Come valutare la risposta clinica: dai RECIST ai PERCIST

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Dai RECIST ai PERCIST

Anatomic Response Criteria

Metabolic Response Criteria

WHO
RECIST 1.0
RECIST 1.1

IRRC
Melanoma

CHOI Criteria in GIST
mRECIST in HCC
CHESON in Lymphoma
PERCIST

RESPONSE CRITERIA IN ONCOLOGY

Development pathway for cancer therapeutic

Management of patients on therapy

ANATOMIC RESPONSE CRITERIA

1981 WHO published the first tumor response criteria

Miller AB et al:Cancer 1981

Table 2
Summary of Key Changes for WHO,

Criterion	WHO
Definition of "measurable" lesions	Should be measurable in two dimensions, no minimum lesion size
Method of measurement	SPD
Lymph nodes	Unspecified
Definition of progressive disease	≥25% increase in SPD
Number of lesions measured	N/A
New lesions	N/A
Guidance for imaging studies	N/A

Note.—MRI = MR imaging, N/A = not applicable.

The WHO Criteria

Introduced the concept of overall assessment of tumor burden on the basis of the sum of the products of diameters (SPD)

Evaluation of changes from baseline during therapy

ANATOMIC RESPONSE CRITERIA

2000 WHO, NCI, EORTC proposed the new RECIST criteria (1.0)

James K et al: J Natl Cancer Inst 1999

Table 2
Summary of Key Changes for WHO, RECIST 1.0,

Criterion	WHO	RECIST 1.0
Definition of "measurable" lesions	Should be measurable in two dimensions, no minimum lesion size	Minimum size = 10 mm at spiral CT, 20 mm at conventional CT
Method of measurement	SPD	Longest diameter
Lymph nodes	Unspecified	Unspecified
Definition of progressive disease	≥25% increase in SPD	20% increase in SLD or new lesions, unequivocal progression considered to indicate progressive disease
Number of lesions measured	N/A	10 lesions (≤5 in any one organ)
New lesions	N/A	N/A
Guidance for imaging studies	N/A	CT, MRI, chest radiography

Note.—MRI = MR imaging, N/A = not applicable.

RECIST 1.0 Key features

- Based on restrospective mesurements obtained in 8 pharmaceutical-sponsored trials (569 tot pts)
- Minimum size of measurable disease
- Unidimensional measures
  - ✓ Sum of longest diameters (SLD)
- N. of lesions to follow up

ANATOMIC RESPONSE CRITERIA

2009 RECIST working group revised the RECIST criteria (1.1)

Bogaerts J et al: Eur J Cancer 2009

Table 2
Summary of Key Changes for WHO, RECIST 1.0, and

Criterion	WHO	RECIST 1.0	RECIST 1.1
Definition of "measurable" lesions	Should be measurable in two dimensions, no minimum lesion size	Minimum size = 10 mm at spiral CT, 20 mm at conventional CT	Minimum size = 10 mm at CT
Method of measurement	SPD	Longest diameter	Longest diameter (except in lymph nodes)
Lymph nodes	Unspecified	Unspecified	Short axis: target lesions ≥15 mm, nontarget lesions = 10–15 mm, nonpathologic lesions <10 mm
Definition of progressive disease	≥25% increase in SPD	20% increase in SLD or new lesions, unequivocal progression considered to indicate progressive disease	>20% increase in SLD; ≥5-mm increase in size; new lesions; detailed description of unequivocal progression
Number of lesions measured	N/A	10 lesions (≤5 in any one organ)	Five lesions (≤2 in any one organ)
New lesions	N/A	N/A	Provides guidance as to when a lesion is considered new (ie, representative of progressive disease)
Guidance for imaging studies	N/A	CT, MRI, chest radiography	CT, MRI, FDG PET

Note.—MRI = MR imaging, N/A = not applicable.

