Idhifa® (enasidenib) – New orphan drug approval

- On August 1, 2017, the FDA announced the approval of Celgene's Idhifa (enasidenib), for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.

- 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 approximately 21,380 Americans will be diagnosed with AML and 10,590 patients will die of the disease this year.

    - For 8 – 19% of AML patients, the mutated IDH2 enzyme blocks normal blood cell development and results in an overabundance of immature blood cells.
    - The majority of patients with AML eventually relapse. Relapsed or refractory AML has a poor prognosis.

- Idhifa contains enasidenib, an IDH2 inhibitor. Blockade of this mutant enzyme leads to decreased 2-hydroxyglutarate levels, reduced blast counts, and increased percentages of mature myeloid cells.

    - Idhifa is the first and only oral targeted IDH2 inhibitor.

- The efficacy of Idhifa was based on an open-label, single-arm trial involving 199 patients with relapsed or refractory AML and an IDH2 mutation. The primary endpoints were the complete response rate (CR)/CR with partial hematologic recovery (CRh), duration of CR/CRh, and rate of conversion from transfusion dependence to transfusion independence.

    - With a minimum of six months of treatment, 19% (95% CI: 13, 25) of patients experienced CR for a median 8.2 months, and 4% (95% CI: 2, 8) of patients experienced CRh for a median 9.6 months.
    - The median duration of CR/CRh was 8.2 months (95% CI: 4.3, 19.4).
    - In addition, of the 157 patients who required transfusions of blood or platelets due to AML at the start of the study, 34% no longer required transfusions after treatment with Idhifa.

- Idhifa carries a boxed warning regarding the risk of differentiation syndrome.

- The other warning and precaution includes the risk of embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Idhifa use were nausea, vomiting, diarrhea, elevated bilirubin, and decreased appetite.

- The recommended starting dose of Idhifa is 100 mg orally once daily until disease progression or unacceptable toxicity.

    - Patients should be selected for treatment based on the presence of IDH2 mutations in the blood or bone marrow.
    - For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response.
    - Healthcare providers should assess blood counts and blood chemistries for leukocytosis and tumor lysis syndrome prior to the initiation of Idhifa and monitor at a minimum of every 2 weeks for at least the first 3 months during treatment. Abnormalities should be managed promptly and the dose interrupted or reduced for toxicities.
    - Do not split or crush Idhifa tablets.

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- The monthly wholesale acquisition cost of AML treatment with Idhifa is $24,872.
- Celgene's plans to launch Idhifa as soon as possible. Idhifa will be available as 50 mg and 100 mg tablets.