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

# Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
# February 26, 2020

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 new drug application 212578 for padeliporfin di-potassium powder for solution for injection, submitted by STEBA Biotech, S.A. The proposed indication (use) for this product is for the treatment of patients with localized prostate cancer, meeting the following criteria: Stage T1-T2a and prostate specific antigen less than or equal to 10 ng/mL and Gleason Grade Group 1 based on transrectal ultrasound guided biopsy or unilateral Gleason Grade Group 2 based on multiparametric magnetic resonance imaging-targeted biopsy with less than 50 percent of cores positive.

During the afternoon session, the committee discussed supplemental biologics license application 125477/S-034, for CYRAMZA (ramucirumab) injection for intravenous use, submitted by Eli Lilly and Company. The proposed indication (use) for this product is in combination with erlotinib, for first-line treatment of patients with metastatic non-small cell lung cancer whose tumors have epidermal growth factor receptor exon 19 deletions or exon 21 (L858R) substitution mutations.

These summary minutes for the February 26, 2020 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on March 19, 2020.

I certify that I attended the February 26, 2020 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

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| **/s/** | **/s/** |
| Lauren Tesh Hotaki, PharmD, BCPS, BCIDP | Philip Hoffman, MD |
| *Designated Federal Officer* | *Chairperson* |
| *ODAC* | *ODAC* |

**Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting**
**February 26, 2020**

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on February 26, 2020, 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 and STEBA Biotech, S.A. and Eli Lilly and Company. 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 160 people in attendance during the morning session and 100 people in attendance during the afternoon session. There were six (6) Open Public Hearing (OPH) speaker presentations during the morning session and four (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.

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**Attendance:**

**Oncologic Drugs Advisory Committee Members Present (Voting):** Massimo Cristofanilli, MD, FACP; Jorge A. Garcia, MD; Susan Halabi, PhD; Christian S. Hinrichs, MD; Philip Hoffman, MD (Chairperson); Heidi D. Klepin, MD, MS

**Oncologic Drugs Advisory Committee Members Not Present (Voting):** Jaffer A. Ajani, MD; David E. Mitchell (Consumer Representative); Alberto S. Pappo, MD; Gregory J. Riely, MD, PhD; Anthony D. Sung, MD; Thomas S. Uldrick MD, MS

**Oncologic Drugs Advisory Committee Member Present (Non-Voting):** Jonathan D. Cheng, MD (Industry Representative)

**Temporary Members (Voting):** John Deeken, MD (Afternoon Session Only); Randy W. Hawkins, MD (Acting Consumer Representative); Maha Hussain, MD, FACP, FASCO (Morning Session Only); Terrence "Terry" Kungel, MBA (Patient Representative; Morning Session Only); Danil V. Makarov, MD, MHS (Morning Session Only); Shakun Malik, MD (Afternoon Session Only); Tracy G. Matson (Patient Representative; Afternoon Session Only); Brian I. Rini, MD (Morning Session Only); Howard Sandler, MD, MS, FASTRO, FASCO (Morning Session Only); Mohummad Minhaj Siddiqui, MD, FACS (Morning Session Only); Daniel Y. Song, MD (Morning Session Only); Eva Szabo, MD (Afternoon Session Only); Patrick C. Walsh, MD (Morning Session Only)

**FDA Participants (Non-Voting):** Richard Pazdur, MD; Paul Kluetz, MD (Morning Session Only); Julia Beaver, MD (Morning Session Only); Chana Weinstock, MD (Morning Session Only); Sundeep Agrawal, MD (Morning Session Only); Xin (Cindy) Gao, PhD (Morning Session Only); Harpreet Singh, MD (Afternoon Session Only); Erin Larkins, MD (Afternoon Session Only); Barbara Scepura, MS, CRNP (Afternoon Session Only); Xiaoxue Li, PhD (Afternoon Session Only)

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

**Open Public Hearing Speakers:** Morning Session: Michael A. Gorin, MD; John Fortin, BS, MS; Peter Prest, MBA; David G. Morse (Men to Men of Sarasota); Diana Zuckerman, PhD (National Center for Health Research); Herbert Lepor, MD
Afternoon Session: Diana Zuckerman, PhD (National Center for Health Research); Samantha Mixon; Anne Phillips; Gina Dietzer

