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NCCN Guidelines Panel: Non-Small Cell Lung Cancer

NCCN Non-Small Cell Lung Cancer Panel: On behalf of Merck & Co., Inc., I respectfully request the NCCN Non-Small Cell Lung Cancer Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to the NCCN Guidelines v3.2020 for Non-Small Cell Lung Cancer (NSCLC).

Specific Changes: We respectfully request that the recommendation for single-agent pembrolizumab as a first-line therapy option for eligible patients with metastatic nonsquamous or squamous NSCLC, PD-L1 expression levels of 1% to 49%, and performance status (PS) of 0-2 be changed from category 2B to category 2A (pages NSCL-29 and MS-54) and added as a category 2A initial systemic therapy option for metastatic nonsquamous or squamous NSCLC with PS 2 on pages NSCL-J 2 of 4 and NSCL-J 3 of 4.

FDA Clearance:

Non-Small Cell Lung Cancer

KEYTRUDA (pembrolizumab), in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA (pembrolizumab), in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

KEYTRUDA (pembrolizumab), as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:

- stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
- metastatic.

KEYTRUDA (pembrolizumab), 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.

Please refer to the KEYTRUDA (pembrolizumab) prescribing information for other FDA-approved indications.[1]

Rationale: Middleton et al. published data from a single-arm, multicenter, phase 2 study (NCT02733159) evaluating the efficacy and safety of pembrolizumab in 60 participants with advanced NSCLC and PS 2, which included the primary outcomes of durable clinical benefit (DCB; the occurrence of complete response, partial response, or stable disease that continues until at least the second CT scan scheduled at 18 weeks) and toxicity (the occurrence at any time of a treatment-related dose delay or treatment discontinuation due to an adverse event). At a median follow-up of 10 months, the observed incidence for DCB in patients on first-line pembrolizumab therapy (n=24) was 38% (95% CI 21–57), and 44.6%, 40.5%, and 18.2% among first-line patients with a tumor proportion score (TPS) ≥50%, TPS 1–49%, and TPS <1%, respectively. The primary toxicity outcome was observed in 28% (95% CI 19–41) of patients, 11 (18%) of 60 due to dose delay and 6 (10%) of 60 due to drug discontinuation. The most common grade 3–4 adverse events were dyspnea (n=9), hyponatremia (n=5), and anorexia (n=4); no grade 5 treatment-related adverse events were observed, and no early deaths were attributed to hyperprogression.[2]

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Middleton G, Brock K, Savage J et al. Pembrolizumab in patients with non-small-cell lung cancer of performance status 2 (PePS2): a single arm, phase 2 trial. Lancet Respir Med. 2020 Mar 19. doi: 10.1016/S2213-2600(20)30033-3. [Epub ahead of print]

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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