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Alectinib vs Crizotinib in ALK+ NSCLC: Final ALEX Data

Ryan Quigley:
This is *AudioAbstracts* on ReachMD. I'm Ryan Quigley, and today we're looking at long-term outcomes in *ALK*-positive non-small cell lung cancer, focusing on the final overall survival analysis from the phase III ALEX trial.

A patient with newly-diagnosed metastatic *ALK*-positive non-small cell lung cancer presents today with a very different outlook than in years past. Targeted therapies have extended survival, and the ALEX trial offers one of the clearest views of how durable those benefits can be with longer follow-up.

This was a global, randomized phase III study comparing first-line alectinib with crizotinib in previously untreated patients with advanced *ALK*-positive non-small cell lung cancer. Just over 300 patients were enrolled, and this final analysis focuses on overall survival, duration of response, and long-term safety after extended follow-up.

With that in mind, let's take a look at the results. At the 2025 data cutoff, median overall survival reached 81.1 months with alectinib versus 54.2 months with crizotinib. This represents a 22 percent lower risk of death with alectinib than with crizotinib, with a hazard ratio of 0.78, ranging from 0.56 to 1.08 in the 95 percent confidence interval. While the analysis wasn't statistically powered for overall survival, the difference remains clinically meaningful. Seven-year survival rates were 48.6 percent with alectinib compared with 38.2 percent for crizotinib, suggesting a sustained long-term benefit.

The central nervous system remains a key differentiation between treatment responses. Among patients with baseline CNS metastases, median overall survival was 63.4 months with alectinib versus 30.9 months with crizotinib. In those without CNS involvement, survival extended to 94 months versus 69.8 months, respectively. These findings reinforce the importance of CNS-active therapy early in the disease course.

Durability of response further supports this advantage. Among responders, median duration of response was 42.3 months with alectinib compared with 11.1 months for crizotinib. In practice, that translates into longer disease control and fewer transitions between therapies.

Treatment sequencing adds further important context. More patients in the crizotinib arm received subsequent next-generation ALK inhibitors, reflecting earlier progression. Even so, adjusted analyses suggest the survival benefit with alectinib may be underestimated.

Safety remained consistent with prior reports despite longer treatment exposure. Rates of grade three to five adverse events were similar between treatment arms. Alectinib was more commonly associated with laboratory abnormalities such as anemia and elevated bilirubin, while crizotinib showed higher rates of gastrointestinal side effects. No new safety signals emerged with extended follow-up.

The longer term findings reported here reinforce alectinib as a preferred first-line option in advanced *ALK*-positive non-small cell lung cancer, supported by durable survival, prolonged response, and manageable long-term safety. Early treatment selection continues to shape outcomes across the disease course, particularly in controlling CNS disease and delaying progression.

This has been an *AudioAbstract*, and I'm Ryan Quigley. To access this and other episodes in our series, visit ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.

Reference:
Peters S, Camidge DR, Dziadziuszko R, et al. Alectinib versus crizotinib in previously untreated ALK-positive advanced non-small cell lung cancer: final overall survival analysis of the phase III ALEX study. *Ann Oncol.* 2026;37(1):92-103. doi:10.1016/j.annonc.2025.09.018