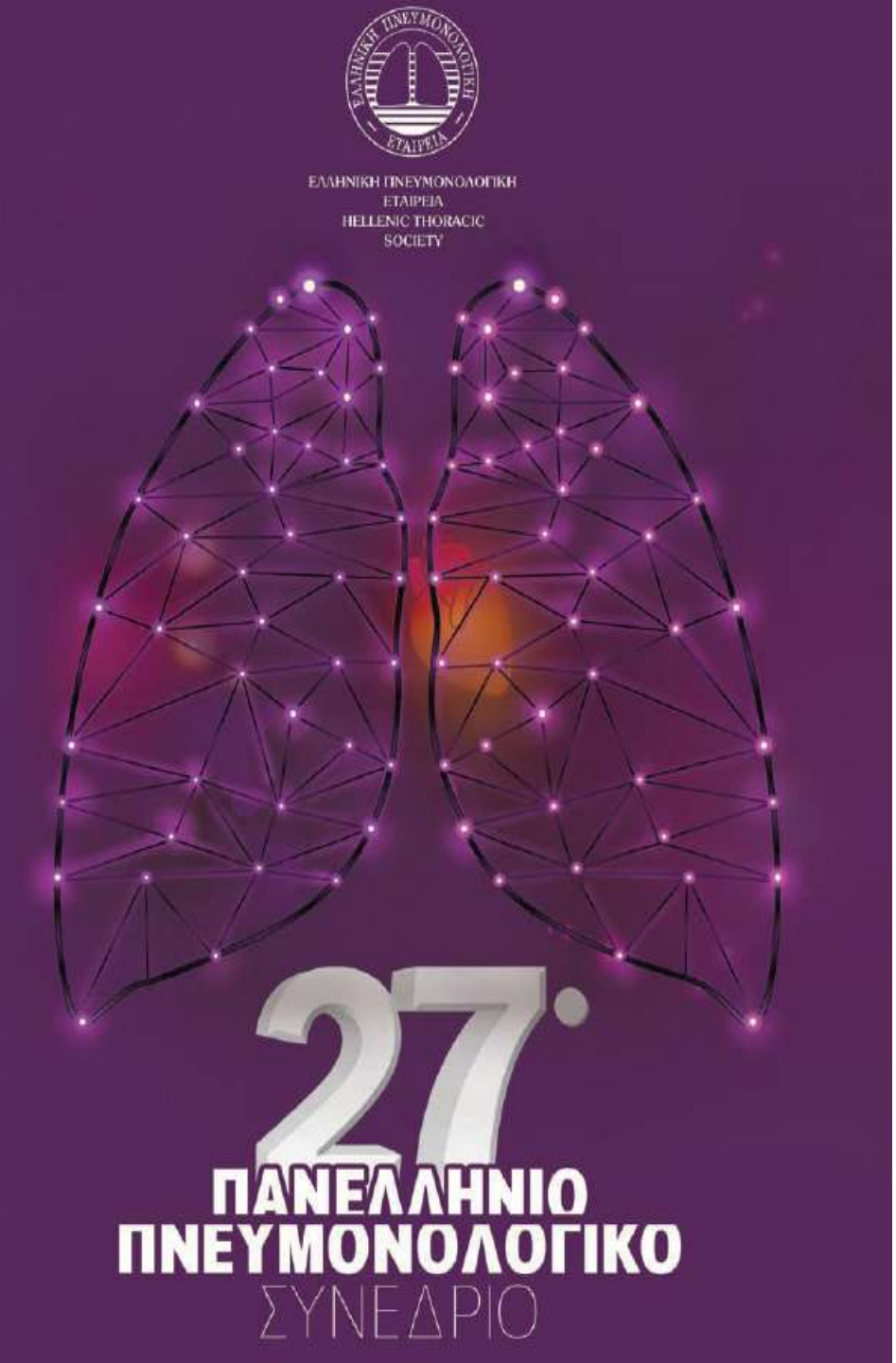


Απεικονιστική Εκτίμηση Ανταπόκρισης στην Ανοσοθεραπεία

Ιωάννης Χ. Γκιόζος
Πνευμονολόγος MD, PhD, FCCP

Ογκολογική Μονάδα
Γ΄Πανεπιστημιακή Παθολογική Κλινική
ΝΝΘΑ "Η Σωτηρία"

TUMOR RESPONSE CRITERIA

A set of published mainly imaging rules that define when cancer patients improve "respond", stay the same "stable" or worsen "progression" during treatments, which is a "common language" between care givers.

