FDA Expands Pembrolizumab Indication for First-line Treatment of NSCLC (TPS ≥1%) Stage III

Approval is based on the results from KEYNOTE 042 study

- **Date**: 12 Apr 2019

On 11 April 2019, the US Food and Drug Administration (FDA) approved pembrolizumab (KEYTRUDA, Merck Inc.) for the first-line treatment of patients with stage III non-small cell lung cancer (NSCLC) who are not candidates for surgical resection or definitive chemoradiation or metastatic NSCLC. Patients' tumours must have no *EGFR* or *ALK* genomic aberrations and express PD-L1 (Tumour Proportion Score [TPS] ≥1%) determined by an FDA-approved test.

Pembrolizumab was previously approved as a single agent for the first-line treatment of patients with metastatic NSCLC whose tumours express PD-L1 TPS ≥50%.

Approval was based on KEYNOTE-042 (NCT02220894), a randomised, multicentre, open-label, active-controlled trial conducted in 1274 patients with stage III or IV NSCLC who had not received prior systemic treatment for metastatic NSCLC and whose tumours expressed PD-L1 (TPS ≥1%). PD-L1 expression was determined by an immunohistochemistry assay using the PD-L1 IHC 22C3 pharmDx Kit.

Patients were randomised (1:1) to receive pembrolizumab 200 mg intravenously every 3 weeks or investigator's choice of a carboplatin-containing regimen with either pemetrexed or paclitaxel. Randomisation was stratified by ECOG performance status, histology, geographic region, and PD-L1 expression (TPS ≥50% vs. TPS 1 to 49%).

Overall survival (OS) in the TPS ≥50% NSCLC subgroup, the TPS ≥20% NSCLC subgroup, and the overall population (TPS ≥1%) were the major efficacy measures. The trial demonstrated statistically significant OS improvements for those randomised to pembrolizumab compared with chemotherapy in all three populations.

In the TPS ≥1% population (overall population), the median OS was 16.7 and 12.1 months for the pembrolizumab and chemotherapy arms, respectively (HR 0.81; 95% CI: 0.71, 0.93; p = 0.0036). For the TPS ≥ 20% subgroup, the median OS was 17.7 months for the pembrolizumab arm and 13.0 months for the chemotherapy arm (HR 0.77; 95% CI: 0.64, 0.92; p = 0.004). For the TPS ≥50% subgroup, the estimated median OS was 20 months and 12.2 months for those receiving pembrolizumab and chemotherapy, respectively (HR 0.69; 95% CI: 0.56, 0.85; p = 0.0006). There were no significant differences in progression-free survival or overall response rate between arms in any population.
The most common adverse reactions reported in at least 10% of patients who received pembrolizumab as a single agent in KEYNOTE-042 include fatigue, decreased appetite, dyspnoea, cough, rash, constipation, diarrhoea, nausea, hypothyroidism, pneumonia, pyrexia, and weight loss.

The recommended pembrolizumab dose for NSCLC is 200 mg as an intravenous infusion over 30 minutes every 3 weeks.

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