Alectinib halts lung cancer growth more than a year longer than crizotinib

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Findings from a phase III clinical trial point to a more effective initial treatment for patients with ALK-positive non-small cell lung cancer (NSCLC). Compared to the current standard of care crizotinib (Xalkori), the newer ALK inhibitor alectinib (Alecensa) halted cancer growth for a median of 15 months longer and caused fewer severe side effects.

The study will be featured in a press briefing today and presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"This is the first global study to compare alectinib with crizotinib in ALK-positive lung cancer and establishes alectinib as the new standard of care for initial treatment in this setting," said lead study author Alice T. Shaw, MD, PhD, Director of Thoracic Oncology at Massachusetts General Hospital Cancer Center in Boston, MA. "Alectinib was especially beneficial in controlling and preventing brain metastases, which can have a major impact on patients' quality of life."

About 5% of NSCLCs are ALK-positive, meaning they have a genetic rearrangement where the ALK gene is fused with another gene. In the United States, about 12,500 people are diagnosed with ALK-positive NSCLC each year.

Crizotinib, the first medicine to specifically target ALK, was approved by the FDA in 2011. Although the majority of patients initially benefit from crizotinib, the cancer typically starts growing again within a year. Alectinib is a more potent, next-generation inhibitor of ALK. It was initially approved in 2015 for use in patients with advanced NSCLC that worsens despite crizotinib.

About the Study

In this open label clinical trial (ALEX), researchers randomly assigned 303 patients with stage IIIB or IV, ALK-positive NSCLC to receive alectinib or crizotinib. The patients had not received prior systemic therapy for advanced NSCLC.

Key Findings

Alectinib reduced the risk of cancer progression or death by 53% compared with crizotinib. Based on independent review, alectinib extended the median time to progression by about 15 months (median progression-free survival was 25.7 months with alectinib and 10.4 months with crizotinib).

"Nobody imagined it would be possible to delay advanced lung cancer progression by this much. Most targeted therapies for lung cancer are associated with a median progression-free survival of roughly 12 months," said Dr. Shaw.

While both treatments cross the blood-brain barrier, alectinib was more effective in preventing brain metastases than crizotinib, because it can better penetrate into the brain. At 12 months, the incidence of brain metastases was much lower with alectinib than with crizotinib (9% vs. 41%).

Overall, severe side effects were less common with alectinib than with crizotinib, occurring in 41% vs. 50% of patients. The most common side effects of alectinib were fatigue, constipation, muscle aches, and swelling, whereas crizotinib caused gastrointestinal problems and liver enzyme abnormalities.

Next Steps

The researchers will continue to follow patients on this study to see if those treated with alectinib live longer than those treated with crizotinib. Meanwhile, several ongoing clinical trials are comparing other next-generation ALK inhibitors to crizotinib in the first-line setting.

More information:
abstracts.asco.org/199/AbstView_199_185951.html

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