Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
March 9, 2023

Location: Please note that due to the impact of the COVID-19 pandemic, all meeting participants joined this advisory committee meeting via an online teleconferencing platform.

Topic: The committee discussed supplemental biologics license application (BLA) 761121/S-008, for POLIVY (polatuzumab vedotin-piiq) for injection, submitted by Genentech, Inc. The proposed indication (use) for this product is in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone for the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL). This product was approved under 21 CFR 601.41 (subpart E, accelerated approval regulations) for use in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory DLBCL, not otherwise specified, after at least two prior therapies. Confirmatory studies are post-marketing studies to verify and describe the clinical benefit of a product after it receives accelerated approval. The new proposed indication is based on the confirmatory study, POLARIX (Study GO39942), conducted to fulfill post-marketing requirement 3630-1 detailed in the June 10, 2019, approval letter, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/761121Orig1s000ltr.pdf. Based on the results of the POLARIX study, the committee will discuss the benefit-risk profile of POLIVY in patients with previously untreated DLBCL.

These summary minutes for the March 9, 2023 meeting of the ODAC of the Food and Drug Administration were approved on May 2 , 2023.

I certify that I attended the March 9, 2023 meeting of the ODAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
She-Chia Chen, PharmD	Jorge A. Garcia, MD, FACP
Designated Federal Officer, ODAC	Chairperson, ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
March 9, 2023

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on March 9, 2023. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing platform. Prior to the meeting, the members and temporary voting members were provided the combined briefing materials from the FDA, and Genentech, Inc. The meeting was called to order by Jorge A. Garcia, MD, FACP (Chairperson). The conflict of interest statement was read into the record by She-Chia Jankowski, PharmD (Designated Federal Officer). There were approximately 1,076 people online. There was one Open Public Hearing (OPH) speaker presentation.

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

Agenda: The committee discussed supplemental biologics license application (BLA) 761121/S-008, for POLIVY (polatuzumab vedotin-piiq) for injection, submitted by Genentech, Inc. The proposed indication (use) for this product is in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone for the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL). This product was approved under 21 CFR 601.41 (subpart E, accelerated approval regulations) for use in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory DLBCL, not otherwise specified, after at least two prior therapies. Confirmatory studies are post-marketing studies to verify and describe the clinical benefit of a product after it receives accelerated approval. The new proposed indication is based on the confirmatory study, POLARIX (Study GO39942), conducted to fulfill post-marketing requirement 3630-1 detailed in the June 10, 2019, approval letter, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/761121Orig1s000ltr.pdf. Based on the results of the POLARIX study, the committee will discuss the benefit-risk profile of POLIVY in patients with previously untreated DLBCL.

Attendance:
ODAC Members Present (Voting): Mark Conaway, PhD; Jorge A. Garcia, MD, FACP (Chairperson); Ravi A. Madan, MD; Anthony D. Sung, MD; Neil Vasan, MD, PhD

ODAC Members Not Present (Voting): Ranjana H. Advani, MD; Jaffer A. Ajani, MD; Pamela L. Kunz, MD; Christopher H. Lieu, MD; David E. Mitchell (Consumer Representative); Jorge J. Nieva, MD; Alberto S. Pappo, MD; Ashley Rosko, MD

ODAC Member Present (Non-Voting): Jonathan D. Cheng, MD (Industry Representative)

Temporary Members (Voting): Christopher S. Coffey, PhD, MS; Louis F. Diehl, MD; Kieron M. Dunleavy, MD; Sandra Finestone, PsyD (Acting Consumer Representative); Paul V. Majkowski, Esq. (Patient Representative); Grzegorz (Greg) S. Nowakowski, MD; Manjunath (Amit) Pai, PharmD, FCP; Mikkael A. Sekeres, MD, MS

FDA Participants (Non-Voting): Richard Pazdur, MD; Marc R. Theoret, MD; Nicole Gormley, MD; Yvette Kasamon, MD; Maryam Yazdy, MD

Designated Federal Officer (Non-Voting): She-Chia Jankowski, PharmD

Open Public Hearing Speaker: Richard Bae

The agenda was as follows:

Call to Order	**Jorge A. Garcia, MD, FACP** Chairperson, ODAC
Introduction of Committee and Conflict of Interest Statement	**She-Chia Jankowski, PharmD** Designated Federal Officer, ODAC
FDA Introductory Comments	**Yvette Kasamon, MD** Clinical Team Leader Division of Hematologic Malignancies II (DHM II) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Genentech, Inc.**
Introduction	**Charles Fuchs, MD** Genentech, Inc.
DLBCL Background & Unmet Need	**Christopher Flowers, MD, MS, FASCO** M.D. Anderson Cancer Center, Houston
POLARIX Efficacy & Safety	**Jamie Hirata, PharmD** Genentech, Inc.
Clinical Perspective	**Jonathan Friedberg, MD, MMSc** Wilmot Cancer Institute, University of Rochester
Closing Remarks	**Charles Fuchs, MD** Genentech, Inc.
FDA PRESENTATION	
Polatuzumab Vedotin-piiq BLA 761121/Supplement 008	**Maryam Yazdy, MD** Clinical Reviewer DHM II, OOD, OND, CDER, FDA
Clarifying Questions to Presenters	
BREAK	
OPEN PUBLIC HEARING	

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Discuss the benefit-risk profile of polatuzumab vedotin-piiq in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the proposed patient population with large B-cell lymphoma (LBCL), including patients with diffused large B-cell lymphoma (DLBCL) not otherwise specified (NOS), considering the results of the POLARIX trial.

   Committee Discussion: *The majority of the Committee members agreed that progression-free survival (PFS) was an appropriate primary endpoint in this setting and patient population and that the difference was clinically meaningful. Furthermore, some Committee members noted that the likelihood of minimizing subsequent lines of therapy was a benefit for this patient population. Some Committee members questioned the meaningfulness of the PFS difference and noted the lack of adequate patient-reported outcomes. Some Committee members shared concerns related to the lack of central pathology review and the heterogeneity of the patients treated in this trial. Please see the transcript for details of the Committee's discussion.*

2. **DISCUSSION:** Based on the results of the POLARIX trial, specifically the overall survival results, discuss whether additional follow-up data from POLARIX should be required to inform the benefit-risk of polatuzumab vedotin-piiq in patients with LBCL in the frontline setting.

   Committee Discussion: *Committee members agreed that it would be beneficial to have additional overall survival data. The majority of the Committee members acknowledged that it might not be feasible or practical to obtain survival data in this patient population and setting. Please see the transcript for details of the Committee's discussion.*

3. **VOTE:** Given the results of the POLARIX trial, does polatuzumab vedotin-piiq have a favorable benefit-risk profile in patients with previously untreated LBCL, including DLBCL NOS?

   Vote Result: Yes: 11 No: 2 Abstain: 0

   Committee Discussion: *The majority of the Committee members voted "Yes", indicating that polatuzumab vedotin-piiq has a favorable benefit-risk profile in patients with previously untreated LBCL, including DLBCL NOS given the results of the POLARIX trial. These Committee members generally agreed that the difference in the primary endpoint, PFS, was considered clinically meaningful. Some Committee members voted "No", sharing concerns*

related to the lack of central pathology review and the heterogeneity of the patients treated in this trial. Please see the transcript for details of the Committee's discussion.

The meeting was adjourned at approximately 5:30 p.m. Eastern Time.