
# FDA Puts Keytruda on Accelerated Approval Track as Combo Lung Cancer Treatment

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The U.S. Food and Drug Administration has put Merck's Keytruda (pembrolizumab) on an **accelerated approval track as a combo treatment for metastatic non-squamous non-small cell lung cancer (NSCLC).**

The accelerated track applies to Keytruda, along with Alimta (pemetrexed) and Paraplatin (carboplatin), as a first-line therapy. The combo can be administered irrespective of a patient's level of the PD-L1 protein, the FDA said. That protein can bind to killer immune cells, inhibiting an immune system response to cancer. The more the protein is expressed, the more it challenges the immune system.

Previous FDA approvals were connected with patients' PD-L1 expression. Expression is the process by which information from a gene is used to create a functional product, like a protein.

Under the accelerated approval program, continued FDA sign-offs can depend on the results of clinical trials that confirm previous studies' evidence of Keytruda's effectiveness.

"This approval marks an important milestone in the treatment of lung cancer. Now, pembrolizumab in combination with pemetrexed and carboplatin can be prescribed in the first-line setting for patients with metastatic nonsquamous non-small cell lung cancer, irrespective of PD-L1 expression," Dr. Corey Langer, director of thoracic oncology at the Hospital of the University of Pennsylvania, said in a press release. "Physicians should continue to use each patient's individual characteristics – including biomarker status, histology, and other clinical factors – to determine the best treatment plan for each person."

The latest FDA approval was based on results of the KEYNOTE-021 Phase 1/2 clinical trial (NCT02039674). It covered 123 metastatic nonsquamous NSCLC patients with no EGFR or ALK gene mutations who had not received previous therapy. Patients were enrolled irrespective of their PD-L1 status.

Participants were randomized to receive one of two therapy regimens. One was Keytruda, Alimta and Paraplatin every three weeks for four cycles, followed by Keytruda every three weeks. The other was Alimta and Paraplatin for four 21-day cycles. At the trial investigator's discretion, Alimta could be administered as a maintenance treatment in both treatment arms.

The study's main measure of effectiveness was patients' objective response to the Keytrude combo therapy. An objective response is either a full or partial response.

Secondary measures of effectiveness included the length of time before a patient's disease progressed, or progression-free survival; duration of patients' response to treatment; and patients' overall survival rate.

Fifty-five percent of patients who received the Keytruda combo responded to it, nearly double the 29% in the control arm. All responses were partial.

Patients' response had no connection with their PD-L1 level, researchers found. Fifty-seven percent of those who were not expressing the protein responded to the Keytruda combo, versus 54 percent of those who were expressing it. The figures in the Alimta-Paraplatin control arm were 13 percent and 38 percent.

Duration of response was longer in the Keytruda arm, the research team said. Ninety-three percent of patients taking the Keytruda combo responded for six or more months, versus 81 percent of patients in the control arm.

Another finding was that the Keytruda combo reduced the risk of disease progression or death by 47 percent. The median time the disease failed to progress among the Keytruda group was 13 months, compared with 8.9 months in the Alimta/Paraplatin arm.

The most common adverse reactions that led to the Keytruda combo treatment being interrupted or halted were acute kidney injury, fatigue, anemia, breathlessness, a lung inflammation known as pneumonitis, and low levels of immune cells called neutrophils.

"The improved responses seen with the Keytruda plus pemetrexed/carboplatin regimen are significant, and highlight the importance of finding new approaches that address the unmet needs of patients with metastatic nonsquamous non-small cell lung cancer," said Dr. Roger M. Perlmutter, the president of Merck Research Laboratories. "Today's approval further supports our commitment to improve the lives of people with cancer."

**Keytruda has already received FDA approval as a stand-alone first-line treatment for metastatic NSCLC patients whose tumors have high rates of PD-L1 expression and no EGFR or ALK mutations. The agency also approved it as a second-line or greater treatment for metastatic NSCLC patients whose tumors express a certain level of PD-L1 and whose disease progressed during or after platinum-based chemotherapy.**

Merck said the latest approval is a milestone for Keytruda. It is now the first anti-PD-1 therapy to be approved with other drugs as a combo treatment for metastatic nonsquamous NSCLC.

"The combination of this immunotherapy with pemetrexed and carboplatin is more good news for patients," said Bonnie J. Addario, a lung cancer survivor who founded the Bonnie J. Addario Lung Cancer Foundation. "Congratulations to Merck and the FDA for moving so swiftly on this important addition to our patients' options for treatment. With this approval, hope for lung cancer patients continues to improve."