Comparison of Key Differences In RECIST v1.1, irRC(irRECIST) and iRECIST

Hitesh Thacker, Covance Clinical Development Pvt. Ltd., Bangalore, India

IASCT
Indian Association for Statistics in Clinical Trials

RECIST v1.1 overview

Response Evaluation Criteria in Solid Tumors (RECIST)
- Initially published in 2000
- Revised in 2009 as version 1.1

Pragmatic methodology to evaluate the activity and efficacy of new cancer therapeutics in solid tumors

Most of oncology trials have typically used RECIST 1.1 to define the primary and secondary efficacy based endpoints

Emergence of irRC and irRECIST

Immuno-therapies
- The novel mechanism of action of immunotherapeutic drugs, with immune and T-cell activation, lead to unusual patterns of response that resemble tumor flare but are more pronounced and more frequent than previously described responses

Pseudo-progression
- In early trials of immune-based therapeutics in melanoma, investigators described unique response patterns, termed pseudo-progression

irRC irRECIST
- In 2009, modified response criteria based on WHO criteria were proposed – the immune-related response criteria (irRC)
- In 2013, researchers published revised irRC based on the original RECIST; subsequent recommendations seem to incorporate RECIST 1.1, often referred to as irRECIST

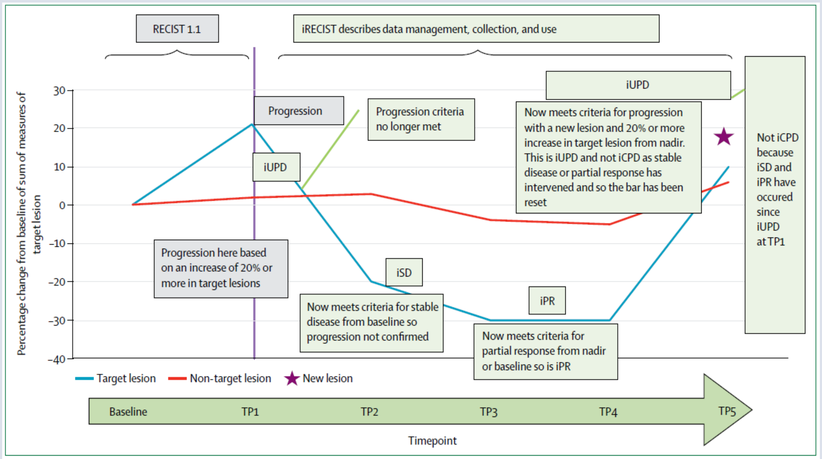
iRECIST

- irRECIST criteria have not always been consistently applied; use of independent imaging review by a commercial entity instead of investigator assessments led to concerns about the comparability of data and poor clarity on new lesion
- Hence, the RECIST working group decided to develop a guideline for the use of a modified RECIST to ensure consistent design and data collection
- iRECIST guidelines were eventually published in 2017
- In iRECIST, objective tumor response principles are largely unchanged from RECIST 1.1, but major change in the concept of progression
- iRECIST responses have a prefix of “i” (i.e., immune) – e.g., “immune” Complete Response (iCR) or “immune” partial response (iPR), etc.

Key differences in response evaluation

	RECIST 1.1	irRECIST	iRECIST
Target and non-target lesions	Sum of the longest diameters of target lesions (uni-dimensional) Measurable lesions are ≥10 mm in diameter (≥15 mm for nodal lesions) Maximum of five lesions (two per organ)		
New lesion	Represents PD	Does not correspond to a formal progression The longest diameter will be added to the total measured tumour burden of all target lesions at baseline.	Does not correspond to a formal progression Is not incorporated in tumour burden
CR	Disappearance of all target and non-target lesions Nodal short axis diameter <10 mm No new lesions		
PR	Decrease of ≥30% in tumour burden relative to baseline Non-unequivocal progression of non-target lesions No new lesions		
SD	Neither PR nor PD		
PD	Increase ≥20% of the sum of LD compared with nadir (minimum 5 mm) or progression of non-target lesions or new lesion	**irPD** Increase ≥ 20% (minimum 5 mm) in TMTB compared with nadir or progression of non-target lesions or new lesion Confirmation of progression recommended minimum 4 weeks after the first irPD assessment	**iUPD** Increase ≥ 20% of the sum of LD compared with nadir (minimum 5 mm) or progression of non-target lesions or new lesion Confirmation of progression recommended minimum 4 weeks after the first iUPD assessment
Confirmed PD	Not required	New unequivocal progression or worsened progression from initial PD visit Appearance of another new lesion	**iCPD** Increased size of target or non-target lesions Increase in the sum of new target lesions > 5 mm Progression of new non-target lesions Appearance of another new lesion

Response assessment in RECIST1.1 vs iRECIST



Assignments of best overall response using iRECIST

	Timepoint response 1	Timepoint response 2	Timepoint response 3	Timepoint response 4	Timepoint response 5	iBOR
Example 1	iCR	iCR, iPR, iUPD, or NE	iCR, iPR, iUPD, or NE	iUPD	iCPD	iCR
Example 2	iUPD	iPR, iSD, or NE	iCR	iCR, iUPD, or NE	iCR, iPR, iSD, iUPD, iCPD, or NE	iCR
Example 3	iUPD	iPR	iPR, iSD, iUPD, or NE	iPR, iSD, iUPD, NE, or iCPD	iPR, iSD, iUPD, NE, or iCPD	iPR
Example 4	iUPD	iSD or NE	iPR	iPR, iSD, iUPD, or NE	iPR, iSD, iUPD, iCPD, or NE	iPR
Example 5	iUPD	iSD	iSD, iUPD, or NE	iSD, iUPD, iCPD, or NE	iSD, iUPD, iCPD, or NE	iSD
Example 6	iUPD	iCPD	Any	Any	Any	iCPD
Example 7	iUPD	iUPD (no iCPD)	iCPD	Any	Any	iCPD
Example 8	iUPD	NE	NE	NE	NE	iUPD

References

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