Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
July 25, 2024

Location: FDA and invited participants attended the meeting at FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. The public participated via an online teleconferencing and/or video conferencing platform, and the meeting presentations were heard, viewed, captioned, and recorded through an online video conferencing platform.

Topic: The Committee discussed supplemental biologics license application (sBLA) 761069/S-043, for IMFINZI (durvalumab) injection, submitted by AstraZeneca UK Limited. The proposed indication (use) is IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by IMFINZI as monotherapy after surgery, for the treatment of adult patients with resectable (tumors ≥ 4 cm and/or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements. The Committee was also asked to discuss whether drug sponsors should be required to adequately justify treatment of patients both before and after surgery for resectable NSCLC prior to an approval that would include both neoadjuvant and adjuvant therapy.

These summary minutes for the July 25, 2024 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on October 14, 2024.

I certify that I attended the July 25, 2024 meeting of the Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	/s/
Takyiah Stevenson, PharmD	Daniel Spratt, MD
Acting Designated Federal Officer, ODAC	Acting Chairperson, ODAC

Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
July 25, 2024

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on July 25, 2024. FDA and invited participants attended the meeting at FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. The public participated via an online teleconferencing and/or video conferencing platform, and 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 and AstraZeneca UK Limited. The meeting was called to order by Daniel Spratt, MD (Acting Chairperson). The conflict of interest statement was read into the record by Takyiah Stevenson, PharmD (Acting Designated Federal Officer). There were approximately 62 people in attendance in-person and approximately 1154 people online. There were 6 Open Public Hearing (OPH) speaker presentations.

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

Agenda: The Committee discussed supplemental biologics license application (sBLA) 761069/S-043, for IMFINZI (durvalumab) injection, submitted by AstraZeneca UK Limited. The proposed indication (use) is IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by IMFINZI as monotherapy after surgery, for the treatment of adult patients with resectable (tumors ≥ 4 cm and/or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements. The Committee was also asked to discuss whether drug sponsors should be required to adequately justify treatment of patients both before and after surgery for resectable NSCLC prior to an approval that would include both neoadjuvant and adjuvant therapy.

Attendance:
Oncologic Drugs Advisory Committee Members Present (Voting): Mark R. Conaway, PhD; Pamela L. Kunz, MD; Ravi A. Madan, MD; Daniel Spratt, MD (*Acting Chairperson*)

Oncologic Drugs Advisory Committee Members Not Present (Voting): Toni K. Choueiri, MD; William J. Gradishar, MD; Neil Vasan, MD, PhD

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

Temporary Members (Voting): Ranjana H. Advani, MD; Azam Ghafoor, MD; Christopher H. Lieu, MD; David E. Mitchell (*Acting Consumer Representative; via video conferencing platform*); Jim Pantelas (*Patient Representative*); Ashley Rosko, MD; Victor van Berkel, MD, PhD

FDA Participants (Non-Voting): Richard Pazdur, MD; Paul Kluetz, MD; Erin Larkins, MD; Bernardo Haddock Lobo Goulart, MD; Gautam Mehta, MD; Shabnam Ford, PhD

Acting Designated Federal Officer (Non-Voting): Takyiah Stevenson, PharmD

Open Public Hearing Speakers: Brendon Stiles, MD (Montefiore Einstein Comprehensive Cancer Center); Grace Drew (National Center for Health Research); Pierre T. Onda, MD, MPH; Heidi Nafman-Onda; Janise Jones; Dave Bjork

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The agenda was as follows:

Call to Order and Introduction of Committee	**Daniel Spratt, MD** Acting Chairperson, ODAC
Conflict of Interest Statement	**Takyiah Stevenson, PharmD** Acting Designated Federal Officer, ODAC
FDA Opening Remarks	**Erin Larkins, MD** Director (Acting) Division of Oncology 2 (DO2) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**AstraZeneca UK Limited**
Introduction	**Leora Horn, MD, MSC, MHPE, FRCPC** Vice President, Head of Clinical Development Late Development Oncology Global Clinical Strategy Head for Lung Cancer AstraZeneca
Disease Background	**Marina Garassino, MD** Professor of Medicine Director, Thoracic Programs Department of Hematology/Oncology University of Chicago
Clinical Efficacy	**Gary Doherty, MB, BChir, MA, PhD, FRCP** Global Clinical Program Lead - Oncology, Lung AstraZeneca
Clinical Safety	**Mayur Patel, PharmD** Vice President, Patient Safety Oncology AstraZeneca

APPLICANT PRESENTATIONS (CONT.)

