Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
March 15, 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: During the morning session, the Committee discussed supplemental biologics license application (sBLA) 125746.74 for CARVYKTI (ciltacabtagene autoleucel), suspension for intravenous infusion, submitted by Janssen Biotech, Inc. The proposed indication for this product is for the treatment of adult patients with relapsed or refractory multiple myeloma, who have received at least one prior line of therapy, including a proteasome inhibitor, and an immunomodulatory agent, and are refractory to lenalidomide. The Committee had a general discussion focused on the overall survival data in the Study MMY3002 (CARTITUDE-4) and the risk and benefit of ciltacabtagene autoleucel in the intended population.

During the afternoon session, the Committee discussed sBLA 125736.218 for ABECMA (idecabtagene vicleucel), suspension for intravenous infusion, submitted by Celgene Corp., a Bristol-Myers Squibb Co. The proposed indication is for the treatment of adult patients with relapsed or refractory multiple myeloma who have received an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. The Committee had a general discussion focused on the overall survival data in the Study MM-003 (KarMMa-3) and the risk and benefit of idecabtagene vicleucel in the intended population**.**

These summary minutes for the March 15, 2024 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on 4/29/2024.

I certify that I attended the March 15, 2024 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

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

Summary Minutes of the Oncologic Drugs Advisory CommitteeMeeting
March 15, 2024

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on March 15, 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, Janssen Biotech, Inc. and Celgene Corporation, a Bristol-Myers Squibb Company. The meeting was called to order by Ravi Madan, MD (Chairperson). The conflict of interest statement was read into the record by Joyce Frimpong, PharmD (Acting Designated Federal Officer). There were approximately 2400 people in attendance. There were 10 Open Public Hearing (OPH) speaker presentations during the morning session and 4 OPH speaker presentations during the afternoon session.

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

Agenda: During the morning session, the Committee discussed supplemental biologics license application (sBLA) 125746.74 for CARVYKTI (ciltacabtagene autoleucel), suspension for intravenous infusion, submitted by Janssen Biotech, Inc. The proposed indication for this product is for the treatment of adult patients with relapsed or refractory multiple myeloma, who have received at least one prior line of therapy, including a proteasome inhibitor, and an immunomodulatory agent, and are refractory to lenalidomide. The Committee had a general discussion focused on the overall survival data in the Study MMY3002 (CARTITUDE-4) and the risk and benefit of ciltacabtagene autoleucel in the intended population.

During the afternoon session, the Committee discussed sBLA 125736.218 for ABECMA (idecabtagene vicleucel), suspension for intravenous infusion, submitted by Celgene Corp., a Bristol-Myers Squibb Co. The proposed indication is for the treatment of adult patients with relapsed or refractory multiple myeloma who have received an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. The Committee had a general discussion focused on the overall survival data in the Study MM-003 (KarMMa-3) and the risk and benefit of idecabtagene vicleucel in the intended population**.**

Attendance:
Oncologic Drugs Advisory Committee Members Present (Voting): Ranjana Advani, MD; William Gradishar, MD; Christopher Lieu, MD; Ravi Madan, MD *(Chairperson)*; Jorge Nieva, MD; Daniel Spratt, MD; Neil Vasan, MD

Oncologic Drugs Advisory Committee Members Not Present (Voting): Toni K. Choueiri, MD; Mark R. Conaway, PhD; Pamela L. Kunz, MD; David E. Mitchell *(Consumer Representative)*; Alberto S. Pappo, MD; Ashley Rosko, MD

Oncologic Drugs Advisory Committee Member Present (Non-Voting): Tara Frenkl MPH, MD *(Industry Representative)*

Temporary Members (Voting): John DeFlice, MD *(Patient Representative)*; Sally Hunsberger, PhD; Mark Kwok, MD; Susan Lattimore, RN, GCPH *(Acting Consumer Representative)*

