FDA Approves Ojemda for Children With Relapsed or Refractory Brain Tumors

Half of pediatric patients treated with tovorafenib experienced tumor shrinkage.

April 25, 2024 By Food and Drug Administration (FDA)

FDA grants accelerated approval to tovorafenib for patients with relapsed or refractory BRAF-altered pediatric low-grade glioma

On April 23, 2024, the Food and Drug Administration granted accelerated approval to tovorafenib (Ojemda, Day One Biopharmaceuticals, Inc.) for patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (LGG) harboring a BRAF fusion or rearrangement, or BRAF V600 mutation.

This represents the first FDA approval of a systemic therapy for the treatment of patients with pediatric LGG with BRAF rearrangements, including fusions.

Full prescribing information for Ojemda is available here.

Efficacy and Safety

Efficacy was evaluated in 76 patients enrolled in FIREFLY-1 (NCT04775485), a multicenter, open-label, single-arm trial in patients with relapsed or refractory pediatric LGG harboring an activating BRAF alteration detected by a local laboratory who had received at least one line of prior systemic therapy.

Patients were required to have documented evidence of radiographic progression and at least one measurable lesion. Patients with tumors harboring additional activating molecular alterations (e.g., IDH1/2 mutations, FGFR mutations) or with a known or suspected diagnosis of neurofibromatosis type 1 were excluded.

Patients received tovorafenib based on body surface area (range: 290 to 476 mg/m2, up to a maximum dose of 600 mg) once weekly until they experienced disease progression or unacceptable toxicity.

The major efficacy outcome measure was overall response rate (ORR), as defined as the

proportion of patients with complete response (CR), partial response (PR), or minor response (MR) by blinded independent central review (BICR) based on Response Assessment in Pediatric Neuro-Oncology Low-Grade Glioma (RAPNO-LGG) criteria. Additional efficacy outcome measures included duration or response (DoR).

The ORR was 51% (95% CI: 40, 63) and median DoR was 13.8 months (95% CI: 11.3, not estimable).

The most common adverse reactions (≥30%) were rash, hair color changes, fatigue, viral infection, vomiting, headache, hemorrhage, pyrexia, dry skin, constipation, nausea, dermatitis acneiform, and upper respiratory tract infection. The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased phosphate, decreased hemoglobin, increased creatinine phosphokinase, increased alanine aminotransferase, decreased albumin, decreased lymphocytes, decreased leukocytes, increased aspartate aminotransferase, decreased potassium, and decreased sodium.

The recommended tovorafenib dose based on body surface area (BSA) is 380 mg/m2 orally once weekly (the maximum recommended dosage is 600 mg orally once weekly) with or without food until disease progression or intolerable toxicity. Tovorafenib is available as an immediate release tablet or as an oral suspension. A recommended dosage for patients with BSA less than 0.3 m2 has not been established.

Expedited Programs

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

This application was granted accelerated approval based on overall response rate and duration of response. Continued approval may be contingent upon verification of clinical benefit in confirmatory trials.

This application was granted priority review, 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.

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