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Low-grade *IDH*-mutant gliomas: from standard post-surgical treatments to novel IDH inhibitors

Roberta Rudà [1], Francesco Bruno [1], Alessia Pellerino [1], Edoardo Pronello [1], Riccardo Soffietti [1]

Affiliations
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Abstract

Introduction: Adult-type IDH-mutant diffuse gliomas grade 2 are rare tumors mainly affecting young patients, classified by WHO 2021 into IDH-mutant astrocytomas and IDH-mutant 1p/19q codeleted oligodendrogliomas. IDH-mutant grade 2 gliomas are slowly growing tumors; however, they grow continuously, and almost all patients will ultimately recur. Surgical resection is the first option, followed by observation with MRI in low-risk patients and radio-chemotherapy in high-risk patients. Early clinical trials and phase 3 INDIGO trial have demonstrated the efficacy of vorasidenib, a dual IDH1/2 inhibitor, in prolonging imaging-based progression-free survival and time-to-next-intervention.

Areas covered: This review covers the following areas: importance of surgical resection, traditional treatments after surgery, mechanisms of IDH mutations and IDH inhibitors in preclinical models, early clinical studies on ivosidenib and vorasidenib, INDIGO trial, the future role of vorasidenib, open issues beyond INDIGO trial, and novel IDH targeting strategies.

Expert opinion: IDH1/2 mutations are ideal targets of therapy and early clinical studies and INDIGO phase 3 trial confirmed the clinical efficacy of vorasidenib. Long-term follow-up is needed to better define the efficacy across different subgroups of patients. Overall, vorasidenib will replace observation with MRI for low-risk patients and allow to delay radiotherapy and chemotherapy and their adverse effects.

Keywords: IDH inhibitors; IDH-mutant grade 2 gliomas; INDIGO trial; novel IDH inhibitor strategies; open issues; radiotherapy and chemotherapy; surgery.