

Paper #AS02

Unravelling the complexity: Efficacy Datasets in Oncology Basket Trials Across Multiple Disease Tumors



INVENTING
FOR LIFE

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About me

- Associate Principal Scientist, Stat programming at Merck & Co., Inc., Rahway, NJ, USA
- 12 Years of experience in SAS programming
- TA: Oncology, Vaccines, Immunology
- Experience using R as a programmer

Agenda

- Introduction
- What are Basket Trials
- Study Design/Overview
- Data Collection
- Efficacy Datasets in Oncology
- Derivation of an endpoint by subject and tumor type
- Conclusion

Introduction

❖ Oncology Basket Trials:

- Clinical trials designed to evaluate a single treatment across multiple tumor types

❖ Challenges:

- Complex subject data with multiple tumor types per cohort

❖ Role of ADaM Standards:

- Standardized datasets ensure consistency, traceability, and compliance.

❖ Focus of the Paper:

- Deriving and analyzing efficacy endpoints for subjects with multiple tumor types.

What are Basket Trials?

❖ Definition:

- Trials that evaluate treatment efficacy across tumor types sharing molecular/genetic markers.

❖ Why are They Important?

- Ideal for rare or heterogenous tumors

❖ Examples of Cohorts:

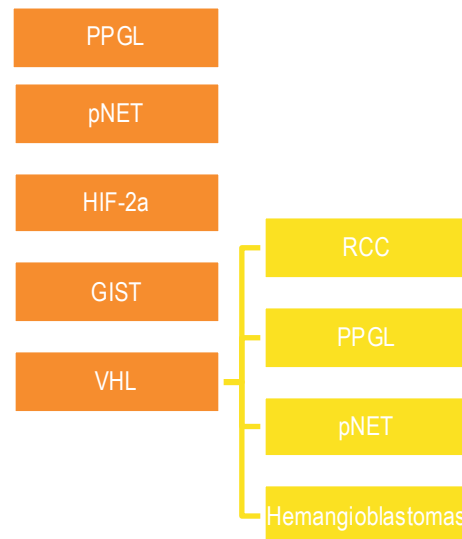
- PPGL, pNET, VHL

❖ Benefits:

- Faster identification of effective treatments
- Optimized trial design for rare diseases.

Study Design and Overview

Study to evaluate the efficacy and safety of a study treatment in Participants With Advanced Pheochromocytoma/Paraganglioma (PPGL), Pancreatic Neuroendocrine Tumor (pNET), Von Hippel-Lindau (VHL) Disease-Associated Tumors, Advanced Gastrointestinal Stromal Tumor (wt GIST), or Advanced Solid Tumors With HIF-2a Related Genetic Alterations.



Study Design and Overview Cont..

Endpoints of Interest:

- Best Overall Response (BOR)
- Tumor Percent Change
- Progression-Free Survival (PFS)
- Overall Survival

Complexity:

- Handling multiple tumors per subject

Data Collection

Key Variables:

- Subject ID
- Tumor Type
- Assessment Dates
- Response Variable

Example for TR/SUPPTR

*TUMORTYP mapped to SUPPXX

USUBJID	TUMORTYP	TRTESTCD	TRTEST	TRTSTDTL	TRDTC	TORRES	TORRESU	TRBLFL
101	RCC	LDIAM	Longest Diameter	TARGET	2024-01-01	50	mm	Y
101	RCC	LDIAM	Longest Diameter	TARGET	2024-01-15	45	mm	
101	PPGL	LDIAM	Longest Diameter	TARGET	2024-01-01	40	mm	Y
101	PPGL	LDIAM	Longest Diameter	TARGET	2024-01-15	35	mm	
101	pNET	LDIAM	Longest Diameter	TARGET	2024-01-01	30	mm	Y
101	pNET	LDIAM	Longest Diameter	TARGET	2024-01-15	28	mm	

Example for RS/SUPPRS

USUBJID	TUMORTYP	RSTESTCD	RSTEST	RSORRES	RSDTC	RSSEQ	RSBLFL
101	RCC	OVRLRESP	Overall Response	PR	2024-01-15	1	
101	PPGL	OVRLRESP	Overall Response	CR	2024-01-15	2	
101	pNET	OVRLRESP	Overall Response	SD	2024-01-15	3	
101	RCC	OVRLRESP	Overall Response	PD	2024-02-01	4	
101	pNET	OVRLRESP	Overall Response	PR	2024-02-01	5	

Key Datasets and Their Roles

ADTL

Captures data related to target Lesions

ADRS

Tracks and analyzes tumor response over time.

ADINTDT

Intermediate dates dataset capturing key dates for efficacy analysis.

ADTTE

Records time-to-event data like survival times and progression-free survival.

ADTL (Analysis Dataset for Target Lesions)

Purpose: ADTL captures tumor measurements overtime to evaluate changes in target lesion size for efficacy endpoints like % **change from baseline** and response assessments.

