



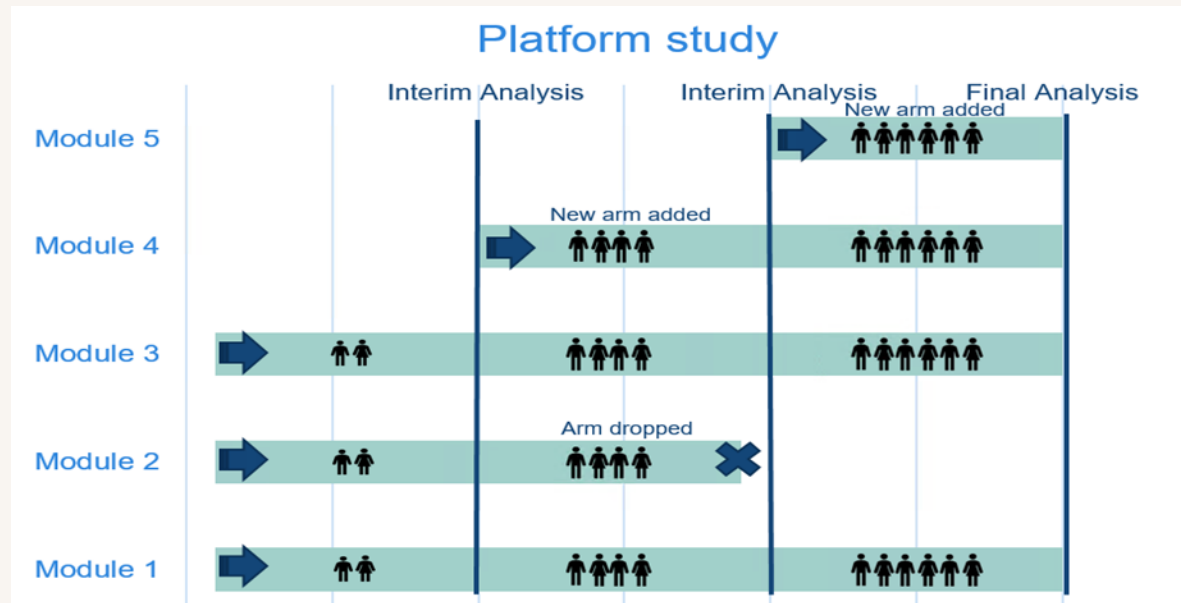
PHUSE EU Connect 2025

SM16 - On the Right Track: Managing Platform Modular Studies with a Central Metadata Switchboard

Dubravka Georgijević – Carla Santillan

Platform Study

A platform modular study is a type of adaptive trial that uses a master protocol to evaluate multiple, targeted therapies within a single disease setting. These trials may not have a planned end date, and treatment arms (and/or modules) can be added, or removed, based on predefined rules.

