Daurismo™ (glasdegib) – New orphan drug approval

- On November 21, 2018, the FDA announced the approval of Pfizer's Daurismo (glasdegib), to be used in combination with low-dose cytarabine (LDAC), for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.
    - Daurismo has not been studied in patients with the comorbidities of severe renal impairment or moderate-to-severe hepatic impairment.
- AML is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of abnormal white blood cells in the bloodstream and bone marrow. The National Cancer Institute estimates that in 2018, approximately 19,520 people will be diagnosed with AML and approximately 10,670 patients with AML will die of the disease.
    - Almost half of the adults diagnosed with AML are not treated with intensive chemotherapy because of comorbidities and chemotherapy related toxicities.
- Daurismo is the first FDA-approved Hedgehog pathway inhibitor for AML. Abnormal activation of this pathway in adults is thought to contribute to the development and persistence of cancer stem cells.
- The efficacy of Daurismo was evaluated in an open-label study of 115 patients age ≥ 55 years with newly-diagnosed AML. Patients were randomized to receive Daurismo with LDAC or LDAC alone until disease progression or unacceptable toxicity.. Efficacy was established based on overall survival (OS).
    - Median OS was 8.3 months (95% CI: 4.4, 12.2) in the Daurismo plus LDAC arm vs. 4.3 months (95 CI%: 1.9, 5.7) in the LDAC arm (hazard ratio = 0.46; 95% CI: 0.30, 0.71; p = 0.0002).
- Daurismo carries a boxed warning for embryo-fetal toxicity.
- An additional warning and precaution of Daurismo includes QTc interval prolongation.
- The most common adverse reactions (≥ 20%) with Daurismo use were anemia, fatigue, hemorrhage, febrile neutropenia, musculoskeletal pain, nausea, edema, thrombocytopenia, dyspnea, decreased appetite, dysgeusia, mucositis, constipation, and rash.
- The recommended dose of Daurismo is 100 mg orally once daily on days 1 to 28 in combination with cytarabine 20 mg subcutaneously twice daily on days 1 to 10 of each 28-day cycle in the absence of unacceptable toxicity or loss of disease control.
    - For patients without unacceptable toxicity, treat for a minimum of 6 cycles to allow time for clinical response.
- Pfizer's launch plans for Daurismo are pending. Daurismo will be available as 25 mg and 100 mg tablets.

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