# Circulating Tumor DNA Dynamics in Hormone Receptor–Positive/Human Epidermal Growth Factor Receptor 2–Negative Early Breast Cancer Using an Ultrasensitive Tumor-Informed Assay

CH Barcenas[1], A Contreras[1], A Alexander[1], H Lopez[1], R Yu[1], S Shete[1], Y Chen[2], CW Abbott[2], K Keough[2], SM Boyle[2], RO Chen[2], D Tripathy[1], V Valero[1]

The University of Texas MD Anderson Cancer Center[1], Personalis, Inc.[2]

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## PURPOSE

- Circulating tumor DNA (ctDNA) in early breast cancer (EBC) is prognostic for distant relapse.
- ctDNA dynamics in hormone receptor–positive (HR+)/human epidermal receptor 2 negative (HER2-) EBC, considered low-shedding, are challenging to track.
- We used an ultrasensitive tumor informed assay (NeXT Personal) to detect molecular residual disease (MRD) and its association with disease recurrence in this subtype.

## METHODS

- Between March 2018 and February 2025 patients with stage I-II HR+/HER2-EBC had serial plasma samples banked while undergoing oncological treatment.
- Eligibility: ≧2 serial plasma samples (n= 28; 26 had adequate tumor material to perform the genomic assay).
- Patients followed over time to assess for disease recurrence.
- ctDNA results were not reported to the patients nor their clinicians.
- Analytical validation of NeXT Personal ctDNA assay published by Northcott et al, Oncotarget 15:200-218, 2024.

**Table 1 Patient Characteristics and MRD Detection**

| Demographics / Tumor / Treatment | N= 26 patients |
|---|---|
| Median age (yrs) at diagnosis (range) | 56 (26 – 71) |
| Tumor stage II / III | 48% / 52% |
| Median follow-up time (yrs) from surgery (range) | 5 (2 – 11) |
| Chemotherapy (n, %) / neoadjuvant | 25 (96%) / 18 (69%) |
| Aromatase inhibitor use (OFS in premenopausal) (n, %) | 26 (100%) |
| Tamoxifen followed by aromatase inhibitor (n, %) | 4 (15%) |
| Adjuvant abemaciclib (n, %) | 3 (12%) |
| Extended endocrine therapy (>5 yrs) (n, %) | 14 (54%) |
| | |
| **MRD Detection** | |
| Number of plasma samples / range samples per patient | 118 / 2 – 9 |
| Median time (months) from breast surgery to first sample (range) | 12.5 (0.7 – 101) |
| Median time (months) interval between samples (IQR) | 7 (6 – 12) |
| ctDNA concentration (PPM) patient-specific panels (median, IQR) | 70.2 (14.9 – 757) |
| ctDNA+ samples in the ultrasensitive range (<100 PPM) | 58% |

**Figure 2**

A) ctDNA levels for ctDNA+ samples
B) Lead time from first post-surgical detection until DRFI event
C) Kaplan-Meier survival curves for DRFI stratified by post-surgical ctDNA dynamics.

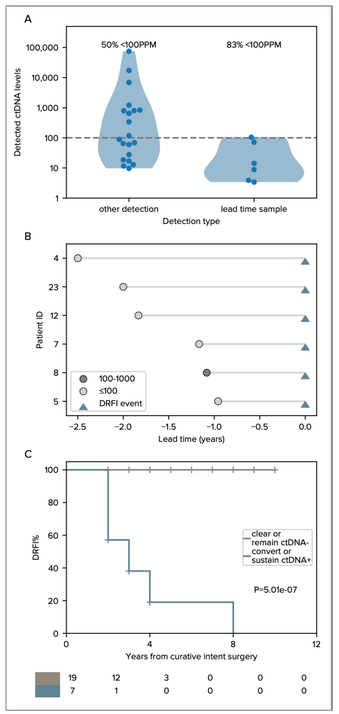
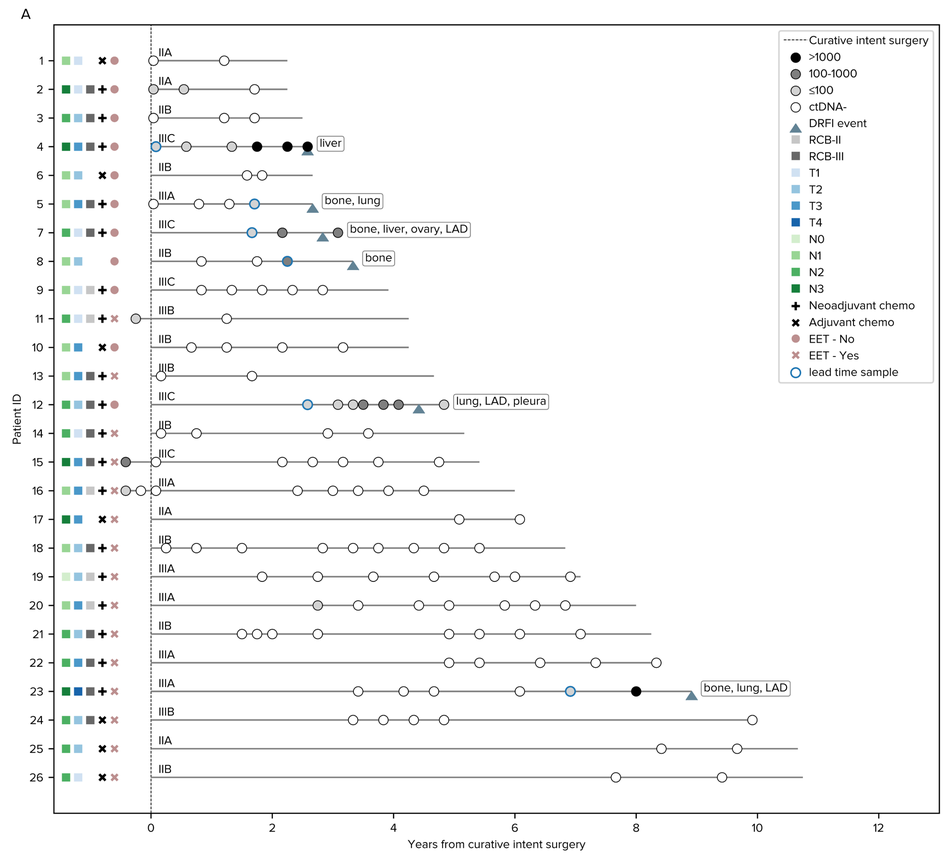



**Table 2 ctDNA Dynamics and Disease Recurrence**

| | Disease recurrence | | Total |
|---|---|---|---|
| | Yes | No | |
| Persistent ctDNA+ | 3 | 0 | 3 |
| Persistent ctDNA-neg | 0 | 15 | 15 |
| ctDNA+ that cleared | 0 | 5 | 5 |
| ctDNA-neg then ctDNA+ | 3 | 0 | 3 |
| Total | 6 | 20 | 26 |

**Figure 1 Swimmer Plot N= 26**




## Conclusions

- Using an ultrasensitive tumor-informed ctDNA assay, all patients with HR+HER2-negative EBC who experienced distant relapse had MRD detected prior to clinical detection, with a median lead time (from first +ctDNA to clinical disease recurrence) of 1.5 years.
- We observed a strong correlation of ctDNA dynamics with oncological outcomes, with 100% sensitivity of the assay for distant relapse.
- Until last follow up, the ctDNA assay showed 100% specificity.