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Date of request: February 16th, 2021
NCCN Guidelines Panel: Non-Small Cell Lung Cancer

Dear NCCN Guidelines Panel for Non-Small Cell Lung Cancer

On behalf of Regeneron Pharmaceuticals, Inc. and Sanofi Genzyme, you will find enclosed an updated request to the Non-Small Cell Lung Cancer (NSCLC) Panel. Our demand is based on our pivotal phase III study EMPOWER-Lung 1 trial recently published in the LANCET. We are respectfully requesting the inclusion of cemiplimab in the NSCLC Guidelines as the preferred systemic treatment option for the management of first-line NSCLC patients with Locally Advanced or Metastatic disease with PD-L1 expression positive (≥50%) tumors.

Specific changes requested: Within the NCCN Non-Small Cell Lung Cancer Guidelines (Version 8.2020)

- Cemiplimab as a preferred first-line treatment option for patients with metastatic NSCLC, PD-L1 (≥50%), PS 0-2 (NSCL-30) for both Adenocarcinoma and Squamous cell carcinoma
- PD-L1 ≥50%: First-line therapy Cemiplimab (NSCL-I)

FDA Approval:

- Cemiplimab is currently FDA-approved[4] the treatment for patients with metastatic cutaneous squamous cell carcinoma (mCSCC) and locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation. An sBLA has been filed with the FDA of cemiplimab for the treatment of patients locally advanced NSCLC and who are not candidates for surgical resection or definitive chemoradiation or have progressed after treatment with definitive chemoradiation or metastatic NSCLC.

Rationale:

Despite positive trials using immune checkpoint inhibitors (ICI)[1,2], not all first-line monotherapy study showed the same magnitude of benefit[2,3]. Findings from the present study, the largest in this setting, showed that cemiplimab was superior to chemotherapy in improving PFS and OS in patients with advanced NSCLC with PD-L1 ≥50%. The study also included a proportion of patients with locally advanced NSCLC who were not candidates for chemoradiation, and those with controlled brain metastases. These patients are usually under-represented in clinical trials, making the present study more reflective of real-world clinical practice. Results from this study provide a strong rationale for cemiplimab as a preferred new monotherapy treatment option for patients with advanced NSCLC with PD-L1 ≥50%.

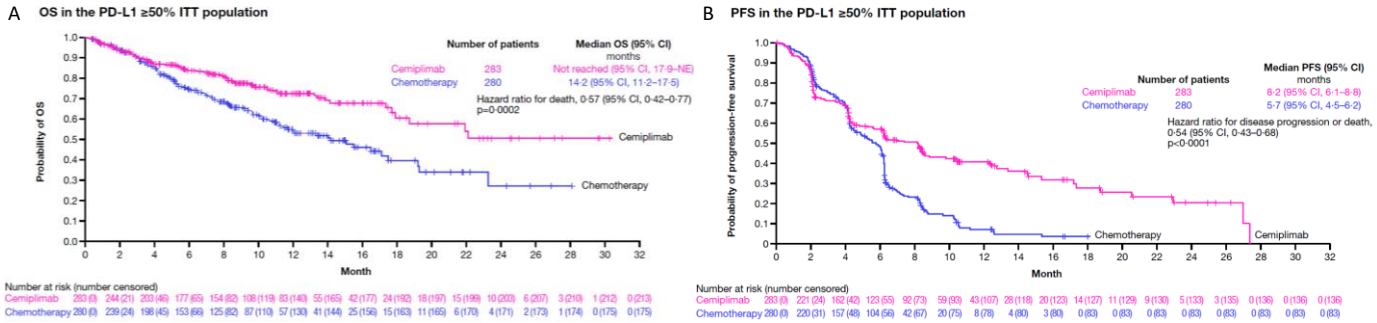
- EMPOWER-Lung 1 is a multicenter, open-label, global, phase 3 study, comparing cemiplimab monotherapy with investigator's choice of platinum-doublet chemotherapy as first-line treatment of patients with advanced NSCLC whose tumors express PD-L1 in ≥50% of tumor cells.

Study Design:

Patients with locally advanced or metastatic NSCLC were randomized (1:1) to either cemiplimab monotherapy 350 mg every 3 weeks or investigator's choice platinum-doublet chemotherapy. The primary endpoints were OS (defined as the time from randomization to death) and PFS (the time from randomization to the date of first disease progression by RECIST 1.1., or death). Secondary endpoints included objective response rate, duration of response, quality of life, and safety. The trial was

stopped after the second interim analysis (249 death events) base on the IDMC recommendation. Cemiplimab met the prespecified boundary for demonstration of superior PFS and OS benefit over chemotherapy.

Figure 1: Primary Efficacy



In the PD-L1 ≥50% ITT population, the median overall survival was significantly improved by cemiplimab (HR, 0.57; 95% CI, 0.42–0.77; p=00002; Figure 1A). The median OS was not reached (95% CI, 17.9–NE*) with cemiplimab versus 14.2 months (95% CI, 11.2–17.5) with chemotherapy. Cemiplimab also significantly improved PFS (HR, 0.54; 95% CI, 0.43–0.68; p<0.0001). Median PFS was 8·2 months (95% CI, 6.1–8.8) with cemiplimab versus 5.7 months (95% CI, 4.5–6.2) with chemotherapy (Figure 1B). Treatment-related AEs (TRAEs) occurred in 204 (57%) of 355 patients who received cemiplimab and 303 (89%) of 342 patients who received chemotherapy; the events were grade 3-4 in 41 (12%) and 127 (37%) of the patients, respectively. The most common grade 3-4 TRAEs were increased aspartate aminotransferase in five (1%) and pneumonia in four (1%) patients treated with cemiplimab, and anemia in 51 (15%) and neutropenia in 35 (10%) patients treated with chemotherapy. TEAEs, regardless of attribution, that led to death occurred in 34 (10%) of 355 patients treated with cemiplimab and 31 (9%) of 342 patients treated with chemotherapy. The events leading to death were considered related to treatment in nine (3%) patients treated with cemiplimab and included autoimmune myocarditis, cardiac failure, cardiopulmonary failure, cardiorespiratory arrest, nephritis, respiratory failure, septic shock, tumor hyperprogression, and unknown cause (n=1 each). The safety profile was consistent with the previously reported profile for cemiplimab and other PD-1/PD-L1 inhibitors in NSCLC and other tumor types.

* NE = Not Evaluable

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

- Sezer et al., Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. LANCET 397; 592–604 (2021)

We appreciate the opportunity to provide this information for review. Thank you for your time and consideration.

Sincerely,

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Clinical References:

1. Reck M, Rodriguez-Abreu D, Robinson AG, et al. Updated Analysis of KEYNOTE-024: Pembrolizumab Versus Platinum-Based Chemotherapy for Advanced Non-Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score of 50% or Greater. J Clin Oncol 2019; 37(7): 537-46.
2. Mok TSK, Wu YL, Kudaba I, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. Lancet 2019; 393(10183): 1819-30.3. Carbone DP, Reck M, Paz-Ares L, et al. First-Line Nivolumab in Stage IV or Recurrent Non-Small-Cell Lung Cancer. N Engl J Med 2017; 376(25): 2415-26.
3. Carbone DP, Reck M, Paz-Ares L, et al. First-Line Nivolumab in Stage IV or Recurrent Non-Small-Cell Lung Cancer. N Engl J Med 2017; 376(25): 2415-26.
4. Regeneron, Sanofi Genzyme. LIBTAYO® (cemiplimab-rwlc) [US prescribing information].