	WHO (bidimensional response asses)	RECIST v1.1 (unidimensional response asses)
CR	Disappearance of all target lesions without any residual lesion; confirmed at 4 weeks	Disappearance of all target lesions; confirmed at 4 weeks
PR	50% or more decrease in target lesions, without a 25% increase in any one target lesion; confirmed at 4 weeks	≥30% reduction in the sum of the longest diameter of target lesions, taking as reference the baseline study; confirmed at 4 weeks
SD	Neither PR or PD criteria are met	Neither PR nor PD criteria are met, taking as reference the smallest sum of the longest diameter recorded since treatment started
PD	≥25% increase in the size of measurable lesion or appearance of new lesions	≥20% increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum longest diameter recorded since treatment started or appearance of new lesions

Padhani AR, Ollivier L. *Br J Radiol*. 2001;74:983–986

Essentials for immunotherapy effects on Response Assessment

Immune-related Response Criteria

RECIST1.1 remains the gold standard for evaluating treatment response in solid tumors

- However, new lesions or flare equals progressive disease under RECIST1.1 guidelines
- Inaccurate interpretation of response can result in premature termination of therapy and patient removal from a trial

Need new response criteria

- **Immune-related response criteria (irRC)**, 2009
  - Based on WHO criteria
- **Immune-related RECIST (irRECIST)**, 2013
  - Combines elements of irRC and RECIST
- **Immune RECIST (iRECIST)**, 2017
  - Standardizes and validates immune response criteria
- All account for novel response patterns seen with immunotherapies

irRC – irRECIST – iRECIST

Measurement Modality	irRC: Bidimensional (Longest Diameter × Longest Perpendicular Diameter)	irRECIST: Unidimensional (Longest Diameter)	iRECIST: Unidimensional (Longest Diameter)
Baseline lesion size, mm	5 × 5	≥ 10	≥ 10
Minimum no. of lesions to be measured for assessment	10 lesions in total; 5 per organ	5 lesions in total; 2 per organ	5 lesions in total; 2 per organ
Appearance of new lesions	Incorporated in the sum of the measurements	Incorporated in the sum of the measurements	iUPD; becomes iCPD if PD is eventually confirmed
CR	Disappearance of all lesions	Disappearance of all lesions	Disappearance of all lesions
PR	≥ 50% decrease from baseline	≥ 30% decrease from baseline	≥ 30% decrease from baseline
SD	Neither CR nor PD is met	Neither CR nor PD is met	Neither CR nor PD is met
PD	≥ 25% increase in the nadir of the sum of target lesions	≥ 20% increase in the nadir of the sum of target lesions with a minimum of 5 mm	≥ 20% increase in the nadir of the sum of target lesions with a minimum of 5 mm
Confirmation of PD	Yes	Yes, at least 4 weeks after, and up to 12 weeks	Yes, at least 4 weeks after, and up to 8 weeks

Abbreviations: irRC, immune-related response criteria; irRECIST, immune-related RECIST; iRECIST, immunotherapy RECIST; iUPD, immune unconfirmed progressive disease; iCPD, immune confirmed progressive disease; PD, progressive disease; CR, complete response; PR, partial response; SD, stable disease.

