# アレクチニブは肺がんの無増悪生存期間を改善する(Abstract LBA9008)

## 新たなALK阻害剤は現在の標準治療よりも肺がんの増殖を1年以上長く停止させる

## New ALK inhibitor halts lung cancer growth more than a year longer than current standard of care

2017年American Society of Clinical Oncology年次集会で発表された第III相臨床試験の結果は、ALK融合遺伝子陽性非小細胞肺がん患者に対し、より有効な初回治療を指し示した。現在の標準治療であるクリゾチニブに比べ、新たなALK阻害剤アレクチニブは、がん増殖を期間中央値で15か月長く停止させ（無増悪生存期間中央値はアレクチニブで25.7か月、クリゾチニブで10.4か月）、重篤な副作用は少なかった。さらに、12か月後の脳転移率はアレクチニブ治療群の方がはるかに低かった（9% vs. 41%）。

## Full Text

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 crizotinib, the current standard of care, the newer ALK inhibitor alectinib halted cancer growth for a median of 15 months longer and caused fewer severe side effects.

The study was featured 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.

Crizotinib is the first medicine to specifically target ALK. 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.

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.

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.

"The fact that this second-generation targeted treatment halted advanced lung cancer growth for more than two years while preventing brain metastases is a remarkable result in this difficult disease," said ASCO Expert John Heymach, MD, PhD. "Thanks to this advance, we are on the road to helping these patients live longer and better."

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.

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