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NCCN Guidelines Panel: Non-Melanoma Skin Cancer

On behalf of Merck & Co., Inc., I respectfully request the NCCN Non-Melanoma Skin Cancer Panel to review the enclosed information on KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V2.2019 for Squamous Cell Skin Cancer.

Specific changes requested:

We respectfully request the inclusion of pembrolizumab as a systemic therapy option for patients with recurrent or metastatic (R/M) cutaneous squamous cell carcinoma, who are not candidates for curative surgery or curative radiation therapy, in the appropriate sections of the guidelines, including section SCC-4, based on evidence demonstrated in the study KEYNOTE-629.

FDA approval:

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

Rationale:

A multicenter, open-label, single-arm, ongoing phase II study (KEYNOTE-629; NCT03284424) is being conducted to evaluate pembrolizumab in the treatment of adult patients with locally advanced or recurrent/metastatic cutaneous squamous cell carcinoma, not amenable to surgery or radiation. All patients received pembrolizumab 200mg every 3 weeks, with treatment planned to continue for 35 administrations (approximately 2 years) or until documented disease progression, unacceptable toxicity, investigator's decision, intercurrent illness preventing treatment, or administrative reasons requiring cessation. The primary endpoint is ORR per RECIST v1.1. Secondary endpoints are DOR, DCR, PFS, OS, and safety.[2]

Results from the first interim analysis in the R/M cohort (cutoff date: April 8, 2019): At data cutoff, median follow up of the 105 patients enrolled was 9.5 months (range 0.4-16.3 months). The objective response rate (ORR) was 34.3% (n=36; 95% CI: 25.3-44.2%; 4 complete responses, 32 partial responses). The disease control rate (DCR; DCR=CR+ PR + SD ≥ 12 weeks) was 52.4% (n=55; 95% CI: 42.4-62.2%) with stable disease seen in 31 patients (29.5%). Of the 76 patients with baseline and post-baseline data, 58 (76.3%) of patients experienced reduction in target lesion size, with 44 (57.9%) of patients experiencing

reductions of ≥30%. Median duration of response (DOR) was not reached (range 2.7-13.1+ months). Median progression free survival (PFS) was 6.9 months (95% CI: 3.1-8.5) for the overall population. Median overall survival (OS) was not reached (95% CI: 10.7 months to not reached). Treatment-related adverse events occurred in 66.7% of patients (n=70); the most common were pruritis (n=15; 14.3%), asthenia (n=14; 13.3%), and fatigue (n=13; 12.4%). Grade 3-5 treatment-related adverse events occurred in 5.7% (n=6) of patients. One patient died of treatment-related cranial nerve neuropathy.[2]

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

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

2. Grob JJ, Gonzalez R, Basset-Seguin N, et al. Pembrolizumab for Recurrent/Metastatic Cutaneous Squamous Cell Carcinoma (cSCC): Efficacy and Safety Results From the Phase 2 KEYNOTE-629 Study. Presented at European Society for Medical Oncology (ESMO); September 27-October 1, 2019; Barcelona, Spain.

Thank you for considering this request. Should you need additional information, please do not hesitate to contact me.

Sincerely,

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