



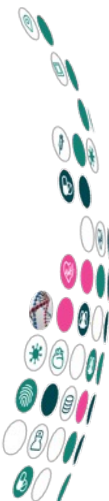
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ICON Plc

Agenda

- Overview
- Current Process
- Macro Goals
- Automation Method
- Conclusion
- Q & A



Overview

A SAS Tool for Generating Adverse Event Summaries in XML Format Using ADaM Datasets ADSL and ADAE for **ClinicalTrial.gov** and **EudraCT** Submissions

ClinicalTrials.gov Adverse Events

<https://clinicaltrials.gov/>

[View this study on Beta.ClinicalTrials.gov](#)

Sponsor:
GlaxoSmithKline

Collaborator:
ITeos Belgium SA

Information provided by (Responsible Party):
GlaxoSmithKline

[Study Details](#) [Tabular View](#) [Study Results](#) [Disclaimer](#) [How to Read a Study Record](#)

Study Type	Interventional
Study Design	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: None (Open Label); Primary Purpose: Treatment
Condition	Neoplasms
Interventions	Drug: Docetaxel Drug: Feladilimab
Enrollment	105

Participant Flow ⓘ

Go to ▼

Recruitment Details			
Pre-assignment Details			
Arm/Group Title		Docetaxel 75 mg/m^2	Feladilimab 80 mg Plus Docetaxel 75 mg/m^2
▼ Arm/Group Description		Participants with NSCLC were administered with Docetaxel 75 milligram per meter square (mg/m^2) monotherapy as intravenous (IV) infusion once every 3 weeks (Q3W).	Participants with NSCLC were administered with Feladilimab 80 mg IV infusion Q3W in combination with Docetaxel 75 mg/m^2 IV infusion Q3W.
Period Title: Overall Study			
Started		35	70
Completed		0	0
Not Completed		35	70

ClinicalTrials.gov Adverse Events

Adverse Events

Go to

Time Frame	All cause mortality, non-SAEs and SAEs were collected up to 2 years.			
Adverse Event Reporting Description	Safety population included all randomized participants who received at least one dose of SoC or experimental regimen based on actual treatment received.			
Arm/Group Title	Docetaxel 75 mg/m^2		Feladilimab 80 mg Plus Docetaxel 75 mg/m^2	
▼ Arm/Group Description	Participants with NSLC were administered with Docetaxel 75 milligram per meter square (mg/m^2) monotherapy as intravenous (IV) infusion once every 3 weeks (Q3W).		Participants with NSLC were administered with feladilimab 80 mg IV infusion once Q3W in combination with Docetaxel 75 mg/m^2 IV infusion Q3W.	
All-Cause Mortality ⓘ				
	Docetaxel 75 mg/m^2		Feladilimab 80 mg Plus Docetaxel 75 mg/m^2	
	Affected / at Risk (%)		Affected / at Risk (%)	
Total	25/34 (73.53%)		62/70 (88.57%)	
▼ Serious Adverse Events ⓘ				
	Docetaxel 75 mg/m^2		Feladilimab 80 mg Plus Docetaxel 75 mg/m^2	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	16/34 (47.06%)		34/70 (48.57%)	
Blood and lymphatic system disorders				
Febrile neutropenia † †	3/34 (8.82%)	3	4/70 (5.71%)	4
Anaemia † †	1/34 (2.94%)	1	2/70 (2.86%)	2
Neutropenia † †	0/34 (0.00%)	0	2/70 (2.86%)	2
Leukopenia † †	0/34 (0.00%)	0	1/70 (1.43%)	1
Pancytopenia † †	0/34 (0.00%)	0	1/70 (1.43%)	1
Cardiac disorders				
Acute coronary syndrome † †	0/34 (0.00%)	0	1/70 (1.43%)	1
Cardiac arrest † †	0/34 (0.00%)	0	1/70 (1.43%)	1
Cardiac failure † †	0/34 (0.00%)	0	1/70 (1.43%)	1
Cardiopulmonary failure † †	0/34 (0.00%)	0	1/70 (1.43%)	1
Right ventricular failure † †	1/34 (2.94%)	1	0/70 (0.00%)	0

