL	PFS	20	1	6

Case 3: In the Online CDISC ADaM Oncology Examples, PARQUAL is used in the ADEXSUM Dataset to describe drug names (All, Drug Z) for summaries/evaluations of individual treatments and "All" for summaries/evaluations across all treatments (refer to Figure 11).

Figure 11: PARQUAL Example Sourced from Online CDISC ADaM Oncology Examples

ADEXSUM

Row	STUDYID	USUBJID	PARAMCD	PARAM	AEVLINT	PARQUAL	AVAL
1	ABC123	ABC123- 0201	TRTDURD	Treatment Duration Actual in Days	Overall	All	32
3	ABC123	ABC123- 0201	NADMIN	Nr of Actual Study Drug Administrations	Overall	All	4
4	ABC123	ABC123- 0201	NUMCYC	Number of Actual Cycles	Overall	All	4
5	ABC123	ABC123- 0201	NUMPCYC	Number of Planned Cycles	Overall	All	5
6	ABC123	ABC123- 0201	CUMPLDOS	Cumulative Planned Dose	Overall	Drug Z	42.5
7	ABC123	ABC123- 0201	CUMACDOS	Cumulative Actual Dose	Overall	Drug Z	30

Case 4: In Pilot OCE/OOD Standard Safety Data Requests v1.3, PARQUAL is applied in the ADEXSUM Dataset to define treatments. Equal to EXTRT for summaries/evaluations of individual treatments, or 'All' for summaries / evaluations across all treatments (refer to Figure 12).

Figure 12: PARQUAL Example Sourced from Pilot OCE/OOD Standard Safety Data Requests v1.3

ADEXSUM: Exposure Summary Analysis Dataset (adexsum.xpt)

Structure: One record per subject per parameter per analysis interval

ADEXSUM Variable Name	Variable Label	Type	Codelist/ Controlled Terms	CDISC Core (SDTM or ADaM)	OCE/OOD Core	CDISC Variable (ADaMIG v1.1 or SDTM v3.3 or OCE/OOD v1.3=FDA)	OCE/OOD Additional Information
PARQUAL	Parameter Qualifier	Char		N/A	Req	FDA	Description of the treatment summarized on each record. Equal to EXTRT for summaries/ evaluations of individual treatments, or 'All' for summaries / evaluations across all treatments.

These examples highlight how PARQUAL is applied in different contexts to specify the source of the parameter or to describe the parameters, whether it is from investigator, central, or protocol-based assessments or specify which drugs are involved in the treatment summaries/evaluations.

PARQTYP AND PARQUAL USED IN THE ADSTOI DATASET

Figure 13 illustrates the use of PARQTYP and PARQUAL in the ADSTOI dataset. PARQTYP is used to specify that the parameter identifier type corresponds to Safety Topics of Interest (STOIs), while PARQUAL is used to associate specific STOIs with the parameter (PARAM). For example, it identifies two specific STOIs: Serious Infection and Anemia, as shown in Figure 13.

In this figure, data for Serious Infection is concatenated from Figures 4, 6, and 8. The PARAM contains three values (as shown in Figure 14): 1) Time to STOI Onset in Cycle (days), 2) Time to STOI Resolution in Cycle (days), and 3) Med x to Treat STOI in Cycle by Grade. Anemia data is also incorporated. PARQUAL links these PARAM values to either Serious Infection or Anemia. Without PARQUAL, the information for Serious Infection or Anemia would be embedded within PARAM, resulting in six values (as shown in Figure 14). If a study/an ISS includes 10 STOIs, PARAM will contain 30 values. The use of PARQTYP and PARQUAL in the ADSTOI Dataset not only categorizes PARAM by STOI but also reduces the number of values in PARAM, thereby enhancing the clarity of data analysis.

The inclusion of PARQTYP and PARQUAL in the ADSTOI Dataset helps reduce the number of values in PARAM. Additionally, PARQUAL and PARAM can be used together to select the record for a specific parameter and STOI, enhancing the clarity of data analysis.