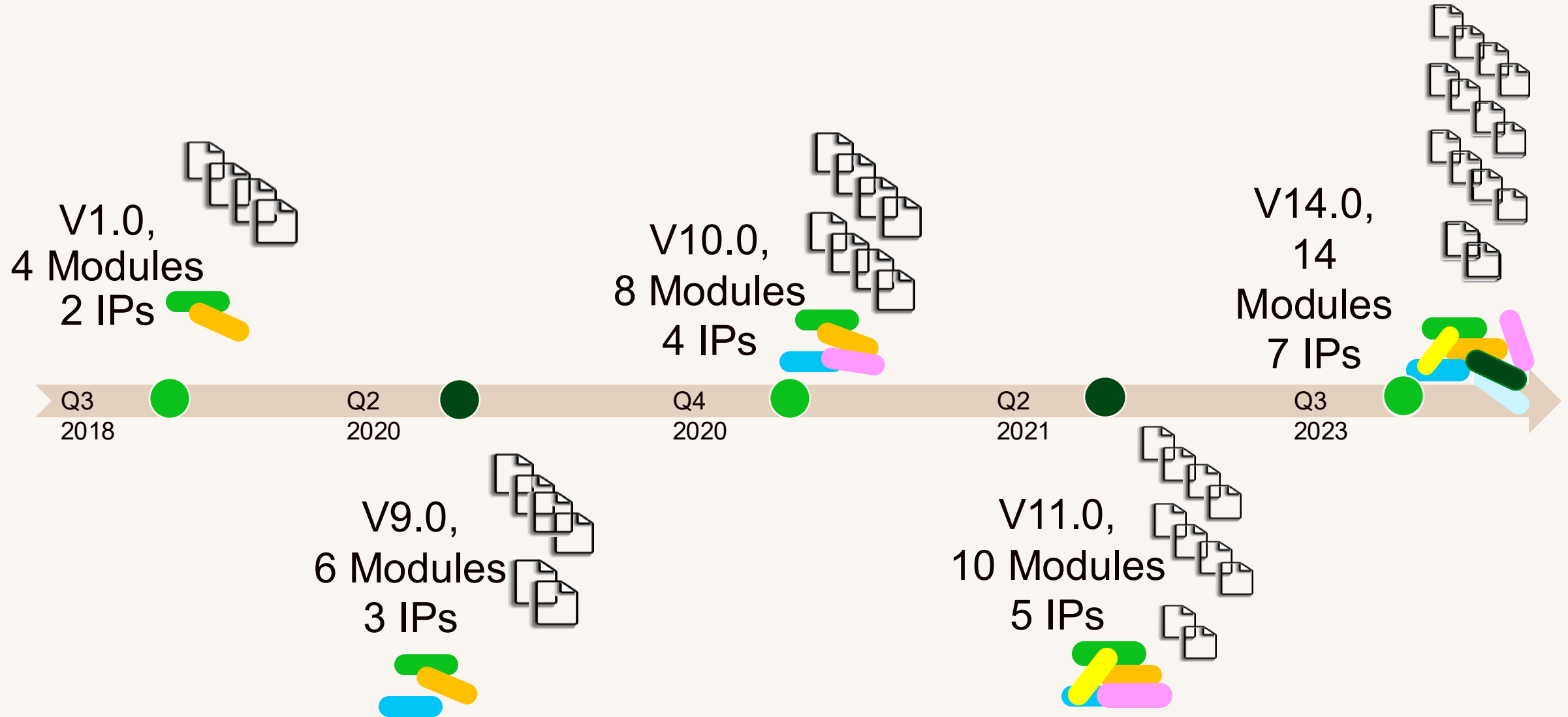


Jay J.H. Park [September 2020], *An overview of platform trials with a checklist for clinical readers [online]*, available from:
<https://www.sciencedirect.com/science/article/pii/S2451865420300521#:~:text=A%20master%20protocol%20is%20a%20unifying%20study%20design%20that%20includes,multiple%20drugs%20to%20treat%20it>

Platform Study Characteristics

- Longer trial timelines
- Higher number of protocol substantial amendments
 - Higher number of Case Report Forms (CRF) amendments
 - Complex trial designs continually evolving and incremental in nature
- Increased data requirements
 - Large number of amendments for Statistical Analysis Plan (SAP), Table of Contents (TOC) and Table, Figure, Listing (TFL) Mock Shells
 - Highly Complex Safety and Efficacy endpoints derivations
 - Large number of TFLs to produce