FDA Participants (Non-Voting): Richard Pazdur, MD *(afternoon sessiononly)*; Marc Theoret, MD; Nicole Verdun, MD; Bindu Kanapuru, MD; Robert Sokolic, MD; Helkha Peredo-Pinto, MD, MPH *(morning session only)*; Cong Wang, PhD *(morning session only)*; Poornima Sharma, MD *(afternoon session only)*; Xue (Mary) Lin, PhD (*afternoon session only*)

Acting Designated Federal Officer (Non-Voting): Joyce Frimpong, PharmD

Open Public Hearing Speakers:
Morning session: Mary DeRome (Multiple Myeloma Research Foundation); Cynthia Chmielewski; Saad Usmani, MD; Aparajita and Ajai Puri; Surbhi Sidana, MD; Jack Aiello; Yelak Biru (Internaational Myeoloma Foundation); Deborah Haustein; Jenny Ahlstrom (HealthTree Foundation); Douglas Keller

Afternoon session: Mary DeRome (Multiple Myeloma Research Foundation); Sanjay Singh; Carl Burgman; Brian G.M. Durie, MD International Myeloma Foundation

The agenda was as follows:

Call to Order	**Ravi A. Madan, MD** Chairperson, ODAC
Introduction of Committee/ Conflict of Interest Statement	**Joyce Frimpong, PharmD** Acting Designated Federal Officer, ODAC
FDA Opening Remarks	**Robert Sokolic, MD** Branch Chief Malignant Hematology Branch (MHB) Division of Clinical Evaluation Hematology (DCEH) Office of Clinical Evaluation (OCE) Office of Therapeutic Products (OTP) Center for Biologics Evaluation and Research (CBER) FDA
GUEST SPEAKER PRESENTATION Current Management of Multiple Myeloma	**Sham Mailankody, MBBS** Clinical Director, Cellular Therapy Service Research Director, Myeloma Service Associate Attending Physician and Associate Member Memorial Sloan Kettering Cancer Center
Clarifying Questions to Guest Speaker	
APPLICANT PRESENTATIONS	**Janssen Biotech Inc.**

Introduction	**Sen Zhuang, MD, PhD** Vice President, Oncology Research & Development Johnson & Johnson
Unmet Need	**Irene Ghobrial, MD** Professor of Medicine Dana Farber Cancer Institute Harvard Medical School
CARTITUDE-4 Efficacy and Safety Data	**Jordan Schecter, MD** Vice President Research & Development Johnson & Johnson
Clinical Perspective	**Sundar Jagannath, MBBS** Director of Center of Excellence for Multiple Myeloma Tisch Cancer Institute Professor of Medicine at Icahn School of Medicine Mount Sinai

FDA PRESENTATIONS

Ciltacabtagene Autoleucel (CARVYKTI) sBLA 125746.74	**Helkha Peredo-Pinto, MD, MPH** Clinical Reviewer MHB, DCEH, OCE, OTP, CBER, FDA **Cong Wang, PhD** Statistical Reviewer Therapeutics Evaluation Branch 1 (TEB1) Division of Biostatistics (DB) Office of Biostatistics and Pharmacovigilance (OBPV) CBER, FDA
Clarifying Questions	

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion	

LUNCH

Call to Order	**Ravi A. Madan, MD** Chairperson, ODAC
Introduction of Committee/ Conflict of Interest Statement	**Joyce Frimpong, PharmD** Acting Designated Federal Officer, ODAC

