

September 28, 2018

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NCCN Guidelines Panel: Non-Small Cell Lung Cancer

On behalf of Merck & Co., Inc., I respectfully request the NCCN Non-Small Cell Lung Cancer (NSCLC) Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V6.2018 for Non-Small Cell Lung Cancer.

Specific changes requested:

We respectfully request that KEYTRUDA (pembrolizumab) in combination with carboplatin and paclitaxel/nab-paclitaxel chemotherapy be recommended as first-line therapy for patients with metastatic squamous non-small cell lung cancer (NSCLC) as category 1 in the appropriate sections of the NCCN guidelines, including the section NSCL-J (3/4).

FDA Approval:

Non-Small Cell Lung Cancer

KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations.

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) $\geq 50\%$] 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 $\geq 1\%$) 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.

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

Rationale:

In a double-blind, phase 3 trial (KEYNOTE-407; NCT02775435), 559 patients with untreated metastatic, squamous NSCLC were randomly assigned (1:1 ratio) to receive 200 mg of pembrolizumab or saline placebo for up to 35 cycles; all patients also received carboplatin and either paclitaxel or nab-paclitaxel for the first 4 cycles. Primary end points were overall survival (OS) and progression-free survival (PFS), which was assessed by blinded, independent central review of radiologic images. After a median follow-up of 7.8 months, the median OS was 15.9 months (95% CI, 13.2-NR) in the pembrolizumab-combination group and 11.3 months (95% CI, 9.5-14.8) in the placebo-combination group (HR for death: 0.64; 95% CI, 0.49-0.85; $P < 0.001$). The OS benefit was observed in all prespecified subgroups, including the subgroups defined according to PD-L1 tumor proportion score. The median PFS was 6.4 months (95% CI, 6.2-8.3) in the pembrolizumab-combination group and 4.8 months (95% CI, 4.3-5.7) in

the placebo-combination group (HR for disease progression or death: 0.56; 95% CI, 0.45-0.70; P<0.001). Adverse events of grade 3 or higher occurred in 69.8% of the patients in the pembrolizumab-combination group and in 68.2% of the patients in the placebo-combination group. Discontinuation of treatment because of adverse events was more frequent in the pembrolizumab-combination group than in the placebo-combination group (13.3% vs. 6.4%).²

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Paz-Ares L, Luft A, Vicente D, et al. Pembrolizumab Plus Chemotherapy for Squamous Non-Small-Cell Lung Cancer [published online September 25, 2018]. N Engl J Med. 2018 doi: 10.1056/NEJMoa181086.

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 from the end of the signature.

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