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Current Treatment Options for Adult Grade 2 IDH-mutant Diffuse Gliomas in the Vorasidenib Era: Patient Selection, Sequencing, and Practical Management

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Abstract

Management of adult WHO CNS grade 2 IDH-mutant diffuse gliomas has entered a more precise postoperative era. Vorasidenib has changed the discussion because it can slow progression and delay the next intervention in selected patients, but the key therapeutic question is not whether mutant IDH inhibition is active; it is where it should be placed relative to observation, reoperation, radiotherapy, and alkylating chemotherapy. We believe treatment should begin with maximal safe resection, integrated molecular diagnosis, and a careful assessment of residual non-enhancing disease, growth kinetics, symptoms, seizure burden, neurocognitive priorities, fertility goals, and patient preference. Observation remains appropriate after gross-total or near-total resection, in patients with absent or minimal residual disease, stable serial MRI, controlled seizures, and no immediate need for durable cytoreduction. Vorasidenib is best framed as an active-delay strategy for patients with measurable, non-enhancing, clinically stable residual or recurrent grade 2 IDH-mutant astrocytoma or oligodendroglioma, particularly when radiotherapy and chemotherapy can reasonably be deferred and preservation of cognition, work capacity, quality of life, or fertility options is a major priority. It should not be presented as a universal substitute for definitive local or adjuvant therapy. Radiotherapy followed by PCV, or selected temozolomide-based approaches when PCV is not feasible, remains appropriate for rapid growth, symptomatic mass effect, new or nodular enhancement, neurological decline, uncontrolled seizures, high-risk molecular pathology such as CDKN2A/B homozygous deletion, or suspected grade transformation. During surveillance or vorasidenib, treatment failure should be judged by trajectory rather than a single scan. Sustained T2/FLAIR volumetric growth, new enhancement, worsening seizures, steroid requirement, functional decline, or need for next intervention should prompt multidisciplinary re-review, repeat tissue sampling when useful, and timely transition to radiochemotherapy, salvage surgery, or clinical-trial enrollment.

Keywords: Astrocytoma; IDH-mutant glioma; Low-grade glioma; Oligodendroglioma; Treatment sequencing; Vorasidenib.