Brocoman E, 2018 ASCO Educational Book

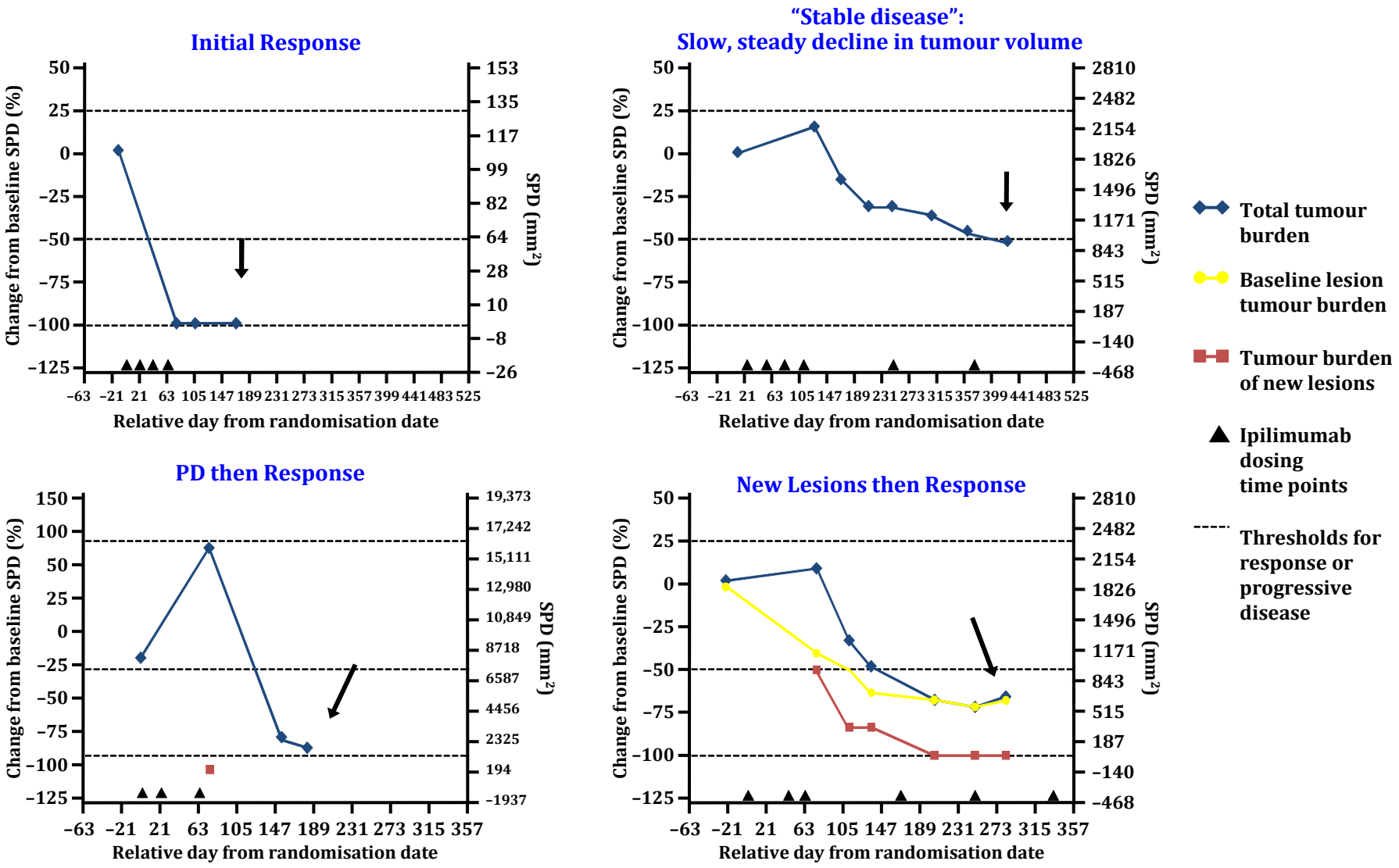
iRECIST 2017

Seymour et al. Lancet Oncol 2017;18:e143-52

- Developed by the RECIST working group
- Standardizes and validates immune response criteria
- Addresses key questions about tumor assessment with immunotherapy

- Resetting the bar if RECIST Progressive Disease (PD) is followed at next time point (TP) by tumor shrinkage
- New overall response is defined as “iUPD” or immune unconfirmed progressive disease

