Ojemda™ (tovorafenib) – New orphan drug approval

- On April 23, 2024, the FDA announced the approval of Day One Pharmaceuticals' Ojemda (tovorafenib), 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.
    - This indication is approved under accelerated approval based on response rate and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- pLGG is the most common brain tumor diagnosed in children. BRAF is the most commonly altered gene in pLGG, with up to 75% of children having a BRAF alteration.
- Ojemda is a Type II RAF kinase inhibitor of mutant BRAF V600E, wild-type BRAF, and wild-type CRAF kinases.
    - Ojemda is the first FDA approved systemic therapy for the treatment of patients with pLGG with BRAF rearrangements, including fusions.
- The efficacy of Ojemda was established in FIREFLY-1, an open-label, single-arm study in 76 patients with relapsed or refractory pLGG harboring an activating BRAF alteration. Patients received Ojemda until disease progression or unacceptable toxicity. The major efficacy measure was overall response rate (ORR). An additional efficacy measure was DOR.
    - The ORR was 51% (95% CI: 40, 63).
    - The median DOR was 13.8 months (95% CI: 11.3, not estimable).
- Warnings and precautions for Ojemda include hemorrhage, skin toxicity including photosensitivity, hepatotoxicity, effect on growth, embryo-fetal toxicity, and NF1 associated tumors.
- The most common adverse reactions (≥ 30%) with Ojemda use 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 dosage of Ojemda based on body surface area (BSA) is 380 mg/m^2 orally once weekly (the maximum recommended dosage is 600 mg orally once weekly) with or without food until disease progression or intolerable toxicity. Ojemda may be administered as an immediate release tablet or as an oral suspension.
    - A recommended dosage for patients with BSA less than 0.3 m^2 has not been established.
    - Refer to the Ojemda drug label for complete dosing and administration recommendations.

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- Day One Pharmaceuticals' launch plans for Ojemda are pending. Ojemda will be available as a 100 mg tablet and 25 mg/mL oral suspension.