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# Clinical experience with tovotafenib in adults with treatment-refractory high- and low-grade gliomas

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## Abstract

**Background:** BRAF alterations are common in pediatric low-grade gliomas (LGG) and a subset of high-grade gliomas (HGG) in adults and children. BRAF-targeted therapy can be effective at preventing tumor growth, though resistance commonly emerges in HGG. Recently, tovotafenib was FDA approved for recurrent or refractory LGG with BRAFV600 alterations or BRAF rearrangements. While the trial showed it is effective for children with LGG previously treated with BRAF or MEK inhibitors, the safety in adults and efficacy in HGG is unknown.

**Methods:** A cohort of appropriate patients was identified through routine clinical care. This research was conducted in accordance with IRB regulations with a waiver of written consent.

**Results:** Seven adults (5 HGG, 2 LGG) who received tovotafenib were identified. All patients had received prior BRAF-targeted therapy, and all patients with HGG had received prior radiation and temozolomide as well. Three individuals (2 HGG, 1 LGG) experienced stable disease or better for 4 or more months. Median duration of treatment was 8 weeks (range 3 weeks to 10 months). Two individuals experienced CTCAE grade 4 intratumoral hemorrhage (1 HGG, 1 LGG). Two patients remain on therapy at 4 and 10 months of treatment (1 HGG, 1 LGG).

**Conclusion:** Our experience with tovotafenib indicates some limited efficacy in HGG in combination with other standard treatments. These observations demonstrate the need for further clinical trials in patients with HGG to understand potential clinical utility, either earlier in the disease course or in combination with other therapies.

**Keywords:** BRAF-targeted therapy; glioma.

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