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The Use of Minor Response, Volumetric Assessment and Growth Rate Kinetics as Endpoints in Grade 1–3 Glioma Clinical Trials: a RANO perspective

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Abstract

The RANO criteria for response to treatment in glioma make a distinction between enhancing and unenhancing tumors, which reflects assessment of a different biological process underlying the MRI findings in enhancing and non-enhancing tumors. The recent regulatory approval of tovorafenib has also considered the patients with minor responses (25% - 50% decrease) based on the 2D measurement on T2/FLAIR MR imaging, while incorporating other measures of patient benefit. The INDIGO placebo controlled trial led to the regulatory approval of vorasidenib based on the increase in PFS in the active treatment arm, as measured by blinded independent radiology review using the 2D RANO criteria. With that, more insight in the regulatory requirements for approval in low grade tumors has been obtained, but other issues in assessing outcome in studies on low grade enhancing tumors remain. These include the added value of volumetric assessment instead of 2D assessments, and assessment of tumor growth rate as an early marker of outcome. This manuscript gives an overview of the current perspective on and challenges of assessing outcome in trials on unenhancing glioma, with both regulatory and clinical perspectives.

Keywords: Minor Response; RANO; Tumor Growth rate; unenhancing tumors; volumetric (3D) assessment.

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