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Data Handling for Subjects Participating in Multiple Cohorts in Oncology Platform Trials: Considerations for Data Collection, SDTM, and ADaM Mappings

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Abstract

Platform trials have emerged as a transformative approach in oncology research, facilitating the investigation of multiple targeted therapies across diverse cohorts based on molecular subtypes. These trials offer the unique advantage of flexibility, allowing for the exclusion of ineffective interventions and the seamless addition of new treatments during the trial. Notably, platform trials may encounter scenarios where subjects exhibit multiple molecular subtypes, initially enrolling in one cohort, but the cohort being discontinued at an interim analysis due to lack of efficacy. The eligible subjects from the discontinued cohort are re-screened and re-enrolled in a newly added cohort. The poster presents practical examples of trial design domains, data collection methodologies for re-enrollers, emphasizing the SDTM data mapping to essential domains such as DM (Demographics) and DC (Demographics as Collected). The collection and mapping of biomarker data are also discussed. Additionally, it highlights the handling of data for analysis purposes, presenting subject-level data in ADSL, ADTP (Trial Participation Analysis Dataset), and laboratory data in ADLB.

Platform Trial – Ability to drop arms early and flexibility to add new arms- the scenario for the re-enrolled subjects

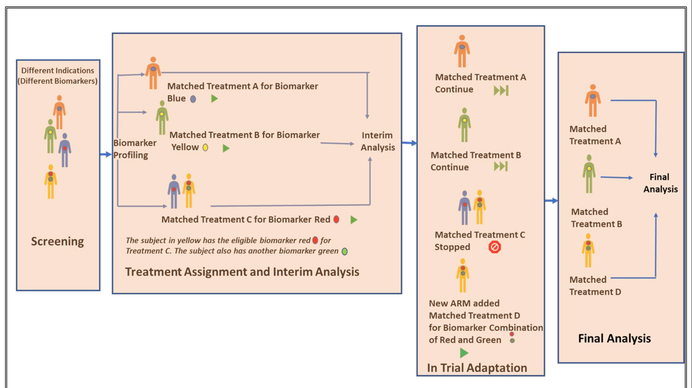


Fig.1: Platform Trial with Re-enrollment. This figure shows a platform trial with subjects assigned to treatments (A, B, C) based on their biomarker colors (blue, yellow, red). Treatment C is discontinued, and a new treatment arm (D) is added for subjects with a red-green biomarker combination. Subjects with both red and green biomarkers are re-enrolled in Treatment D. The final analysis includes Treatments A, B, and D.

Representation of Platform Trial in the database using SDTM Trial Arms (TA) & Trial Elements (TE)

ta.xpt

STUDYID	DOMAIN	ARMCD	ARM	TAETORD	ETCD	Element	TABRANCH	TATRANS	EPOCH
ABC123	TA	A	TRTA	1	SCRN	Screen	Assigned to Treatment A following biomarker match		SCREENING
ABC123	TA	A	TRTA	2	TRTA	Matched Treatment A		If early stop due to interim analysis, start new treatment matching the biomarker allowed by the protocol	TREATMENT
ABC123	TA	A	TRTA	3	FU	Follow-up			FOLLOW-UP
ABC123	TA	B	TRTB	1	SCRN	Screen	Assigned to Treatment B following biomarker match		SCREENING
ABC123	TA	B	TRTB	2	TRTB	Matched Treatment B		If early stop due to interim analysis, start new treatment matching the biomarker allowed by the protocol	TREATMENT
ABC123	TA	B	TRTB	3	FU	Follow-up			FOLLOW-UP
ABC123	TA	C	TRTC	1	SCRN	Screen	Assigned to Treatment C following biomarker match		SCREENING
ABC123	TA	C	TRTC	2	TRTC	Matched Treatment C		If early stop due to interim analysis, start new treatment matching the biomarker allowed by the protocol	TREATMENT
ABC123	TA	C	TRTC	3	FU	Follow-up			FOLLOW-UP
ABC123	TA	D	TRTD	1	SCRN	Screen	Assigned to Treatment D following biomarker match		SCREENING
ABC123	TA	D	TRTD	2	TRTD	Matched Treatment D		If early stop due to interim analysis, start new treatment matching the biomarker allowed by the protocol	TREATMENT
ABC123	TA	D	TRTD	3	FU	Follow-up			FOLLOW-UP