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***The morning session agenda was as follows:***

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| Call to Order and Introduction of Committee | **Philip C. Hoffman, MD**<br>Chairperson, ODAC |
| Conflict of Interest Statement | **Lauren Tesh Hotaki, PharmD, BCPS, BCIDP**<br>Designated Federal Officer, ODAC |
| FDA Opening Remarks | **Chana Weinstock, MD**<br>Team Leader, Genitourinary Cancers Team<br>Division of Oncology 1 (DO1)<br>Office of Oncologic Diseases (OOD)<br>Office of New Drugs (OND), CDER, FDA |
| Contemporary Diagnosis and Treatment of Localized Prostate Cancer | **Jim C. Hu, MD, MPH**<br>Ronald P. Lynch Professor of Urologic Oncology<br>Director of the LeFrak Center for Robotic Surgery,<br>Weill Cornell Medicine |

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| | New York Presbyterian/Weill Cornell<br>New York, New York |
| **APPLICANT PRESENTATIONS** | **STEBA Biotech, S.A.** |
| Introduction | **John C. Rewcastle, PhD**<br>Head, US Regulatory<br>STEBA Biotech, S.A. |
| Current Management of Clinically Localized Prostate Cancer | **Peter T. Scardino, MD**<br>Attending Surgeon and Member<br>Departments of Surgery and Molecular Pharmacology and Therapeutics<br>Memorial Sloan Kettering Cancer Center<br>Professor of Urology<br>Weill Cornell College of Medicine<br>New York, New York |
| Prostate Hemiablation with TOOKAD VTP: Procedure and Mechanism of Action | **Neal D. Shore, MD, FACS**<br>Medical Director, CPI<br>Carolina Urologic Research Center<br>National Urology Research Director<br>21st Century Oncology<br>Atlantic Urology Clinics<br>Myrtle Beach, South Carolina |
| Efficacy and Safety and Confirmatory Study | **Henri W. Boodée, MD**<br>Head, US Medical Affairs and Clinical Development<br>STEBA Biotech, S.A. |
| Clinical Perspective | **Inderbir S. Gill, MD**<br>Chair and Distinguished Professor of Urology<br>Keck School of Medicine<br>University of Southern California<br>Los Angeles, California |
| **FDA PRESENTATION** | |
| NDA 202578: padeliporfin di-potassium powder for solution for injection (TOOKAD) | **Sundeep Agrawal, MD**<br>Clinical Reviewer, Genitourinary Cancers Team<br>DO1, 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:***

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| Call to Order and Introduction of Committee | **Philip C. Hoffman, MD**<br>Chairperson, ODAC |
| Conflict of Interest Statement | **Lauren Tesh Hotaki, PharmD, BCPS, BCIDP**<br>Designated Federal Officer, ODAC |
| FDA Opening Remarks | **Erin Larkins, MD, CDR, USPHS**<br>Cross-Discipline Team Lead<br>Thoracic and Head & Neck Cancers Team<br>Division of Oncology 2 (DO2)<br>OOD, OND, CDER, FDA |
| **APPLICANT PRESENTATIONS** | **Eli Lilly and Company** |
| Introduction | **Allen Melemed, MD, MBA**<br>Distinguished Medical Scholar and Senior Director<br>Global Regulatory Affairs, Oncology<br>Eli Lilly and Company |
| Unmet Medical Need | **Everett Vokes, MD**<br>John E. Ultmann Professor of Medicine and Radiation Oncology<br>Physician-in-Chief, University of Chicago Medicine and Biological Sciences Chair Department of Medicine |
| Efficacy | **Paolo Abada, MD, PhD**<br>Senior Medical Director<br>Cyramza Global Product Development, Oncology<br>Eli Lilly and Company |
| Safety | **Carla Visseren, MD**<br>Global Medical Lead RELAY<br>Eli Lilly and Company |