RECIST 1.1 Key features

- **Larger database (over 6,500 pts)**
- **Assessment of nodes**
- **N. of lesions to follow up**
- **Overall definition of PD**

ANATOMIC RESPONSE CRITERIA: LIMITATIONS

Reduction of continuous data on tumor size and response in 4 groups: (CR, PR, SD, PD)

Reliability of measuremets: misclassification rates ~30% for PD and 14% for PR

Developed to assess response to cytotoxic chemotherapy

Newer cancer therapy may be more cytostatic than cytotoxic

Unable to distinguish viable tumor from non viable component

Is it time to move from anatomical to functional assessment?

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CHOI RESPONSE CRITERIA in GIST

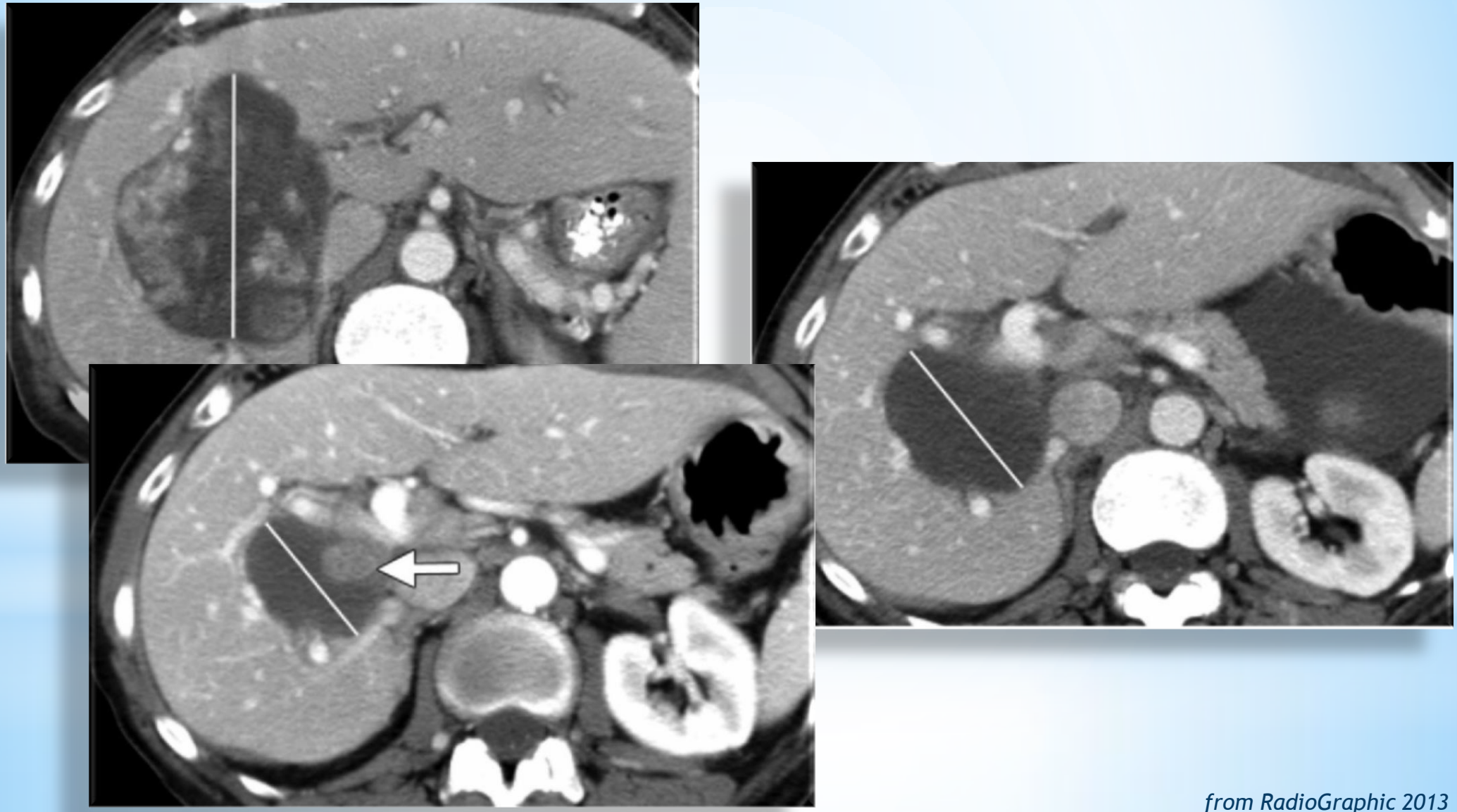
Comparison of WHO, RECIST 1.1, Choi,

Response	WHO*	RECIST 1.1	Choi†
Complete response	No lesions detected for at least 4 weeks	Disappearance of all target lesions or lymph nodes <10 mm in the short axis	Disappearance of all target lesions
Partial response	≥50% decrease in SPD (confirmed at 4 weeks)	>30% decrease in sum of longest diameters (SLD) of target lesions	≥10% decrease in tumor size or ≥15% decrease in tumor attenuation at computed tomography (CT); no new lesions
Progressive disease	≥25% increase in SPD in one or more lesions; new lesions	>20% increase in SLD of target lesions with an absolute increase of ≥5 mm; new lesions	≥10% increase in SLD of lesions; does not meet the criteria for partial response by virtue of tumor attenuation, new intratumoral nodules, or an increase in the size of the existing intratumoral nodules
Stable disease	None of the above	None of the above	None of the above

The CHOI response criteria for GIST proposed that tumor attenuation could provide an additional measure of response to imatinib therapy.