FDA Opening Remarks	**Robert Sokolic, MD** Branch Chief MHB, DCEH, OCE, OTP, CBER, FDA
APPLICANT PRESENTATIONS	**Celgene Corporation, a Bristol-Myers Squibb Company**
Introduction	**Anne Kerber, MD** Senior Vice President, Head of Late Clinical Development, Hematology, Oncology, and CT Bristol Myers Squibb
Disease Background	**Sagar Lonial, MD** Chief Medical Officer, Winship Cancer Institute of Emory University Professor and Chair, Department of Hematology and Medical Oncology Anne and Bernard Gray Family Chair in Cancer Emory University School of Medicine
KarMMa-3 Design and PFS Results	**Eric Bleickardt, MD** Vice President, Late Clinical Development, Cell Therapy Bristol Myers Squibb
KarMMa-3 Overall Survival Results	**Eric Bleickardt, MD**
Clinical Safety	**Mark Cook, MBChB, PhD** Senior Clinical Trial Physician Bristol Myers Squibb
Clinical Perspective on Benefits and Risks of Ide-cel Treatment for Triple-class Exposed Multiple Myeloma Patients	**Noopur Raje, MD** Director, Center for Multiple Myeloma Massachusetts General Hospital Professor of Medicine Harvard Medical School
FDA PRESENTATIONS	
Idecabtagene Vicleucel (ABECMA) sBLA 125736.218	**Poornima Sharma, MD** Clinical Reviewer MHB, DCEH, OCE, OTP, CBER, FDA
	Xue (Mary) Lin, PhD Statistical Reviewer TEB1, DB, OBPV, CBER, FDA
Clarifying Questions	

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

Morning session

1. **DISCUSSION:** Discuss whether the results of CARTITUDE-4 are sufficient to support a positive risk-benefit assessment of ciltacabtagene autoleucel for the proposed indication.

   Committee Discussion: *Committee members discussed that, while there are some risks, the benefit of the progression free survival allows patients freedom from treatment. Committee members highlighted that it was a benefit to have a treatment option that could be given one time without having patients come back and forth for treatment. Please see the transcript for details of the Committee's discussion.*

2. **DISCUSSION:** Is the risk of early death associated with ciltacabtagene autoleucel treatment acceptable in the context of the PFS benefit?

   Committee Discussion: *Committee members acknowledged that the risk of the death up front was concerning,but noted that the risk may or may not be mitigated for the future. Please see the transcript for details of the Committee's discussion.*

3. **VOTE:** Is the risk-benefit assessment for ciltacabtagene autoleucel for the proposed indication, favorable?

   Vote Result: Yes: 11 No: 0 Abstain: 0

   Committee Discussion: *The Committee unanimously agreed that the risk-benefit assessment was favorable. Committee members acknowledged the risk of early death could be related to an inadequate bridging regimen, which was not optimized. The Committee noted that the risk should be addressed in the future, but there was agreement that the progression free survival data was strong, and it outweighed the risk. Please see the transcript for details of the Committee's discussion.*

Afternoon session

1. **DISCUSSION:** Discuss whether the results of KarMMa-3 are sufficient to support a positive risk-benefit assessment of idecabtagene vicleucel for the proposed indication.

   Committee Discussion: *Committee members generally agreed that it was difficult to evaluate the overall survival given the amount of crossover presented, and that the benefit observed was in regard to the progression free survival. Please see the transcript for details of the Committee's discussion.*

2. **DISCUSSION**: Is the risk of early death associated with idecabtagene vicleucel treatment acceptable in the context of the PFS benefit?

   Committee Discussion: *Overall, Committee members agreed that the progression free survival benefit was clear, and the risk of early death was a concern. Some panel members suggested that the risk of the early death could be related to an inadequate bridging regimen, which was not optimized. Please see the transcript for details of the Committee's discussion.*

3. **VOTE:** Is the risk-benefit assessment for idecabtagene vicleucel for the proposed indication, favorable?

   Vote Result: Yes: 8 No: 3 Abstain: 0

   Committee Discussion: *The majority of the panel agreed that the risk-benefit assessment for idecabtagene vicleucel for the proposed indication was favorable. Members who voted "Yes," commented that the progression free survival data was encouraging and beneficial to the patient and that time off of therapy was valuable. They also noted that in the future the bridging regimen should be optimized. Those who voted "No," expressed concerns about the lack of improvement in OS with earlier ide-cel treatment, the possibility that crossing over of the OS curves was from a higher rate of death in the SOC arm upon cross over to ide-cel arm and the lack of plateau in the PFS curves. Please see the transcript for details of the Committee's discussion.*

The morning session was adjourned at approximately 1:00 p.m. and the afternoon session was adjourned at approximately 5:05 p.m.