Clin Cancer Res. 2025 Jan 14. doi: 10.1158/1078-0432.CCR-24-3439. Online ahead of print.

FDA Approval Summary: Tovorafenib for Relapsed or Refractory BRAF-altered Pediatric Low-Grade Glioma

Sonia Singh [1], Diana Bradford [2], Somak Chatterjee [3], Xiaoxue Li [2], Stephanie L Aungst [2], Amy M Skinner [3], Claudia P Miller [2], Sarah Kim-McOlash [2], Jeanne Fourie Zirkelbach [1], Ye Xiong [1], Youwei Bi [2], Ying-Hong Wang [2], Yuching Yang [1], Jielin Sun [2], Jeffrey Kraft [4], Rosane Charlab [2], Stacy S Shord [3], Shenghui Tang [2], Barbara Scepura [3], Ilynn Bulatao [1], Opeyemi Udoka [5], Haleh Saber [1], Nam Atiqur Rahman [3], Richard Pazdur [2], Harpreet Singh [5], Martha Donoghue [2], Nicole Drezner [1]

Affiliations

PMID: 39808502 DOI: 10.1158/1078-0432.CCR-24-3439

Abstract

On April 23, 2024, FDA granted accelerated approval to tovorafenib, a type II RAF kinase inhibitor, for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (pLGG) harboring a BRAF fusion or rearrangement, or BRAF V600 mutation. Efficacy was evaluated in FIREFLY-1 (NCT04775485), a single-arm, open-label, multicenter trial that enrolled patients 6 months to 25 years of age with relapsed or refractory pLGG with an activating BRAF alteration who had received prior systemic therapy. The major efficacy outcome measure was radiologic overall response rate (ORR), defined as the proportion of patients with complete response, partial response, or minor response as determined by blinded independent central review using Response Assessment in Pediatric Neuro-Oncology (RAPNO) criteria. A key secondary endpoint was duration of response (DoR). In an efficacy population of 76 patients, the ORR was 51% (95% confidence interval (CI): 40, 63), and the median DoR was 13.8 months (95% CI: 11.3, not estimable). The required post-marketing clinical trial (FIREFLY-2) was well underway at the time of accelerated approval. This represents the first FDA approval of a systemic therapy for the treatment of patients with pLGG with BRAF fusions or rearrangements.