te.xpt

STUDYID	DOMAIN	ETCD	ELEMENT	TESTRL	TEENRL
ABC123	TE	SCRN	Screen	Informed Consent	1 week after start of Element
ABC123	TE	TRTA	Matched Treatment A	subject matches blue biomarker and receives Matched Treatment A	At either end of trial or if Matched Treatment A meets stopping rules at any pre-planned interim analysis, whichever comes first
ABC123	TE	TRTB	Matched Treatment B	subject matches yellow biomarker and receives Matched Treatment B	At either end of trial or if Matched Treatment B meets stopping rules at any pre-planned interim analysis, whichever comes first
ABC123	TE	TRTC	Matched Treatment C	subject matches green biomarker and receives Matched Treatment C	At either end of trial or if Matched Treatment C meets stopping rules at any pre-planned interim analysis, whichever comes first
ABC123	TE	TRTD	Matched Treatment D	subject matches green and red biomarkers and receives Matched Treatment D.	At end of trial
ABC123	TE	FU	Follow-up	End of the treatment	30 days from the end of the teratment or beginning of a new treatment

Fig.2: Representation of Trial Arms (TA) &Trial Elements (TE): The TA dataset captures Trial Arms and Elements. The Platform trial requires the use of the TATRANS variable to represent the rule describing the conditions under which a subject will go to the new ARM. The Trial Elements (TE) dataset contains the definitions of the elements that appear in the Trial Arms (TA) dataset.

Data Collection, SDTM Mapping of Data to DC & DM Domains

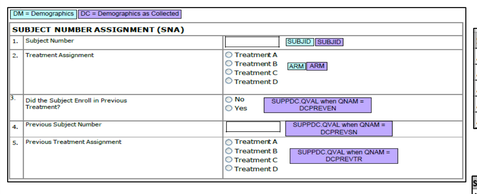


Fig.3: Annotated CRF collecting new SUBJID for each enrollment. Information on previous cohorts is collected and mapped to DC, SUPPDC, and DM domains. Although participants have a new SUBJID for each participant, they have a common USUBJID throughout the trial.

dc.xpt

STUDYID	DOMAIN	USUBJID	SUBJID	DCSEQ	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	AGE	AGEU	ARMCD	ARM
ABC123	DC	ABC1231001001	1001A	1	2021-03-01	2023-04-01	2021-03-01	2023-04-01	35	YEARS	TRTA	Treatment A
ABC123	DC	ABC1231001002	1002A	1	2021-03-16	2023-04-30	2021-03-16	2023-04-30	32	YEARS	TRTB	Treatment B
ABC123	DC	ABC1231001003	1003A	1	2021-05-29	2022-06-02	2021-05-29	2022-06-02	40	YEARS	TRTC	Treatment C
ABC123	DC	ABC1231001004	1004A	1	2021-05-20	2022-05-20	2021-05-20	2022-05-20	46	YEARS	TRTC	Treatment C
ABC123	DC	ABC1231001004	1004B	2	2022-06-15	2023-05-30	2022-06-15	2023-05-30	47	YEARS	TRTD	Treatment D

suppdc.xpt

STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
ABC123	DC	ABC1231001001	DCSEQ	1	DCPREVEN	Previous Treatment Enrollment	N	CRF	
ABC123	DC	ABC1231001002	DCSEQ	1	DCPREVEN	Previous Treatment Enrollment	N	CRF	
ABC123	DC	ABC1231001003	DCSEQ	1	DCPREVEN	Previous Treatment Enrollment	N	CRF	
ABC123	DC	ABC1231001004	DCSEQ	1	DCPREVEN	Previous Treatment Enrollment	N	CRF	
ABC123	DC	ABC1231001004	DCSEQ	2	DCPREVEN	Previous Treatment Enrollment	Y	CRF	
ABC123	DC	ABC1231001004	DCSEQ	2	DCPREVSN	Previous Subject Number	1004A	CRF	
ABC123	DC	ABC1231001004	DCSEQ	2	DCPREVTR	Previous Treatment	Treatment C	CRF	

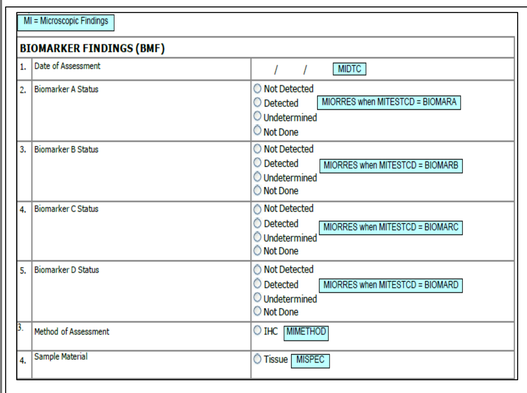
Fig.4: Illustrates the utilization of DC (Demographics as Collected) and SUPPDC in storing subject-level information within the platform trial. DC allows multiple records for the same subject, representing each participant within the trial. SUPPDC, on the other hand, collects enrollment data from previous cohorts, if applicable. It serves as a supplementary dataset, capturing additional information from prior cohort participation.

