

PP02

The Journey of Deriving the Best Overall Response (BOR) for Solid Tumors – A Programmer’s Perspective

INTRODUCTION

- BOR** = Best tumor response until progression or discontinuation.
- Best Overall Response (BOR)** captures the most favorable tumor response observed over the course of treatment.
- Key for **Objective Response Rate (ORR)** in early phase trials.
- Influenced by **response criteria** (*RECIST*, *mRECIST*, *iRECIST*), **assessment timing**, and **confirmation rules**.
- Trial completion status** (*completed*, *ongoing*, *discontinued*) directly affects response confirmation.
- Incomplete follow-up** or **missing data** can alter final BOR interpretation.
- BOR** should be interpreted alongside **ORR**, **OS**, **PFS** and Safety.

METHODOLOGICAL IMPACT ON BOR

Differences in tumor measurement, response thresholds, confirmation rules, and handling of new lesions across response criteria contribute to variability in BOR derivation.

	RECIST 1.1	mRECIST 1.1	iRECIST 1.1
Tumor Measurement	Size-based	Viable Tumor	Size-based
Confirmation Requirement	Trial Specific	Usually Required	Mandatory
New Lesion Handling	Immediate PD	PD if Viable	iUPD Confirmation Pending
Sensitivity to Pseudo Progression	Low	Low	High

IMPLECATION & RECOMMANDATIONS

- Pre-specify response criteria and confirmation rules in protocol and analysis plans.
- Align response criteria with **therapeutic mechanism of action**.
- Clearly define handling of **trial completion status**.
- Report **sensitivity analyses** using alternative criteria.

CONCEPTUAL FRAMWORK OF BOR

- BOR as a Derived Endpoint** – Retrospective from serial tumor assessments post baseline.
- Sensitive to follow-up duration, assessment timings, and trial specific confirmation rules.

BOR
Responder

ORR
Objective
Response
Rate

DoR
Duration of
Response

Any inaccuracy or inconsistency in BOR determination can propagate to these downstream metrics, potentially impacting conclusions about therapeutic efficacy and trial success.

Limitations

- Does not reflect durability of response or timing of response onset.
- Limited ability to capture clinical benefit in patients with stable disease.

IMPACT OF TRIAL COMPLETION STATUS ON BOR

	Initial Response	Confirmation	BOR
Completed	PR	Yes	Confirmed PR
Ongoing	PR	Pending	Unconfirmed PR
Early Disc.	PR	No	PR not confirmed
Lost to follow-up	PR	No	NE

CONCLUSION

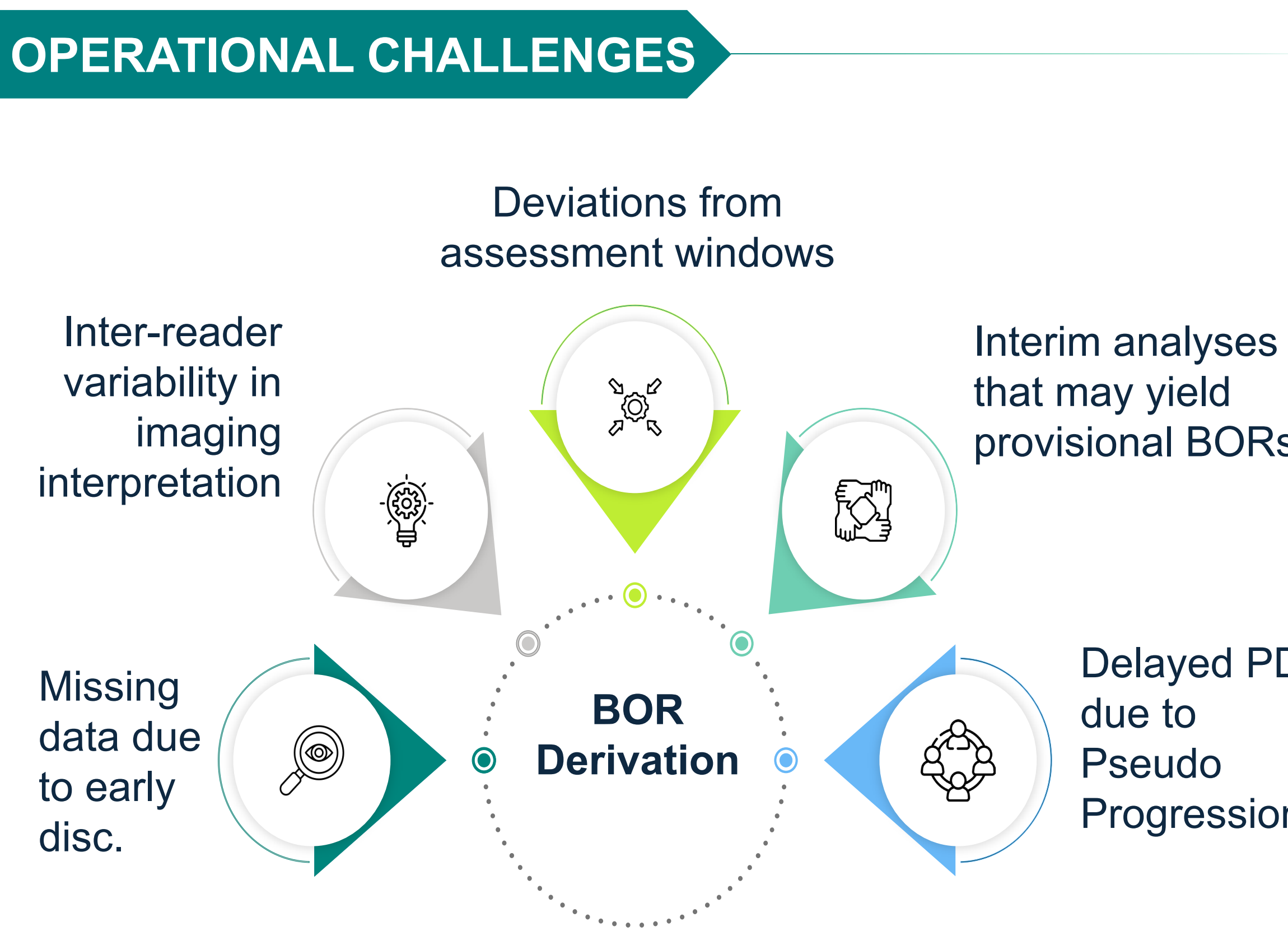
BOR captures the best tumor response over time in oncology trials.

BOR varies by criteria (RECIST, mRECIST, iRECIST) and trial completion status.

Methodology and confirmation rules drive interpretation and regulatory confidence.

RESPONSE EVALUATION CRITERIA IN SOLID TUMOR

	RECIST 1.1	mRECIST 1.1	iRECIST 1.1
CR Complete Response	Disappearance of all lesions	Disappearance of viable tumor	iCR (confirmed)
PR Partial Response	>30% decrease in lesion size	>30% decrease in viable tumor	iPR (confirmed)
SD Neither PR nor PD	Neither PR not PD	Neither PR nor PD	iSD
PD >20% increase/new lesion	>20% increase / new lesion	Increase in viable tumor	iUPD/iCPD
NE Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data



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