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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 consolidation KEYTRUDA (pembrolizumab) monotherapy be included as treatment recommendation for patients with **unresectable Stage III Non-small Cell Lung Cancer (NSCLC)** whose disease has not progressed following concurrent chemoradiation therapy in the appropriate sections of the NCCN guidelines, including the section NSCL-E.

FDA Approvals:

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 nab-paclitaxel, 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 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.

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

Rationale:

A single-arm, multi-center, investigator-initiated phase 2 trial (LUN 14-179) evaluating consolidation pembrolizumab monotherapy was conducted in 93 patients with unresectable stage III NSCLC whose disease has not progressed following concurrent chemoradiation therapy (CCRT). Study patients received chemoradiation with cisplatin/etoposide or carboplatin/paclitaxel or cisplatin/pemetrexed in addition to 59.4-66.6 Gy of radiation. Patients could receive up to two cycles of consolidation chemotherapy at the discretion of the treating physician. Treatment response or stable disease was assessed on imaging (CT or PET) 4-8 weeks after completion. Patients with stable disease or response were enrolled and received pembrolizumab 200 mg IV every 3 weeks for up to 12 months.

Primary endpoint was time to metastatic disease or death (TMDD). Secondary endpoints were progression-free survival (PFS), overall survival (OS), and toxicity. The hypothesis was that pembrolizumab would increase the TMDD from 12 months (historical control) to 18 months.[2,3]

Preliminary results were presented at ASCO 2018 in Chicago IL based on a median follow-up of 18.6 months for the study population.[2] The following data are from the updated analysis presented at the 19th World Conference on Lung Cancer (WCLC 2018) in Toronto, Canada based on a median follow-up of 23.9 months for the study population. Median TMDD was 30.7 months (95% CI, 17.9-NR) with TMDD rates of 76.3% (95% CI, 66.0-83.9) at 12 months, 60.0% (95% CI, 48.4-69.9) at 18 months and 52.3% (95% CI, 40.0-63.3) at 24 months. Median PFS was 15.0 months (95% CI, 11.9-25) with PFS rates of 60.8% (95% CI, 49.5-70.3) at 12 months, 46.9% (95% CI, 35.5-57.5) at 18 months and 41.4% (95% CI, 29.9-52.4) at 24 months. Median OS has not been reached (95% CI, 22.4-NR); 12-month, 18-month, and 24-month OS rates were 81.3% (95%CI, 71.7-88.0), 65.3% (95% CI, 54.2-74.4), and 61.5% (95% CI, 49.8-71.3), respectively.[3]

The most common adverse events (all grades) were fatigue (47.3%), cough (25.8%), dyspnea (21.5%), anorexia (17.2%), arthralgia (16.1%), diarrhea (16.1%), rash (15.1%), nausea (14.0%), hypothyroidism (12.9%) and pruritus (10.8%). Sixteen patients (17.2%) developed grade $\geq$ 2 pneumonitis: 10 patients (10.8%) with grade 2, 4 patients (4.3%) with grade 3, 1 patient (1.1%) with grade 4. There was one pneumonitis-related death (1.1%).[3]

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

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

2. Durm G, Althouse S, Sadiq A et al. Phase II Trial of Concurrent Chemoradiation with Consolidation Pembrolizumab in Patients with Unresectable Stage III NSCLC: Hoosier Cancer Research Network LUN 14-179. Presented at ASCO 2018; June 1-5, Chicago IL

3. Durm G, Althouse S, Sadiq A et al. Phase II Trial of Concurrent Chemoradiation with Consolidation Pembrolizumab in Patients with Unresectable Stage III NSCLC: Hoosier Cancer Research Network LUN 14-179. Presented at 19th WCLC 2018; September 23-26, 2018 Toronto, Canada.

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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