Choi H et al: Am J Roentjenol 2004

CHOI RESPONSE CRITERIA in GIST



from RadioGraphic 2013

mRECIST CRITERIA in HCC

Comparison of WHO, RECIST 1.1, Choi, mRECIST,

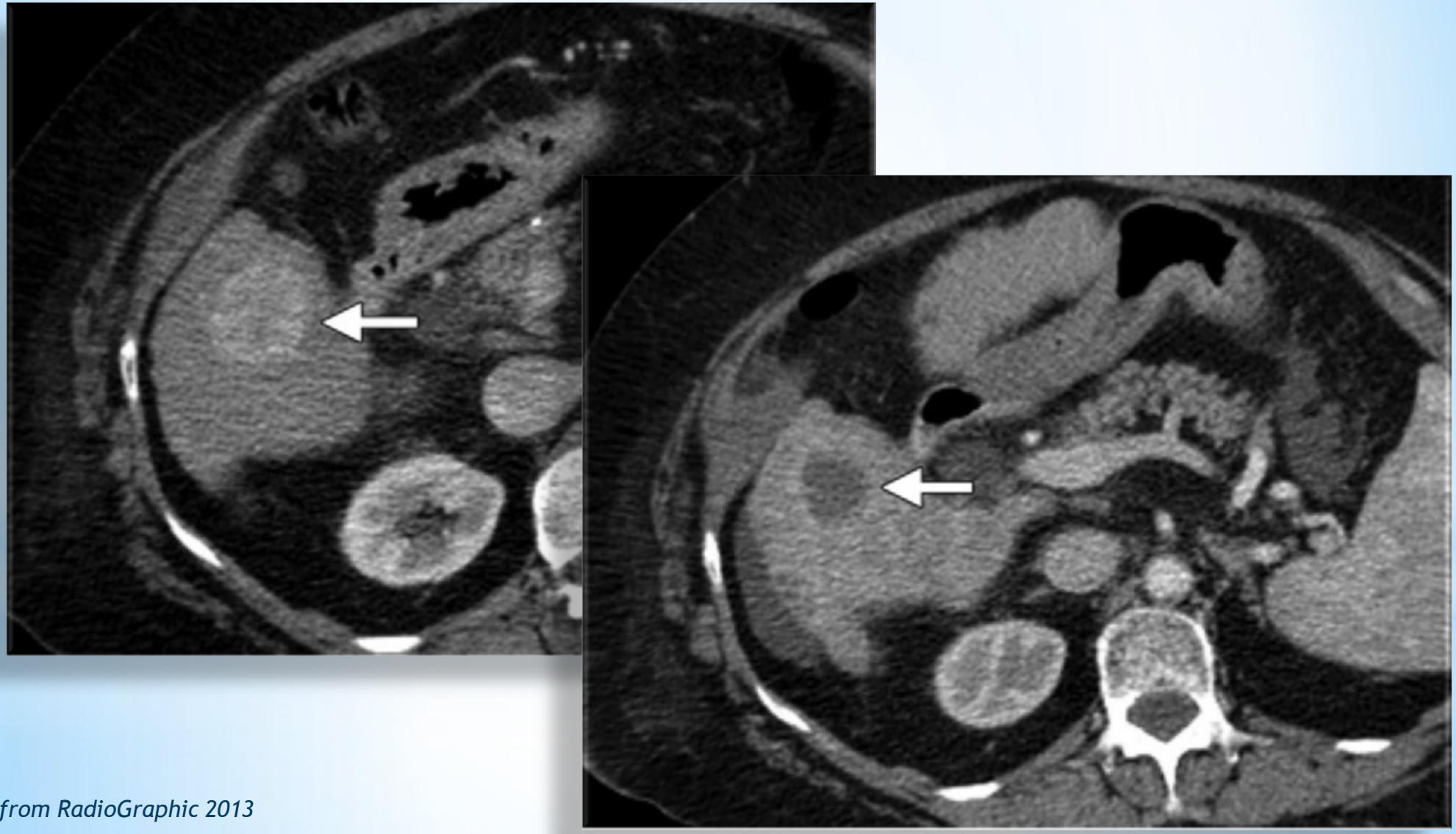
Response	WHO*	RECIST 1.1	Choi†	mRECIST‡
Complete response	No lesions detected for at least 4 weeks	Disappearance of all target lesions or lymph nodes <10 mm in the short axis	Disappearance of all target lesions	Disappearance of arterial phase enhancement in all target lesions
Partial response	≥50% decrease in SPD (confirmed at 4 weeks)	>30% decrease in sum of longest diameters (SLD) of target lesions	≥10% decrease in tumor size or ≥15% decrease in tumor attenuation at computed tomography (CT); no new lesions	>30% decrease in SLD of "viable" target lesion (arterial phase enhancement)
