Inqovi® (decitabine/cedazuridine) – New orphan drug approval

- On July 7, 2020, the FDA announced the approval of Astex Pharmaceuticals' Inqovi (decitabine/cedazuridine), for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System (IPSS) groups.

- Inqovi is a fixed-dose combination of the approved anti-cancer DNA hypomethylating agent, decitabine, together with cedazuridine, an inhibitor of cytidine deaminase. By inhibiting cytidine deaminase in the gut and the liver, Inqovi is designed to allow for oral delivery of decitabine.

    - Inqovi is the first orally administered hypomethylating agent approved by the FDA.
    - Decitabine is also available generically as an intravenous infusion for a similar indication as Inqovi.

- The efficacy of Inqovi was established in ASTX727-01-B, an open-label, randomized, 2-cycle, 2-sequence crossover study that included 80 adult patients with MDS (IPSS Intermediate-1, Intermediate-2, or high-risk) or CMML. Patients were randomized to receive Inqovi in cycle 1 and decitabine intravenously in cycle 2 or the reverse sequence. Both Inqovi and intravenous decitabine were administered once daily on days 1 through 5 of the 28-day cycle. Starting with cycle 3, all patients received Inqovi on days 1 through 5 of each 28-day cycle until disease progression or unacceptable toxicity. Efficacy was established on the basis of complete response (CR) and the rate of conversion from transfusion dependence to transfusion independence.

    - The CR rate was 18% (95% CI: 10, 28).
    - Among the 41 patients who were dependent on red blood cell (RBC) and/or platelet transfusions at baseline, 20 (49%) became independent of RBC and platelet transfusions during any consecutive 56-day post-baseline period.
    - Of the 39 patients who were independent of both RBC and platelet transfusions at baseline, 25 (64%) remained transfusion-independent during any consecutive 56-day post-baseline period.

- The efficacy of Inqovi was also evaluated in ASTX727-02, an open-label, randomized, 2-cycle, 2-sequence crossover study that included 133 adult patients with MDS or CMML, including all French-American-British classification criteria and IPSS Intermediate-1, Intermediate-2, or high-risk prognostic scores. The study had similar treatment arms as ASTX727-01-B. Efficacy was established on the basis of CR and the rate of conversion from transfusion dependence to transfusion independence.

    - The CR rate was 21% (95% CI: 15, 29).
    - Among the 57 patients who were dependent on RBC and/or platelet transfusions at baseline, 30 (53%) became independent of RBC and platelet transfusions during any 56-day post-baseline period.
    - Of the 76 patients who were independent of both RBC and platelet transfusions at baseline, 48 (63%) remained transfusion-independent during any 56-day post-baseline period.

- Warnings and precautions for Inqovi include myelosuppression and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Inqovi use were fatigue, constipation, hemorrhage, myalgia, mucositis, arthralgia, nausea, dyspnea, diarrhea, rash, dizziness, febrile

Continued . . .

neutropenia, edema, headache, cough, decreased appetite, upper respiratory tract infection, pneumonia, and increased transaminase.

- The most common Grade 3 or 4 laboratory abnormalities (≥ 50%) with Inqovi use were decreased leukocytes, decreased platelet count, decreased neutrophil count, and decreased hemoglobin.

- The recommended dosage of Inqovi is 1 tablet (containing 35 mg decitabine and 100 mg cedazuridine) orally once daily on days 1 through 5 of each 28-day cycle for a minimum of 4 cycles until disease progression or unacceptable toxicity. A complete or partial response may take longer than 4 cycles.

    — Inqovi should NOT be substituted for an intravenous decitabine product within a cycle.
    — Antiemetics prior to each dose of Inqovi should be considered to minimize nausea and vomiting.

- Astex Pharmaceuticals' launch plans for Inqovi are pending. Inqovi will be available as a tablet containing 35 mg decitabine and 100 mg cedazuridine.