FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Oncologic Drugs Advisory Committee (ODAC) Meeting

September 26, 2024

AGENDA

During the morning session, the Committee will discuss the use of immune checkpoint inhibitors in patients with unresectable or metastatic gastric and gastroesophageal junction adenocarcinoma. The current labeling for approved checkpoint inhibitors in this indication reflect broad approvals in the intent to treat patient populations agnostic of programmed death cell ligand-1 (PD-L1) expression. Cumulative data has shown that PD-L1 expression appears to be a predictive biomarker of treatment efficacy in this patient population; however, clinical trials have used different approaches to assess PD-L1 expression and different thresholds to define PD-L1 positivity. FDA would like the Committee's opinion on the:

- *adequacy of PD-L1 expression as a predictive biomarker for patient selection in this patient population,*
- *differing risk-benefit assessments in different subpopulations defined by PD-L1 expression, and*
- *adequacy of the cumulative data to restrict the approvals of immune checkpoint inhibitors based on PD-L1 expression.*

The Committee will discuss the existing supplemental biologics license applications (sBLA) which were approved for patients with previously untreated HER2-negative unresectable or metastatic gastric or gastroesophageal adenocarcinoma:

- *sBLA 125554/S-091 for OPDIVO (nivolumab) injection, submitted by Bristol Myers-Squibb Co. and*
- *sBLA 125514/S-143 for KEYTRUDA (pembrolizumab) injection, submitted by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.*

The Committee will also discuss BLA 761417 for tislelizumab injection, submitted by BeiGene USA, Inc., for the same proposed indication.

8:00 a.m.	Call to Order and Introduction of Committee	**Christopher Lieu, MD** Acting Chairperson, ODAC
8:05 a.m.	Conflict of Interest Statement	**Joyce Frimpong, PharmD** Acting Designated Federal Officer, ODAC
8:10 a.m.	FDA Introductory Remarks	**Steven Lemery, MD, MHS** Director Division of Oncology 3 (DO3) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
8:30 a.m.	**APPLICANT PRESENTATIONS**	**Bristol-Myers Squibb Co.**
	Introduction	**Ian Waxman, MD** Vice President, Late Development Oncology Bristol Myers Squibb

	APPLICANT PRESENTATIONS (CONT.)	
	Benefit Risk Profile in PD-L1 Subgroups	**Dana Walker, MD, MSCE** Vice President, Global Program Lead, Opdivo/Yervoy, GI & GU Bristol Myers Squibb
	PD-L1 Testing in Clinical Practice	**Robert A. Anders, MD, PhD** Division of GI and Liver Pathology The Johns Hopkins University
	Conclusion	**Ian Waxman, MD**
8:50 a.m.	**BREAK**	
9:00 a.m.	**APPLICANT PRESENTATIONS**	**Merck Sharp & Dohme LLC,** **a subsidiary of Merck & Co., Inc.**
	Overview of Pembrolizumab and PD-L1 22C3 PharmDx	**M. Catherine Pietanza, MD** Vice President, Clinical Research Global Clinical Development, Late-Stage Oncology Merck Sharp & Dohme LLC
	KEYNOTE-859 Results in HER2-Negative Gastric Cancer	**Pooja Bhagia, MD** Executive Director Global Clinical Development, Late-Stage Oncology Merck Sharp & Dohme LLC
	Clinical Management of Gastric Cancer	**Yelena Y. Janjigian, MD** Chief Attending Gastrointestinal Oncology Memorial Sloan Kettering Cancer Center
	Concluding Remarks	**M. Catherine Pietanza, MD**
9:20 a.m.	**BREAK**	

9:30 a.m.	**APPLICANT PRESENTATIONS**	**BeiGene USA, Inc.**
	Tislelizumab Background	**Mark Lanasa, MD, PhD** Senior Vice President Chief Medical Officer Solid Tumor BeiGene
	Rationale 305 Results	**Mark Lanasa, MD, PhD**
	PD-L1 Subgroup Analyses	**Mark Lanasa, MD, PhD**
	Clinical Perspective	**Nataliya Uboha, MD, PhD** Hematology and Medical Oncology Associate Professor University of Wisconsin School of Medicine
9:50 a.m.	**FDA PRESENTATIONS**	
	PD-L1 Expression and Immune Checkpoint Inhibitors for the Treatment of Patients with HER2 Negative Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma	**Vaibhav Kumar, MD, MS** Clinical Reviewer DO3, OOD, OND, CDER, FDA
10:30 a.m.	**BREAK**	
10:45 a.m.	Clarifying Questions	
11:15 a.m.	**OPEN PUBLIC HEARING**	
11:45 a.m.	Questions to the Committee/Committee Discussion	
12:45 p.m.	**LUNCH**	

