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**NCCN Guidelines Panel: Head and Neck Cancers**

On behalf of Merck & Co., Inc., I respectfully request the NCCN Head and Neck Cancers Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V2.2017 for Head and Neck Cancers.

Specific changes requested:

We respectfully request that KEYTRUDA (pembrolizumab) be added as an anti-PD-1 immunotherapy for previously treated, PD-L1-positive patients with recurrent or metastatic nasopharyngeal carcinoma in the NCCN guidelines for Head and Neck Cancers, including the section CHEM-A.

FDA approval:

On August 5, 2016, FDA approved KEYTRUDA for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma with disease progression on or after platinum-containing chemotherapy. 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.[1]

Rationale:

This publication reports results from KEYNOTE-028, a nonrandomized, multicohort, phase 1b trial (NCT02054806) in patients with PD-L1–positive recurrent or metastatic nasopharyngeal carcinoma (RM-NPC). Key eligibility criteria for the NPC cohort included unresectable or metastatic disease, failure on prior standard therapy, and PD-L1 expression in 1% or more of tumor cells or tumor-infiltrating lymphocytes. Patients received pembrolizumab for up to 2 years or until disease progression or unacceptable toxicity. Primary end point (EP) was objective response rate (ORR) per investigator review according to RECIST version 1.1. Twenty-seven patients received pembrolizumab; median age was 52 years; 66.7% (18/27) of patients had WHO class II and III histology; 92.6% received prior therapies for RM-NPC; 70.4% had received three or more therapies for advanced disease. Partial response (PR) was observed in seven patients over a median follow-up of 20 months; there were no complete responses (CR). ORR per investigator review (primary EP) was 25.9%. ORR by central review was similar (26.3%). Stable disease (SD) was observed in 14 patients (51.9%). Disease control rate (CR + PR + SD ≥6 months) was 37% and disease control rate regardless of SD duration was 77.8%. Drug-related adverse events (DRAEs) that occurred in ≥15% of patients included rash (25.9%), pruritus (25.9%), pain (22.2%), hypothyroidism (18.5%), and fatigue (18.5%). Grade ≥3 DRAEs occurred in eight patients (29.6%), and there was one drug-related death (sepsis). Pembrolizumab monotherapy has shown antitumor activity and a manageable safety profile in PD-L1-positive RM-NPC patients for whom treatment options are limited and who have a generally poor outcome.[2]

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

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

2. Hsu C, Lee SH, Ejadi S *et al*. Safety and Antitumor Activity of Pembrolizumab in Patients With Programmed Death-Ligand 1–Positive Nasopharyngeal Carcinoma: Results of the KEYNOTE-028 Study. Published at jco.org on August 24, 2017. DOI: https://doi.org/10.1200/JCO.2017.73.3675

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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