FDA Gives Green Light to Zykadia (Ceritinib) as First-line Therapy for ALK-positive NSCLC

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The U.S. Food and Drug Administration has approved Norvartis' Zykadia (ceritinib) to be used as first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive.

In 2014, Zykadia was granted accelerated approval for patients with ALK-positive NSCLC who progressed or are intolerant to Xalkori (crizotinib). More recently, in January 2017, the FDA granted Zykadia breakthrough therapy status for the treatment of ALK-positive metastatic NSCLC with metastasis to the brain, and priority review status for first-line metastatic NSCLC.

The May 26 approval "represents the next step in the development of Zykadia as a treatment option for ALK-positive metastatic NSCLC, bringing this important medication to a patient population where a need still exists," Bruno Strigini, CEO,

Novartis Oncology, said in a press release. “At Novartis, we are tireless in our pursuit of developing novel medicines to treat lung cancer, and the first-line approval of Zykadia for ALK-positive metastatic NSCLC illustrates our commitment to cancer patients.”

Lung cancer is the second-most common cancer in both men and women, with more than 222,000 new cases expected to be diagnosed this year in the U.S. alone, according to estimates from the American Cancer Society.

Among patients with NSCLC, the most common subtype of lung cancer, 3% to 7% percent of patients have an ALK rearrangement. In these patients, the ALK gene is fused with a constitutively active gene, and as a consequence, ALK becomes uncontrollably expressed and active even in the absence of an activating signal.

ALK is a member of the insulin receptor family and participates in the activation of several cancer-driving pathways. In cells with ALK rearrangements, the over-activation of these pathways often leads to cancer.

The FDA’s decision was based on results from the ASCEND-4 Phase 3 trial (NCT01828099), an open-label, randomized, multicenter, global study designed to assess the safety and effectiveness of Zykadia vs. standard chemotherapy: Alimta (pemetrexed) plus Platinol (cisplatin) or Alimta plus Paraplatin (carboplatin), in previously untreated patients.

The trial was conducted at 134 medical centers across 28 countries, and included a total of 376 patients with stage 3B or 4 ALK-positive NSCLC.

Results revealed that patients treated with Zykadia had a median progression-free survival (PFS) of 16.6 months, which more than doubled the 8.1 months seen in the chemotherapy arm.

Zykadia’s beneficial effects were seen in patients with or without brain metastasis, demonstrating the drug’s intracranial efficacy. Patients without brain metastasis receiving Zykadia had a median PFS of 26.3 months, compared to 8.3 months in chemotherapy-treated patients.

Among patients with brain metastatis, Zykadia treatment induced a median PFS of 10.7 months, versus 6.7 months in the chemotherapy arm.

Overall intracranial response rate was 57% among patients with measurable brain metastasis treated with Zykadia, compared to 22% in patients treated with chemotherapy. Zykadia-treated patients had an overall response rate of 73%.

The most common adverse events were diarrhea, nausea, vomiting, fatigue, abdominal pain, loss of appetite, and cough. Grade 3 or 4 adverse effects were mainly fatigue, vomiting and diarrhea.