dm.xpt

STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	AGE	AGEU	SITEID	COUNTRY	ARMCD	ARM
ABC123	DM	ABC1231001001	1001A	2021-03-01	2023-04-01	2021-03-01	2023-04-01	35	YEARS	100	USA	TRTA	Treatment A
ABC123	DM	ABC1231001002	1002A	2021-03-16	2023-04-30	2021-03-16	2023-04-30	32	YEARS	100	USA	TRTB	Treatment B
ABC123	DM	ABC1231001003	1003A	2021-05-29	2022-06-02	2021-05-29	2022-06-02	40	YEARS	100	USA	TRTC	Treatment C
ABC123	DM	ABC1231001004	1004B	2022-06-15	2023-05-30	2022-06-15	2023-05-30	47	YEARS	100	USA	TRTD	Treatment D

Fig. 5: DM (Demographics) has only one record per USUBJID. The last participating SUBJID is used as a record to be represented in DM for re-enrollers.

Data Collection, SDTM mapping of Biomarker Data to MI (Microscopic Findings) Domain



STUDYID	DOMAIN	USUBJID	MISEQ	MITESTCD	MITEST	MIORRES	MISTRESC	MISPEC	MIMETHOD	MIDTC
ABC123	MI	ABC1231001001	1	BIOMARA	Biomarker A	DETECTED	DETECTED	TISSUE	IHC	2021-02-01
ABC123	MI	ABC1231001001	2	BIOMARB	Biomarker B	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-02-01
ABC123	MI	ABC1231001001	3	BIOMARC	Biomarker C	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-02-01
ABC123	MI	ABC1231001001	4	BIOMARD	Biomarker D	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-02-01
ABC123	MI	ABC1231001002	1	BIOMARA	Biomarker A	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-02-16
ABC123	MI	ABC1231001002	2	BIOMARB	Biomarker B	DETECTED	DETECTED	TISSUE	IHC	2021-02-16
ABC123	MI	ABC1231001002	3	BIOMARC	Biomarker C	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-02-16
ABC123	MI	ABC1231001002	4	BIOMARD	Biomarker D	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-02-16
ABC123	MI	ABC1231001003	1	BIOMARA	Biomarker A	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-04-29
ABC123	MI	ABC1231001003	2	BIOMARB	Biomarker B	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-04-29
ABC123	MI	ABC1231001003	3	BIOMARC	Biomarker C	DETECTED	DETECTED	TISSUE	IHC	2021-04-29
ABC123	MI	ABC1231001003	4	BIOMARD	Biomarker D	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-04-29
ABC123	MI	ABC1231001004	1	BIOMARA	Biomarker A	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-04-20
ABC123	MI	ABC1231001004	2	BIOMARB	Biomarker B	NOT DETECTED	NOT DETECTED	TISSUE	IHC	2021-04-20
ABC123	MI	ABC1231001004	3	BIOMARC	Biomarker C	DETECTED	DETECTED	TISSUE	IHC	2021-04-20
ABC123	MI	ABC1231001004	4	BIOMARD	Biomarker D	DETECTED	DETECTED	TISSUE	IHC	2021-04-20

Fig.6: Annotated CRF and SDTM compliant MI dataset. Subjects ABC1231001001, ABC1231001002 and ABC1231001003 have shown detectable levels of biomarkers A, B and C respectively. Subject ABC1231001004 exhibits detectable levels of both biomarkers C and D.

