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ALEX trial results show alectinib further outpacing crizotinib in ALK+ NSCLC

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D. Ross Camidge, MD, PhD. Credit: University of Colorado Cancer Center

Updated results of the global phase III ALEX trial comparing alectinib with crizotinib as first-line treatment against ALK-positive non-small cell lung cancer show a median progression-free survival (PFS) of 34.8

months in 152 patients treated with alectinib versus 10.9 months in 151 patients treated with crizotinib.

"Think of it like a horse race, only it's not about who crosses the finish line first, but how far the horses can run," says D. Ross Camidge, MD, Ph.D., the Joyce Zeff Chair in Lung Cancer Research at the University of Colorado Cancer Center, director of Thoracic Oncology at the CU School of Medicine, and the study's first author. "In this trial, it's as if half of the people 'riding' crizotinib had exhausted their horses at about 11 months. For patients on alectinib, when this trial first started reporting data last year, more than half were still on their horses, still running. Now enough time has elapsed to estimate the median performance of these alectinib 'horses' more accurately."

Camidge's analogy explains the results above: At 10.9 months half of the cancers treated with crizotinib had restarted their growth, whereas it took 34.8 months for patients on alectinib to reach this same "median progression free survival". Impressively, the PFS was almost identical in patients without brain metastases at the point of diagnosis, demonstrating the drug's success broad overall cancer control.

"When preliminary data were reported last year, estimates were looking to be more like 25 months PFS on alectinib, so this jump to 34.8 months is huge and may surprise people," Camidge says. "In reality, it's just that patients' progression tends to be rather sparse around the time of the 50 percent point, and when that happens the median can jump around a lot."

Additionally, 45 percent of patients treated with crizotinib went on to develop brain metastases while on trial, compared with only 12 percent of patients treated with alectinib. The overall response rate for alectinib was 82.9 percent, compared with 75.5 percent for crizotinib. And alectinib was also associated with fewer overall side effects than crizotinib, with 16 percent of alectinib patients requiring dose reduction

and 22 percent requiring dose interruption, compared with 21 and 25 percent of crizotinib patients, respectively.

"In addition to median progression-free survival, another way to describe the duration of a drug's benefit is to compare the risk, over time, that each 'horse' will 'stop running'. We call this a hazard ratio. It's a little harder to understand, but in a comparison trial it's probably the better way to really show the difference. Last year, when the data were presented the risk of progression or death—the 'hazard ratio' - of alectinib was reported as 47 percent of what it was on crizotinib, and now we show that the risk of progression or death for patients on alectinib was even lower, just 43 percent that of patients on crizotinib," says Camidge.

Both drugs target lung cancers in which the gene ALK becomes improperly fused with a partner gene, such as EML4, to code for a protein made from bits of both genes. These ALK fusion proteins have been shown to drive about 4 percent of all lung cancers, resulting in about 12,000 diagnoses of ALK-positive non-small cell lung cancer in the United States every year. Crizotinib earned FDA approval in 2011 to treat advanced ALK-positive lung cancer, and now next-generation ALK inhibitors such as alectinib, which have shown activity post-crizotinib, are replacing or vying to replace crizotinib in many settings.

In Camidge's opinion, these updated data further consolidate alectinib as the standard-of-care for first-line treatment of ALK+ non-small cell lung cancer.

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