Progressive disease	≥25% increase in SPD in one or more lesions; new lesions	>20% increase in SLD of target lesions with an absolute increase of ≥5 mm; new lesions	≥10% increase in SLD of lesions; does not meet the criteria for partial response by virtue of tumor attenuation, new intratumoral nodules, or an increase in the size of the existing intratumoral nodules	>20% increase in SLD of "viable" target lesion (arterial phase enhancement)
Stable disease	None of the above	None of the above	None of the above	None of the above

In 2000 a panel of expert on HCC proposed that estimation of viable tumor with contrast-enhanced imaging (dynamic CT or MR arterial phase) should be optimal method for assessing treatment response

The new criteria, referred to as **mRECIST**, were endorsed by the AASLD

Bruix et al: J Hepatol 2001

mRECIST CRITERIA in HCC



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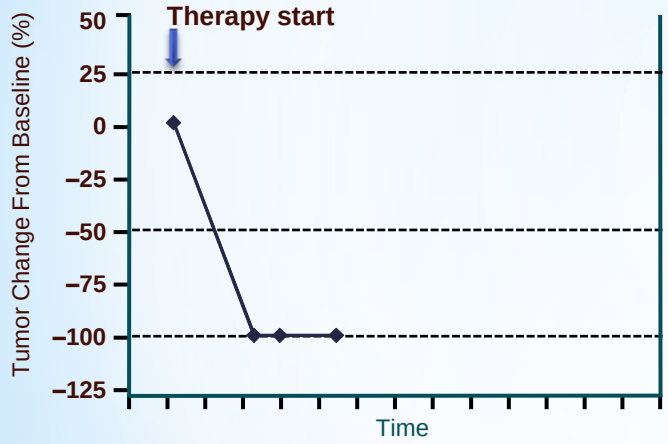
TUMOR RESPONSE PATTERNS TO I-O THERAPY