EudraCT Adverse Events

<https://www.clinicaltrialsregister.eu/>

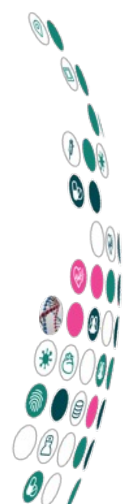
Adverse events  Top of page	
Adverse events information	
Timeframe for reporting adverse events	Occurring on the Day of Vaccination and the following 28 Days after any Dose
Adverse event reporting additional description	Subjects who became unblinded and/or received a licensed/authorized vaccine were censored at the day after unblinding or at the day after receiving the licensed/authorized vaccine, whichever is earlier.
Assessment type	Systematic
Dictionary used for adverse event reporting	
Dictionary name	MedDRA
Dictionary version	24.0
Reporting groups	
Reporting group title	6 ug
Reporting group description	6 ug
Reporting group title	Active control
Reporting group description	Active control
Reporting group title	12 ug
Reporting group description	12 ug

EudraCT Adverse Events

Serious adverse events	6 ug	Active control	12 ug
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 61 (0.00%)	8 / 584 (1.37%)
number of deaths (all causes)	0	1	3
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 23 (0.00%)	0 / 61 (0.00%)	1 / 584 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 23 (0.00%)	0 / 61 (0.00%)	1 / 584 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Extraocular muscle paresis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 61 (0.00%)	1 / 584 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

EudraCT Adverse Events

Frequency threshold for reporting non-serious adverse events: 5%			
Non-serious adverse events	6 ug	Active control	12 ug
Total subjects affected by non serious adverse events			
subjects affected / exposed	21 / 23 (91.30%)	55 / 61 (90.16%)	557 / 584 (95.38%)
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	2 / 23 (8.70%)	0 / 61 (0.00%)	10 / 584 (1.71%)
occurrences all number	3	0	10
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	4 / 23 (17.39%)	0 / 61 (0.00%)	4 / 584 (0.68%)
occurrences all number	4	0	4
Anaemia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 61 (0.00%)	8 / 584 (1.37%)
occurrences all number	2	0	8
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 23 (56.52%)	30 / 61 (49.18%)	378 / 584 (64.73%)
occurrences all number	21	41	668



Current Process

Manual Data entry

ClinicalTrials.gov PRS

Protocol Registration and Results System

Org: PrahsAdmin: SKannattikuni

Home > Record Summary > Results Section > Adverse Events

ID: NCT02794285TULIP SLE LTE[NCT ID not yet assigned]

Adverse Events Overview

Results SectionDownload/UploadSort...HelpDefinitions

Show All

Edit	Time Frame	Up to 1114 days	
	Adverse Event Reporting Description	FAS - LTE Study: consist of all participants who were randomised and received at least 1 dose of investigational product in the LTE Study. All cause - participant flow. SAEs - Table 14.3.4.1.2.1	
	Source Vocabulary Name for Table Default	MedDRA (24.1)	
	Collection Approach for Table Default	Systematic Assessment	

Edit	Arm/Group Title	Anifrolumab 300 mg	Placebo
	Arm/Group Description	Anifrolumab (300 mg) administered v...	Placebo administered via an IV infu...

All-Cause Mortality
Information is required

		Anifrolumab 300 mg	Placebo
		Affected / at Risk (%)	Affected / at Risk (%)
Edit	Total	--- /---	--- /---

▼ Serious Adverse Events
Information is required

		Anifrolumab 300 mg	Placebo
		Affected / at Risk (%)	Affected / at Risk (%)
Edit	Total	--- /---	--- /---

Project Goals, Objectives and Benefits

Problem Statement

- Uploads to CT.gov and EudraCT currently rely on manual process to prepare and submit data.
- Inefficient business process that is prone to data entry errors and compliance risk.