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| Clinical Perspective | **John Heymach, MD, PhD**<br>Chair, Department of Thoracic Head and Neck Medical Oncology<br>MD Anderson Cancer Center<br>David Bruton, Jr. Chair in Cancer Research |

**FDA PRESENTATION**

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| BLA: 125477 s:34 Ramucirumab | **Barbara Scepura, MS, CRNP**<br>Clinical Reviewer<br>Thoracic and Head & Neck Cancers Team<br>DOP2, OOD, OND, CDER, FDA |

Clarifying Questions to Presenters

**BREAK**

**OPEN PUBLIC HEARING**

Questions to the Committee/Committee Discussion

**ADJOURNMENT**

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***Questions to the Committee:***

**Morning Session:**

1. **VOTE:** Do the results of PCM301 represent a favorable benefit/risk profile for TOOKAD in patients with low-risk early stage prostate cancer?

   **Vote Result: Yes: 2 No: 13 Abstain: 0**

   ***Committee Discussion***: *The majority of the members agreed that, the PCM301 trial ultimately did not support a favorable benefit/risk profile for patients with low-risk early stage prostate cancer treated with Tookad. The committee agreed with the general concept of using progression in a manner that resulted in a delay of morbidity from definitive therapy. The committee members that voted "No" did not accept that the results of PCM301 represented a favorable benefit/risk profile for TOOKAD in patients with low-risk early stage prostate cancer. There was concern about the flawed study trial design, the low risk population studied in which active surveillance is an accepted management option, short study duration, missing biopsy data, and trial conduct. Members also questioned if the study population could be generalized to the US population due to differences in low risk classification versus the classification used for study enrollment at the time of trial conduct,and were apprehensive of lack of long term safety data. Concern was raised, too,*

*about the learning curve required to master the technique of this modality. The two committee members that voted "Yes" noted that the trial met its co-primary endpoints, and that an "in-between" option is needed for patients who would otherwise receive active surveillance versus definitive therapy. Please see the transcript for details of the committee discussion.*

**Afternoon Session:**

1. **DISCUSSION:** Discuss whether the results of the RELAY trial, with a demonstrated improvement in progression free survival (PFS), support a positive benefit/risk assessment given the uncertain effect on overall survival (OS) and the increased toxicity associated with the addition of ramucirumab to erlotinib.

   ***Committee Discussion***: *In addition to concerns surrounding increased cardiovascular toxicity, i.e. Grade 3 hypertension, with the combination of ramucirumab and erlotinib, members weighed the meaningfulness of using PFS vs. OS as the primary endpoint for the RELAY trial. One member noted that PFS as a primary endpoint is clinically meaningful especially when using OS as a primary endpoint is difficult to obtain or will take a very long time to study. Some members mentioned that it is unknown if there is a detriment in OS if a PFS proven regimen is used before an OS proven regimen (in this case, osimertinib) in the treatment cascade of a patient. Members also questioned the role of the combination in the current treatment landscape for non-small cell lung cancer (e.g. first-line or otherwise), and whether this combination would be of benefit to patients seeking additional options. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Is the benefit/risk profile of ramucirumab plus erlotinib favorable for patients with untreated metastatic EGFR-positive non-small cell lung cancer?

   **Vote Result: Yes: 6 No: 5 Abstain: 0**

   ***Committee Discussion***: *The committee members that voted "Yes" agreed that the benefit/risk profile of ramucirumab plus erlotinib is favorable for patients with untreated metastatic EGFR-positive non-small cell lung cancer and noted it should be available as a treatment option for patients during the shared-decision making process with their physician. Members also noted that the RELAY trial met its primary PFS endpoint. The committee members that voted "No" were concerned that impact on OS was uncertain, and that the trial did not demonstrate evidence of improved quality of life, and increased adverse events. While some members expressed reservations about the need for regular IV infusions with this regimen as compared to an oral drug alone, and the effect that might have on quality of life, others opined that it was not within the purview of ODAC to mandate how a company would eventually market a drug or what regimen patients and physicians might choose if the data on efficacy and safety appeared promising. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:48 p.m.