Errata to FDA Briefing Document

Oncologic Drugs Advisory Committee Meeting

March 14, 2024

This erratum contains corrections to FDA's briefing information for the March 14, 2024, ODAC Meeting. The committee will discuss new drug application (NDA) 217779 for imetelstat, submitted by Geron Corporation, for the following proposed indication: for the treatment of transfusion-dependent anemia in adult patients with low- to intermediate-1 risk myelodysplastic syndromes (MDS) who have failed to respond, or have lost response to, or are ineligible for erythropoiesis stimulating agents (ESA).

1. In Section 2.3 Pertinent Drug Development and Regulatory History, the first bullet point states that the original IND 072072 for imetelstat was submitted on May 11, 2005. It should state that the original IND 072072 for imetelstat was submitted on April 8, 2005, and was deemed safe to proceed on May 11, 2005.

2. In Section 3.2.1 Magnitude and Durability of RBC Transfusion Independence, Table 2 states that the 95% confidence interval for 24-week RBC-TI for the placebo arm was (12.6, 34.2). It should state that the 95% confidence interval was (0.4, 11.5).

3. In Section 3.2.7 Lack of evidence of reduction in medical resource utilization, Table 5 states that the total number of medical encounters (average per patient) was 97 (0.8/patient) for imetelstat versus 51 (0.9/patient) for placebo. It should state that the total number of medical encounters (average per patient) was 157 (1.3/patient) for imetelstat versus 96 (1.6/patient) for placebo. Additionally, the footnote under the table which states "Source: Study MSD3001 Phase 3 Clinical Study Report" should state "Source: Study MDS3001 Phase 3 Clinical Study Report and FDA analysis using ADHO dataset."

4. In Section 3.3 Safety summary, Table 9, "neutrophils decreased", the risk difference for grade 3-4 is listed as +6.4. It should be +64. In "alkaline phosphatase increased", the all grade imetelstat value states 49 and placebo value states 14. The corrected values are 45 for imetelstat and 12 for placebo with the risk difference for the corrected values of +33.

5. In Section 3.4.1.1 Neutropenia, Table 14 states that 42 (36%) patients required myeloid growth factor on treatment with imetelstat. It should state that 41 (35%) patients received myeloid growth factor during on treatment with imetelstat, and the * footnote should be removed.

6. In Table 15 (Section 3.4.1.1 Neutropenia), Table 21 (Section 3.4.1.2 Thrombocytopenia), and Table 27 (Section 4 Benefit-Risk Assessment), the analyses presented used data from the 120-day safety update (data cut-off date 10 May 2023) rather than the initial submission (data cut-off date 13 Oct 2022) as stated in the footnotes. Tables using the initial submission (data cut-off date 13 Oct 2022) will be in the FDA slide presentation.

7. In Section 3.4.2 Hepatic toxicity, the third paragraph states:
   "The abnormalities resolved when both medications were stopped and recurred after restarting first imetelstat then deferiprox. The Applicant attributed the abnormalities to deferiprox, but the timing of the dechallenge and rechallenge events makes attribution difficult."

   This should state:
   "The abnormalities resolved when both medications were stopped and no recurrence of transaminase and bilirubin abnormalities that met laboratory criteria for Hy's law were observed, although increases in transaminases to grade 2 and in bilirubin to grade 1 were observed after re-challenge with deferasirox. The Applicant attributed the abnormalities to deferasirox, but the timing of the dechallenge makes attribution difficult. The Applicant's hepatic adjudication committee did not attribute the event to imetelstat and did not identify any confirmed Hy's law cases."

   Note that the spelling of "deferasirox" was corrected in this sentence.

8. In Section 3.4.3 Fractures, paragraph 1 states:
   "Finally, fractures were documented in 61 patients (8%) who received imetelstat as monotherapy or as part of combination therapy at any dose and in a variety of hematologic and solid tumors, including 47 (8%) who received imetelstat as monotherapy at any dose and 20 (10%) who received imetelstat monotherapy at a dose of 7.1 mg/kg."

   This should state:
   "Finally, when using broad search criteria to screen for the occurrence of fractures, including non-specific terms such as bone pain, screening identified 61 patients (8%) who received imetelstat as monotherapy or as part of combination therapy at any dose and in a variety of hematologic and solid tumors, including 47 (8%) who received imetelstat as monotherapy at any dose and 20 (10%) who received imetelstat monotherapy at a dose of 7.1 mg/kg. Using the narrow definition of fracture including only those cases in which a fracture was definitively documented in the dataset (preferred terms hand fracture, hip fracture, lumbar vertebral spine fracture, femur fracture, humerus fracture), 20 patients experienced fractures all of whom received imetelstat at a dose equivalent to or higher than 7.1 mg/kg every 4 weeks. This represents 3% of patients in the safety database and 4% of those who received at least 7.1 mg/kg every 4 weeks. The narrow search terms were used in the description of adverse events for the primary study MDS3001, in order to avoid over-attribution."