Monitoring of molecular response during immunotherapy by circulating tumor dna using patient-tailored assays in non-small cell lung cancer

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Abstract

Background

Patients diagnosed with non-small cell lung cancer (NSCLC), can be treated with immune checkpoint blockade (ICB), which are antibodies against PD-1/PD-L1. However, only 20-40% of patients will respond to ICB. Analysis of circulating tumor DNA (ctDNA) in blood plasma is a non-invasive method that can be used as a biomarker to monitor treatment. Detection of ctDNA has shown to predict clinical response earlier compared with standard radiological examination.

Objective

The study aims to evaluate the amounts and detection of somatic tumor-specific DNA-variants in ctDNA during early treatment cycles to identify response pattern.

Methods

33 stage III-IV NSCLC ICB-treated patients were included in this prospective study. The amount of ctDNA was analyzed longitudinally at baseline and up to five timepoints during treatment. From the initial tumor sequencing, four to sixteen somatic patient-specific DNA-variants were chosen based on driver capacity, classification and variant allele frequency. The variants were monitored and analyzed at each timepoint using ultrasensitive sequencing assays (Simsen Diagnostics). Patients were considered clinical responders or non-responders based on RECIST criteria from CT scans every third month after ICB initiation.

Results

16 patients with partial or complete response at 3 months had at baseline low or non-detectable levels of ctDNA, which decreased during early follow-up timepoints. Two of these patients had progressive disease at 6-months and showed increasing ctDNA levels at early timepoints. Also, two other responders had high levels of ctDNA that rapidly decreased and remained non-detectable during follow-up. 14 patients had progressive disease and were considered non-responders, for 12 of the non-responders, ctDNA levels increased at or prior to progression. Non-responders generally had higher ctDNA levels at baseline which increased over time. None of the patients with long-term response had an increase of ctDNA.

Conclusion

CtDNA can be used for monitoring treatment by detecting tumor-specific DNA-variants. The ctDNA amount correlated well with response or non-response in patients. During early treatment cycles a probable response can be determined, indicating clinical progress earlier compared with current radiological settings. The earlier determination of treatment response by analyzing patient-specific ctDNA assays at several timepoints might indicate clinical benefit or not for the patients.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.