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Use, access, and initial outcomes of off-label ivosidenib in patients with IDH1 mutant glioma

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Abstract

Background: Isocitrate dehydrogenase (IDH) is commonly mutated (mIDH) in gliomas, and this mutant enzyme produces the oncometabolite 2-hydroxyglutarate (2HG). 2HG promotes gliomagenesis and is implicated in epileptogenesis. Ivosidenib (IVO), a small molecule oral mIDH1 inhibitor, is FDA-approved for mIDH1 newly diagnosed and relapsed/refractory acute myeloid leukemia. Moreover, IVO has efficacy in clinical trials for recurrent mIDH1 gliomas. Given the lack of targeted treatments for gliomas, we initiated off-label IVO for mIDH glioma patients in October 2020.

Methods: Retrospectively, we sought to assess early outcomes in our patients and describe their experience on IVO from October 2020 through February 2022. Our objective was to report on the following variables of off-label use of IVO: radiographic response, seizure control, tolerability, and access to the medication. All patients initially received single-agent IVO dosed at 500 mg orally once daily.

Results: The cohort age range was 21-74 years. Tumor types included astrocytoma (n = 14) and oligodendroglioma (n = 16), with most being grade 2 (n = 21). The best radiographic response in nonenhancing disease (n = 22) was 12 stable diseases, 5 minor responses, 3 partial responses, and 2 progressive diseases. Seizure frequency was stable to improved for most patients (70%, n = 21). IVO was well-tolerated, with the most common toxicities being diarrhea, elevated creatine kinase, and QTc interval prolongation. Most patients (66.7%, n = 20) received drugs via the patient assistance program, with insurance initially covering a third of patients and with ongoing use, later covering 60%.

Conclusions: Targeted therapies like IVO are options for mIDH glioma patients and can provide positive oncologic and neurological outcomes.

Keywords: glioma; isocitrate dehydrogenase; ivosidenib; radiographic response.