## Vanflyta® (quizartinib) – New orphan drug approval

- On July 20, 2023, Daiichi Sankyo announced the FDA approval of Vanflyta (quizartinib), in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test.
    - Vanflyta is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with Vanflyta in this setting has not been demonstrated.
- AML is one of the most common forms of leukemia in adults and an estimated 20,380 new cases will be diagnosed in the U.S. in 2023. Up to 37% of newly diagnosed patients with AML have a FLT3 gene mutation and approximately 80% of these are FLT3-ITD mutations, which drive cancer growth and contribute to increased risk of relapse and shorter overall survival.
- The efficacy of Vanflyta was established in a QuANTUM-First, a randomized, double-blind, placebo-controlled study in 539 patients with newly diagnosed FLT3-ITD positive AML. Patients were randomized to receive Vanflyta or placebo in combination with induction and consolidation therapy and as maintenance monotherapy according to the initial assignment. Patients who proceeded to HSCT initiated maintenance therapy after recovery from the HSCT. Efficacy was established on the basis of overall survival (OS), measured from the date of randomization until death by any cause.
    - A statistically significant improvement in OS was demonstrated for the Vanflyta arm compared to placebo (hazard ratio [HR] 0.78, 95% CI: 0.62, 0.98; p = 0.0324).
    - In an exploratory subgroup analysis of the 89/208 (43%) of patients who received maintenance therapy with Vanflyta or placebo following consolidation chemotherapy, the OS HR was 0.40 (95% CI: 0.19, 0.84). Of 119/208 (57%) of patients who received maintenance therapy with Vanflyta or placebo following HSCT, the OS HR was 1.62 (95% CI: 0.62, 4.22).
- Vanflyta carries a boxed warning for QT prolongation, torsades de pointes, and cardiac arrest.
    - Vanflyta is available only through a restricted program called the Vanflyta Risk Evaluation and Mitigation Strategy (REMS).
- Vanflyta is contraindicated in patients with severe hypokalemia, severe hypomagnesemia, long QT syndrome, or in patients with a history of ventricular arrhythmias or torsades de pointes.
- An additional warning and precaution for Vanflyta is embryo-fetal toxicity.
- The most common adverse reactions (> 20%), including laboratory abnormalities, with Vanflyta use were decreased lymphocytes, decreased potassium, decreased albumin, decreased phosphorus, increased alkaline phosphatase, decreased magnesium, febrile neutropenia, diarrhea, mucositis, nausea, decreased calcium, abdominal pain, sepsis, neutropenia, headache, increased creatine phosphokinase, vomiting, and upper respiratory tract infection.
- A treatment course with Vanflyta consists of up to 2 cycles of Vanflyta in combination with induction cytarabine and anthracycline, up to 4 cycles of Vanflyta in combination with high-dose cytarabine consolidation, and up to 36 cycles of Vanflyta as maintenance therapy or until disease progression or unacceptable toxicity. Vanflyta maintenance therapy should be initiated following consolidation

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chemotherapy upon blood count recovery of absolute neutrophil count > 500/$mm^3$ and platelet count > 50,000/$mm^3$.

  - Vanflyta is administered orally, and the dose depends on the phase of therapy. Refer to the drug label for complete dosing and administration recommendations.

- Patients should be selected for the treatment of AML with Vanflyta based on the presence of FLT3-ITD mutation positivity. Information on FDA-approved tests for the detection of FLT3-ITD mutation in AML is available at: http://www.fda.gov/CompanionDiagnostics.

- Daiichi Sankyo plans to launch Vanflyta in the coming weeks. Vanflyta will be available as a 17.7 mg and 26.5 mg tablet.

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