



Know breast cancer's next move with MRD testing

- How can I assess if my patient will benefit from additional therapy?
- Can we detect relapse earlier during surveillance?
- What do I do with a positive ctDNA result?

Ultrasensitive, personalized molecular residual disease (MRD) testing to inform critical decisions for breast cancer care

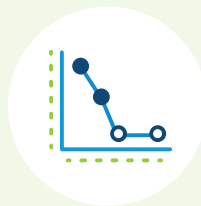


1 in 3 women will experience relapse. Signatera™ can detect this earlier.

30%



Up to 30% of women with no evidence of disease will eventually relapse and experience cancer progression.¹

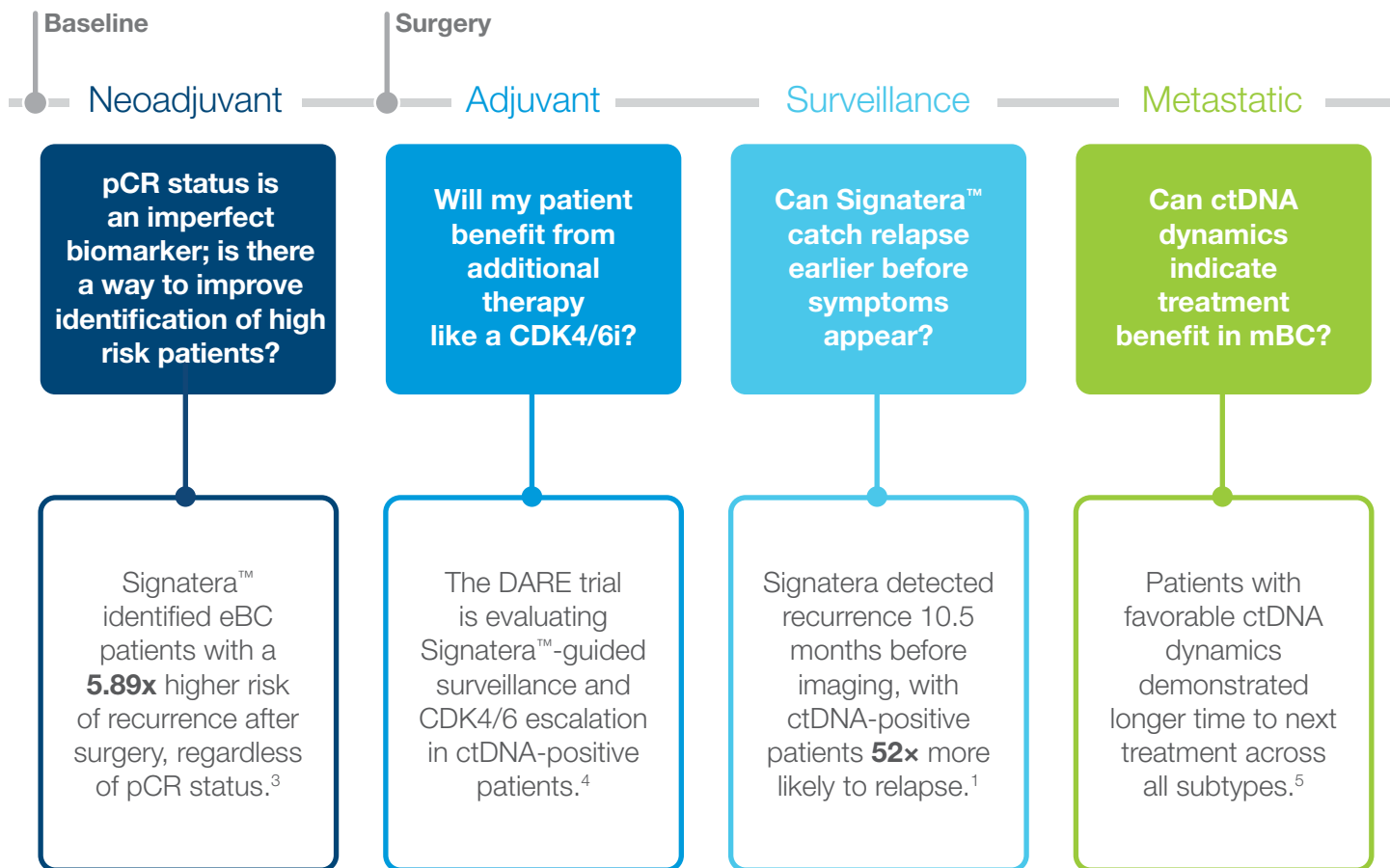


Additionally, 10-15% of patients experience reduced performance status, which limits treatment options.²



Existing tools fall short at identifying recurrence early, before the patient becomes symptomatic.