Clinical Perspective	**John Heymach, MD, PhD** Chair and Professor, Department of Thoracic/Head and Neck Medical Oncology Division of Cancer Medicine University of Texas MD Anderson Cancer Center
Concluding Remarks & Future Perspectives	**Leora Horn, MD, MSC, MHPE, FRCPC**

FDA PRESENTATIONS

Durvalumab Before and After Surgery for the Treatment of Resectable Non-Small Cell Lung Cancer (AEGEAN)	**Bernardo Haddock Lobo Goulart, MD** Clinical Reviewer Cures Senior Physician DO2, OOD, OND, CDER, FDA
Contribution of Treatment Phase in Perioperative Trials	**Shabnam Ford, PhD** Senior Mathematical Statistician Division of Biometrics V Office of Biostatistics Office of Translational Sciences, CDER, FDA
Clarifying Questions	

LUNCH

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion – AEGEAN

Questions to the Committee/Committee Discussion – Future Perioperative Trial Designs to Support Contribution of Sequence

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** In light of the uncertainty around the need for both phases of treatment, discuss whether an additional trial should be conducted to clarify the contribution of treatment phase for the durvalumab perioperative regimen prior to approval.

Committee Discussion: *Overall, the Committee agreed that an additional trial should not be conducted to clarify the contribution of treatment phase for the durvalumab perioperative regimen prior to approval. While several Committee members expressed concerns that the design of the AEGEAN trial does not provide clarity on the contribution of each treatment phase, the Committee emphasized that this is a beneficial regimen that should be made available to patients sooner rather than later. Committee members concurred that the AEGEAN trial met its primary endpoints and demonstrated a clinically meaningful improvement in event-free survival. However, Committee members agreed that there is unclear evidence of the contribution of the adjuvant phase of treatment to the efficacy findings, and mentioned concerns of exposing patients to safety risks during this phase of the regimen, potentially without any benefits. A few committee members expressed confidence that clinicians would work with patients to manage adverse events and discontinue durvalumab as necessary. As a result, the Committee discussion generally favored moving forward with approval of durvalumab instead of requiring an additional trial, which could significantly delay access to this regimen. Please see the transcript for details of the Committee's discussion.*

Following discussion of the AEGEAN trial results for perioperative durvalumab, the Committee moved its attention to voting and discussion about the design of future perioperative trials, particularly trials for resectable NSCLC adding a new therapy to an existing perioperative immune checkpoint inhibitor backbone. The discussion focused on the need for designs that would better characterize the contribution of each sequence of therapy to avoid the uncertainty associated with two arm perioperative trial designs.

2. **VOTE:** Should FDA require that new trial design proposals for perioperative regimens for resectable NSCLC include adequate within trial assessment of contribution of treatment phase?

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

   Committee Discussion*: The Committee unanimously agreed that FDA should require that new trial design proposals for perioperative regimens for resectable NSCLC include adequate within trial assessment of contribution of treatment phase. Committee members acknowledged that addressing this issue after a trial has been conducted is not ideal and would take a significant amount of time. Therefore, it is important to determine upfront how to best incorporate new therapies into perioperative regimens for resectable NSCLC. Several Committee members agreed that new trial designs will be important for limiting overtreatment in this setting. Committee members also noted that novel endpoints may support more efficient trials in this space that include this within trial assessment of contribution of treatment phase. While Committee members acknowledged that future trials implementing new designs will likely result in higher costs, larger sample sizes, increased complexity, and longer study durations, several members agreed that this is feasible and will clarify the contribution of treatment phases for perioperative regimens. Some committee members noted that the added upfront complexity and cost of the premarket trial could be*

offset by a reduction in the risk of potentially years of overtreatment and would preclude the expense of post-marketing de-escalation studies which may or may not be feasible to run. Finally, some committee members stated that these considerations should not be limited to resectable NSCLC and should apply to trials including patients with other cancers as well. Please see the transcript for details of the Committee's discussion.

The meeting was adjourned at approximately 1:50 p.m.