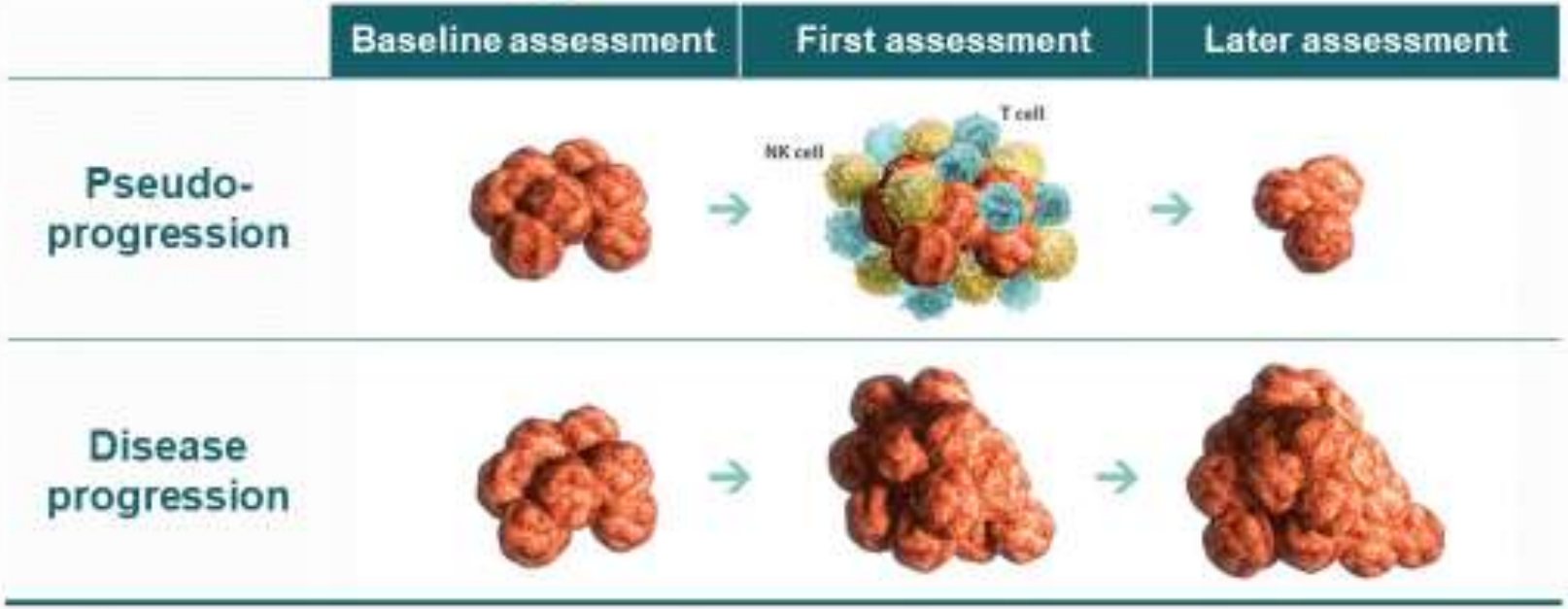
Patterns of response to cancer immunotherapy can be heterogeneous



RECIST OR WHO CRITERIA MAY NOT BE APPROPIATE TO ASSESS

Wolchok JD, et al. *Clin Cancer Res* 2009;15:7412–7420

Pseudoprogression



- Pseudoprogression may be due to
  - tumor infiltration by immune cells *or*
  - continued tumor growth until a sufficient response develops (transient progression)

Radiologic Pseudoprogression during Anti-PD-1 Therapy for Advanced Non-Small Cell Lung Cancer

Sharyn I. Katz, MD, MTR,[a,*] Mark Hammer, MD,[a,b] Stephen J. Bagley, MD,[c] Charu Aggarwal, MD, MPH,[c] Joshua M. Bauml, MD,[c] Jeffrey C. Thompson, MD,[c] Arun C. Nachiappan, MD,[a] Charles B. Simone II, MD,[d] Corey J. Langer, MD[c]

