Abstract #3058: Leveraging a hybrid tumor-informed and tumor-agnostic ctDNA assay for optimal ctDNA-MRD detection: A real-world study in Southeast Asia

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BACKGROUND

- The typical **tumor-informed method** of ctDNA testing requires **tissue specimens of high quality**, which is a challenge in developing countries.
- **Developed** a **hybrid tumor-informed and tumor-agnostic approach** to overcome this constraint and evaluate its performance in real-world samples.

STUDY DESIGN AND WORKFLOW

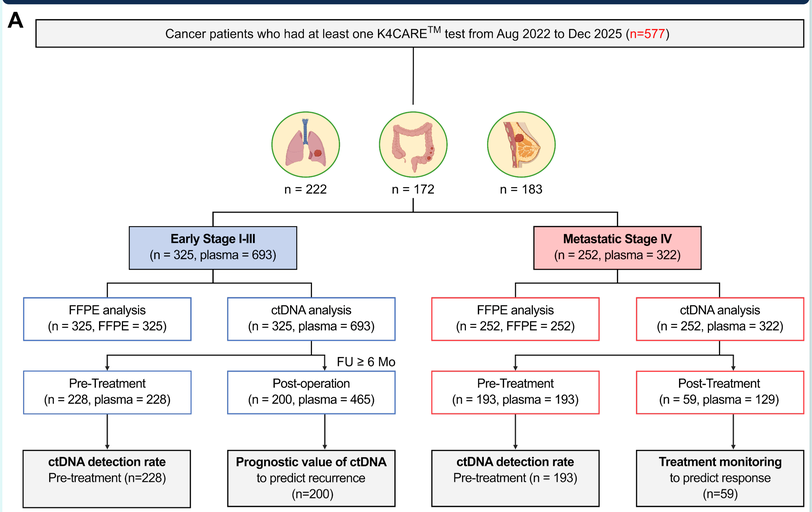


Figure 1. Study design and ctDNA analysis workflow. (A) Diagram showing the number of cancer patients that were included in the study. The patients had at least 1 ctDNA test from Aug 2022 to Dec 2025 and selected patients were followed up for at least 6 months from the last ctDNA test. **(B)** gDNA of paired FFPE and WBC samples were sequenced to identify tumor-specific mutations in 515 cancer-associated genes. Top personalized mutations with the highest scores were used to detect ctDNA in plasma samples by mPCR and ultra-deep sequencing. Besides personalized mutations, an additional panel of ~500 hotspot mutations specific to breast cancer was added to the analysis.

PRE-TX DETECTION RATE OF ctDNA

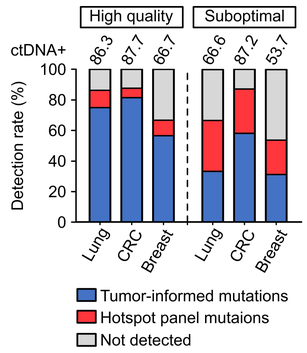
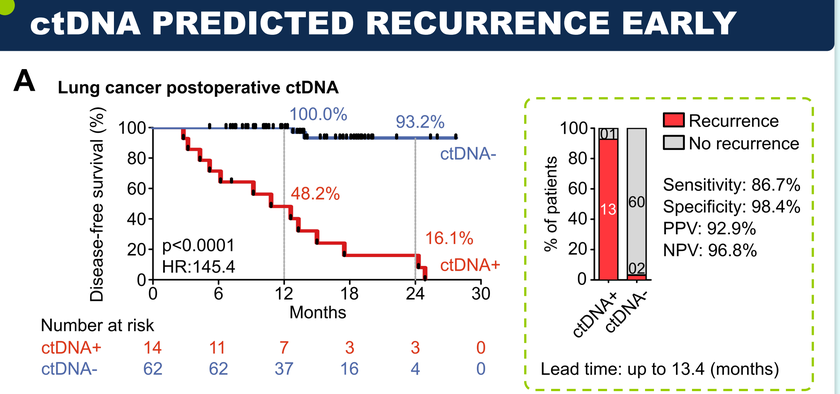


Figure 2. Detection rate of ctDNA in early stage and metastatic cancer. (Left) ctDNA detection rate in pre-treatment plasma among cancer types in high quality samples. The addition of the hotspot panel improved the detection rate for patients with no highly-scored mutations (increased by 6.5-18.6%). **(Right)** ctDNA detection rate in pre-treatment plasma among cancer types in suboptimal samples (increased by 33.3-48.8%). The addition of the hotspot panel improved the detection rate.

EARLY STAGE ctDNA PREDICTED RECURRENCE EARLY



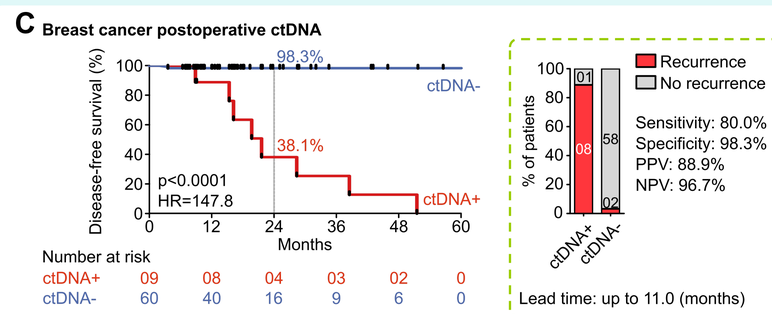


Figure 4. Prognostic value of post-operative ctDNA. (A-C) Kaplan-Meier plots showed that patients with ctDNA(+) after surgery were more likely to relapse than those with ctDNA(-) among cancer types. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of post-operative ctDNA to predict recurrence in different types of cancer and the maximal lead time before clinical diagnosis.

METASTATIC STAGE ctDNA PREDICTED Tx RESPONSE

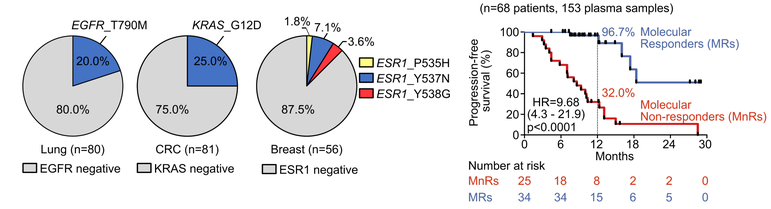


Figure 5. Plasma ctDNA monitoring to identify tumor-agnostic mutations and predict disease progression. (A) Venn diagram showing the proportion Tumor-agnostic hotspot panel helped identify new and resistance mutations including EGFR in lung (20.0%), ESR1 in breast (12.5%), and KRAS in colorectal (25.0%) cancers. **(B)** Kaplan-Meier analysis of progression-free survival (PFS) for 40 patients as stratified by ctDNA dynamics. Patients who had more than 50% ctDNA decrease from baseline showed significantly longer PFS than patients with less than 50% ctDNA decrease ($p<0.0001$).

CONCLUSION

Our **hybrid tumor-informed and tumor-agnostic ctDNA assay** improved **ctDNA detection,** particularly in cases with **suboptimal tissue** samples, and **predicted** cancer recurrence and progression with **high sensitivity and specificity**

Ethical approval by the institutional ethics review board of the MGI for the analysis of de-identified genomic and clinical data (approval #: 03/2023/CT-VDTYH; 03/2024/CT-VDTYH).
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