

April 6, 2018

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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 Cancer Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V1.2018 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 patients with recurrent or metastatic, PD-L1 positive, salivary gland carcinoma in the NCCN guidelines for Head and Neck Cancers, including the section SALI-4.

**FDA Approval:**

KEYTRUDA (pembrolizumab) is not approved for the treatment of patients with recurrent or metastatic salivary gland carcinoma, with the exception of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) salivary gland carcinoma 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 details on the MSI-H cancer indication and other FDA-approved indications.<sup>1</sup>

**Rationale:**

A multicenter, open-label, multicohort phase 1b study (KEYNOTE-028; NCT02054806) of pembrolizumab was conducted in patients with recurrent or metastatic, PD-L1 positive, salivary gland carcinoma (SGC). Eligibility criteria for the SGC cohort included locally advanced or metastatic SGC of any subtype (except sarcomas or mesenchymal tumors) for which standard therapy was ineffective, did not exist, or was not considered appropriate; PD-L1-positive disease ( $\geq 1\%$  of tumor or stroma cells); ECOG PS 0-1; and adequate organ function. Patients received pembrolizumab every 2 weeks for 24 months or until confirmed disease progression, unacceptable toxicity or investigator/patient decision to withdraw. The primary objective of the study was objective response rate (ORR) by investigator review, per RECIST v1.1. Twenty-six patients with PD-L1-positive SGC were enrolled; median age was 57 years, 88% were men and 74% had received prior therapy for recurrent/metastatic disease. After a median follow-up of 20 months, confirmed ORR was 12% with 3 patients achieving partial response; there were no complete responses. Median duration of response was 4 months. Twelve patients (46%) had stable disease. Treatment-related adverse events occurred in 22 patients (85%), resulting in discontinuation in 2 patients. Six patients experienced immune-mediated AEs, including 4 cases of hypothyroidism (3 G2, one G1), 1 case of hepatitis (G3), and one treatment-related death from interstitial lung disease (G5). Adverse events that occurred in  $\geq 15\%$  of patients were fatigue, diarrhea, decreased appetite, and pruritus.<sup>2</sup>

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Cohen RB, Delord JP, Doi T *et al.* Pembrolizumab for the Treatment of Advanced Salivary Gland Carcinoma: Findings of the Phase 1b KEYNOTE-028 Study. Am J Clin Oncol 2018 - Early Online - Feb 21, 2018. DOI: 10.1097/COC.0000000000000429

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

Sincerely,

A handwritten signature in black ink, appearing to read 'Suzana Giffin', with a horizontal line extending to the right.

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