PACE-ctDNA: Impact of circulating tumor DNA monitoring on patient anxiety and clinician decision-making in early-stage breast cancer

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Devora Isseroff[1], Nathalie Wiesendanger[1], Adriana Kahn[1], Daniel O'Neil[1], Michael Cohenuram[1], Anca Bulgaru[1], Kathleen Fenn[1], Johanna LaSala[1], Kert Sabbath[1], Neal Fischbach[1], Jane Kanowitz[1], Robert Legare[1], Michael DiGiovanna[1], Andrea Silber[1], Tara Sanft[1], Sarah Schellhorn[1], Ian Krop[1], Eric Winer[1], Wei Wei[1], Maryam Lustberg[1], Lajos Pusztai[1], Mariya Rozenblit[1]

[1]Yale Cancer Center, Yale School of Medicine, New Haven, CT

Background

- Circulating tumor DNA (ctDNA) is a promising biomarker for detecting molecular residual disease and predicting breast cancer recurrence.
- The Signatera™ assay (Natera, Inc.) is a tumor-informed, personalized ctDNA test reimbursed by CMS for recurrence monitoring in stage IIB/III breast cancer.
- While ctDNA testing has become more common, its impact on patient anxiety and physician decision-making remains unclear, and there are no standardized protocols for managing positive results.
- This registry study evaluated patient-reported anxiety and physician-decision making confidence during ctDNA surveillance in the adjuvant setting

Methods

- Single-institution registry study of ctDNA surveillance in early-stage hormone receptor-positive (HR+), triple-negative breast cancer (TNBC) patients with residual disease after neoadjuvant therapy, or patients with ctDNA testing for other reasons.
- Patients were administered Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety surveys at baseline and q6m for 1 year of follow-up. T Scores range 0-100, where higher scores reflect higher anxiety.
- Physicians completed Physician Decision Making Tool (PDAT) at baseline and q6m following ctDNA results.

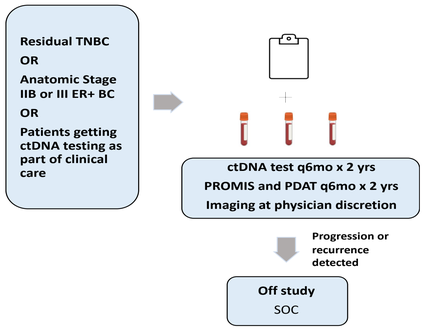


Table 1: Patient Characteristics

		Overall Population N (%)	TNBC N (%)	HR+ (%)
Total Patients		67	45	22
Age (range)		53(24-84)	53(24-84)	51(29-73
Stage	I	12 (18)	9 (20)	3 (14)
	II	39 (58)	24 (53)	15 (68)
	III	16 (24)	12 (27)	4 (19)
Adjuvant Therapy	Chemotherapy+/- Immunotherapy	31(46)	30 (67)	1 (5)
	Endocrine Therapy +/-CDK4/6i	25 (37)	4 (9)	21 (95)
	Other	11 (16)	11 (24)	0 (0)
	None	4 (6)	3 (7)	1 (5)
Baseline ctDNA drawn		64 (96)	42 (93)	22 (100)
Positive ctDNA at anytime		11 (16)	10 (22)	1 (5)
ctDNA Positive with negative imaging		4 (36)	3 (30)	1 (100)
ctDNA Positive with disease recurrence		7 (63)*	7 (70)	0 (0)

* For ctDNA-positive patients with recurrence: 2 were Stage I, 4 were Stage II, 1 was Stage III.

Results

- 11 patients had ctDNA positive results at any time
  - 7 patients were positive at baseline assessment
    - 4 were confirmed to have metastatic disease
    - 3 had ctDNA clearance on adjuvant therapy (olaparib or aromatase inhibitor) and remain disease-free after one year
    - 1 (treated with capecitabine) had ctDNA clearance but was later found to have bone only metastatic disease
  - 4 became ctDNA positive on adjuvant therapy
    - 3 were found to have metastatic disease or locoregional recurrence
    - 1 had subsequent clearance on adjuvant therapy and remains disease free

Patient-Reported PROMIS Results

- Median T-scores in the overall population were 52.7 (Range: 33.5-71.4) at baseline to 55.1(range: 33.5-74.2) at 6 months, and 55.8 (range: 33.5-73) at 12 months
- Fig. 2, 3, and 5a and 5b summarizes T scores in ctDNA positive and negative patients
- All 11 patients with positive ctDNA findings completed at least one PROMIS survey of whom 4 completed surveys both before and after a positive results (Fig 3.)
- Follow up T scores were not available for patients with metastatic or local recurrence as they went off study.