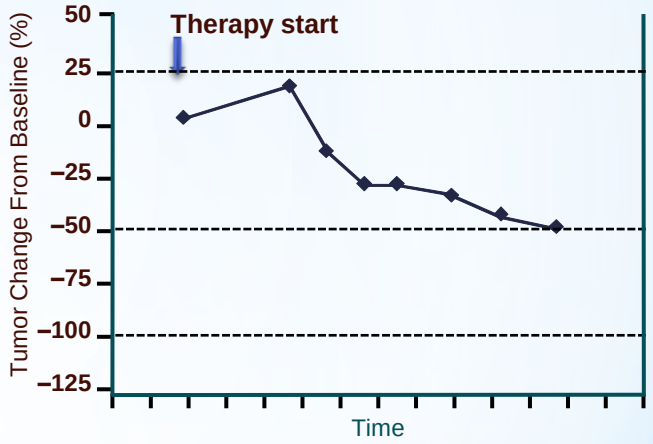
A patient with response in baseline lesions
Seen with chemotherapy, but also I-O therapies Captured by existing RECIST and WHO criteria



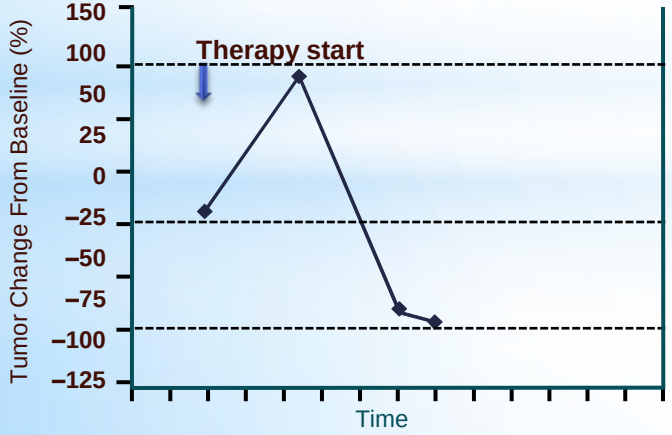
----- Thresholds for response or progressive disease (RECIST)

Graphs for illustrative purposes showing responses to ipilimumab in individual patients with advanced melanoma

A patient with "stable disease": Slow, steady decline in tumor volume seen with chemotherapy, targeted and I-O therapies. Captured by existing RECIST and WHO criteria

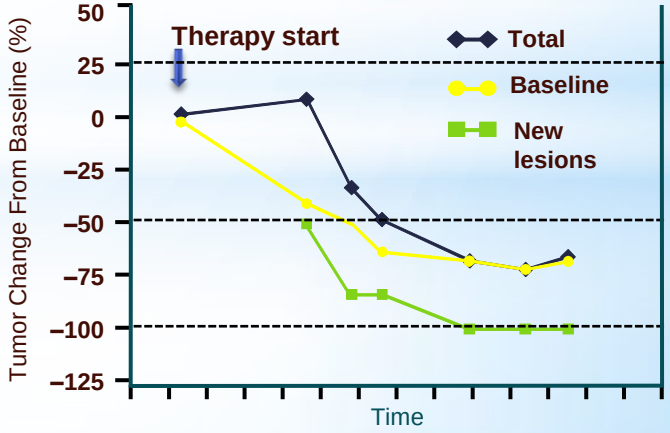


A patient with response after initial increase in tumor volume. Novel and specific to I-O therapy
RECIST or WHO criteria may not be optimal



Some vaccines may not have response patterns like other I-O therapies

A patient with reduction in tumor burden after appearance of new lesions; novel and specific to I-O therapy
RECIST or WHO criteria may not be optimal



Wolchok JD, et al. Clin Cancer Res. 2009;
. Hoos A, et al. Ann Oncol. 2012;23(suppl 8)

