Bristol Myers Squibb™

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NCCN Guidelines® Panel: Esophageal and Esophagogastric Junction Cancers

Dear Panel Members,

On behalf of Bristol Myers Squibb Company, I respectfully submit the enclosed Opdivo® (nivolumab) clinical data that was presented at the 2020 European Society for Medical Oncology (ESMO) Annual Meeting to the NCCN Esophageal and Esophagogastric Junction Cancers Panel for your consideration.[1,2]

CheckMate 577 is a global, randomized, double-blind, placebo-controlled, phase 3 study, which evaluated nivolumab in the adjuvant setting for esophageal cancer or gastroesophageal junction cancer (EC/GEJC). Patients with stage II/III EC/GEJC who completed neoadjuvant chemoradiation therapy followed by surgery were randomized (2:1) to receive either nivolumab or placebo for a duration of up to 1 year. The primary endpoint was disease-free survival (DFS) per investigator assessment. The first results of the CheckMate 577 study (N = 794) were presented at the 2020 ESMO Annual Meeting.[1]

CheckMate 649 is a global, randomized, open-label, phase 3 study, which evaluated nivolumab plus chemotherapy in the first-line setting for patients with advanced gastric cancer, gastroesophageal junction cancer, or esophageal adenocarcinoma (GC/GEJC/EAC). Patients with previously untreated, unresectable, advanced or metastatic GC/GEJC/EAC were randomized (1:1:1) to receive nivolumab plus ipilimumab, nivolumab plus chemotherapy (1 of 2 regimens: oxaliplatin plus leucovorin plus fluorouracil [FOLFOX] or oxaliplatin plus capecitabine [CapeOX]), or chemotherapy alone. The dual primary endpoints were overall survival (OS) and progression-free survival (PFS) in patients whose tumors expressed PD-L1 CPS ≥ 5. Secondary endpoints included OS and PFS in all randomized patients. The first results of the CheckMate 649 study, comparing nivolumab plus chemotherapy versus chemotherapy alone (N = 1581, including 955 patients with PD-L1 CPS ≥ 5), were presented at the 2020 ESMO Annual Meeting.[2]

Specific Changes: I request that the Panel consider:

- the inclusion of nivolumab as a Category 1 treatment option in the adjuvant setting for patients with stage II/III EC/GEJC who complete neoadjuvant chemoradiation therapy followed by surgery (ESOPH-F, page 1 of 15)
- the inclusion of nivolumab in combination with FOLFOX or CapeOX as a Category 1 treatment option for patients with previously untreated, unresectable, advanced or metastatic GEJC or EAC (ESOPH-F, page 3 of 15).

FDA Clearance in Esophageal Cancer: Nivolumab is approved for the treatment of patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based chemotherapy.[3]

The use of nivolumab in the adjuvant setting for EC/GEJC is considered investigational. The use of nivolumab plus chemotherapy as first-line treatment for unresectable, advanced or metastatic GC/GEJC/EAC is considered investigational.[3]

Rationale: This information is being submitted in response to a standing request from NCCN for new data.

As part of this submission, the following resources are included for your review. We would like to acknowledge the contributions of NCCN panel members who are also co-authors of these presentations.

1. Kelly RJ, Ajani JA, Kuzdzal J, et al. Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiation therapy: first results of the CheckMate 577 study. Oral Presentation presented at the ESMO 2020 Annual Meeting; September 19-21, 2020; Virtual Meeting.
2. Moehler M, Shitara K, Garrido M, et al. Nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma: first results of the CheckMate 649 study. Oral Presentation presented at the ESMO 2020 Annual Meeting; September 19-21, 2020; Virtual Meeting.
3. Product information, OPDIVO® (nivolumab) injection, for intravenous infusion. Bristol Myers Squibb Company, Princeton, NJ. September 2020.

Thank you for your consideration of this request.

Sincerely,

Samantha Gothelf

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