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Advances in IDH-mutant glioma management: IDH inhibitors, clinical implications of INDIGO trial, and future perspectives

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Abstract

The discovery of isocitrate dehydrogenase (IDH) mutation in gliomas marked the new era of molecular classification of CNS tumors. Understanding the complex role of IDH mutation in oncogenesis led to the evaluation of novel small molecules targeting this enzyme as a potential therapeutic intervention. Vorasidenib, a brain-penetrant inhibitor of both IDH1 and IDH2-mutant enzymes, was one such agent. The phase 3 INDIGO trial evaluated vorasidenib and demonstrated its efficacy in IDH-mutant low-grade gliomas (LGG). This study established vorasidenib as an effective inhibitor of both IDH1 and IDH2-mutant enzymes, highlighting its great potential in advancing the therapeutic armamentarium for patients with LGG. While vorasidenib has been recently included in several treatment guidelines for CNS tumors, further research on the use of this novel agent, as monotherapy or in combination with other drugs, becomes imperative to exploit fully its potential in the management of IDH-mutant gliomas.

Keywords: 2-hydroxyglutarate (2-HG); Glioma; IDH inhibitor; isocitrate dehydrogenase (IDH); vorasidenib.