

Vorasidenib- A Paradigm Shift in IDH1- or IDH2-Mutant Low-Grade Glioma Treatment

Hurais Malik, Muhammad Hudaib, Abdul Rehman

Low-grade gliomas (LGGs) pose significant challenges in cancer research and treatment due to their infiltrative nature and tendency for recurrence, making them the most common brain tumour in adults. Most of the LGGs have the propensity to cause notable alterations in the microenvironment of the tumour thus making them difficult to treat. These alterations can be attributed to the prevalent mutations in the genes that produce isocitrate dehydrogenase (IDH) enzymes, especially in grade 2 diffuse gliomas.¹ Despite its inability to provide a complete cure, chemoradiation has been adopted as the standard therapy in grade 3 gliomas since it can lead to long-lasting remission. Chemoradiotherapy, when administered promptly, can help prevent tumour progression, and recurrence after surgery and improve long-term outcomes. Nevertheless, immediate adjuvant chemoradiotherapy is not administered in patients afflicted with tumours containing IDH mutant grade 2 gliomas. This decision is often made to circumvent potential harm such as radiation-induced cognitive problems, chemotherapy-related DNA mutations, and other negative effects on their health.² Due to the intricacies associated with the treatment decisions and the inclination to delay aggressive therapies to avoid adverse events, creates a necessity for a novel therapeutic strategy that is both effective and well tolerated.

Vorasidenib, an oral medication specifically designed to deal with IDH mutations has displayed promise despite existing challenges. By aiming to specifically target aberrant metabolic pathways triggered by mutant IDH enzymes, Vorasidenib offers a potential treatment

capable of interrupting tumour growth and could subsequently result in better patient outcomes. Among the many reasons that make Vorasidenib an appealing option are its capability to penetrate the blood-brain barrier and its promising safety profile, resulting in effective treatment while alleviating potential side effects.³

Vorasidenib's efficacy is derived from its ability to halt the metabolic cascades driven by mutant IDH enzymes thus leading to decreased progression of the gliomas. Clinical studies elicit the substantial value Vorasidenib has to offer by enhancing progression-free survival and postponing the advancement of the illness in patients with grade 2 IDH-mutant gliomas. This offers an optimistic prospect for delaying the need for more aggressive treatments in these patients.^{2,4}

Hence, to conclude Vorasidenib can transform treatment norms and enhance outcomes for those suffering from IDH-mutant LGG. Furthermore, it is crucial to investigate different treatment combinations, finding markers that would help assess clinical response to treatment, which in turn would be an important milestone in the treatment journey.

DOI: <https://doi.org/10.47391/JPMA.20428>

Disclaimer: None.

Conflict of Interest: None.

Funding disclosure: The authors declare that no financial grants were obtained for the completion of this paper.

References

- Solomou G, Finch A, Asghar A, Bardella C. Mutant IDH in gliomas: Role in cancer and treatment options. [Online] 2023 [Cited 2024 March 15]. Available from: URL: <http://dx.doi.org/10.3390/cancers15112883>
- Mellinghoff IK, van den Bent MJ, Blumenthal DT, Touat M, Peters KB, Clarke J, et al. Vorasidenib in IDH1- or IDH2-mutant low-grade glioma. [Online] 2023 [Cited 2024 March 13]. Available from: URL: <https://pubmed.ncbi.nlm.nih.gov/37272516/>

.....
Final Year MBBS Student, Fazaia Ruth Pfau Medical College, Karachi, Pakistan.

Correspondence: Hurais Malik. Email: huraismalik38@gmail.com

ORCID ID: 0009-0005-0647-8181

.....
Submission complete: 06-04-2024 **Review began:** 21-05-2024

Acceptance: 13-06-2024 **Review end:** 08-06-2024

3. Gatto L, Di Nunno V, Tosoni A, Bartolini S, Ranieri L, Franceschi E. Vorasidenib in IDH1/2-mutant low-grade glioma: the grey zone of patient's selection. [Online] 2024 [Cited 2024 May 23]. Available from: URL: <https://pubmed.ncbi.nlm.nih.gov/38273856/>
4. Bombino A, Magnani M, Conti A. A promising breakthrough: The potential of VORASIDENIB in the treatment of low-grade glioma. [Online] 2024 [Cited 2024 June 3]. Available from: URL: <https://pubmed.ncbi.nlm.nih.gov/38425121/>

Authors' Contribution:

HM: Concept, writing, review and editing.

MH: Writing, review and editing.

AR: Writing.