FDA Grants Regular Approval for Keytruda Plus Chemotherapy for First-Line Treatment of Metastatic NSCLC

Immunotherapy approved for previously untreated patients with nonsquamous non-small-cell lung cancer.

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FDA grants regular approval for pembrolizumab in combination with chemotherapy for first-line treatment of metastatic nonsquamous NSCLC

On August 20, 2018, the Food and Drug Administration approved pembrolizumab (KEYTRUDA, Merck & Co., Inc.) in combination with pemetrexed and platinum as first-line treatment of patients with metastatic, non-squamous non-small cell lung cancer (NSqNSCLC), with no EGFR or ALK genomic tumor aberrations.

Pembrolizumab was previously granted accelerated approval for this indication in May 2017 based on improvements in overall response rate and progression-free survival for patients randomized to pembrolizumab administered with pemetrexed and carboplatin as compared with pemetrexed and carboplatin alone in the KEYNOTE-021 study.

Today's approval represents fulfillment of a postmarketing commitment demonstrating the clinical benefit of this product. This action is based on the results of KEYNOTE-189 (NCT02578680), a randomized, multicenter, double-blind, active controlled study enrolling 616 patients receiving first-line treatment for metastatic NSqNSCLC.

Patients were randomized (2:1) to receive pembrolizumab (or placebo) in combination with pemetrexed, and investigator's choice of either cisplatin or carboplatin every 3 weeks for 4 cycles followed by pembrolizumab (or placebo) and pemetrexed. Treatment with pembrolizumab continued until disease progression, unacceptable toxicity, or a maximum of 24 months.

The primary efficacy outcome measures were overall survival (OS) and progression-free survival (PFS), as assessed by a blinded independent committee review (RECIST 1.1.).

The trial demonstrated a statistically significant improvement in OS for patients randomized to pembrolizumab and chemotherapy (HR 0.49; 95% CI: 0.38, 0.64; $p<0.00001$) in a pre-specified interim analysis. The median OS was not reached at the time of the data cut-off in the

pembrolizumab plus chemotherapy arm and was 11.3 months for those in the chemotherapy arm. The trial also demonstrated an improvement in PFS for patients randomized to pembrolizumab plus chemotherapy (HR 0.52; 95% CI: 0.43, 0.64; p<0.00001). The median PFS was 8.8 months for patients receiving pembrolizumab plus chemotherapy and 4.9 months for those receiving chemotherapy alone. The overall response rate was significantly higher (48% vs. 19%; p=0.0001) for those in the pembrolizumab plus chemotherapy arm and the median response duration was 11.2 months and 7.8 months, respectively.

The most common adverse reactions reported in ≥20% of patients in KEYNOTE-189 were fatigue/asthenia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, and pyrexia.

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

View full prescribing information for KEYTRUDA.

This is the second FDA approval using the Real Time Oncology Review pilot program that enabled the FDA review team to begin analyzing data before the application submission.

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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