

**Abstract 3834: Tracking CAD-ALK gene translocation in urine and plasma of a colorectal cancer patient treated with ALK blockade** 

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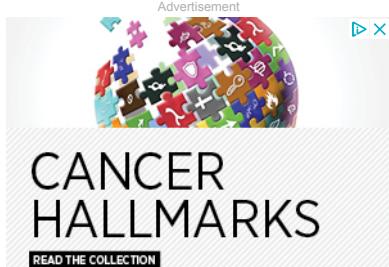
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## Abstract

A metastatic colorectal cancer (mCRC) patient carrying CAD-ALK translocation achieved partial response to an experimental ALK inhibitor and then progressed after 5 months. We studied whether urine cell-free, trans-renal DNA (tr-DNA) could be used to monitor tumor burden and patient's response. A NGS panel was developed to interrogate 52 common cancer gene rearrangements and 14 frequently mutated genes in cancer patients. A TP53 p.R248W mutation and the CAD-ALK genomic breakpoint (rearrangement) were identified in the tumor tissue and matched plasma circulating tumor DNA (ctDNA). Urine samples were longitudinally obtained from the patient during ALK inhibitor treatment in parallel with blood. To detect the CAD-ALK translocation in urine tr-DNA we designed ultra-short (51 bp amplicon) primer pairs spanning the genomic breakpoint as a unique tumor marker. This approach allowed the non-invasive monitoring of the gene fusion in urine with amounts paralleling tumor burden. Of note, CAD-ALK gene fusion was apparent in urine tr-DNA before radiological confirmation of disease progression. The same strategy was applied to plasma ctDNA and the results were compared. To detect point mutations in urine tr-DNA, we exploited a peptide nucleic acids (PNA)-CLAMP PCR coupled with droplet digital PCR (ddPCR) analysis to specifically suppress amplification of wild-type DNA fragments. Custom PNA probes were designed for TP53 codon 248, and a ddPCR assay was optimized to detect the TP53 p.R248W mutation, which was then identified in all urine tr-DNA samples, with absolute copies correlating with tumor burden throughout ALK inhibitor treatment. In conclusion, we find that urine tr-DNA can be exploited to non-invasively monitor tumor burden by detecting tumor-specific gene fusions as well as point mutations.

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