

iRECIST was developed in 2017 by the RECIST working group modifying RECIST 1.1 for use in cancer immunotherapy trials. The goal is to ensure consistent design and data collection to facilitate the ongoing collection of clinical trial data and ultimate validation.



Tumor Response to Immunotherapy

PATTERNS OF RESPONSE OBSERVED WITH IMMUNOTHERAPIES:



Delayed response



Hyperprogression



Response after initial disease progression (flare/pseudoprogression)



Differentiated Response



Key PointsCOMPARING RECIST 1.1

iRECIST starts once PD is determined per RECIST 1.1

AND IRECIST



Progression is sub-divided into unconfirmed (iUPD) and confirmed progression (iCPD). First PD per RECIST 1.1 is "unconfirmed" (iUPD). At following time point, progression can be "confirmed" (iCPD) or tumor shrinkage can be observed (iSD/iPR/iCR). iUPD can be assigned multiple times as long as iUPD is not confirmed or conditions are not met to call for iSD, iPR or iCR.

Key Points	RECIST 1.1	iRECIST
Target Lesions	Measurable lesions ≥10 mm in longest diameter (≥15 mm in short axis for nodal lesions); maximum of five lesions (two per organ)	No change from RECIST 1.1
Non Target Lesions	All other lesions (must be ≥10 mm in short axis for nodal disease)	No change from RECIST 1.1
New Lesions	Appearance of new lesions causes PD	New lesions are assessed as per RECIST 1.1 and recorded separately New Lesions Target: Measurable lesions ≥10 mm in longest diameter (≥15 mm in short axis for nodal lesions); maximum of five lesions (two per organ). Measurements are not included in baseline SOD New Lesions Non Target: All other lesions (must be ≥10 mm in short axis for nodal disease)
Progression Confirmation	Not required	Required
Clinical Status	Not considered	Considered when deciding whether treatment is continued after iUPD





Confirmation of Progression

PROGRESSION IS CONFIRMED (iCPD) IF:

Worsening is observed in the lesion category where progression was first identified (further increase in size or in number of lesions)

OR

Progression as defined by RECIST 1.1 is observed in lesion categories that had not previously met RECIST 1.1 progression criteria







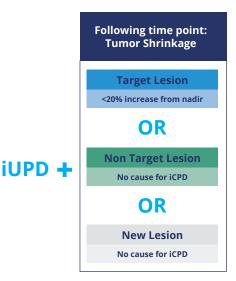


Resetting the BarTHE BAR IS RESET WHEN:

Baseline tumor shrinkage is observed meeting the criteria of iCR, iPR or iSD. When the bar is reset there is no impact on the nadir values

Target Lesions weight more heavily than Non Target Lesions or New Lesions. iUPD resolves to iSD or iPR when:

- No drivers of iCPD are observed (i.e., no new cause of PD or worsening of any existing cause)
- Target Lesions are below the PD threshold whether they were or were not PD at the initial iUPD scan even if New Lesions are still present or Non Target Lesions have not reduced in size.



= iSD/iPR

iUPD



Progression

AFTER THE BAR WAS PREVIOUSLY RESET:



CONCEPTS & LEXICON

iCR = Immune Complete Response

iNADIR = Smallest Sum of New Lesions Target

iPR = Immune Partial Response

iSD = Immune Stable Disease

iUPD = Immune Unconfirmed Progression

iCPD = Immune Confirmed Progression

NADIR = Smallest Sum of Target Lesions

NLT = New Lesion Target

NLNT = New Lesion Non Target

UNEQ. = Unequivocal

"PSEUDOPROGRESSION":

The stimulation of the immune system falsely interpreted as progression on imaging (e.g., inflammation around the tumor). PD/iUPD needs to be confirmed at subsequent time point.

"RESETTING THE BAR":

When RECIST 1.1 progression is followed at the next assessment by tumor shrinkage the bar is reset. Progression needs to occur again (compared to nadir values) and be confirmed at subsequent time point to get iCPD.

"WORSENING":

Defined as further progression in the lesion category that triggered an initial PD per RECIST 1.1.