Improved detection of residual disease in solid tumors via combined circulating tumor cell and cell-free dna profiling

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Abstract

Background

Accurate detection of minimal residual disease (MRD) and disease progression is critical for guiding treatment decisions in patients with solid tumors. Liquid biopsy approaches, including circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs), offer non-invasive options for disease monitoring and early detection of recurrence. However, each modality has limitations that may lead to false-negative results. We report the utility of combined evaluation of cell-free tumor DNA (ctDNA) and circulating tumor cells (CTCs) for improving the detection sensitivity.

Objective

We evaluated the individual and combined cancer-detection sensitivities of ctDNA and CTC-profiling in 366 patients with solid tumors.

Methods

The study included 366 patients (219 females, 147 males; median age: 59 years) with solid tumors, either treatment-naïve or post-therapy. Peripheral blood (20 mL) was collected in EDTA and Streck tubes following informed consent. CTCs were enriched from blood as described by Akolkar et al. This approach utilises label-free, size independent, non-mechanical approach to allow enrichment of viable apoptosis-resistant circulating tumor cells and their clusters using a proprietary cell enrichment media. The enriched cells are labelled with CK, EPCAM and CD45 to detect CTCs with immunofluorescence platform.

cfDNA was isolated from plasma and profiled by semi-conductor based next generation sequencing (NGS) using a targeted 52-gene panel.

Results

In the analysed cohort, 68.9% (252/366) were CTC-positive and 53.8% (197/366) had detectable gene variants in cfDNA. The combined (CTC + cfDNA) sensitivity was 85.5% (313/366).

Conclusion

False negative findings in cfDNA based tumor genomic profiling arise from sensitivity limitations and NGS panel design limitations, i.e., absence of target genes or variants. Similarly, a CTC-only based approach may have lower sensitivity in case of tumors with lower shedding rates or active immune clearance. These limitations can adversely impact residual disease monitoring in the clinical setting. Here, we show that a combinatorial approach of simultaneous CTC and cfDNA profiling can overcome the limitations of cfDNA-only or CTC-only profiling. In the study, combined cfDNA + CTC profiling yielded high cancer detection sensitivity in post-treatment patients, that was comparable to patients with radiologically evident disease.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.