EMA to Review Keytruda Combo as First-line Treatment for Advanced NSCLC Patients in EU

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The European Medicines Agency (EMA) has started the review process for Merck's application seeking approval of Keytruda (pembrolizumab) in combination with Alimta (pemetrexed) and platinum chemotherapy as a first-line treatment for patients with metastatic nonsquamous non-small cell lung cancer (NSCLC).

This decision comes after promising overall survival and progression-free survival data from the Phase 3 KEYNOTE-189 trial (NCT02578680), which were recently presented at the American Association of Cancer Research (AACR) 2018 Annual Meeting in Chicago.

The findings were also published in the *New England Journal of Medicine,* in the study titled "Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer."

"We are very pleased that the centralized review process is underway, and are hopeful that this new combination regimen will soon become available for appropriate patients in Europe who have been diagnosed with metastatic lung cancer," Roger M. Perlmutter, president of Merck Research Laboratories, said in a press release.

Generally, the first-line therapy for patients with advanced NSCLC without any targetable mutations is platinum-based chemotherapy. But for patients whose tumors

have 50% or more of cancer cells producing the PD-L1 factor, the first-line treatment is the immunotherapy Keytruda, a PD-1 inhibitor.

Phase 2 clinical trials have shown that adding Keytruda to platinum chemotherapy and Alimta increases the rates of response and delays tumor progression or death, compared to platinum chemotherapy alone.

The Phase 3 KEYNOTE-189 trial was designed to compare the combination of Alimta and platinum-based chemotherapy with either Keytruda or placebo in patients with nonsquamous NSCLC with any level of PD-L1 expression.

The study's main goal was to determine if Keytruda increases overall survival and progression-free survival — the time until disease worsening or death — as determined by a blinded and independent central radiologic review.

One year after starting the treatment, 69.2% of patients receiving Keytruda were still alive, compared to 49.4% in the control arm who received a placebo. This represented a 51% reduction in the risk of death for those taking Keytruda.

Interestingly, patients across all PD-L1 categories demonstrated an improvement in overall survival, indicating a benefit for all patients.

Progression-free survival was also better in the Keytruda group — 8.8 months vs. 4.9 months — showing that Keytruda reduced the risk of progression or death by 49%.

Grade 3 or higher adverse events occurred at similar rates between the two groups: 67.2% compared to 65.8%.

"In patients with previously untreated metastatic nonsquamous NSCLC without *EGFR* or *ALK* mutations, the addition of [Keytruda] to standard chemotherapy of [Alimta] and a platinum-based drug resulted in significantly longer overall survival and progression-free survival than chemotherapy alone," the investigators wrote.

In 2017, the U.S. Food and Drug Administration granted accelerated approval to the combination of Keytruda, Alimta, and carboplatin for patients with previously untreated metastatic nonsquamous NSCLC.