Physician Reported PDAT Results

- 103 surveys were completed by 16 physicians at baseline, 6-month, or 12-month blood draws. 6 physicians completed PDAT surveys following a positive ctDNA result.
- In response to *"How confident are you in [your] recommendation based on the information that you currently have?"*, physician confidence was lower after positive ctDNA results (mean 3.8; range 3–5) vs negative results (mean 4.5; range 1–5), where 1=Not at all confident and 5=Strongly confident
- Two physicians reported changing therapy after a positive ctDNA result, both in patients with TNBC:
  - 1 changed adjuvant capecitabine → ddAC, no evidence of relapse after 12 months
  - 1 changed adjuvant capecitabine → sacituzumab govitecan, pt also found to have locoregional recurrence

Figure 2: PROMIS T Scores among patient without positive ctDNA result (N=27)

	Baseline	6 Months	12 Months
Median	56.7	54.8	55.3
Min	39.2	33.5	33.5
Max	71.4	74.2	73

PROMIS surveys were administered at the same time as ctDNA blood draw and before participants were aware of their ctDNA result

Figure 3: PROMIS T Scores among 4 ctDNA positive patients with surveys completed before and after a ctDNA result

	Before		After		Follow up	
ctDNA+	Score	ctDNA	Score	ctDNA	Score	ctDNA
Pt1	61	Positive	60.4	Positive	--	--
Pt2	52.7	Positive	57.5	Positive	--	--
Pt3	55.1	Positive	57.1	Negative	55.8	Negative
Pt4	47.7	Positive	50.3	Negative	46.3	Negative

Figure 4:

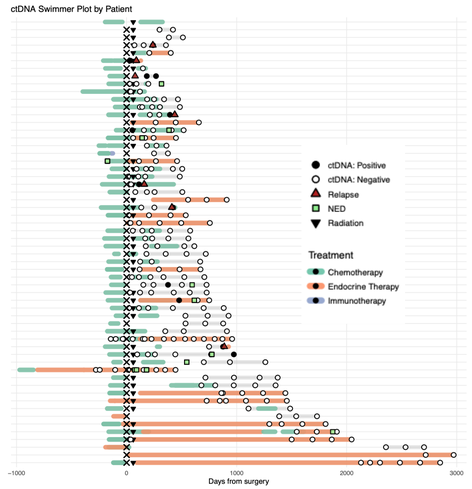
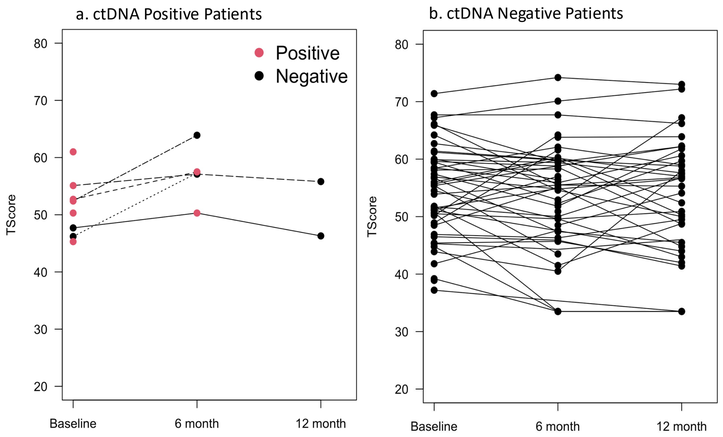


Figure 5: PROMIS T Scores at baseline, 6 months, 12 months by ctDNA positivity



Conclusions

- Overall, median T scores in our study population (52.7) were similar to the general population (50).
- Patient-reported anxiety scores fluctuated but remained overall stable over 12 months in the ctDNA- population. A large number of patients reported high anxiety T scores regardless of ctDNA results, highlighting the need for psychological support in this patient population.
- The small number of ctDNA positive patients in this study limits our ability to generalize how ctDNA positivity affects patient reported anxiety, although the with pre- and post- ctDNA report both had stable PROMIS T scores.
- In the absence of clear clinical guidelines, ctDNA positive results may lead to physician decision making uncertainty.
- National guidelines are needed to standardize ctDNA testing in the adjuvant setting in early-stage breast cancer, especially in cases of ctDNA positive, imaging negative patients

References

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Disclosures

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