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NCCN Guidelines Panel: Esophageal and Esophagogastric Junction Cancers

On behalf of Merck & Co., Inc., I respectfully request the NCCN Esophageal and Esophagogastric Junction Cancers Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V2.2018 for Esophageal and Esophagogastric Junction Cancers.

Specific changes requested:

We respectfully request the addition of KEYTRUDA (pembrolizumab) as a second-line treatment option for patients with advanced gastric or gastro-esophageal junction cancer with PD-L1 CPS of 10 or higher in the appropriate sections of the NCCN guidelines, including the section ESOPH-F (4/13).

FDA Approval:

Gastric Cancer

KEYTRUDA (pembrolizumab) is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

KEYTRUDA (pembrolizumab) is not approved for the second-line treatment of patients with advanced gastric or gastroesophageal junction cancer, with the exception of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) gastric or gastroesophageal cancer that has progressed following prior treatment and who have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Please refer to the KEYTRUDA Prescribing Information for other FDA-approved indications.[1]

Rationale:

A multicenter, open label, randomized phase 3 study (KEYNOTE-061; NCT02370498) was conducted to evaluate pembrolizumab compared to paclitaxel in patients with advanced gastric or gastroesophageal junction (GEJ) cancer that progressed on first-line chemotherapy with a platinum and fluoropyrimidine. Primary endpoints were overall survival (OS) and progression-free survival (PFS) in patients with a PD-L1 combined positive score (CPS) of 1 or higher. Pembrolizumab (n=196) did not significantly improve overall survival compared with paclitaxel (n=199) as

second-line therapy for advanced gastric or GEJ cancer with PD-L1 CPS of 1 or higher with a hazard ratio (HR) of 0.82 (95% CI, 0.66-1.03); one-sided p=0.0421 (the significance threshold for OS was p=0.0135). The HR for PFS for pembrolizumab vs. paclitaxel was 1.27 (95% CI, 1.03-1.57). In the total population, adverse events (AEs) attributed to study treatment occurred in 155 (53%) of 294 patients treated with pembrolizumab and 232 (84%) of 276 patients treated with paclitaxel. These AEs were of grade 3–5 severity in 42 (14%) of 294 patients in the pembrolizumab group and 96 (35%) of 276 patients in the paclitaxel group and led to discontinuation of study treatment in nine (3%) patients and 15 (5%) patients, respectively. The safety profile of pembrolizumab was consistent with that previously observed for pembrolizumab in patients with advanced solid tumors.[2]

In a post-hoc analysis, the pembrolizumab treatment effect was greater for patients with a PD-L1 CPS of 10 or higher (HR 0.64; 95% CI, 0.41-1.02) with a median overall survival of 10.4 months (95% CI, 5.9-17.3) with pembrolizumab vs. 8.0 months (95% CI, 5.1-9.9) with paclitaxel. The objective response rate in patients with PD-L1 CPS≥10 was 24.5% (n=13/53) in the pembrolizumab group vs. 9.1% (n=5/55) in the paclitaxel group. The complete response rates were 9.4% (n=5/53) and 1.8% (n=1/55) for pembrolizumab and paclitaxel, respectively. The partial response rates were 15.1% (n=8/53) and 7.3% (n=4/55) for pembrolizumab and paclitaxel, respectively.[2,3]

The following resources are submitted to assist the committee with their review:

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.

2. Shitara KS, Özgüroğlu M, Bang YJ, et al. Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): a randomised, open-label, controlled, phase 3 trial. Lancet 2018; 392: 123–33.

3. Shitara KS, Özgüroğlu M, Bang YJ, et al. Supplementary Appendix: Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): a randomised, open-label, controlled, phase 3 trial. Lancet 2018; 392: 123–33.

Thank you for considering this request. Below is my contact information should you need to contact me for additional information.

Sincerely,

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