FDA Approves Tibsovo As First-Line Treatment for AML With IDH1 Mutation

More than 40% of patients with acute myeloid leukemia achieved complete remission.

May 3, 2019 By Food and Drug Administration (FDA)

On May 2, 2019, the Food and Drug Administration approved ivosidenib (TIbsovo, Agios Pharmaceuticals, Inc.) for newly-diagnosed acute myeloid leukemia (AML) with a susceptible IDH1 mutation, as detected by an FDA-approved test, in patients who are at least 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy.

Approval was based on an open-label, single-arm, multicenter clinical trial (Study AG120-C-001, NCT02074839) of single-agent ivosidenib for newly-diagnosed AML with an IDH1 mutation detected by the Abbott RealTimeTM IDH1 Assay. Patients enrolled were at least 75 years old or met at least one of the following criteria: baseline Eastern Cooperative Oncology Group performance status of ≥ 2, severe cardiac or pulmonary disease, hepatic impairment with bilirubin > 1.5 times the upper limit of normal, or creatinine clearance < 45 mL/min. The 28 patients treated had a median age of 77 years (range, 64-87 years), and 22 (79%) had therapy-related AML or AML with myelodysplasia-related changes.

Ivosidenib was administered orally at a dose of 500 mg daily until disease progression, development of unacceptable toxicity, or hematopoietic stem cell transplantation. Two of the 28 patients underwent stem cell transplantation following ivosidenib.

Efficacy was based on the rate of complete remission (CR) or complete remission with partial hematologic recovery (CRh), the duration of CR+CRh, and the conversion rate from transfusion dependence to transfusion independence. Twelve (42.9%) of the 28 achieved CR+CRh (95% CI: 24.5, 62.8), and 7 (41.2%) of the 17 transfusion-dependent patients achieved transfusion independence lasting at least 8 weeks.

The adverse reactions that occurred in at least 25% of patients were diarrhea, fatigue, edema, decreased appetite, leukocytosis, nausea, arthralgia, abdominal pain, dyspnea, differentiation syndrome and myalgia. Prescribing information contains a Boxed Warning alerting health care professionals and patients about the risk of differentiation syndrome which may be life-threatening or fatal.

The recommended ivosidenib dose is 500 mg orally once daily with or without food until disease progression or unacceptable toxicity. For patients without disease progression or unacceptable

toxicity, treatment is recommended for a minimum of 6 months to allow time for clinical response.

View full prescribing information for Tibsovo.

This application used the Real-Time Oncology Review pilot program. FDA granted this application priority review and orphan product designation. A description of FDA expedited programs is 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.

Follow the Oncology Center of Excellence on Twitter @FDAOncology.

This announcement was originally published on the Food and Drug Administration website on May 2, 2019.
