Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting

March 14, 2024

Location: All meeting participants were heard, viewed, captioned, and recorded for this advisory committee meeting via an online teleconferencing and/or video conferencing platform.

Topic: The Committee discussed new drug application (NDA) 217779 for imetelstat for injection, submitted by Geron Corporation. The proposed indication for this product is for the treatment of transfusion-dependent anemia in adult patients with low- to intermediate-1 risk myelodysplastic syndromes who have failed to respond or have lost response to or are ineligible for erythropoiesis-stimulating agents.

These summary minutes for the March 14, 2024 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on June 26, 2024.

I certify that I attended the March 14, 2024 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
LaToya Bonner, PharmD	Ravi A. Madan, MD
Acting Designated Federal Officer, ODAC	Chairperson, ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
March 14, 2024

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on March 14, 2024. The meeting presentations were heard, viewed, captioned, and recorded through an online video conferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Geron Corporation. The meeting was called to order by Ravi Madan, MD (Chairperson). The conflict-of-interest statement was read into the record by LaToya Bonner, PharmD (Acting Designated Federal Officer). There were approximately 1527 people online. There was a total of 9 Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda:

The Committee discussed new drug application (NDA) 217779 for imetelstat for injection, submitted by Geron Corporation. The proposed indication for this product is for the treatment of transfusion-dependent anemia in adult patients with low- to intermediate-1 risk myelodysplastic syndromes who have failed to respond or have lost response to or are ineligible for erythropoiesis-stimulating agents.

Attendance:

ODAC Members Present (Voting): Ranjana H. Advani, MD; Toni K. Choueiri, MD; Mark R. Conaway, PhD; Pamela L. Kunz, MD; Christopher H. Lieu, MD; Ravi A. Madan, MD *(Chairperson)*; David E. Mitchell *(Consumer Representative)*; Jorge J. Nieva, MD; Ashley Rosko, MD; Daniel Spratt, MD; Neil Vasan, MD, PhD

ODAC Members Not Present (Voting): William J. Gradishar, MD; Alberto S. Pappo, MD

ODAC Member Present (Non-Voting): Tara L. Frenkl, MD, PhD (*Industry Representative*)

Temporary Members (Voting): Jacqueline Garcia, MD; Anthony Hunter, MD; and Joan D. Powell (*Patient Representative*)

FDA Participants (Non-Voting): Rick Pazdur, MD; Marc Theoret, MD; R. Angelo de Claro, MD; Kelly Norsworthy, MD; Lori Ehrlich, MD, PhD; Nina Kim, MD

Acting Designated Federal Officer (Non-Voting): LaToya Bonner, PharmD

Open Public Hearing Speakers Present: Rena Buckstein, MD; Tracey Irarca and Ashley Moncrief (MDS Foundation); Cyndy Lunsford; Gail J. Roboz, MD; Valeria Santini, MD; Lewis Silverman; Daneen Sekoni (Cancer Support Community); Kenan White; Paul Urken

The agenda was as follows:

Call to Order	**Ravi A. Madan, MD** Chairperson, ODAC
Introduction of Committee and Conflict of Interest Statement	**LaToya Bonner, PharmD** Acting Designated Federal Officer, ODAC
FDA Opening Remarks	**Lori Ehrlich, MD, PhD** Cross-disciplinary Team Leader Division of Hematologic Malignancies I (DHMI) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Geron Corporation**
Introduction	**Sharon McBain, BSc** Senior Vice President, Global Head of Regulatory Affairs Geron Corporation
Clinical Results	**Faye Feller, MD** Chief Medical Officer Geron Corporation
Unmet Medical Need for Treatment in Low-Risk Myelodysplastic Syndromes	**Michael Savona, MD** The Beverly and George Rawlings Director of Hematology Research Professor of Medicine and Cancer Biology Vanderbilt University School of Medicine
Clinical Perspective	**Rami Komrokji, MD** Vice Chair, Malignant Hematology Department Lead Clinical Investigator, MDS Program H. Lee Moffitt Cancer Center & Research Institute Professor of Oncologic Sciences University of South Florida
Conclusion	**Faye Feller, MD**

FDA PRESENTATION

Imetelstat for the Treatment of Transfusion-Dependent Anemia in Patients with Lower Risk Myelodysplastic Syndromes who have Not Responded to or have Lost Response to or are Ineligible for Erythropoiesis-Stimulating Agents	**Nina Kim, MD** Clinical Reviewer DHM1, OOD, OND, CDER, FDA

Clarifying Questions to Presenters

LUNCH

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Discuss the efficacy of imetelstat for patients with lower-risk myelodysplastic syndromes (MDS) based on the results of the MDS3001 trial considering the safety profile.

   Committee Discussion*: Collectively, the Committee members agreed that Study MDS3001 met the statistical goals for the primary endpoint of achievement of red blood cell transfusion independence (RBC-TI) for 8 weeks and the secondary endpoint of RBC-TI for 24 weeks. When it comes to overall safety, the Committee acknowledged the occurrences of cytopenia shown in the data but expressed that these toxicities are not foreign in the population studied and can be well controlled in a real-world setting.*

   Some members noted the lack of measurable outcomes in the study, they suggested for the applicant to establish a true surrogate, in further studies, so a measurable quality of life (QOL) can be captured in the population studied. Other members noted that transfusion independence (TI) is a QOL metric, and the study may have potentially introduced a measurable nuance for future MDS trials.

   The Committee highlighted the current challenges of MDS patients and the limited options available to manage the disease. The members pointed out that avoiding transfusion as long as possible reduces toxicity and cost, which are considered measurable outcomes in the MDS community. Although the data did not show any markers of overall survival or imetelstat preventing the transitioning of MDS to acute myelogenous leukemia, the Committee agreed that the possibility of achieving TI up to 6 months is remarkable to the population affected. Please see the transcript for details of the Committee's discussion.

2. **VOTE:** Do the benefits of imetelstat outweigh its risks for the treatment of transfusion dependent anemia in adult patients with International Prognosis Scoring System (IPSS) low- to intermediate-1 risk MDS who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents?

   Vote Result: Yes: 12 No: 2 Abstain: 0

   Committee Discussion*: The majority of the Committee voted "Yes", that imetelstat's benefits outweigh its risks for the treatment of transfusion dependent anemia in adult patients with International Prognosis Scoring System low- to intermediate-1 risk MDS who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents. The Committee members who voted "Yes", agreed that the study met its primary and secondary endpoints. Although the Committee acknowledged the severity of the side effects observed from imetelstat in the study, the members discussed that these episodes can be well-controlled in a real world setting as the intended population is already closely monitored by specialists who are familiar with neutropenia and cytopenia. One member stated that hematologists are no strangers to neutropenia, and although neutropenia cannot be mitigated, to have an option where patients can potentially benefit is promising in the management of MDS. Another member expressed that the long-term consequences of transfusion dependence are debilitating enough, and the demonstration shown of imetelstat's ability to reduce the number of transfusions is "impressive."*

   Two Committee members voted "No", that the data shown did not convince them of imetelstat's benefits (RBC-TI for eight weeks) outweighing it risks (i.e., cytopenia). Although there was an agreement that the primary and secondary endpoints were met, these members were not persuaded by the trial's outcome relative to the safety profile observed. Please see the transcript for details of the Committee's discussion.

The meeting was adjourned at approximately 3:30 p.m. ET.