Study Protocol History – a Real Study Example

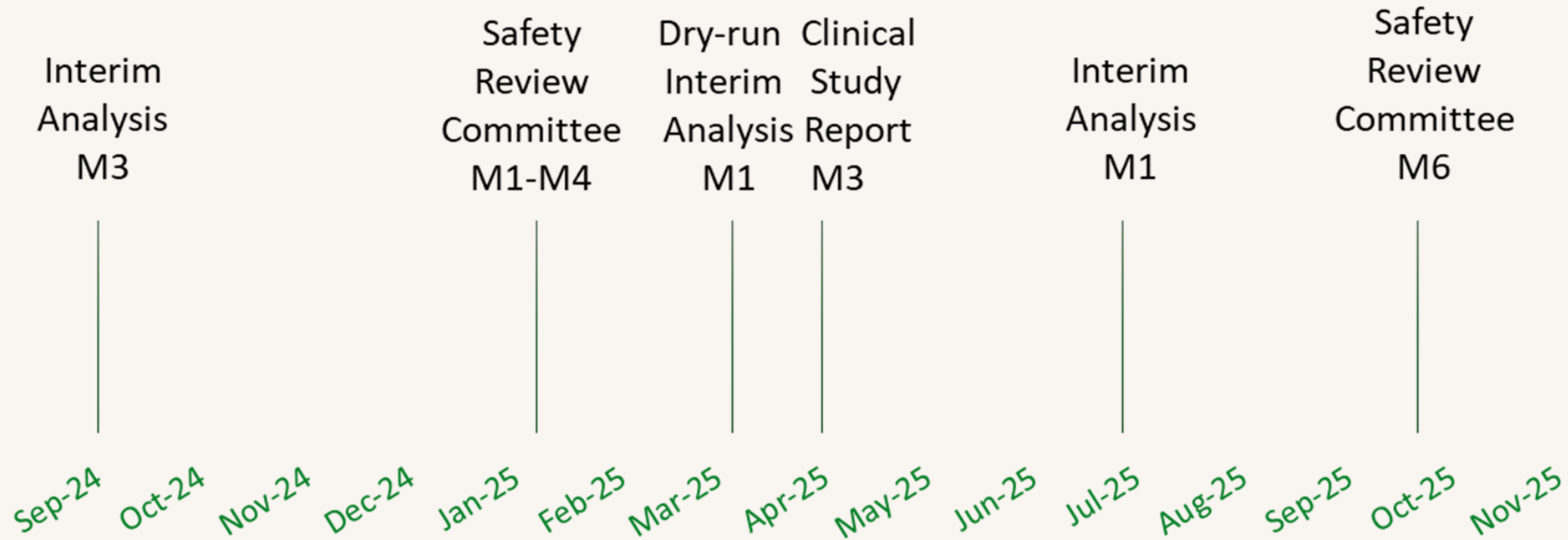


Fortrea Approach to Managing Challenges in Oncology Modular Studies

- Centralized programming (in each program, the logic is present for all modules of the study)
- Centralized data selection (data selection at the raw data level, in one central program, prior to creating SDTM datasets)
- Extensive use of macros and macro variables
- Data-driven and metadata-driven solutions to select the study modules/treatment groups

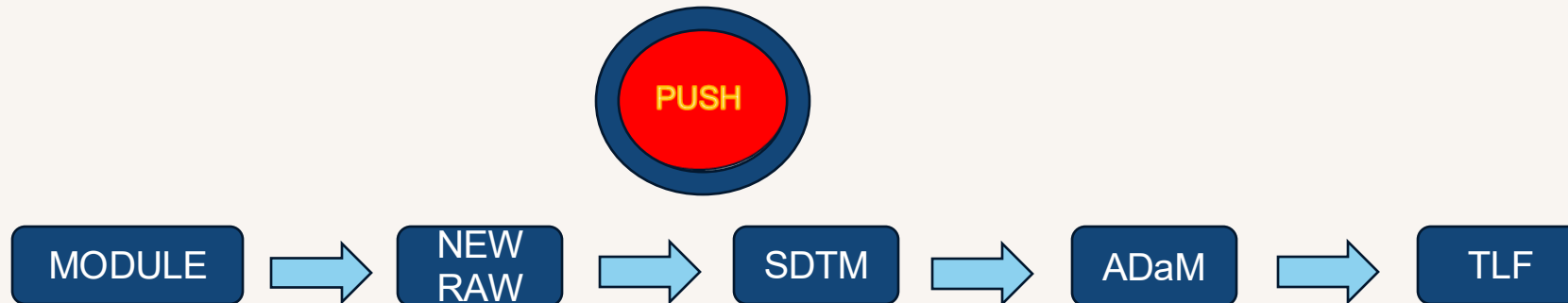
Continuous Module-specific Deliveries

- No new study modules being added
- Each module follows its own development program, with ongoing safety reviews, interim analysis, clinical study report (CSR) dry-run and final CSR.



