Single Institution experience of longitudinal post-surgical circulating tumor DNA monitoring in patients with HER2+ breast cancer

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Background

- Recent studies have demonstrated the utility of longitudinal, tumor-informed, personalized circulating tumor DNA (ctDNA) testing for monitoring response to neoadjuvant treatment and predicting long-term outcomes in patients with breast cancer.[1-3]
- In this study, we evaluated ctDNA detection rates post-surgery in patients with HER2+ breast cancer in the adjuvant treatment and surveillance settings.

Methods

- This retrospective study included 60 patients with stage I-IV HER2+ breast cancer.
- Blood samples were collected after primary resection and serially during surveillance at the physician's discretion for commercial ctDNA testing.
- A clinically validated, personalized, tumor-informed 16-plex PCR-NGS assay (Signatera™, Natera, Inc.) was used for the detection and quantification of ctDNA in blood samples.
- ctDNA status and dynamics were correlated with clinicopathological features and surgical outcomes.

Figure 1. Signatera Workflow

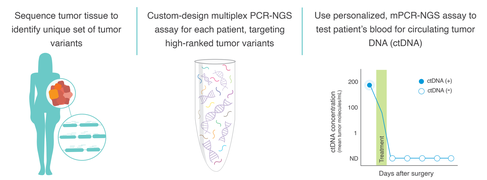


Figure 1. Signatera workflow. A set of up to 16 patient- and tumor-specific single nucleotide variants is selected from whole-exome sequencing of tumor tissue and matched normal blood sample and tracked in the associated patient's plasma using a multiplex PCR-NGS approach to detect ctDNA. ctDNA levels are reported as mean tumor molecules per mL of plasma (MTM/mL).

Acknowledgments and Disclosures

S.S., C.M.B., C.C.P., E.K., J.M., A.R. and M.C.L. are employees at Natera, Inc. with stock or option to own stock. Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from SABCS® and the author.

References

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Longitudinal ctDNA monitoring aids in identifying high-risk HER2+ breast cancer patients and shows potential utility for a ctDNA guided treatment approach

Figure 2. Consort Diagram

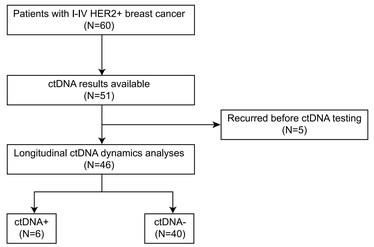


Figure 2. Patient inclusion and ctDNA results.

Table 1. Patient demographics (N = 60)

Patient and tumor characteristic		# Patients (%)
Median age in years [range]		56 [27 - 82]
T Stage	T1	16 (26.7%)
	T2	30 (50.0%)
	T3	12 (20.0%)
	T4	2 (3.3%)
N stage	N0	33 (55.0%)
	N1	22 (36.7%)
	N2	3 (5.0%)
	Not available	2 (3.3%)
Grade	1	4 (6.7%)
	2	24 (40.0%)
	3	32 (53.3%)
Hormone receptor (HR) status		
HR positive		39 (65.0%)
HR negative		21 (35.0%)
Neoadjuvant therapy		
Yes		43 (71.7%)
No		15 (25%)
Not available		2 (3.3%)
Pathologic response status		
Pathologic complete response (pCR)		8 (13.3%)
Residual disease (no pCR)		36 (60.0%)
Not available		16 (26.7%)

Figure 3. Timing of the first ctDNA test and duration of serial ctDNA negativity

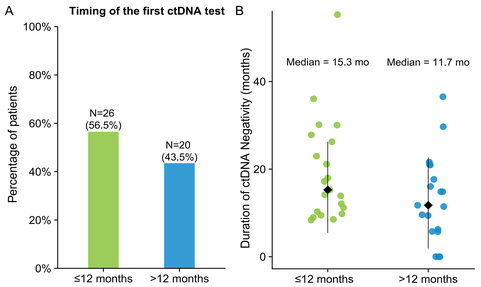


Figure 3. A. Bar plot showing the proportion of patients stratified by the interval between surgical resection and the first postoperative ctDNA assessment. More than half of patients (56.5%) underwent ctDNA testing within 12 months of surgery, while 43.5% were tested after >12 months postoperatively.

