June 7, 2018

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NCCN Guidelines Panel: Small Cell Lung Cancer

On behalf of Merck & Co., Inc., I respectfully request the NCCN Small Cell Lung Cancer (SCLC) Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V2.2018 for Small Cell Lung Cancer.

Specific changes requested:

We respectfully request the addition of KEYTRUDA (pembrolizumab) as a treatment option for patients with advanced SCLC who had progression on or are intolerant to standard therapy in the appropriate sections of the NCCN guidelines, including the section SCL-E (1 of 3).

FDA Approval:

Small Cell Lung Cancer

KEYTRUDA (pembrolizumab) is not approved for the treatment of patients with advanced SCLC, with the exception of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) SCLC 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.

Non-Small Cell Lung Cancer

KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥50%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.

KEYTRUDA, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. 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 phase 2 multicohort study (KEYNOTE-158; NCT02628067) was conducted to evaluate pembrolizumab in patients with advanced small-cell lung cancer (SCLC) regardless of biomarker status. Enrolled patients had prior progression on or intolerance to standard therapy and received pembrolizumab 200 mg every 3 weeks for 2 years or until disease progression or intolerable toxicity. Primary endpoint was ORR (RECIST v1.1, central review). Secondary endpoints included PFS, OS, duration of response (DOR) and safety. At the data cutoff date (Jan 15, 2018), median follow-up was 9.3 months (range, 0.5–22.3). Among 107 SCLC patients enrolled, 81 (76%) had received 1-2 prior therapies for recurrent/metastatic disease and 16 (15%) had stable brain metastasis. PD-L1-positive was defined as PD-L1 combined positive score ≥1. Tumors were PD-L1–positive in 39% and PD-L1–negative in 47% of patients (14% non-evaluable). ORR was 18.7% in the overall population (20/107; 95% CI, 11.8–27.4), 35.7% (15/42; 95% CI, 21.6–52.0) in patients with PD-L1–positive tumors, and 6.0% (3/50; 95% CI, 1.3–16.5) in PD-L1–negative tumors. Overall, median DOR had not been reached (range, 2.1+ to 18.7+) and 12 patients had DOR ≥12 months. Median PFS was 2.0 months (95% CI, 1.9–2.1) in all patients, 2.1 months (95% CI, 2.0–8.1) in patients with PD-L1–positive tumors, and 1.9 months (95% CI, 1.6–2.0) in PD-L1–negative tumors. Median OS was 8.7 months (95% CI, 5.6–12.0) overall, 14.9 months (95% CI, 5.6–NR) in patients with PD-L1–positive tumors, and 5.9 months (95% CI, 3.3–10.1) in PD-L1–negative tumors. Treatment-related AEs occurred in 64 patients (60%) with Grade ≥3 AEs in 13 patients (12%); there were two fatal treatment-related AEs (pneumonia and encephalopathy). The most common AEs (≥10%) were fatigue (14%), pruritus (12%), hypothyroidism (12%), decreased appetite (10%) and nausea (10%).[2]

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

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

2. Chung HC, Lopez-Martin J, Kao S, et al. Phase 2 Study of Pembrolizumab in Advanced Small-Cell Lung Cancer: KEYNOTE-158. Presented at American Society of Clinical Oncology (ASCO); June 1-5, 2018; Chicago IL, USA.

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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