

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.

## 1

## Tumor Response to Immunotherapy

PATTERNS OF RESPONSE OBSERVED WITH IMMUNOTHERAPIES:



**Delayed response**



**Hyperprogression**



**Response after initial disease progression (flare/pseudoprogression)**



**Differentiated Response**

## 2

## Key Points

COMPARING RECIST 1.1 AND iRECIST

**+** iRECIST starts once PD is determined per RECIST 1.1

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

## 3

## 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



## 4

## Resetting the Bar

THE 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.

iUPD +

Following time point:  
Tumor Shrinkage

Target Lesion

&lt;20% increase from nadir

OR

Non Target Lesion

No cause for iCPD

OR

New Lesion

No cause for iCPD

= iSD/iPR

## 5

## Progression

AFTER THE BAR WAS PREVIOUSLY RESET:

iSD/iPR +

Following time point: Progression

Target Lesion

≥20% Increase

OR

Non Target Lesion

Any progression if previously progressed or uneq. progression

OR

New Lesion

 NLT: ≥5mm Increase (iNadir)  
 NLNT: Any Progression New New Lesion

= iUPD

## CONCEPTS &amp; 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.