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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 V2.2018 for Head and Neck Cancers.

Specific changes requested:

We respectfully request the NCCN panel to consider the inclusion of KEYTRUDA monotherapy as a first-line treatment recommendation in patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) that expresses PD-L1 combined positive score (CPS) ≥1 in the appropriate sections of the guidelines, including section CHEM-A.

We also respectfully request the NCCN panel to consider the inclusion of KEYTRUDA in combination with chemotherapy with a platinum and 5-FU as a first-line treatment recommendation in patients with recurrent or metastatic HNSCC in the appropriate sections of the guidelines, including section CHEM-A.

FDA Approval:

KEYTRUDA (pembrolizumab) is approved for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) 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.

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

Rationale:

A multicenter, randomized, active-controlled, open-label, ongoing phase III study (KEYNOTE-048; NCT02358031) was conducted to evaluate pembrolizumab or pembrolizumab plus chemotherapy versus standard of care with cetuximab and platinum chemotherapy (EXTREME regimen) in the first-line treatment of patients with recurrent or metastatic (R/M) HNSCC. Key eligibility criteria included confirmed R/M HNSCC in the oropharynx (with known p16 status), oral cavity, hypopharynx or larynx considered incurable by local therapies, with no prior systemic therapy administered in the R/M setting, and ECOG PS of 0 or 1. Patients were randomized (1:1:1) to receive pembrolizumab monotherapy, pembrolizumab and chemotherapy (carboplatin or cisplatin + 5-FU), or EXTREME regimen (cetuximab + carboplatin or cisplatin + 5-FU). Progression-free survival (PFS) and overall survival (OS) were dual primary endpoints and were analyzed in these populations: CPS ≥20, CPS ≥1, and total population. Key secondary endpoints included safety, objective response rate (ORR), PFS at 6 months and 12 months, and quality of life measures. Results from the second interim analysis are reported below (data cutoff date: June 13, 2018).

Pembrolizumab monotherapy significantly improved OS vs. EXTREME regimen in the CPS ≥20 population with a hazard ratio (HR) of 0.61 (95% CI, 0.45-0.83; P=0.0007) as well as in the CPS ≥1 population with a HR of 0.78 (95% CI, 0.64-0.96; P=0.0086). There was no PFS or ORR benefit for pembrolizumab monotherapy over the EXTREME regimen in these populations. Median duration of response (DOR) for pembrolizumab monotherapy patients in the CPS ≥20 population was 20.9 months (range: 2.7 to 34.8+) vs. 4.2 months (range: 1.2+ to 22.3+) for EXTREME regimen patients. Median DOR for pembrolizumab monotherapy in the CPS ≥1 population was 20.9 months (range: 1.5+ to 34.8+) vs. 4.5 months (range: 1.2+ to 28.6+) for EXTREME regimen patients. Pembrolizumab monotherapy had a favorable safety profile vs. EXTREME regimen, with a lower incidence of any-grade, grade 3-4, and grade 5 treatment-related adverse events (AEs), and a lower incidence of treatment-related AEs leading to discontinuation.

Pembrolizumab in combination with chemotherapy significantly improved OS vs. EXTREME regimen in the total population regardless of PD-L1 status with a HR of 0.77 (95% CI, 0.63-0.93; P=0.0034). There was no PFS or ORR benefit for pembrolizumab plus chemotherapy over the EXTREME regimen. Median DOR for pembrolizumab plus chemotherapy patients in the total population was 6.7 months (range: 1.6+ to 30.4+) vs. 4.3 months (range: 1.2+ to 27.9+). Pembrolizumab plus chemotherapy had a comparable safety profile vs. EXTREME regimen. There was a similar incidence of any-grade, grade 3-4, and grade 5 treatment-related AEs. There was no unexpected toxicity in the pembrolizumab plus chemotherapy arm. The totality of these data supports our requests for the inclusion of pembrolizumab monotherapy (CPS ≥1 population) and pembrolizumab in combination with chemotherapy (irrespective of biomarker) as first-line treatment in patients with R/M HNSCC.[2]

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

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

2. Burtness B, Harrington K, Greil R et al. KEYNOTE-048: Phase 3 Study of First-Line Pembrolizumab for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma (R/M HNSCC). Presented at European Society for Medical Oncology (ESMO); October 19-23, 2018; Munich, Germany.

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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