ADaM Datasets for Analysis Needs

adsl.xpt

STUDYID	USUBJID	SUBJID	BIOMRKSTT	COHORT	TRT01A	AAGE	AGEU	SAFFL	TRTSDT	TRTEDT
ABC123	ABC1231001001	1001A	BIOA	A	Treatment A	35	YEARS	Y	2021-03-01	2023-04-01
ABC123	ABC1231001002	1002A	BIOB	B	Treatment B	32	YEARS	Y	2021-03-16	2023-04-30
ABC123	ABC1231001003	1003A	BIOC	C	Treatment C	40	YEARS	Y	2021-05-29	2022-06-02
ABC123	ABC1231001004	1004B	BIOC+BIOD	D	Treatment D	47	YEARS	Y	2022-06-15	2023-05-30

Fig.7: ADSL contains one record per USUBJID. The ADSL dataset is derived from primary SUBJID in DM.

adtp.xpt

STUDYID	USUBJID	SUBJID	BIOMRKSTT	COHORT	TRT01A	AAGE	AGEU	SAFFL	TRTSDT	TRTEDT
ABC123	ABC1231001001	1001A	BIOA	A	Treatment A	35	YEARS	Y	2021-03-01	2023-04-01
ABC123	ABC1231001002	1002A	BIOB	B	Treatment B	32	YEARS	Y	2021-03-16	2023-04-30
ABC123	ABC1231001003	1003A	BIOC	C	Treatment C	40	YEARS	Y	2021-05-29	2022-06-02
ABC123	ABC1231001004	1004A	BIOC+BIOD	C	Treatment C	46	YEARS	Y	2021-05-20	2022-05-20
ABC123	ABC1231001004	1004B	BIOC+BIOD	D	Treatment D	47	YEARS	Y	2022-06-15	2023-05-30

Fig.8: ADTP (Trial Participation Analysis Dataset): The ADTP captures subject level analysis dataset at participate level. It contains one record per SUBJID as collected in DC

adlb.xpt

STUDYID	USUBJID	SUBJID	TRTA	PARAMCD	AVISIT	AVAL	ABLFL	BASETYPE	SAFFL	BASE	CHG
ABC123	ABC1231001004	1004A	TREATMENT C	ALT	Cycle 1 Day 1	30	Y	COHORT C	Y	30	
ABC123	ABC1231001004	1004A	TREATMENT C	ALT	Cycle 2 Day 1	31		COHORT C	Y	30	1
ABC123	ABC1231001004	1004A	TREATMENT C	ALT	Cycle 3 Day 1	110		COHORT C	Y	30	80
ABC123	ABC1231001004	1004A	TREATMENT C	ALT	End of Treatment	554		COHORT C	Y	30	524
ABC123	ABC1231001004	1004B	TREATMENT D	ALT	Cycle 1 Day 1	25	Y	COHORT D	Y	25	
ABC123	ABC1231001004	1004B	TREATMENT D	ALT	Cycle 2 Day 1	35		COHORT D	Y	25	10
ABC123	ABC1231001004	1004B	TREATMENT D	ALT	Cycle 3 Day 1	31		COHORT D	Y	25	6
ABC123	ABC1231001004	1004B	TREATMENT D	ALT	End of Treatment	31		COHORT D	Y	25	6

Fig. 9: ADLB, an analysis dataset generated by merging ADTP (Trial Participation Analysis Dataset) and LB/SUPPLB datasets. ADLB utilizes SUBJID and USUBJID as key identifier variables to accurately identify subjects. This allows analysis based on multiple participations by a subject by setting proper baseline flags and treatment values. BASETYPE identifies of baseline that corresponds to the value of BASE in each row.

Conclusions

- ❖ Platform trials have emerged as transformative approaches in oncology, significantly improving the efficiency of clinical trials.
- ❖ In the context of multiple enrollments in platform trials, careful attention is required for data collection and mapping to SDTM (Study Data Tabulation Model) standards.
- ❖ The trial design domains, TA (Trial Arms) and TE (Trial Elements), provide essential structure and information for platform trials.
- ❖ The DM domain captures one record per USUBJID, while the DC (Demographics as Collected) domain captures one record per enrollment (SUBJID).
- ❖ Biomarker data entry and mapping processes are crucial components of platform trials.
- ❖ The ADSL dataset is structured similarly to the DM domain.
- ❖ The ADTP (Trial Participation Analysis Dataset), akin to the DC domain, captures one record per trial participation, enabling comprehensive presentation of subject engagement.
- ❖ ADLB is created by merging ADTP and LB/SUPPLB datasets, facilitating the capture of lab data for each participating cohort by subject. This allows for analysis based on multiple participations, incorporating appropriate baseline flags and treatment values.

In conclusion, this presentation provides valuable insights into the practical aspects of data entry and data mappings to SDTM and ADaM standards, with a focus on addressing the challenges posed by re-enrollers in platform trials. The examples presented offer guidance for designing effective data entry and standardization systems to accommodate the complexities of clinical trials involving subjects participating in multiple cohorts.

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