FDA Approves New Targeted Therapy for Brain Cancer

Voranigo was approved for astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation.

August 8, 2024 By Food and Drug Administration (FDA)

FDA approves vorasidenib for Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation

On August 6, 2024, the Food and Drug Administration approved vorasidenib (Voranigo, Servier Pharmaceuticals LLC), an isocitrate dehydrogenase-1 (IDH1) and isocitrate dehydrogenase-2 (IDH2) inhibitor, for adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation, following surgery including biopsy, sub-total resection, or gross total resection.

Full prescribing information for Voranigo will be posted on Drugs@FDA.

This is the first approval by the FDA of a systemic therapy for patients with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation.

Efficacy and Safety

Efficacy was evaluated in 331 patients with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation following surgery enrolled in INDIGO (NCT04164901), a randomized, multicenter, double-blind, placebo-controlled trial. Patients were randomized 1:1 to receive vorasidenib 40 mg orally once daily or placebo orally once daily until disease progression or unacceptable toxicity. IDH1 or IDH2 mutation status was prospectively determined by the Life Technologies Corporation Oncomine Dx Target Test. Patients randomized to placebo were allowed to cross over to vorasidenib after documented radiographic disease progression. Patients who received prior anti-cancer treatment, including chemotherapy or radiation therapy, were excluded.

The major efficacy outcome measure was progression-free survival (PFS) using a blinded independent review committee per modified Response Assessment in Neuro-Oncology for Low Grade Glioma (RANO-LGG) criteria. An additional efficacy outcome measure was time to next intervention. The hazard ratio for PFS was 0.39 (95% CI: 0.27, 0.56), p-value <0.0001. The median time to next intervention was not reached for the vorasidenib arm and was 17.8 months for the placebo arm (HR=0.26; 95% CI: [0.15, 0.43], p <0.0001).

The most common (≥15%) adverse reactions were fatigue, headache, COVID-19 infection, musculoskeletal pain, diarrhea, nausea, and seizure. The most common Grade 3 or 4 laboratory abnormalities (>2%) were increased alanine aminotransferase, increased aspartate aminotransferase, GGT increased, and decreased neutrophils.

The recommended vorasidenib dose in adult patients is 40 mg orally once daily until disease progression or unacceptable toxicity. The recommended vorasidenib dose in pediatric patients 12 years and older is based on body weight:

- Patients weighing ≥ 40 kg: 40 mg orally once daily.
- Patients weighing < 40 kg: 20 mg orally once daily.

This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, FDA collaborated with the Australian Therapeutic Goods Administration (TGA), the Brazilian Health Regulatory Agency (ANVISA), Health Canada, Switzerland's Swissmedic, and Israel's Ministry of Health (IMoH). The application reviews are ongoing at the other regulatory agencies.

Expedited Programs

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment.

This application was granted priority review, fast track designation, breakthrough designation and orphan drug designation. FDA expedited programs are described in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

This announcement was published by the Food and Drug Administration/National Institutes of Health on August 6, 2024.
