Rytelo™ (imetelstat) – New orphan drug approval

- On June 6, 2024, the FDA announced the approval of Geron's Rytelo (imetelstat), for the treatment of adult patients with low-to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring 4 or more red blood cell units over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESA).

- Lower-risk MDS is a blood cancer that often progresses to require increasingly intensified management of key symptoms such as anemia and resulting fatigue. These symptomatic patients frequently become red blood cell transfusion dependent.

- The efficacy of Rytelo was established in IMerge, a randomized, double-blind, placebo-controlled study in 178 patients with low- or intermediate-1 risk MDS who were transfusion-dependent. Patients were required to have failed to respond or have lost response or be ineligible for ESAs. Participants were randomized to Rytelo or placebo. Efficacy was established based upon the proportion of patients who achieved ≥ 8-week and ≥ 24-week red blood cell transfusion independence (RBC-TI), defined as the absence of RBC transfusion(s) during any consecutive 8-week period, and during any consecutive 24-week period, respectively, from randomization until the start of subsequent anti-cancer therapy (if any).

    - The proportion of patients with ≥ 8-week RBC-TI was 39.8% with Rytelo vs. 15.0% with placebo (difference 24.8, 95% CI: 9.9, 36.9; $p < 0.001$).
    - The proportion of patients with ≥ 24-week RBC-TI was 28.0% with Rytelo vs. 3.3% with placebo (difference 24.6, 95% CI: 12.6, 34.2; $p < < 0.001$).

- Warnings and precautions for Rytelo include thrombocytopenia, neutropenia, infusion-related reactions, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 10% with a difference between arms of > 5% compared to placebo), including laboratory abnormalities, with Rytelo use were decreased platelets, decreased white blood cells, decreased neutrophils, increased aspartate aminotransferase, increased alkaline phosphatase, increased alanine aminotransferase, fatigue, prolonged partial thromboplastin time, arthralgia/myalgia, COVID-19 infections, and headache.

- The recommended dose of Rytelo is 7.1 mg/kg administered as an intravenous infusion over 2 hours every 4 weeks. Rytelo should be discontinued if a patient does not experience a decrease in RBC transfusion burden after 24 weeks of treatment (administration of 6 doses) or if unacceptable toxicity occurs at any time.

- Geron plans to launch Rytelo by the end of June 2024. Rytelo will be available as a 47 mg and 188 mg powder in single-dose vials.