Xospata™ (gilteritinib) – New orphan drug approval

- On November 28, 2018, the FDA announced the approval of Astellas' Xospata (gilteritinib), for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.

- AML is a rapidly progressing cancer that crowds out normal cells in the bone marrow and bloodstream, resulting in low numbers of normal blood cells and a continuous need for transfusions. The National Cancer Institute estimates that approximately 19,520 people will be diagnosed with AML this year; approximately 10,670 patients with AML will die of the disease in 2018.

    — Approximately 25 to 30% of patients with AML have a mutation in the FLT3 gene.

- Xospata is a tyrosine kinase inhibitor, including FLT3.

    — Xospata is the first drug to be approved that can be used alone in treating patients with FLT3-mutated AML who have relapsed or who don't respond to initial treatment.

- The efficacy of Xospata was evaluated in the ADMIRAL study, which included 138 adult patients with relapsed or refractory AML having a FLT3 mutation. Patients received Xospata until unacceptable toxicity or lack of clinical benefit. Efficacy was established on the basis of the rate of complete remission (CR)/complete remission with partial hematologic recovery (CRh), the duration of CR/CRh (DOR), and the rate of conversion from transfusion dependence to transfusion independence.

    — Overall, 21% (95% CI: 14.5, 28.8) of patients achieved CR or CRh. The median DOR was 4.6 months (range: 0.1 to 15.8).
    — Among the 106 patients who were dependent on red blood cell (RBC) and/or platelet transfusions at baseline, 31% became independent of RBC and platelet transfusions during any 56-day post-baseline period. For the 32 patients who were independent of both RBC and platelet transfusions at baseline, 53% remained transfusion-independent.

- Warnings and precautions of Xospata include posterior reversible encephalopathy syndrome, prolonged QT interval, pancreatitis, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Xospata use were myalgia/arthralgia, transaminase increase, fatigue/malaise, fever, noninfectious diarrhea, dyspnea, edema, rash, pneumonia, nausea, stomatitis, cough, headache, hypotension, dizziness, and vomiting

- The recommended starting dose of Xospata is 120 mg orally once daily with or without food. Response may be delayed. In the absence of disease progression or unacceptable toxicity, treatment for a minimum of 6 months is recommended to allow time for a clinical response.

    — Patients should be selected for the treatment of AML with Xospata based on the presence of FLT3 mutations in the blood or bone marrow. Information on FDA-approved tests for the detection of a FLT3 mutation in AML is available at http://www.fda.gov/CompanionDiagnostics.
    — Refer to the Xospata label for additional dosing recommendations.

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- Astellas' launch plans for Xospata are pending. Xospata will be available as 40 mg tablets.