

Serial analysis of CTCs may provide biomarker predictive of NSCLC response to crizotinib

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Among patients with non-small cell lung cancer (NSCLC) fueled by ALK gene alterations who were being treated with crizotinib (Xalkori), a decrease in the number of circulating tumor cells (CTCs) harboring increased copies of the ALK gene over the first two months of treatment was associated with increased progression-free survival.

The study is published in *Cancer Research*, a journal of the American Association for Cancer Research, by Françoise Farace, PhD, leader of the circulating cells team at Gustave Roussy, INSERM, Université Paris-Saclay, Villejuif, France.

About 4 percent of NSCLCs are driven by genetic aberrations called ALK gene rearrangements, according to Farace.

"The approval of the ALK-targeted therapeutic crizotinib has improved outcomes for [patients](#) with ALK-rearranged NSCLC, but the duration of responses varies widely, from a few months to several years," she said.

Farace and colleagues prospectively recruited 39 patients with ALK-rearranged NSCLC to the study. All patients had a blood sample taken before starting crizotinib treatment. Blood samples were taken about two months later for 29 of these patients; 10 patients received follow-up care at a different center and no serial blood samples were available for analysis.

After enriching for CTCs, the researchers analyzed the samples for ALK rearrangements and for an increase in the number of copies of the ALK gene. All patients had both CTCs with ALK rearrangements and CTCs with ALK copy number gain before treatment and at two months.

Analysis of CTC numbers at the different time

points showed that the one measurement that was statistically significantly associated with progression-free survival was a change in the number of CTCs with ALK copy number gain over time. Median progression-free survival for the 13 patients who had a decrease in the number of CTCs with ALK copy number gain was 14.0 months, while the median progression-free survival for the 16 patients who had stable or increased numbers of CTCs with ALK copy number gain was 6.1 months. In addition, in multivariate analysis, patients who had a decrease in the number of CTCs with ALK copy number gain were 4.5 times more likely not to have had disease progression compared with those who had stable or increased numbers of CTCs with ALK copy number gain.

"In this study, we showed that analysis of ALK copy number in CTCs before starting crizotinib treatment and after two months of crizotinib treatment may provide a biomarker for predicting the effectiveness of the therapeutic," said Farace. "This is important because there is currently no means of distinguishing those patients likely to gain long-term benefit from crizotinib from those who are not and who should consider trying some of the newer ALK-targeted therapeutics that have been more recently developed.

"Although this is a proof-of-concept study that needs validating in larger studies at different sites before it can be used in the clinic, the results reflect the potential of liquid biopsies to monitor [treatment](#) response in real time and tailor treatments at the individual patient level," she said.

According to Farace, the main limitation of the study is that CTCs are very rare and the identification of ALK copy number gain in CTCs is complex and requires a very specific know-how and high technical expertise. As a result, large-scale

application of the assay will require technological advances, she said.

Provided by American Association for Cancer Research

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