Continuous Module-specific Deliveries continued

Many releases will come, short timelines between releases will be proposed, because everything (SDTM, ADaM, TLFs) is programmed.



The Central Deliveries Metadata File

- A central study file stores metadata related to the study programming needs - among other metadata, program and output file names, output titles and footnotes
- It is read into SAS to apply the metadata when generating the outputs.
- In addition, the file contains a list of macro variables that get created in the SAS session when the file is read into SAS and are used for multiple purposes while programming:

macro_var_name	macro_var_value	macro_var_purpose
meta_sponsor	Sponsor A	Text to be displayed in all outputs
meta_study	ABCD0003	Text to be displayed in all outputs
meddra_version	28.1	Dictionary version used for programs and to display in the output
whodde_version	March 2025	Dictionary version used for programs and to display in the output

Switches for Selection of Subjects and Data Cutoff (DCO) Date for the Release

- For some modular study deliveries there is a need to select data up to the DCO date, containing the desired selection of subjects based on the study modules they belong to.
- Data selection at the raw data level, in one central program, prior to creating SDTM datasets – this program uses the following macro variables:

macro_var_name	macro_var_value	macro_var_purpose
apply_dco	Y	Apply or not DCO rules on raw data (if not, then only subject selection based on the module will be done)
raw_dco	2025-09-02	Used as the DCO date to apply DCO rules on raw data
dcutdt	2025-09-02	Used in ADaM derivations as analysis cutoff date
module	1	Used in multiple programs to select subjects or perform module-specific derivations
meta_dco	Module 1 IA1: Data cut-off = 2025-09-02	Title to be displayed in the top left corner in all outputs

Switches for Selection of Output Programs and Treatment Groups

Module 1

Part A Group 1 (N = xx)	Part A Group 2 (N = xx)	Part A Total (N = xx)	Part B Group 1 (N = xx)	Part B Group 2 (N = xx)	Part B Total (N = xx)
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Module 6

Part A Group 1 (N = xx)	Part A Group 2 (N = xx)	Part A Group 3 (N = xx)	Part A Group 4 (N = xx)	Total (N = xx)
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output_number	program_name	output_name	program_select
14.x.y.1	table xy	table xy 1	CSRM3/M1IA1/SRCM6
14.x.y.2	table xy	table xy 2	CSRM3/M1IA1
14.x.y.3	table xy	table xy 3	CSRM3/M1IA1
14.x.y.4	table xy	table xy 4	CSRM3
14.x.z.1	table xz	table xz 1	CSRM3/M1IA1/SRCM6
14.x.z.2	table xz	table xz 2	
14.x.z.3	table xz	table xz 3	M1IA1
14.x.z.4	table xz	table xz 4	SRCM6

Switches for Selection of Output Programs and Treatment Groups continued

Module 1						
	Part A Group 1 (N = xx)	Part A Group 2 (N = xx)	Part A Total (N = xx)	Part B Group 1 (N = xx)	Part B Group 2 (N = xx)	Part B Total (N = xx)

Module 6				
	Part A Group 1 (N = xx)	Part A Group 2 (N = xx)	Part A Group 3 (N = xx)	Part A Group 4 (N = xx)
	Total (N = xx)			

output_number	program_name	output_name	program_select
14.x.y.1	table_xy	table_xy_1	CSRM3/M1IA1/SRCM6
14.x.y.2	table_xy	table_xy_2	CSRM3/M1IA1
14.x.y.3	table_xy	table_xy_3	CSRM3/M1IA1
14.x.y.4	table_xy	table_xy_4	CSRM3
14.x.z.1	table_xz	table_xz_1	CSRM3/M1IA1/SRCM6
14.x.z.2	table_xz	table_xz_2	
14.x.z.3	table_xz	table_xz_3	M1IA1
14.x.z.4	table_xz	table_xz_4	SRCM6

macro_var_name	macro_var_value	macro_var_purpose
current_release	M1IA1	Used to select tlf programs to run
m1ia1	Y	Used in tlf macros to select trt columns and in multiple programs to perform release-specific derivations
srcm6	N	Used in tlf macros to select trt columns and in multiple programs to perform release-specific derivations

Switches for Analysis Sets Definition

For an IA analysis:

Interim evaluable for efficacy analysis set: All dosed subjects who received first dose at least 17 weeks prior to or on data cut-off.