Figure 13: Example of PARQTYP and PARQUAL Variables in BDS ADSTOI Dataset

SCENARIO	ROW	USUBJID	TRT01A	ACYSTDT	ASTDT	AENDT	AVISIT	AVISITN	PARQTYP	PARQUAL	PARAM	PARAMCD	AVAL	AVALC	ATOXGR	DTYPE	ANL01FL	ANL02FL
1 & 2	1	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	2		2		Y	Y
	2	101	TRT1	1/4/2024	1/10/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	6		1			Y
	3	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	3		3		Y	Y
	4	101	TRT1	3/4/2024	3/8/2024	3/12/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	4		3		Y	Y
	5	101	TRT1	3/4/2024	3/14/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Onset in Cycle (days)	TTAEONS	10		3			
3	6	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	2		2			
	7	101	TRT1	1/4/2024	1/10/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	2		1			
	8	101	TRT1	1/4/2024	1/6/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	6			Merged	Y	
	9	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	1		3		Y	
	10	101	TRT1	3/4/2024	3/8/2024	3/12/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	4		3			
	11	101	TRT1	3/4/2024	3/14/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	2		3			
	12	101	TRT1	3/4/2024	3/8/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Time to STOI Resolution in Cycle (days)	TTAERES	8			Merged	Y	
4	18	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG			2			
	19	101	TRT1	1/4/2024	1/10/2024	1/12/2024	Cycle 1	1	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDTTAEG		Y	1		Y	
	20	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDTTAEG		Y	3		Y	
	21	101	TRT1	3/4/2024	3/8/2024	3/12/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDTTAEG		Y	3		Y	
	22	101	TRT1	3/4/2024	3/14/2024	3/16/2024	Cycle 3	3	Safety Topics of Interest	Serious Infection	Med x Use to Treat STOI in Cycle by Grade	MEDTTAEG		Y	3			
1 & 2	23	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Anemia	Time to STOI Onset in Cycle (days)	TTAEONS	2		2		Y	Y
	24	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Anemia	Time to STOI Onset in Cycle (days)	TTAEONS	3		3		Y	Y
3	25	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Anemia	Time to STOI Resolution in Cycle (days)	TTAERES	2		2		Y	
	26	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Anemia	Time to STOI Resolution in Cycle (days)	TTAERES	1		3		Y	
4	29	101	TRT1	1/4/2024	1/6/2024	1/8/2024	Cycle 1	1	Safety Topics of Interest	Anemia	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG			2			
	30	101	TRT1	2/4/2024	2/7/2024	2/8/2024	Cycle 2	2	Safety Topics of Interest	Anemia	Med x Use to Treat STOI in Cycle by Grade	MEDUTAEG		Y	3		Y	

Figure 14: PARAM Values

PARAM (PARQTYP/PARQUAL Included in ADSTOI data set)	PARAM (PARQTYP/PARQUAL not Included in ADSTOI data set)
Time to STOI Onset in Cycle (days)	Time to Serious Infection Onset in Cycle (days)
Time to STOI Resolution in Cycle (days)	Time to Serious Infection Resolution in Cycle (days)
Med x to Treat STOI in Cycle by Grade.	Med x to Treat Serious Infection in Cycle by Grade.
	Time to Anemia Onset in Cycle (days)
	Time to Anemia Resolution in Cycle (days)
	Med x to Treat Anemia in Cycle by Grade.

CONCLUSION

This paper introduces the BDS ADSTOI dataset, designed to analyze the time to events of STOIs across four distinct scenarios. The ADSTOI Dataset has several key features:

1. It follows the ADAE occurrence principle, including all the observations where STOI occurs.
2. Unlike the ADTTE dataset, the ADSTOI Dataset does not include the required censoring variable (CNSR) and the permissible variables of analysis date (ADT) and Time to Event Origin Date for Subject (STARTDT), which are typically included in ADTTE datasets.
3. The ADSTOI Dataset includes three date variables—ASTDT, AENDT, and ACYSTDT—which represent the analysis start date, analysis end date, and the most recent dose date associated with the analysis start date. These date variables are essential for calculating various time to STOI events. As a result, the structure of this Dataset supports clear and traceable calculations.
4. The ADSTOI Dataset includes two variables, PARQTYP and PARQUAL, which help improve the clarity of data analysis involving multiple STOIs. PARQTYP has been discussed within the CDSIC ADaM teams, and PARQUAL is already used in CDSIC ADaM examples and FDA documentation. The ADSTOI Dataset provides an example where PARQTYP represents the type of Safety Topics of Interest and PARQUAL represents various STOIs, providing a case to support the discussion and decision-making regarding PARQTYP and PARQUAL in ADaM.

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