B. Scatter plot showing the duration between the first and last ctDNA-negative results, stratified by the time of ctDNA monitoring initiation post-surgery. Patients who began ctDNA testing within 12 months of surgery demonstrated similar durations of ctDNA negativity compared with those initiating testing after >12 months.

Figure 4. Post-surgical ctDNA dynamics and patient outcomes

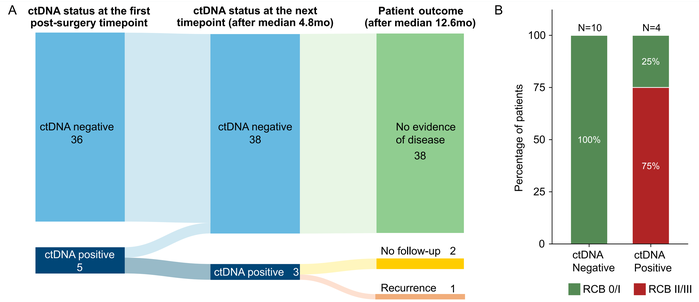


Figure 4. A. Sankey plot showing ctDNA status ctDNA dynamics and corresponding patient outcomes. All patients with serial ctDNA negativity or ctDNA clearance had no evidence of disease at a median of 12.6 months after the second ctDNA test, while persistently ctDNA-positive patients had recurrence or no follow-up data. **B. Relationship between postoperative ctDNA status and Residual Cancer Burden (RCB) category.** Among patients with RCB and ctDNA status within 12 months post-surgery available (N=14), all ctDNA negative patients achieved RCB 0/I, whereas 75% (3/4) of ctDNA positive patients had RCB II/III.

Figure 5. A. Event-free survival probability; B. Longitudinal ctDNA dynamics in a representative patient

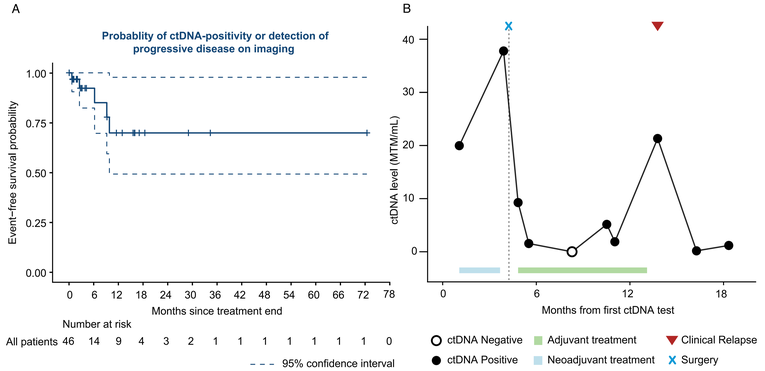


Figure 5. A. Event-free survival probability. Kaplan-Meier estimates of event-free survival for all patients in the cohort (N=46). An event was defined as a positive ctDNA test or detection of progressive disease on imaging. The upper and lower 95% confidence intervals are plotted as dashed lines. **B. Longitudinal ctDNA dynamics in a representative patient with recurrence.** Serial ctDNA results in response to treatment plotted over time from the first postoperative test. The patient had increased ctDNA levels after neoadjuvant therapy. Surgical resection followed by adjuvant therapy resulted in transient ctDNA clearance. However, the patient turned back ctDNA positive and later had clinical recurrence, with ctDNA levels (measured as MTM/mL) increasing before detection of recurrence. Abbreviations: MTM/mL, mean tumor molecules per mL of plasma.

Conclusions

- In addition to clinicopathological features and surgical outcomes, longitudinal ctDNA monitoring helps identify patients with HER2+ breast cancer who may be at high risk of recurrence.
- Further research is needed to assess the true utility of a ctDNA-guided treatment approach in this patient population.

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