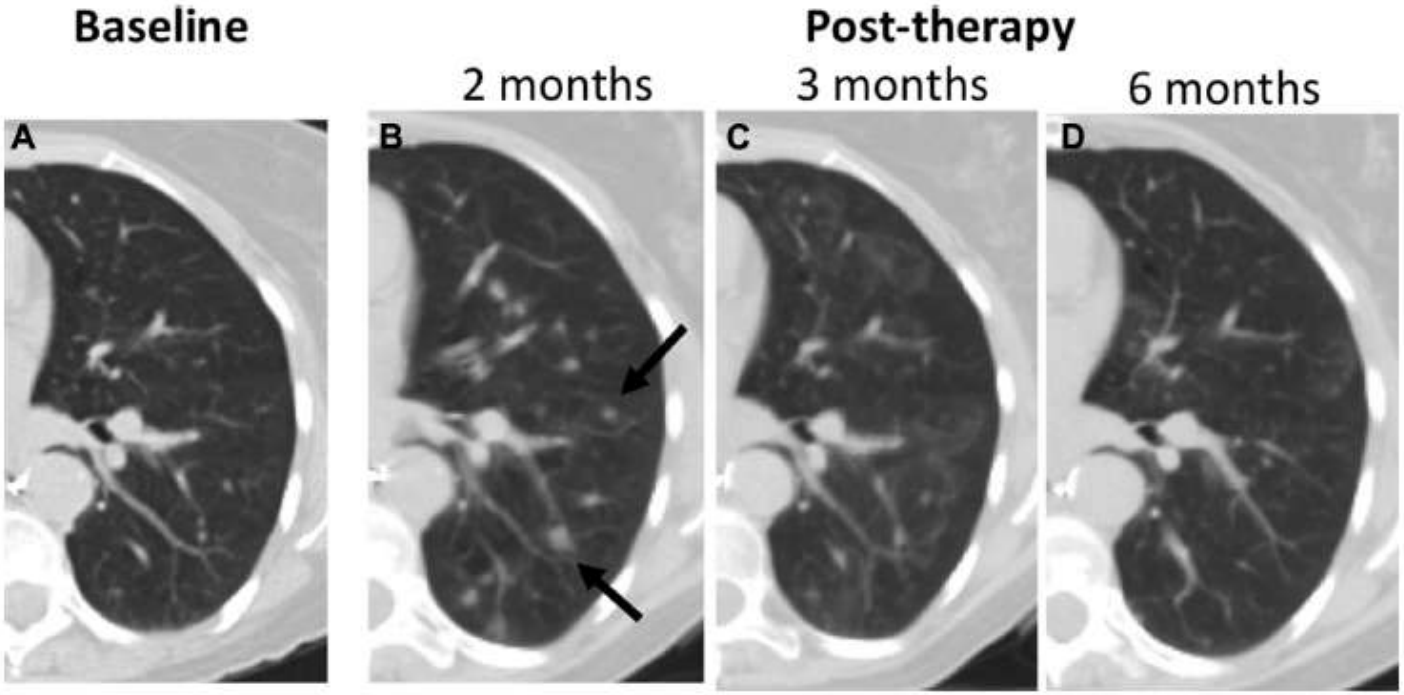


Figure 2. Radiologic pseudoprogression in a patient with NSCLC who was receiving nivolumab therapy. (*A*) Axial computed tomography images from a 68-year-old patient with adenocarcinoma of the lung after a lobectomy with known pulmonary metastasis (*arrows*) at baseline. (*B*) At 2 months of therapy there were new and enlarged pulmonary nodules. By 3 months of therapy, the pulmonary nodules had decreased in size and number (*C*) and at 6 months of therapy they had nearly resolved (*D*).

Most Clinically Suspected Cases of Radiologic Pseudoprogression in NSCLC Being Treated with Anti-PD-1 Agents Were True Cancer Progression

Last Evaluation of Response is iRECIST in Immunotherapies

iRECIST: guidelines for response criteria for use in trials testing immunotherapeutics

Lesley Seymour, Jan Bogaerts, Andrea Perrone, Robert Ford, Lawrence H Schwartz, Sumithra Mandrekar, Nancy U Lin, Saskia Litière, Janet Dancey, Alice Chen, F Stephen Hodi, Patrick Therasse, Otto S Hoekstra, Lalitha K Shankar, Jedd D Wolchok, Marcus Ballinger, Caroline Caramella, Elisabeth G E de Vries, on behalf of the RECIST working group