Guidelines for the Evaluation of Immune Therapy Activity in Solid Tumors: Immune-Related Response Criteria

Table 1. Comparison between WHO criteria and the irRC

	WHO	irRC
New, measurable lesions (i.e., ≥5 × 5 mm)	Always represent PD	Incorporated into tumor burden
New, nonmeasurable lesions (i.e., <5 × 5 mm)	Always represent PD	Do not define progression (but preclude irCR)
Non-index lesions	Changes contribute to defining BOR of CR, PR, SD, and PD	Contribute to defining irCR (complete disappearance required)
CR	Disappearance of all lesions in two consecutive observations not less than 4 wk apart	Disappearance of all lesions in two consecutive observations not less than 4 wk apart
PR	≥50% decrease in SPD of all index lesions compared with baseline in two observations at least 4 wk apart, in absence of new lesions or unequivocal progression of non-index lesions	≥50% decrease in tumor burden compared with baseline in two observations at least 4 wk apart
SD	50% decrease in SPD compared with baseline cannot be established nor 25% increase compared with nadir, in absence of new lesions or unequivocal progression of non-index lesions	50% decrease in tumor burden compared with baseline cannot be established nor 25% increase compared with nadir
PD	At least 25% increase in SPD compared with nadir and/or unequivocal progression of non-index lesions and/or appearance of new lesions (at any single time point)	At least 25% increase in tumor burden compared with nadir (at any single time point) in two consecutive observations at least 4 wk apart

Wolchok JD et al: Clin Cancer Res 2009

PERCIST CRITERIA

Comparison of WHO, RECIST 1.1, Choi, mRECIST, and PERCIST Tumor Response Criteria

Response	WHO*	RECIST 1.1	Choi†	mRECIST‡	PERCIST§
Complete response	No lesions detected for at least 4 weeks	Disappearance of all target lesions or lymph nodes <10 mm in the short axis	Disappearance of all target lesions	Disappearance of arterial phase enhancement in all target lesions	Disappearance of all metabolically active tumors
Partial response	≥50% decrease in SPD (confirmed at 4 weeks)	>30% decrease in sum of longest diameters (SLD) of target lesions	≥10% decrease in tumor size or ≥15% decrease in tumor attenuation at computed tomography (CT); no new lesions	>30% decrease in SLD of "viable" target lesion (arterial phase enhancement)	>30% (0.8-unit) decline in SUL peak between the most intense lesion before treatment and the most intense lesion after treatment
Progressive disease	≥25% increase in SPD in one or more lesions; new lesions	>20% increase in SLD of target lesions with an absolute increase of ≥5 mm; new lesions	≥10% increase in SLD of lesions; does not meet the criteria for partial response by virtue of tumor attenuation, new intratumoral nodules, or an increase in the size of the existing intratumoral nodules	>20% increase in SLD of "viable" target lesion (arterial phase enhancement)	>30% (0.8-unit) increase in SUL peak or confirmed new lesions
Stable disease	None of the above	None of the above	None of the above	None of the above	None of the above

PET Response Criteria in Solid Tumors PERCIST (1.0)