Options Discussed:

- Option 1
Create a unique PARAMCD for each tumor type. Pros: Clear distinction
- Option 2
Use a single PARAMCD with a TUMORTYP variable. Pros: Simplified structure; Cons: Potential validation issues.

Solving Validation Issues:

Introducing the BASETYPE variable can resolve P21 validation issues.

USUBJID	PARAMCD	PARAM	AVISIT	AVAL	ADT	ABLFL
101	RCC_SLD	SLD (RCC)	Baseline	50.0	2024-01-01	Y
101	RCC_SLD	SLD (RCC)	Week 2	45.0	2024-01-15	
101	PPGL_SLD	SLD (PPGL)	Baseline	40.0	2024-01-01	Y
101	PPGL_SLD	SLD (PPGL)	Week 2	35.0	2024-01-15	
101	pNET_SLD	SLD (pNET)	Baseline	30.0	2024-01-01	Y
101	pNET_SLD	SLD (pNET)	Week 2	28.0	2024-01-15	

USUBJID	PARAMCD	PARAM	AVISIT	AVAL	ADT	ABLFL	TUMORTYP	BASETYPE
101	SLD	SLD	Baseline	50.0	2024-01-01	Y	RCC	RCC
101	SLD	SLD	Week 2	45.0	2024-01-15		RCC	RCC
101	SLD	SLD	Baseline	40.0	2024-01-01	Y	PPGL	PPGL
101	SLD	SLD	Week 2	38.0	2024-01-15		PPGL	PPGL
101	SLD	SLD	Baseline	30.0	2024-01-01	Y	pNET	pNET
101	SLD	SLD	Week 2	28.0	2024-01-15		pNET	pNET

ADRS (Analysis Dataset for Response)

ADRS captures derived response assessments such as Best Overall Response (BOR) – Complete Response (CR), and Partial Response (PR).

Derivation: Deriving the BOR per subject and tumor type by sorting the dataset by subject, tumor type, and analysis time point and pick the best response within each subject-tumor combination.

USUBJID	PARAMCD	AVISIT	ADT	AVAL	AVALC	TUMORTYP	BOR
101	OVRRESP	Baseline	2024-01-01	2	PR	RCC	PR
101	OVRRESP	Week 4	2024-02-01	1	CR	RCC	CR
101	OVRRESP	Week 8	2024-03-01	3	SD	RCC	CR
101	OVRRESP	Baseline	2024-01-01	3	SD	PPGL	SD
101	OVRRESP	Week 4	2024-02-01	2	PR	PPGL	PR
101	OVRRESP	Week 8	2024-03-01	4	PD	PPGL	PR

ADINTDT (Intermediate Dates Dataset for ADTTE)

ADINTDT dataset captures essential dates for analyzing efficacy endpoints such as DOR, PFS, and OS

Derivation: Date parameters, such as Date of Progression and date of First CR, are derived by subject and tumor type. The dataset is sorted by subject, tumor type, and analysis date to identify the required record within each subject-tumor type combination.

USUBJID	PARAMCD	ADT	TUMORTYP
101	DISCDT	2024-05-15	
101	DTHDT	2024-06-01	
101	IRCPDDT	2024-02-15	RCC
101	IRCPDDT	2024-03-10	PPGL
101	IRCPDDT	2024-03-20	pNET
101	IRCPDDT	2024-04-05	CNS
102	DTHDT	2024-04-15	
102	IRCPDDT	2024-01-25	CNS

ADTTE (Time to Event Analysis Dataset)

This dataset records time-to-event data (PFS, DOR, OS) per subject and tumor type. Events are derived using ADINTDT dataset by transposing date variables and capturing separate progression-free survival endpoints for each tumor type.

Derivation: Time-to-event endpoints (e.g., PFS, DOR, TTR) are derived per subject and tumor type, not just per subject. Date variables (e.g., progression or response dates) are extracted from the transposed ADINTDT dataset, structured by USUBJID, TUMORTYP, and PARAMCD, ensuring independent calculations for each tumor type.

USUBJID	TUMORTYP	DISCDT	DTHDT	IRCPDDT
101	RCC	2024-05-15	2024-06-01	2024-02-15
101	PPGL	2024-05-15	2024-06-01	2024-03-10
101	pNET	2024-05-15	2024-06-01	2024-03-20
101	CNS	2024-05-15	2024-06-01	2024-04-05
102	CNS		2024-04-15	2024-01-25

USUBJID	TUMORTYP	EVENTDESC	CNSDTDSC	PARAMCD	ADT	CNSR
101	RCC	Documented Progression		PFS	2024-07-15	0
101	PPGL	Documented Progression		PFS	2024-07-10	0
101	pNET	No adequate post-baseline disease assessment	First dose date	PFS	2024-03-25	1
101	CNS	No adequate post-baseline disease assessment	First dose date	PFS	2024-04-01	1
102	CNS	Documented Progression		PFS	2024-06-25	0
102	CNS	No adequate post-baseline disease assessment	First dose date	PFS	2024-02-15	1

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Your comments and questions are valued and encouraged. You may contact authors at:

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Questions?

Thank you!