

Ultrasensitive ctDNA analysis as a biomarker for immunotherapy response across multiple cancer types.

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Abstract

Tracking a limited set of mutations in circulating tumor DNA (ctDNA) has demonstrated biomarker potential in cancer patients receiving immune checkpoint inhibitors (ICIs). Here, we extend prior research by integrating tumor whole-genome-based ultrasensitive ctDNA analysis, enabling the detection of ~1,800 tumor-specific mutations per patient. Our study includes both retrospective (n=136) and prospective validation (n=66) cohorts spanning 24 cancer types treated with ICIs alone or in combination with bispecific antibodies or immune cell engagers.

Across 1,455 longitudinal plasma samples, ctDNA molecular response at day 21 post-treatment initiation was significantly associated with improved progression-free (PFS) and overall survival (OS), while ctDNA clearance at any timepoint strongly correlated with radiologic response and extended survival. Furthermore, ctDNA dynamics effectively differentiated true progression from pseudoprogression and provided predictive insights for patients continuing immunotherapy beyond initial progression.

These findings underscore the broad applicability of ultrasensitive ctDNA as a dynamic biomarker across diverse cancers and immunotherapy regimens, offering a powerful tool for real-time treatment monitoring and response assessment.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.