

**Food and Drug Administration
Center for Drug Evaluation and Research**

**Final Summary Minutes of the Oncologic Drugs Advisory Committee (ODAC) Meeting
December 17, 2019**

Location: FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland

Topic: During the morning session, the committee discussed supplemental new drug application (sNDA) 208558/010 for LYNPARZA (olaparib) tablets, submitted by AstraZeneca Pharmaceuticals LP. The proposed indication (use) for this product is for the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic adenocarcinoma of the pancreas whose disease has not progressed on first-line platinum-based chemotherapy.

During the afternoon session, the committee discussed supplemental biologics license application (sBLA) 125514/066 for KEYTRUDA (pembrolizumab) for injection, submitted by Merck Sharpe & Dohme Corp. The proposed indication (use) for this product is for the treatment of patients with bacillus Calmette-Guérin-unresponsive, high-risk, non-muscle invasive bladder cancer with carcinoma in-situ with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

These summary minutes for the December 17, 2019 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on January 14, 2020.

I certify that I attended the December 17, 2019 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/

Lauren Tesh Hotaki, PharmD, BCPS, BCIDP
Designated Federal Officer
ODAC

/s/

Philip Hoffman, MD
Chairperson
ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting December 17, 2019

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on December 17, 2019, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA, AstraZeneca Pharmaceuticals LP and Merck Sharpe & Dohme Corp. The meeting was called to order by Philip C. Hoffman, MD (Chairperson). The conflict of interest statement was read into the record by Lauren Tesh Hotaki, PharmD, BCPS, BCIDP (Designated Federal Officer). There were approximately 150 people in attendance during the morning and afternoon sessions. There were four (4) Open Public Hearing (OPH) speaker presentations during the morning session and two (2) 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.

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Attendance:

Oncologic Drugs Advisory Committee Members Present (Voting): Massimo Cristofanilli, MD, FACP; Susan Halabi, PhD; Christian S. Hinrichs, MD; Philip Hoffman, MD (Chairperson); Heidi D. Klepin, MD, MS; Anthony D. Sung, MD (Morning Session Only); Thomas S. Uldrick, MD, MS

Oncologic Drugs Advisory Committee Members Not Present (Voting): Jaffer A. Ajani, MD; Jorge A. Garcia, MD; David E. Mitchell (Consumer Representative); Alberto S. Pappo, MD; Gregory J. Riely, MD, PhD

Oncologic Drugs Advisory Committee Member Present (Non-Voting): Albert L. Kraus, PhD (Industry Representative (alternate))

Oncologic Drugs Advisory Committee Member Not Present (Non-Voting): Jonathan D. Cheng, MD (Industry Representative)

Temporary Members (Voting): Piyush Agarwal, MD (Afternoon Session Only); Dawn Aldrich, PhD (Patient Representative; Morning Session Only); Andrea B. Apolo, MD (Afternoon Session Only); Randy W. Hawkins, MD (Acting Consumer Representative); Colette Johnson (Patient Representative; Afternoon Session Only); Matthew H. Kulke, MD (Morning Session Only); Diane Reidy Lagunes, MD (Morning Session Only); Jonah Murdock, MD, PhD, FACS (Afternoon Session Only); Christian P. Pavlovich, MD (Afternoon Session Only); Hanna K.Sanoff, MD, MPH (Morning Session Only); Mohummad Minhaj Siddiqui, MD FACS (Afternoon Session Only)

FDA Participants (Non-Voting): Richard Pazdur, MD; Steven Lemery, MD (Morning Session Only); Lola Fashoyin-Aje, MD MPH (Morning Session Only); Martha Donoghue, MD (Morning Session Only); Naomi Horiba, MD, MPH (Morning Session Only); Julia Beaver, MD (Afternoon Session Only); Daniel Suzman, MD (Afternoon Session Only); Jamie Brewer, MD (Afternoon Session Only); Joyce Cheng, PhD (Afternoon Session Only)

Designated Federal Officer (Non-Voting): Lauren Tesh Hotaki, PharmD, BCPS, BCIDP

Open Public Hearing Speakers: Morning Session: Lisa Schlager (Facing Our Risk of Cancer Empowered); Julie Fleshman, JD, MBA (Pancreatic Cancer Action Network); Allison Perlis; Nina Zeldes, MS (National Center for Health Research)
Afternoon Session: Andrea Maddox-Smith (Bladder Cancer Advocacy Network); Diana Zuckerman, PhD (National Center for Health Research)

The morning session agenda was as follows:

Call to Order and Introduction of Committee	Philip C. Hoffman, MD Chairperson, ODAC
Conflict of Interest Statement	Lauren Tesh Hotaki, PharmD, BCPS, BCIDP Designated Federal Officer, ODAC
FDA Opening Remarks	Martha Donoghue, MD Cross-Discipline Team Leader Gastrointestinal Cancers Team Division of Oncology 3 (DO3) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	AstraZeneca Pharmaceuticals LP

Introduction

Susan Galbraith, MB, BChir, PhD, MRCP, FRCR, FMedSci
Senior Vice President
Head of Research and Early Development
Oncology R&D, AstraZeneca

