Cell-free tumor DNA analysis during immunotherapy to monitor clinical response for patients with non-small cell lung cancer

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Background & objectives

Patients diagnosed with Non-Small Cell Lung Cancer (NSCLC) can be treated with antibodies against PD-1/PD-L1, called immune checkpoint blockade (ICB). In spite of the success of ICB only approximately 1 in 3 will respond to the therapy. Thus, analysis of biomarkers to the monitor therapy response in a patient over time is warranted. Levels of cell-free tumor DNA (ct-DNA) analysis in circulation is a non-invasive method that can be used to monitor the effect of ICB treatment at several timepoints during the treatment cycles, and has been shown to predict clinical response earlier compared with standard radiological investigation. This study

aims to evaluate both the amounts and detection of specific somatic DNA-variants in ct-DNA during the treatment cycles to identify patients most likely to derive clinical benefit over time.

Methods

Fifteen stage III and IV NSCLC patients' treated with ICB were included in the study. The amount of ct-DNA was analyzed at up to six different timepoints during treatment. Four to nine specific somatic DNA variants selected from the initial tumor analysis were analyzed at each timepoint, by using an ultrasensitive sequencing assay (Simsen Diagnostics). Patients were categorized as clinical responders or non-responders based on the 9 months' clinical assessment after the start of ICB.

Results

Nine of the 15 patients were responders based on the clinical examination. Five of these patients had no ct-DNA at baseline or follow up timepoints. In the remaining four responders ct-DNA was detectable at baseline and was decreasing during treatment cycles or ctDNA clearance was seen. Six patients were non-responders according to the clinical examination. In non-responders the ct-DNA level was higher at baseline and increased over time.

Conclusion

Ct-DNA can be used to monitor treatment by detecting several specific somatic DNA-variants and at several timepoints. The ct-DNA amount is correlated with response or non-response in the patients. By measuring ct-DNA at several timepoint using several specific somatic DNA variants an early determination of treatment response can be found, which can indicate clinical benefit or not for the patients.