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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 V3.2019 for Non-Small Cell Lung Cancer

Specific changes requested:

We respectfully request that KEYTRUDA (pembrolizumab) monotherapy be recommended as first-line treatment of patients with stage III NSCLC (who are not candidates for surgical resection or definitive chemoradiation) or metastatic non-small cell lung cancer (NSCLC) of any histology whose tumors express PD-L1 with a tumor proportion score (TPS) ≥1% as determined by an FDA-approved test, with no sensitizing EGFR or ALK genomic tumor aberrations as a category 1 in the appropriate sections of the NCCN guidelines, including the section NSCL-E and I.

FDA Approvals (NSCLC indications):

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, 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, as a single agent, is indicated for the first-line treatment of patients with stage III NSCLC who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC, and whose tumors express PD L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations [see Dosage and Administration (2.1)].

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 [see Dosage and Administration (2.1)], 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:

KEYTRUDA is now approved as monotherapy for the first-line treatment of patients with stage III NSCLC who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC of any histology whose tumors have PD-L1 expression TPS ≥1%, with no sensitizing EGFR or ALK genomic tumor aberrations based on the phase III randomized, open-label trial (KEYNOTE-042, NCT02220894) which was conducted in 1274 patients with previously untreated locally advanced or metastatic NSCLC without a sensitizing EFGF mutation or ALK translocation and an

Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1, life expectancy 3 months or longer, and a PD-L1 TPS of 1% or greater. Enrolled patients were randomly assigned 1:1 to receive pembrolizumab 200 mg every 3 weeks for up to 35 cycles or the investigator's choice of platinum-based chemotherapy for up to four to six cycles. Primary endpoints were overall survival (OS) in patients a TPS of 50% or greater, 20% or greater, and 1% or greater in the intent-to-treat population.

Overall survival was significantly longer in the pembrolizumab group than the chemotherapy group in all three TPS populations (≥50% hazard ration 0.69, 95% CI 0.56-0.85, p=0.0003; ≥20% 0.77, 0.64-0.92, p=0.0020, and ≥1% 0.81, 0.71-0.93, p=0.0018). The median survival values by TPS population were 20.0 months (95% CI 15.4-24.9) for the pembrolizumab verses 12.2 months (10.4-14.2) for chemotherapy, 17.7 months (15.3-22.1) verses 13.0 months (11.6-15.3) and 16.7 months (13.9-19.7) verses 12.1 months (11.3-13.3), respectively.

Treatment-related adverse events (AE) of any grade occurred in 399 (63%) of the 636 patients in the pembrolizumab group and 553 (90%) of 615 patients in the chemotherapy group. Treatment-related adverse events of grade 3 or worse occurred in 133 (18%) in the pembrolizumab group and in 252 (41%) in the chemotherapy group. Grade 3 or worse AEs that occurred in 20 or more patients were pneumonitis in the pembrolizumab group and anemia, decreased neutrophil count, neutropenia, decreased white blood cell count and decreased platelet count in the chemotherapy group. Death occurred in 13 (2%) of the pembrolizumab group and 14 (2%) of the chemotherapy group.[2]

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

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

2. Mok S, Wu Y, Kudaba I, et al. Pembrolizumab verses chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (Keynote-042): a randomized open-label, controlled, phase 3 trial. Lancet 2019; http://dx.doi.org/10.1016/s0140-6736(18)32409-7

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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