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"Liquid biopsy" may help earlier detection of lung cancer treatment resistance

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A blood test to regularly monitor for the presence of rearrangement of the EML4-ALK gene fusion in patients with non-small cell lung cancer (NSCLC) may help clinicians predict the outcome of treatment with crizotinib, according to research presented here at the AACR Annual Meeting 2015, April 18-22.

"By using the platelets isolated from venous blood specimen collections we have an opportunity to follow the therapy in real time by determining alterations occurring in the tumor during treatment, and this makes it possible to tailor the therapy for each patient," said Jonas A. Nilsson, PhD, a researcher in the Department of Radiation Sciences at Umeå University in Sweden. "As a complement to imaging modalities, we may help doctors to be informed on when the tumor starts to regrow, when to switch therapy, and whether second-generation ALK inhibitors may be effective."

A subgroup of patients with NSCLC harbors EML4-ALK rearrangements in their tumors, making them responsive to targeted treatment with crizotinib, an ALK inhibitor. Although the drug is effective in these patients, many eventually develop resistance to the treatment.

In this study, Nilsson and colleagues analyzed the efficacy of a blood-based "liquid biopsy" in assessing the presence in blood platelets of EML4-ALK in patients with NSCLC. Unlike assessment with advanced imaging techniques, such as computed tomography, the researchers

theorized that the liquid biopsy would allow for real-time monitoring of the disease and earlier identification of patients who have developed resistance to treatment.

The researchers analyzed blood samples from 77 patients with NSCLC with known mutation status, and among them, 38 patients had EML4-ALK rearrangements in the tumor.

The liquid biopsy identified 65 percent of the patients with confirmed EML4-ALK rearrangement. In the 29 patients treated with crizotinib, those whose blood test was EML4-ALK-positive had a progression-free survival of 3.7 months compared with 16 months in those with EML4-ALK-negative blood tests.

"We showed that if we detected EML4-ALK in the platelet fraction before therapy starts and it does not disappear during treatment, it indicates that the patient is not responding to the therapy, which is associated with a shorter time to recurrence and, therefore, other therapies could be tried," Nilsson said.

Finally, in a case study of a patient followed for 2.5 years during crizotinib therapy, the researchers detected the presence of EML4-ALK in the liquid biopsy two months before disease progression could be confirmed using imaging modalities.

"This study shows that platelet-powered diagnostics may add another layer of information to clinicians, and this information can be used to help in the clinical decision-making process," Nilsson said. "Therefore, the platelet platform is an interesting biosource for the next generation of liquid biopsies and in the development of personalized health care."

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