

iRANO criteria

The [immunotherapy](#) response assessment for neuro-oncology (iRANO) criteria have been developed as a modification of [RANO criteria](#) to address the challenges of emerging novel immunotherapy for high-grade gliomas.

This approach utilizes post-contrast and T2/FLAIR MRI sequences. Advancements of imaging modalities that distinguish a specific response due to treatment, versus the non-specific contributions due to disease progression, would be of particularly high value for patients with intracranial tumors and treated with immunotherapy. Accordingly, an early confirmation that a patient was responding to an immunotherapeutic modality would prevent the unnecessary continuation of ineffective treatments, even while the patients may undergo progressive worsening according to conventional imaging results and/ or symptoms associated with clinical worsening ¹⁾.

Key differences between iRANO and RANO criteria

new enhancing lesion outside the main radiation field are encountered in immunotherapy and therefore do not automatically denote progressive disease in iRANO the onset of therapeutic effect in immunotherapy can be delayed and thus iRANO requires a repeat scan (3 months later) to confirm disease progression on imaging criteria

Progressive disease

Progressive disease can be diagnosed in the setting of immunotherapy in the following scenarios 1:

Clinical features

significant clinical deterioration (not attributable to other non-tumour causes and not due to steroid decrease)

Imaging features

6 months of the current immunotherapeutic regime

same as RANO progressive disease criteria

≤6 months of the current immunotherapeutic regime requires a second scan confirming further progressive disease 3 months after the initial scan showing features of progressive disease during this interval, immunotherapy can continue if toxicity is minimal, at the discretion of treating clinicians

iRANO is a multinational and multidisciplinary panel of neuro-oncology immunotherapy experts

Among patients who demonstrate imaging findings meeting **RANO** criteria for progressive disease within 6 months of initiating immunotherapy, including the development of new lesions, confirmation of radiographic progression on follow-up imaging is recommended provided that the patient is not significantly worse clinically. The proposed criteria also include guidelines for the use of corticosteroids.

They reviewed the role of advanced imaging techniques and the role of measurement of clinical benefit endpoints including neurological and immunological functions. The iRANO guidelines put forth in the Review of Okada et al. will evolve successively to improve their usefulness as further experience from immunotherapy trials in neuro-oncology accumulate ²⁾.

¹⁾

Lukas RV, Juhász C, Wainwright DA, James CD, Kennedy E, Stupp R, Lesniak MS. Imaging tryptophan uptake with positron emission tomography in glioblastoma patients treated with indoximod. *J Neurooncol*. 2018 Nov 10. doi: 10.1007/s11060-018-03013-x. [Epub ahead of print] PubMed PMID: 30415456.

²⁾

Okada H, Weller M, Huang R, Finocchiaro G, Gilbert MR, Wick W, Ellingson BM, Hashimoto N, Pollack IF, Brandes AA, Franceschi E, Herold-Mende C, Nayak L, Panigrahy A, Pope WB, Prins R, Sampson JH, Wen PY, Reardon DA. Immunotherapy response assessment in neuro-oncology: a report of the RANO working group. *Lancet Oncol*. 2015 Nov;16(15):e534-e542. doi: 10.1016/S1470-2045(15)00088-1. Review. PubMed PMID: 26545842; PubMed Central PMCID: PMC4638131.

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