Review Curr Neurol Neurosci Rep. 2024 Sep 20. doi: 10.1007/s11910-024-01378-3.

Online ahead of print.

The Role of Mutant IDH Inhibitors in the Treatment of Glioma

Vihang Nakhate [1 2 3], Aleksandra B Lasica [4 5], Patrick Y Wen [4 5]

Affiliations

PMID: 39302605 DOI: 10.1007/s11910-024-01378-3

Abstract

Purpose of review: The identification of isocitrate dehydrogenase (IDH) mutations has led to a transformation in our understanding of gliomas and has paved the way to a new era of targeted therapy. In this article, we review the classification of IDH-mutant glioma, standard of care treatment options, clinical evidence for mutant IDH (mIDH) inhibitors, and practical implications of the recent landmark INDIGO trial.

Recent findings: In the phase 3 randomized placebo-controlled INDIGO trial, mIDH1/2 inhibitor vorasidenib increased progression-free survival among non-enhancing grade 2 IDH-mutant gliomas following surgery. This marks the first positive randomized trial of targeted therapy in IDH-mutant glioma, and led to the US Food and Drug Administration's approval of vorasidenib in August 2024 for grade 2 IDH-mutant glioma. Vorasidenib is a well-tolerated treatment that can benefit a subset of patients with IDH-mutant glioma. Targeting mIDH also remains a promising strategy for select groups of patients excluded from the INDIGO trial. Ongoing and future studies, including with new agents and with combination therapy approaches, may expand the benefit and unlock the potential of mIDH inhibitors.

Keywords: Glioma; IDH inhibitor; IDH mutant; INDIGO; Vorasidenib.