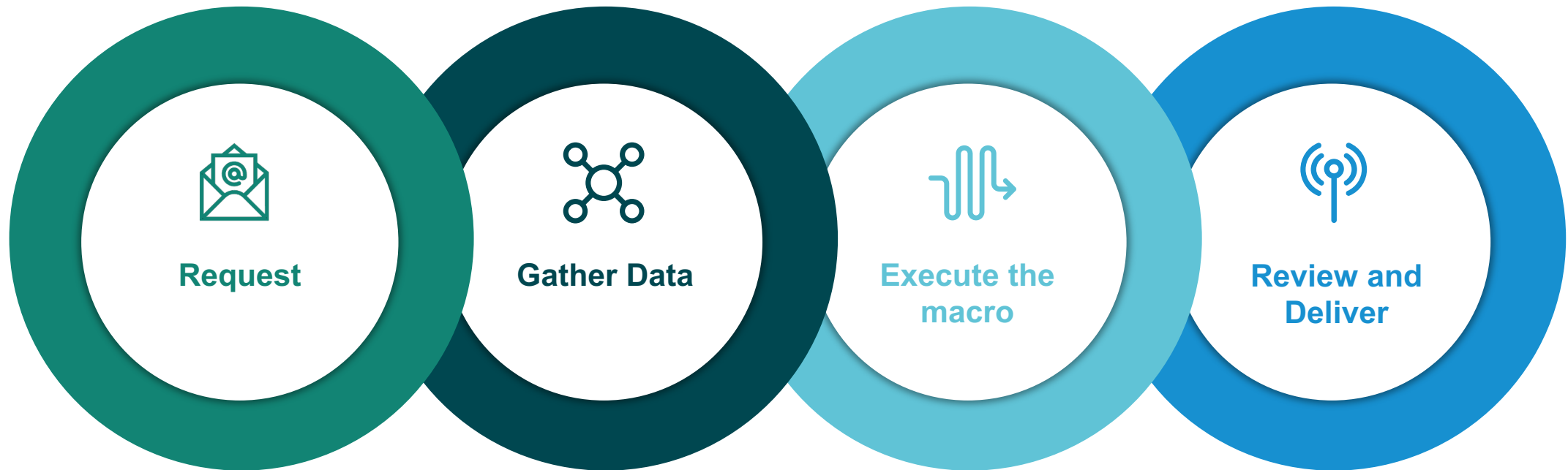
Why Now?

- Lack of more automated process was contributing factor to loss of multiple RFPs (Request for Proposals) and is frequently requested by sponsors.



Automation Method

Macro process



The Clinical Safety department will initiate the request.

Gather Study Specific data (ADSL and ADAE datasets)

Provide input parameters and execute the macro

Review the outputs and Deliver to the clinical Safety team

Key inputs and Outputs

Inputs

- ADaM Datasets
 - ADSL
 - ADAE
- Additional information from
 - Protocol
 - SAP/Shell
- If available
 - Serious Adverse Events Summary table
 - Frequent Non-Serious Adverse Events Summary table

Outputs

- CT_GOV.XML
- EUDRACT.XML
- AE Tabulation.xls
- Full_Summary.sas7bdat

Assigning study specific parameters in the Setup program

```
*****;  
* Edit Study specific parameters below;  
*****;  
/*Study specific parameters*/  
%let sponsor = %str(); * Name of the Sponsor;  
%let protocol = %str(); * Protocol Number;  
%let title = %str( ); *This will appear in the Brief title section in the ClinicalTrials.gov website;  
%let xmlfile_US = %str(&protocol._CT_GOV.xml); * Name of the US XML file;  
%let xmlfile_EU = %str(&protocol._EUDRACT.xml); * Name of the EU XML file;  
  
/*ASSESSTYPE - Method used to assess the adverse events (e.g., Systematic Assessment)*/  
%let assesstype = %str(Systematic Assessment); /*or Non-Systematic Assessment */  
  
/*DICTIONARY - Dictionary used for reporting (e.g. MedDRA with version number)*/  
%let dictionary=%str(meddra); /*Used meddra or snomed*/  
%let DictionaryVersion = %str(24.0);  
%let OtherDictionary = %str();  
  
/*TIMEFRAME - Period in which the reported adverse event data were collected*/  
%let timeframe = %str();  
  
/*ClinicalTrials.gov: Adverse Event Reporting Description*/  
/*EudraCT: Adverse event reporting additional Description*/  
%let AEAdditionalDescription = %str();  
  
/* DESC1 - DESC9 - Long description of each reporting group (treatment) matching the number in the group_n variable*/  
%let desc1=%str();  
%let desc2=%str();  
%let desc3=%str();  
%let desc4=%str();  
%let desc5=%str();  
%let desc6=%str();
```