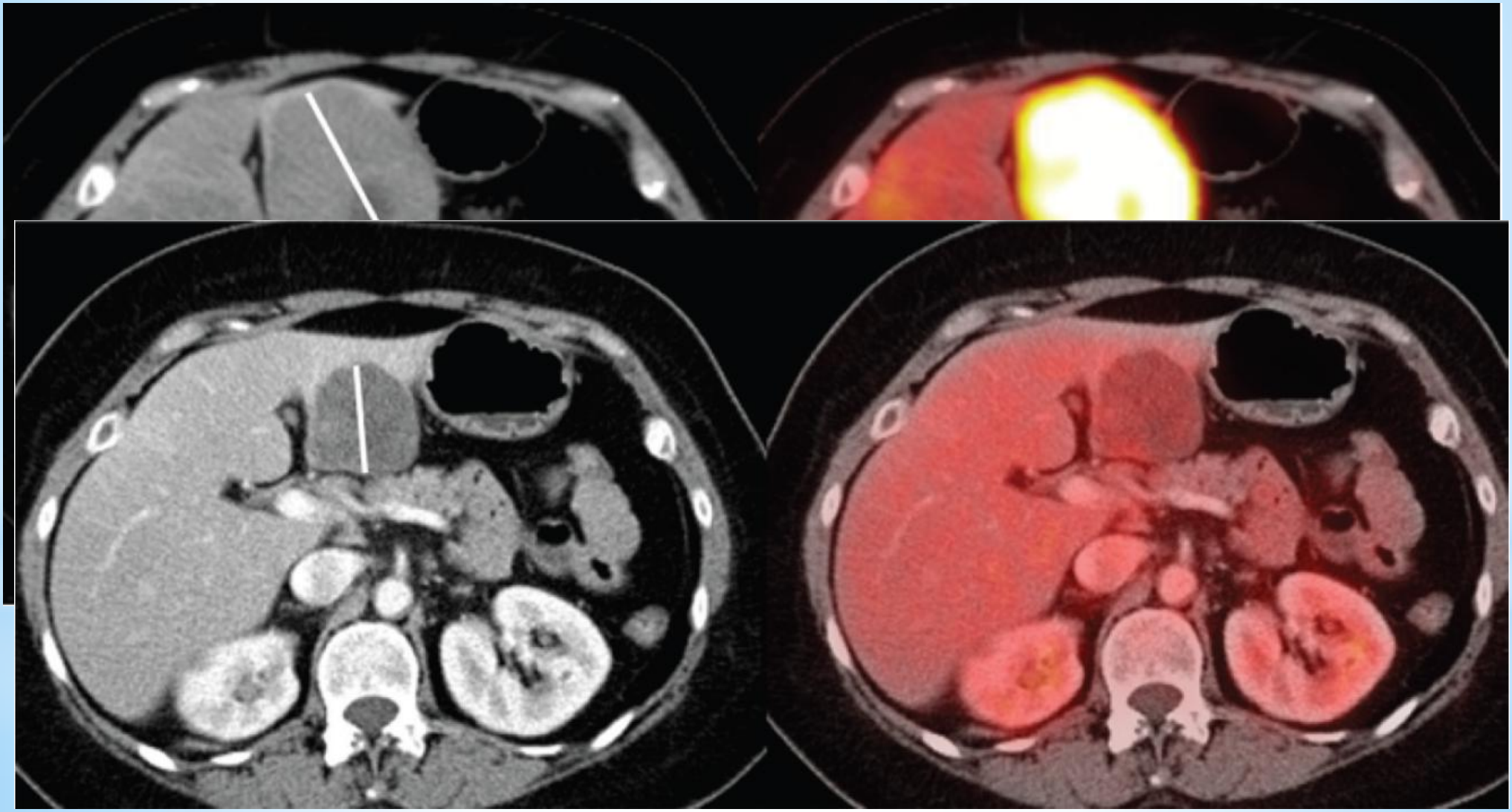
Many new drugs are cytostatic

Tumor response associated with decrease in metabolism

No reduction in size

Wahl RL et al:J Nucl Med 2009

PERCIST vs RECIST



from RadioGraphic 2013

FUTURE PERSPECTIVE

Radiology will continue to adapt to the new tumor response concept

Tumor response criteria adapt to treatment and type of tumor

Integration with current clinical image-viewing

Costs?

CONCLUSIONS

Assessment of tumor burden important feature in evaluation of cancer therapy

Tumor shrinkage and time to progression important endpoints in clinical trials

Usefull only if based on widely accepted and readily applied standard criteria

RECIST 1.1 the most widely accepted criteria for response evaluation in clinical trials and practice

No sufficient standardization and widespread availability to recommend adoption of alternative assessment methods

GRAZIE PER L'ATTENZIONE