Disease Background and Unmet Need

Hedy Kindler, MD
Professor of Medicine
University of Chicago

POLO Clinical Development Program
and Efficacy

Carsten Goessl, MD
Global Development Lead for Olaparib
AstraZeneca

Clinical Safety

Mayur Patel, PharmD
Vice President, Patient Safety
Oncology/Immuno Oncology, AstraZeneca

Clinical Perspective

Margaret Tempero, MD
Director, UCSF Pancreas Center
University of California at San Francisco

Summary

Susan Galbraith, MB, BChir, PhD, MRCP, FRCR, FMedSci

FDA PRESENTATION

sNDA 208558 s10: Olaparib

Naomi Horiba, MD, MPH
Clinical Reviewer
Gastrointestinal Cancers Team
DO3, OOD, OND, CDER, FDA

Clarifying Questions to Presenters

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee
Discussion

LUNCH

The afternoon session agenda was as follows:

Call to Order and Introduction of Committee	Philip C. Hoffman, MD Chairperson, ODAC
Conflict of Interest Statement	Lauren Tesh Hotaki, PharmD, BCPS, BCIDP Designated Federal Officer, ODAC
FDA Opening Remarks	Daniel Suzman, MD Acting Clinical Team Leader Genitourinary Team 2 Division of Oncology 1 (DO1) OOD, OND, CDER, FDA
APPLICANT PRESENTATIONS	Merck Sharpe & Dohme Corp
Introduction	Jeffrey N. Stuart, PhD Executive Director, Global Regulatory Affairs Merck & Co., Inc.
Unmet Need	Gary D. Steinberg, MD Professor and Director Goldstein Bladder Cancer Program NYU Langone Health
Efficacy and Safety	Ekta Kapadia, MD Senior Clinical Director, Oncology Merck & Co., Inc.
Clinical Perspective	Ashish M. Kamat, MD, MBBS, FACS Professor of Urologic Oncology (Surgery) Wayne B. Duddleston Professor of Cancer Research MD Anderson Cancer Center, Houston, Texas President, International Bladder Cancer Group (IBCG) Co-President, International Bladder Cancer Network (IBCN)
Benefit-Risk	Scot Ebbinghaus, MD Vice President, Clinical Research, Oncology Merck & Co., Inc.

FDA PRESENTATION

Keytruda® (pembrolizumab)

Jamie Brewer, MD
Clinical Reviewer
Genitourinary Team 2
DO1, OOD, OND, CDER, FDA

Clarifying Questions to Presenters

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OPEN PUBLIC HEARING

Questions to the Committee/Committee
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ADJOURNMENT

Questions to the Committee:

Morning Session:

1. **VOTE:** Is the risk-benefit assessment for olaparib as a maintenance therapy in patients with gBRCAm pancreatic cancer favorable?

Vote Result: Yes: 7 No: 5 Abstain: 0

Committee Discussion: *Members of the Committee agreed that an imaging-based endpoint like progression free survival, was an appropriate endpoint to support an assessment of clinical benefit in gBRCAm metastatic pancreatic cancer. The committee members who voted “Yes” stated that the statistically significant improvement in progression free survival, without evidence to demonstrate an improvement in overall survival, was sufficient to demonstrate the clinical benefit of olaparib in the indicated population, which consists of a small subset of patients with pancreatic cancer and noted that consistency with the known safety profile of olaparib supported favorable risk-benefit assessment. Committee members noted the convenience of providing a treatment option that permits a delay in the initiation of cytotoxic chemotherapy with its associated toxicity profile, the challenges with conducting a study to demonstrate OS in a rare biomarker selected population, and the high unmet medical need of patients with gBRCAm metastatic pancreatic adenocarcinoma, as important considerations in the recommendation for approval. Committee members who voted “No” acknowledged that having an oral medication may provide a more convenient treatment option to patients, and stated that treatment with olaparib appeared to confer benefit in a subset of patients with gBRCAm metastatic pancreatic cancer; however, these members viewed the absence of a demonstrated benefit in OS or improvement in quality of life, to be a significant limitation to concluding that the risk:benefit assessment is favorable.*

Afternoon Session:

1. **VOTE:** Do the observed complete response rate and duration represent a favorable risk/benefit profile in patients with BCG-unresponsive high-risk NMIBC with CIS treated with pembrolizumab?

Vote Result: Yes: 9 No: 4 Abstain: 0

Committee Discussion: The majority of the committee agreed that the observed complete response rate and duration do represent a favorable risk/benefit profile in patients with bacillus Calmette-Guérin-unresponsive, high-risk, non-muscle invasive bladder cancer with carcinoma in-situ treated with pembrolizumab. The committee members that voted “Yes” agreed that the response data presented, although immature, seemed to be clinically meaningful in patients who want to delay cystectomy and have another option for treatment. It was further commented that it will be important for physicians and patients to have an informed discussion regarding risks and benefits associated with pembrolizumab for use in this indication. The committee members that voted “No” stated that data presented by the Applicant was immature and that the subset of patients who experienced prolonged benefit may be too small for approval in the setting of a systemic therapy. Some committee members were concerned that deferring cystectomy may result in a higher-risk operation if and when cystectomy is subsequently required. Some committee members noted that presentation of quality of life data may have been helpful to better understand the risk/benefit of pembrolizumab in this setting. One member noted concern with using systemic therapy for a localized disease. Please see the transcript for details of the committee discussion.

The meeting was adjourned at approximately 4:36 p.m.