During the afternoon session, the Committee will discuss the use of immune checkpoint inhibitors in patients with metastatic or unresectable esophageal squamous cell carcinoma. The current labeling for approved checkpoint inhibitors in this indication reflect broad approvals in the intent to treat patient populations agnostic of programmed death cell ligand-1 (PD-L1) expression. Cumulative data has shown that PD-L1 expression appears to be a predictive biomarker of treatment efficacy in this patient population; however, clinical trials have used different approaches to assess PD-L1 expression and different thresholds to define PD-L1 positivity. FDA would like the Committee's opinion on the:

- *adequacy of PD-L1 expression as a predictive biomarker for patient selection in this patient population,*
- *differing risk-benefit assessments in different subpopulations defined by PD-L1 expression, and*
- *adequacy of the cumulative data to restrict the approvals of immune checkpoint inhibitors based on PD-L1 expression.*

The Committee will discuss the existing sBLAs which were approved for patients with previously untreated unresectable or metastatic esophageal squamous cell carcinoma:

- *sBLA 125514/S-096 for KEYTRUDA (pembrolizumab) injection, submitted by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.;*
- *sBLAs 125554/S-105 and S-106 for OPDIVO (nivolumab) injection, submitted by Bristol Myers-Squibb Co.; and*
- *sBLA 125377/S-122 for YERVOY (ipilimumab) injection, submitted by Bristol Myers-Squibb Co.*

The Committee will also discuss the new BLA 761380 for tislelizumab, submitted by BeiGene USA, Inc., for the same proposed indication.

1:30 p.m.	Call to Order and Introduction of Committee	**Christopher Lieu, MD** Acting Chairperson, ODAC
1:35 p.m.	Conflict of Interest Statement	**Joyce Frimpong, PharmD** Acting Designated Federal Officer, ODAC
1:40 p.m.	FDA Introductory Remarks	**Sandra Casak, MD** Clinical Team Leader (Acting) Gastrointestinal Malignancies DO3, OOD, OND, CDER, FDA
2:00 p.m.	**APPLICANT PRESENTATIONS**	**Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.**
	Overview of Pembrolizumab and PD-L1 22C3 PharmDx	**M. Catherine Pietanza, MD**
	KEYNOTE-590 Results in Esophageal Cancer	**Pooja Bhagia, MD**

	APPLICANT PRESENTATIONS (CONT.)	
	Clinical Management of Esophageal Cancer	**Peter Enzinger, MD** Gastrointestinal Oncologist Dana-Farber Cancer Institute
	Concluding Remarks	**M. Catherine Pietanza, MD**
2:20 p.m.	**BREAK**	
2:30 p.m.	**APPLICANT PRESENTATIONS**	**Bristol-Myers Squibb Co.**
	Introduction	**Ian Waxman, MD**
	Benefit Risk Profile in PD-L1 Subgroups	**Dana Walker, MD, MSCE**
	Clinical Perspective	**Ronan J. Kelly, MBBCh, MBA, FASCO** Charles A. Sammons Cancer Center Baylor University Medical Center
	Conclusion	**Ian Waxman, MD**
2:50 p.m.	**BREAK**	
3:00 p.m.	**APPLICANT PRESENTATIONS**	**BeiGene USA, Inc.**
	Rationale-306 Results	**Mark Lanasa, MD, PhD**
	PD-L1 Subgroup Analyses	**Mark Lanasa, MD, PhD**
	Clinical Perspective	**Nataliya Uboha, MD, PhD**
3:20 p.m.	**FDA PRESENTATIONS**	
	PD-L1 Expression and Immune Checkpoint Inhibitors for the First Line Treatment of Metastatic or Unresectable Esophageal Squamous Cell Carcinoma (ESCC)	**Geetika Srivastava, MD, MSPH** Clinical Reviewer DO3, OOD, OND, CDER, FDA
4:00 p.m.	Clarifying Questions	

AGENDA (cont.)

4:30 p.m.	**BREAK**
4:45 p.m.	**OPEN PUBLIC HEARING**
5:15 p.m.	Questions to the Committee/Committee Discussion
6:15 p.m.	**ADJOURNMENT**