BRAIN CANCER SUPPORT & SOLUTIONS ALLIANCE (BCSSA)

Supporting Information Sheet

Vorasidenib (Brand name Voranigo®)

Vorasidenib, an oral dual inhibitor of mutant IDH1 and IDH2 enzymes, received FDA approval on August 6, 2024 for the treatment of 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, subtotal resection, or gross total resection.

The primary evidence supporting vorasidenib's approval comes from the pivotal Phase 3 INDIGO trial, a global, randomized, double-blind, placebo-controlled study. This trial enrolled 331 patients with residual or recurrent grade 2 glioma harboring an IDH1/2 mutation who had undergone surgery as their only treatment. Patients were randomized to receive either vorasidenib or placebo orally once daily in 28-day cycles.

The INDIGO trial met its primary endpoint of progression-free survival (PFS) as assessed by blinded independent review committee. The median PFS was 27.7 months in the vorasidenib arm versus 11.1 months in the placebo arm. At 18 months, the PFS rate was 60.4% with vorasidenib compared to 26.7% with placebo.

The trial also met its key secondary endpoint of time to next intervention. At 18 months, there was an 85.6% likelihood of not requiring intervention in the vorasidenib group, compared to a 47.4% likelihood in the placebo group.

Vorasidenib was generally well-tolerated, with patients reporting only minor side effects. Common adverse reactions (≥15%) included fatigue, headache, COVID-19, musculoskeletal pain, diarrhea, nausea, and seizure. Vorasidenib may affect fertility, so patients should discuss fertility concerns with their healthcare provider before starting the drug.

The FDA approval of vorasidenib represents the first targeted therapy approved specifically for IDH-mutant diffuse glioma in over 20 years. (A few other IDH inhibitor drugs have been approved but not specifically for brain cancer.) While there has been some criticism of vorasidenib, this FDA approval may significantly change the standard of care for patients with grade 2 astrocytoma and oligodendroglioma by offering a well-tolerated targeted treatment option that can potentially delay the need for more aggressive therapies like chemotherapy or radiation, which often come with harsh, long-term side effects.

While vorasidenib is a promising new option for low-grade gliomas, the benefit for higher-grade IDH-mutant brain tumors remains uncertain. More research is needed to determine if and how IDH inhibitors can be effectively incorporated into treatment strategies for grade 3 and 4 gliomas with IDH mutations.

KEY TAKEAWAY: Vorasidenib is a newly approved oral medication for Grade 2 astrocytoma and oligodendroglioma harboring IDH mutations. It can significantly delay tumor growth and postpone the need for more aggressive treatments, potentially allowing patients to maintain a better quality of life for a longer period. Each patient's situation is unique, and treatment decisions should be made in consultation with your neuro-oncology care team.