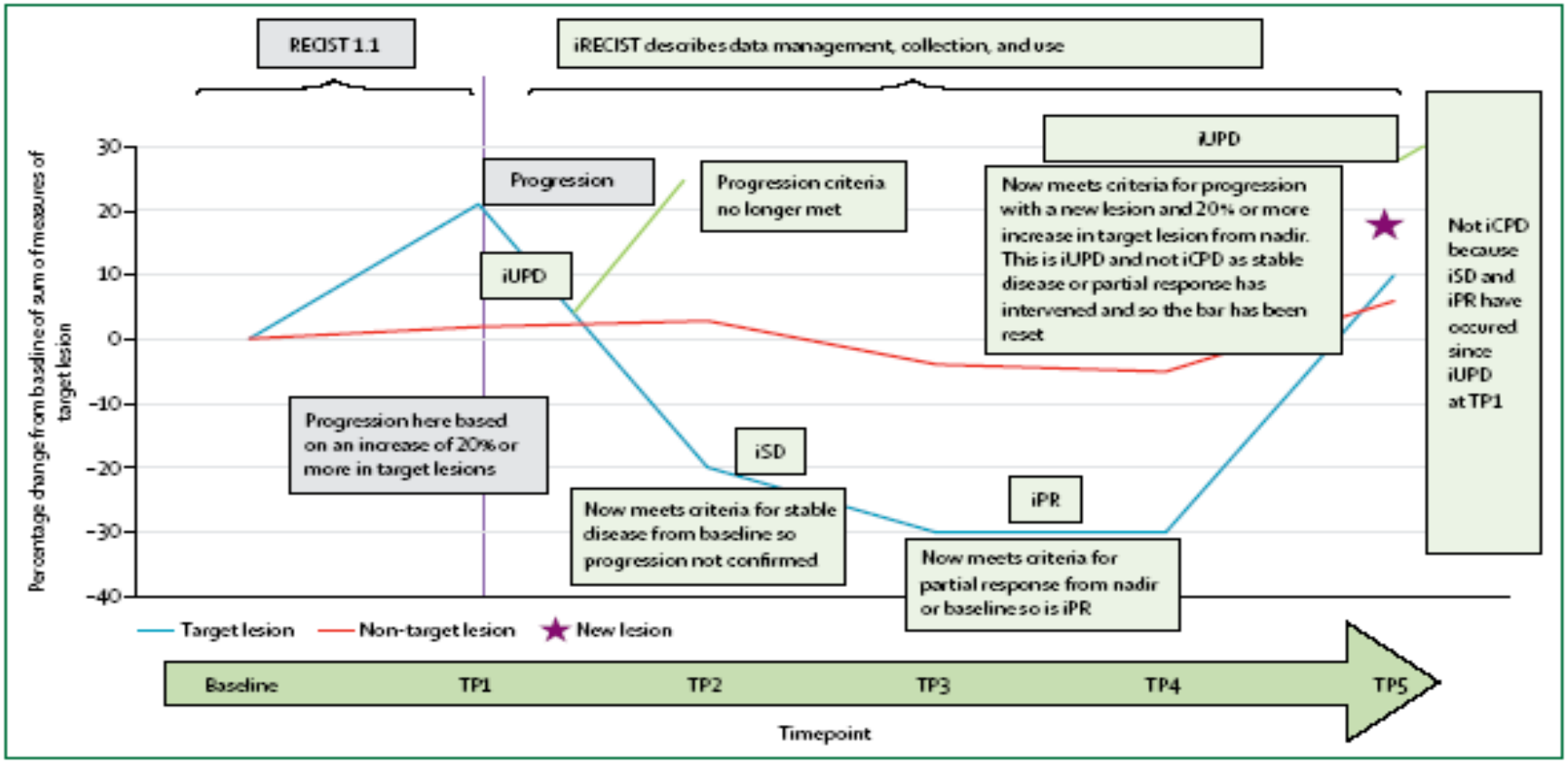


Figure 2: RECIST 1.1 and IRECIST: an example of assessment

Prefix "I" indicates immune responses assigned using IRECIST; others without "I" are confirmed by RECIST 1.1. RECIST=Response Evaluation Criteria in Solid Tumours. ICR=complete response. ICPD=complete progression. IPR=partial response. ISD=stable disease. IUPD=unconfirmed progression. TP=timepoint.

These guidelines are not intended to define or guide clinical practice or treatment decisions, but rather to provide a consistent framework for the management of data collected in clinical trials of immune-based therapies. Treatment decisions rest with the patient and their health-care team.

RECIST

RECIST Working Group

RECIST (Response Evaluation Criteria in Solid Tumours) provides a simple and pragmatic methodology to evaluate the activity and efficacy of new cancer therapeutics in solid tumors, using validated and consistent criteria to assess changes in tumor burden. The RECIST Working Group comprises representatives of the European Organization for Research and Treatment of Cancer (EORTC), National Cancer Institute (NCI) of the United States and Canadian Cancer Trials Group (CCTG), as well as several pharmaceutical companies. Its mission is to ensures that RECIST undergoes

http://www.eortc.org/recist/contact-us/

- New Imaging Assessment Tool for Response Rate Evaluation of Immunotherapy, Based on Clinical Trials

- The Understanding of full potential of Immunotherapies depends on new tools such as iRECIST