FDA approves pembrolizumab in combination with chemotherapy for first-line treatment of metastatic squamous NSCLC

On October 30, 2018, the Food and Drug Administration approved pembrolizumab (KEYTRUDA, Merck & Co. Inc.) in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of metastatic squamous non-small cell lung cancer (NSCLC).

Approval was based on KEYNOTE-407 (NCT02775435), a randomized, multi-center, double-blind, placebo-controlled trial in 559 patients with metastatic squamous NSCLC, regardless of PD-L1 tumor expression status, who had not previously received systemic therapy for metastatic disease. Patients were randomized (1:1) to pembrolizumab 200 mg or placebo in combination with carboplatin, and investigator's choice of either paclitaxel every 3 weeks or nab-paclitaxel weekly on a 3-week cycle for 4 cycles followed by pembrolizumab or placebo. Patients continued pembrolizumab or placebo until disease progression, unacceptable toxicity, or a maximum of 24 months.

The main efficacy outcome measures were overall survival (OS), progression-free survival (PFS) and overall response rate (ORR) as assessed by blinded independent review. The trial demonstrated statistically significant improvements in OS, PFS and ORR for patients receiving pembrolizumab plus chemotherapy compared with those randomized to placebo plus chemotherapy. The median OS was 15.9 and 11.3 months for the pembrolizumab plus chemotherapy and placebo plus chemotherapy arms, respectively (HR 0.64; 95% CI: 0.49, 0.85; p=0.0017). The median PFS was 6.4 and 4.8 months for the pembrolizumab plus chemotherapy and placebo plus chemotherapy arms, respectively (HR 0.56; 95% CI: 0.45, 0.70; p<0.0001). The analysis of ORR was limited to the initial 204 patients randomized. The ORRs were 58% and 35%, favoring

the pembrolizumab-containing arm (difference of 23.6%; 95% CI: 9.9, 36.4; p=0.0008). The estimated median response durations were 7.2 and 4.9 months, respectively.

The most common adverse reactions in at least 20% of patients who received pembrolizumab on KEYNOTE-407 were fatigue/asthenia, nausea, constipation, diarrhea, vomiting, pyrexia, decreased appetite, rash, cough, dyspnea, alopecia, and peripheral neuropathy.

The recommended pembrolizumab dose for metastatic squamous NSCLC is 200 mg intravenously every 3 weeks, prior to chemotherapy when given on the same day, until disease progression, unacceptable toxicity, or 24 months after initiation.

View full prescribing information for KEYTRUDA.

FDA granted this application priority review.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

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