Perioperative Minimal Residual Disease Monitoring Using a Tumor-informed ctDNA Assay in Stage II-III Breast Cancer

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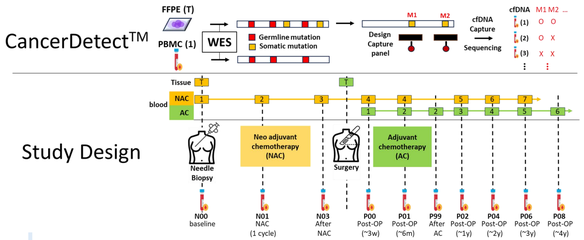
Background

- Recent studies have established an association between ctDNA-based minimal residual disease (MRD) tracking results and therapeutic efficacy and recurrence.
- We conducted a prospective study, encompassing both pre- and post-operative time points, to investigate the association between ctDNA and clinical features in breast cancer using tumor-informed ctDNA monitoring.

Materials and Methods

- Stage II/III breast cancer patients were prospectively enrolled from February 2023 to July 2024 at Seoul National University Hospital.
- Whole exome sequencing was performed on FFPE blocks and PBMCs. Somatic variants selected for individual patients were then tracked by targeted capture of cfDNA from corresponding time points (CancerDetect™).

Figure 1. Overview of the CancerDetect™ assay and study design.



- Patients were stratified into the neoadjuvant chemotherapy (NAC) and adjuvant chemotherapy (AC) groups.
- Majority of the patients received NAC, with cfDNA samples collected and analyzed (or scheduled for collection/analysis) at the following time points: baseline (N00), after NAC cycle 1 (N01), after NAC completion (N03), either post-surgery (~3 weeks, P00) or 6 months post-surgery (P01), and subsequently at 1 year (P02), 2 years (P04), and 3 years (P06) post-surgery.
- Similarly, the Adjuvant Chemotherapy (AC) group underwent collection at the following time points: P00, either P01 or post-AC (P99), P02, P04, P06, and 4 years post-surgery (P08).

Results

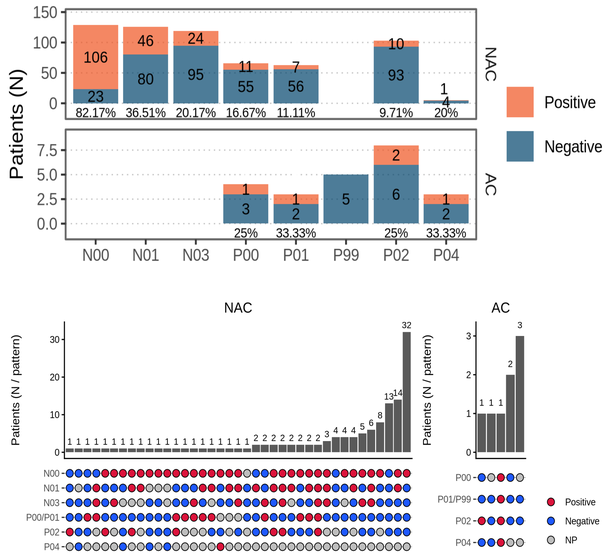
- A total of 130 patients in the NAC group and 8 patients in the AC group have been analyzed to date (Table 1).

Table 1. Patient characteristics

Demographics	N (%)
Age (years) : median [range]	51 [25-83]
Sex	
Female	138 (100)
Subtype	
HR+/HER2+	28 (20.3)
HR-/HER2+	30 (21.7)
HR+/HER2-	32 (23.2)
HR-/HER2-	48 (34.8)
Clinical Stage	
II	81 (58.7)
III	57 (41.3)
Clinical T stage	
Stage 1 or 2	100 (72.5)
Stage 3 or 4	37 (26.8)
Other	1 (0.7)
Clinical N status	
Node-positive	108 (78.3)
Node-negative	30 (21.7)
Pathologic complete response	
pCR	61 (44.2)
non-pCR	69 (50.0)
ND	8 (5.8)
RCB class	
0	73 (52.9)
1	17 (12.3)
2	31 (22.5)
3	8 (5.8)
ND	9 (6.5)

- The ctDNA positivity rate decreased from 82.17% (106/129) at N00 to 20.17% (24/119) at N03 (Figure 2).
- Among patients who remained ctDNA positive at N03, a significantly higher proportion (83.33%, 20/24) failed to achieve pCR, compared to 48.42% (46/95) of ctDNA-negative patients (p=0.002). A slightly weaker association with pCR was observed at N01 (p=0.015), while no statistically significant correlation was found at the other time points.

Figure 2. Distribution of ctDNA positivity across time points in each patient group and pattern



- Analysis of ctDNA detection and pCR status by subtype in the NAC group across pre-operative (N01, N03) and post-operative (P00, P01) time points revealed a characteristically low pCR rate in HR+/HER2- (Figure 3).
- Based on the last observation date, the median follow-up period was 722 days (range: 345–977). A total of 5 recurrences were observed, including 4 in the NAC group and 1 in the AC group.
- Among the recurrent patients, one was HR+/HER2- and four were triple negative breast cancer. The Kaplan-Meier plot based on post-operative ctDNA detection status demonstrated a difference in Recurrence-Free Survival (p = 0.011; Figure 4).

Figure 3. Pre- and post-operative ctDNA detection and pCR status by subtype in the NAC group

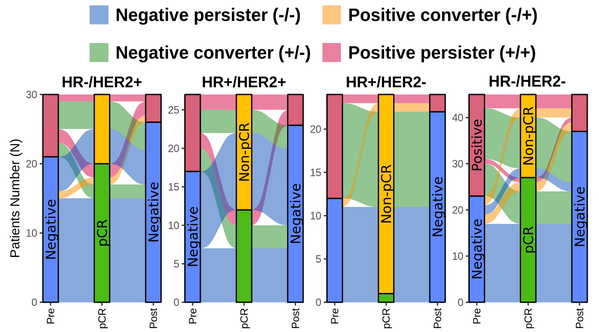
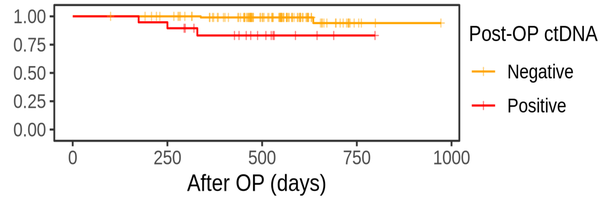


Figure 4. Kaplan-Meier plot based on post-operative ctDNA status



Conclusions

- Prospective, multi-time point ctDNA monitoring demonstrates an association between ctDNA and established clinical parameters.
- Post-operative ctDNA detection may be useful for predicting future prognosis.
- The confirmation of additional recurrence cases through subsequent follow-up will further clarify the relationship between ctDNA and recurrence.

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