Execution of SAS Macros

```
%m_AE (AE_in = ADAE
      ,SL_in=ADSL
      ,DT_in=ADAE      /* input datasets for AEs, groups, deaths */
      ,POP_fl=SAFFL     /* population to select from both AE and SL datasets */
      ,TE_fl=           /* Treatment Emergent flag to select TEAEs from AE dataset */
      ,SER_fl=AESER     /* Serious flag to select SAEs from AE dataset - otherwise non-serious */
      ,REL_fl = AEREL   /*Related to study medication information*/
      ,DT_fl=AEOUT      /*Outcome*/
      ,DT_val=FATAL     /* Fatal AE indicator from AE dataset */
      ,group_c=TRT01A
      ,group_n=TRT01AN
      ,TH_perc=5        /* Percent Threshold to count non-serious frequent, e.g., enter the number 5 for 5 percent*/
      ,where_ADAE =%str() /*Additional filter conditions from ADAE*/
      ,where_ADSL = %str() /*Additional filter conditions from ADSL*/
      ,ExcelTable = Y /*Option to generate Excel table*/
      ,CLEANUP = Y); /*Delete intermediate datasets*/
```

Individual Macros

m_AE_datacheck

This program checks the compatibility of the source datasets ADSL and ADAE. It also verifies the required and conditionally required macro parameters, terminating the program if any issues arise.

m_AE_FullSummary

After the data check m_AE_FullSummary program will generate a full summary SAS dataset required for the XML generation. This dataset consists of below specified variables:

m_AE_XML_US

This program will generate the XML file required for ClinicalTrial.gov submission according to the required schemas.

m_AE_XML_EU

This program will generate the XML file required for EudraCT submission according to the required schemas.

m_AE_ExcelTable

In addition to the XML files, we have created an Excel version of the output to facilitate a manual review of the generated Adverse Event summary counts.

Validation of XML files

- Given that the XML file has a different structure than the typical SAS dataset, the m_AE_ExcelTable macro generates an Excel version of summary outputs, making it easier for review purposes.
- This can be utilized to compare adverse event summary tables prepared for CSR delivery.
- We have successfully validated this tool across more than six studies and subsequently submitted those studies for inclusion in both ClinicalTrial.gov and EudraCT submissions.

Conclusion

- The automation process facilitates the direct generation of XML files that can be seamlessly loaded into the registry systems of ClinicalTrials.gov and/or EudraCT.
- Leveraging source data for Analysis Datasets ADSL and ADAE, this automated approach ensures precision, efficiency, and consistency in consolidating adverse event summary data as mandated by FDA/EMA.



References

- ClinicalTrials.gov. Accessed on May 5th, 2023
<https://www.clinicaltrials.gov/>
- ClinicalTrials.gov Protocol Registration System (PRS)
“ClinicalTrials.gov Results Data Element Definitions”.
Accessed May 5th, 2023.
https://prsinfo.clinicaltrials.gov/results_definitions.html
- EU Clinical Trials Register. Accessed May 5th 2023.
www.clinicaltrialsregister.eu
- EudraCT Results related documentation. Accessed May 5th 2023. <https://eudract.ema.europa.eu/result.html>



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Questions



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