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Introduction to RANO 2.0

The Response Assessment in Neuro-Oncology (RANO) criteria have long been the standard for evaluating treatment response in brain tumors. The latest update, RANO 2.0, incorporates new guidelines to address challenges associated with modern therapies, such as immunotherapy and targeted treatments. It provides refined criteria for lesion assessment, pseudoprogression, and the integration of advanced imaging techniques, aiming to enhance accuracy in clinical trials and patient care.

History of Response Criteria by RANO Working Group

CNS Assessment Criteria	Indication	Description
Macdonald Criteria (1990)	Glioma	Initial response criteria for primary brain cancer
RANO Criteria for HGG (2010)	HGG	Assessment of HGG improvement and addressing limitations of Macdonald Criteria
RANO-LGG (2011)	LGG	Assessment of LGG using T2/FLAIR
RANO-BM (2015)	Brain metastasis	Assessment of brain metastasis, to be used with RECIST 1.1 for extra-CNS disease with unidimensional measurement
iRANO (2015)	Glioma with immunotherapy	Assessment addressing potential pseudoprogression due to immunotherapy
mRANO (2017)	Glioma	Modification of RANO HGG with confirmation of PD and PsP, post-RT scan to be used as baseline scan for newly diagnosed glioma
RANO-LM (2017)	Leptomeningeal disease	Assessment of leptomeningeal disease
RANO 2.0 (2023)	Glioma	Most recent update by RANO working group addressing various challenges and incorporation of new guidance from RANO, RANO LGG, iRANO, mRANO

Changes & Updates in RANO 2.0

Response assessment categorization

- Response assessment by lesion enhancement feature rather than WHO grade
- Enhancing tumors, Non-enhancing tumors, Mixed enhancing and non-enhancing tumors
- Enhancing and non-enhancing tumor burdens to be tracked separately
- Choice of applying each assessment type to be determined prospectively

T2/FLAIR assessment for GBM

- Glioblastoma Multiforme (GBM) assessment excludes T2/FLAIR assessment unless anti-angiogenic agents are used

Baseline scan designation

- Post Radiotherapy (RT) scan to be used as Baseline scan for newly diagnosed glioma
- Post-RT scan to be acquired about 3-5 weeks after the completion of the RT

Definition of PD for enhancing lesions

- Preliminary PD is assigned when 25% increase in sum of product of diameter (SPD) of target lesions from baseline or nadir
- Confirmed PD is assigned when subsequent 25% increase in SPD of target lesions compared to prior visit which preliminary PD has been assigned

Confirmation of Progression (PD) and Pseudoprogression (PsP)

- Still required within 12 weeks of RT for enhancing lesions
- Assessment beyond 12 weeks from RT is recommended if investigational drug is associated with high PsP rate
- Confirmation of PD is not needed for non-enhancing lesions

Management of non-target lesion, new lesion, and PD

- Non-measurable lesions that increase by 5mm in each short and long axis is added to target SPD
- Any new measurable enhancing lesions are added to target SPD

Measurement Consideration

- Mixed enhancing/non-enhancing lesions: enhancing lesions within non-enhancing lesions can be measured
- Measurement of lesions should not included surgical cavities and cyst
- Measurement of bidimensional measurement should not be outside of the lesion

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