Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
April 21, 2022

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: On April 21, 2022, the committee discussed the appropriate approach for phosphatidylinositol-3-kinase inhibitors currently under development in patients with hematologic malignancies and whether randomized data should be required to support a demonstration of substantial evidence of effectiveness and that the drug is safe for its intended use in the proposed population.

These summary minutes for the April 21, 2022 meeting of the ODAC of the Food and Drug Administration were approved on June 1, 2022.

I certify that I attended the April 21, 2022 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	Acting Chairperson, ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
April 21, 2022

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on April 21, 2022. 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 briefing materials from the FDA. The meeting was called to order by Jorge A. Garcia, MD, FACP (Acting Chairperson). The conflict of interest statement was read into the record by She-Chia Chen, PharmD (Designated Federal Officer). There were approximately 1,057 people online. There were no 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 the appropriate approach for phosphatidylinositol-3-kinase inhibitors currently under development in patients with hematologic malignancies and whether randomized data should be required to support a demonstration of substantial evidence of effectiveness and that the drug is safe for its intended use in the proposed population.

Attendance:

ODAC Members Present (Voting): Ranjana H. Advani, MD; Mark R. Conaway, PhD; Massimo Cristofanilli, MD, FACP; Jorge A. Garcia, MD, FACP (Acting Chairperson); Christopher H. Lieu, MD; Ravi A. Madan, MD; David E. Mitchell (Consumer Representative); Jorge J. Nieva, MD; Anthony D. Sung, MD

ODAC Members Not Present (Voting): Jaffer A. Ajani, MD; Pamela K. Kunz, MD; Alberto S. Pappo, MD; Ashley Rosko, MD

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

Temporary Members (Voting): Jessie Lai-Sim Au, PharmD, PhD; Andy I. Chen, MD, PhD; Christopher S. Coffey, PhD, MS; Louis F. Diehl, MD; Kieron M. Dunleavy, MD; Walter K. Kraft, MD, MS, FACP; Michele Nadeem-Baker, MS (Patient Representative); Gita Thanarajasingam, MD

FDA Participants (Non-Voting): Richard Pazdur, MD; Marc R. Theoret, MD; Nicole Gormley, MD; Nicholas Richardson, DO, MPH; Yvette Kasamon, MD; Thomas Gwise, PhD; Brian Booth, PhD

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

Open Public Hearing Speakers: None

The agenda was as follows:

Call to Order	**Jorge A. Garcia, MD, FACP** Acting Chairperson, ODAC
Introduction of Committee and Conflict of Interest Statement	**She-Chia Chen, PharmD** Designated Federal Officer, ODAC
FDA Introductory Comments	**Nicole Gormley, MD** Director Division of Hematologic Malignancies II (DHM II) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
FDA PRESENTATION	
Phosphatidylinositol 3-kinase (PI3K) Inhibitors in Hematologic Malignancies	**Nicholas Richardson, DO, MPH** Clinical Reviewer Leader 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:** Please discuss the observed toxicity of the PI3K inhibitor class and whether randomized data are warranted with an assessment of overall survival (OS) to support the evaluation of benefit-risk in patients with hematologic malignancies.

   Committee Discussion: *The members noted that while the class of PI3K inhibitors appear to exhibit efficacy, there are significant safety concerns related to adverse events and the overal toxicity profile of the agents in question. Some members also commented on the pattern of the frequent withdrawal of agents in the PI3K inhibitor class. It was acknowledged by the members that these safety issues raise concerns about the potential detrimental impact in patients quality of life and overall survival reported. Members also expressed that the benefit-risk assessment remain critical for drug development. Other comments from members included the recommendation to encourage drug developers to innovate new endpoints including patient reported outcomes (PROs) in clinical trials; however members also expressed that raising the approval bar on the drug class could stifle progress and delay*

products for patients with hematologic malignancies. Please see the transcript for details of the Committee's discussion.

2. **VOTE:** Given the observed toxicities with this class, previous randomized trials with a potential detriment in OS, and a narrow range between effective and toxic doses, should future approvals of PI3K inhibitors be supported by randomized data?

   Vote Result: Yes: 16 No: 0 Abstain: 1

   Committee Discussion: *The vast majority of the members agreed that the future approvals of PI3K inhibitors should be supported by randomized data, given the observed toxicities with this class, previous randomized trials with a potential detriment in OS, and a narrow range between effective and toxic doses. The members that voted, "Yes" were in favor of the randomized trials to address the acute and long-term toxicities of PI3K inhibitors. The member who abstained commented that randomized data should be done if there is concern with the Phase 1 studies; however, was not comfortable requiring all future drugs in this class to be supported by randomized data. Please see the transcript for details of the Committee's discussion.*

The meeting was adjourned at approximately 3:45 p.m.