FDA Approves New Lung Cancer Combo

Two targeted therapies, Tafinlar and Mekinist, for non-small-cell lung cancer with a specific BRAF mutation have been approved.

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The Food and Drug Administration (FDA) last week approved a new oral treatment combination for people with metastatic non-small-cell lung cancer (NSCLC) that carries the BRAF V600E mutation.

Just over 60 percent of patients with advanced BRAF V600E positive lung cancer responded to treatment with Tafinlar (dabrafenib) plus Mekinist (trametinib) in a Phase II study, according to drugmaker Novartis.

Non-small-cell lung cancer, which accounts for more than 80 percent of all lung cancers, is often detected late and has a high mortality rate. It is the leading cause of cancer-related death for both men and women, according to the Centers for Disease Control and Prevention.

Lung cancer is difficult to treat, but targeted therapies and immunotherapy have improved outcomes. Targeted therapy works against cancer with specific genetic characteristics. This type of treatment is often better tolerated than traditional chemotherapy, which kills not only cancer cells but also rapidly dividing healthy cells throughout the body.

BRAF is a proto-oncogene, or a gene that can trigger cancer when it mutates. The gene produces the protein B-Raf, which helps regulate cell division. A specific BRAF mutation known as V600E can cause uncontrolled cell growth.

Tafinlar is a kinase inhibitor that blocks the B-Raf protein. Mekinist blocks the activity of two other kinase enzymes, MEK1 and MEK2, that regulate cell signaling. Tafinlar comes in a capsule; Mekinist is a tablet.

Tafinlar plus Mekinist is the first targeted treatment approved in the United States specifically for lung cancer with the BRAF V600E mutation, according to Novartis. The combination is also approved for metastatic melanoma with the same type of mutation and is currently being studied for other tumor types.

The new approval was based on a non-randomized Phase II trial that enrolled 93 participants.
with BRAF V600E positive NSCLC that had metastasized (spread beyond the lungs); 36 were previously untreated, while 57 had received prior chemotherapy. They were treated with 150 milligrams Tafinlar taken twice daily plus 2 mg Mekinist taken once daily.

Overall response rates were 61 percent for the previously untreated patients and 63 percent for those who had tried chemotherapy. The median duration of response was 12.6 months in the prior chemotherapy group but could not be determined in the newly treated group because most were still responding. The combination regimen worked better than Tafinlar or Mekinist alone.

The most common adverse events were fever, fatigue, nausea, vomiting, diarrhea, decreased appetite, swelling, rash, chills, hemorrhage, cough and shortness of breath. Safety information for Tafinlar plus Mekinist states that treatment can cause more serious side effects, including new cancers, bleeding in the brain or stomach, blood clots, and heart, lung and eye problems.

Tafinlar plus Mekinist is indicated only for people with cancer that carries the BRAF V600E mutation as determined by an FDA-approved genetic test. This group accounts for around 1 to 3 percent of NSCLC patients worldwide. Although this type of cancer is rare, it is aggressive and associated with poor outcomes.

With the approval of Tafinlar plus Mekinist, BRAF V600E is now the fourth NSCLC genetic mutation with approved targeted therapies, Bruce Johnson, MD, of the Dana-Farber Cancer Institute, noted in a Novartis press release.

The others are EGFR, ALK and ROS-1. Two studies presented at the recent American Society of Clinical Oncology (ASCO) annual meeting in Chicago showed that the experimental EGFR inhibitor dacomitinib and the ALK inhibitor Alecensa (alectinib) improved survival of advanced lung cancer patients with the corresponding mutations.

Taken together, about 30 percent of people with NSCLC have one of these four mutations and can potentially be treated with targeted therapies.

“This is an important milestone for the lung cancer community as we are continuing to better understand the genomic drivers of cancer and develop effective treatments targeted for these biomarkers,” Johnson said.