For an SRC analysis:

Interim evaluable for efficacy analysis set: All dosed subjects who received first dose at least 13 weeks prior to or on data cut-off.

macro_var_name	macro_var_value	macro_var_purpose
iafl	Y	Apply IA definitions of interim analysis sets in ADSL
srcfl	N	Apply SRC definitions of interim analysis sets in ADSL
iaefftxt	17 weeks	Footnote text for outputs using IA definition of interim evaluable for efficacy analysis set
iaeffdays	118	Number of days from DCO date to use in the IA definition of interim evaluable for efficacy analysis set
srcefftxt	13 weeks	Footnote text for outputs using SRC definition of interim evaluable for efficacy analysis set
srceffdays	91	Number of days from DCO date to use in the SRC definition of interim evaluable for efficacy analysis set

Switches for Other Specific Module Differences

Table 14.x.y.z.w Progression-free survival (Evaluable for efficacy analysis set)

Module x

	Part A Total (N = xx)	Part B Group 1 (N = xx)	Part B Group 2 (N = xx)	Part B Total (N = xx)
Total events, n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Individual Part A cohorts are not displayed.

Programming Guidance:
In case of Modules for which no subject included in Part B and individual Part A cohorts should be displayed, not present footnote "Individual Part A cohorts are not displayed.". Add the footnote: "BRCAm plus corresponds to BRCA1/BRCA2/PALB2/RAD51C/RAD51D mutations." in all outputs where BRCAm plus grouping is displayed

macro_var_name	macro_var_value	macro_var_purpose
daysafteot	35	Number of days (xx) to use in ADaM derivations and in footnotes that need ADSL.EOTDT+xx
brcafn	Y	Display or not the module 1 specific footnote with the definition of BRCAm plus
partB	Y	Used for efficacy outputs to NOT display individual part A cohorts when partB=Y

Summary

macro_var_name	macro_var_value
meta_sponsor	Sponsor A
meta_study	ABCD0003
meddra_version	28.1
whodde_version	March 2025
current_release	M1IA1
module	1
m1ia1	Y
srcm6	N
raw_dco	2025-09-02
dcutdt	2025-08-02
meta_dco	Module 1 IA1: Data cut-off = 2025-09-02
apply_dco	Y
iafl	Y
srcfl	N
iaeffttx	17 weeks
iaefftays	118
srceffttx	13 weeks
srcefftays	91
daysafteot	35
brcafn	Y
partB	Y

Summary

macro_var_name	macro_var_value
meta_sponsor	Sponsor A
meta_study	ABCD0003
meddra_version	28.1
whodde_version	March 2025
current_release	M1IA1
module	1
m1ia1	Y
srcm6	N
raw_dco	2025-09-02
dcutdt	2025-08-02
meta_dco	Module 1 IA1: Data cut-off = 2025-09-02
apply_dco	Y
iafl	Y
srcfl	N
iaeffttx	17 weeks
iaefftays	118
srceffttx	13 weeks
srcefftays	91
daysafteot	35
brcafn	Y
partB	Y



macro_var_name	macro_var_value
meta_sponsor	Sponsor A
meta_study	ABCD0003
meddra_version	28.1
whodde_version	March 2025
current_release	SRCM6
module	6
m1ia1	N
srcm6	Y
raw_dco	2025-10-02
dcutdt	2025-10-02
meta_dco	Module 6 SRC: Data cut-off = 2025-10-02
apply_dco	N
iafl	N
srcfl	Y
iaeffttx	17 weeks
iaefftays	118
srceffttx	13 weeks
srcefftays	91
daysafteot	42
brcafn	N
partB	N

Thank You!

Questions?

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PHUSE EU Connect 2025

CONTACT INFORMATION

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