Guiding treatment decisions in breast cancer starts with actionable insights.



Personalized, tumor-informed MRD testing: ultrasensitive, next-generation precision from the most trusted name in breast cancer

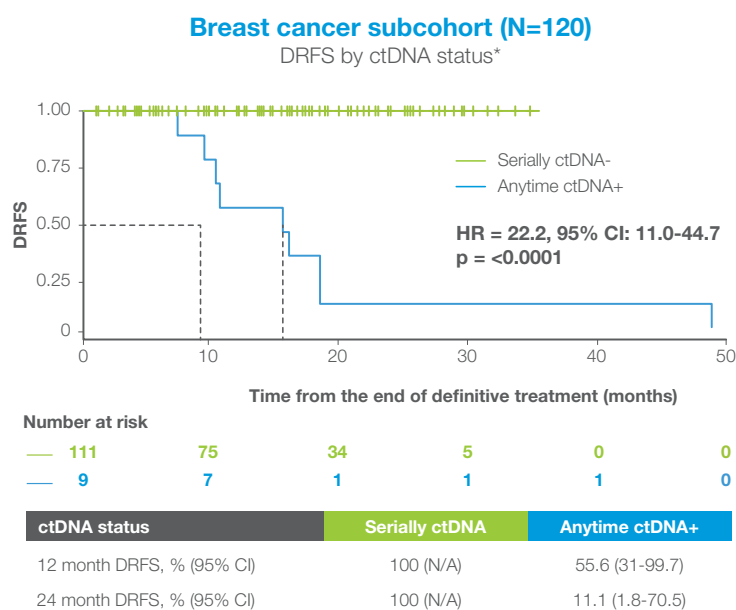
Signatera™ Genome is ready for prime time.

>99%
Sensitivity⁶

>99%
Specificity⁶

100%
Confidence

Signatera™ Genome is prognostic of outcomes and predictive of adjuvant benefit.



*DRFS = Distant Recurrence Free Survival

In breast cancer, **ctDNA-positivity** after treatment strongly predicted **worse distant relapse-free survival**, while serial negativity signaled better outcomes.

Signatera™ Genome can **detect recurrence up to 13.5 months before imaging⁶**—empowering you to personalize follow-up, intensify surveillance, and guide patients with great clarity.

Detect earlier



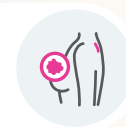
Detect residual disease at the earliest possible stage.

Trust the result



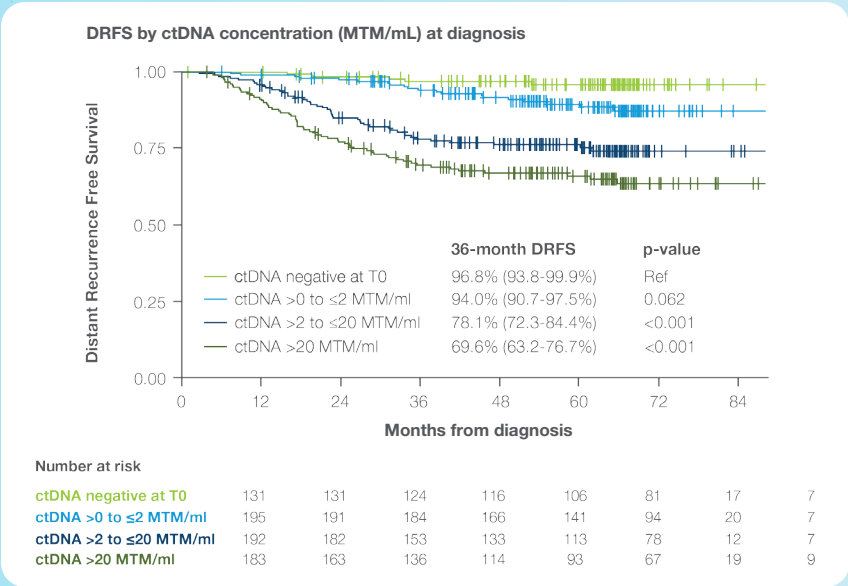
Minimize false positives, maximize clinical confidence.

Look beyond the breast



Mammograms focus on the breast; Signatera™ Genome looks for recurrence systemically.

Order Signatera™ at diagnosis to establish a molecular baseline

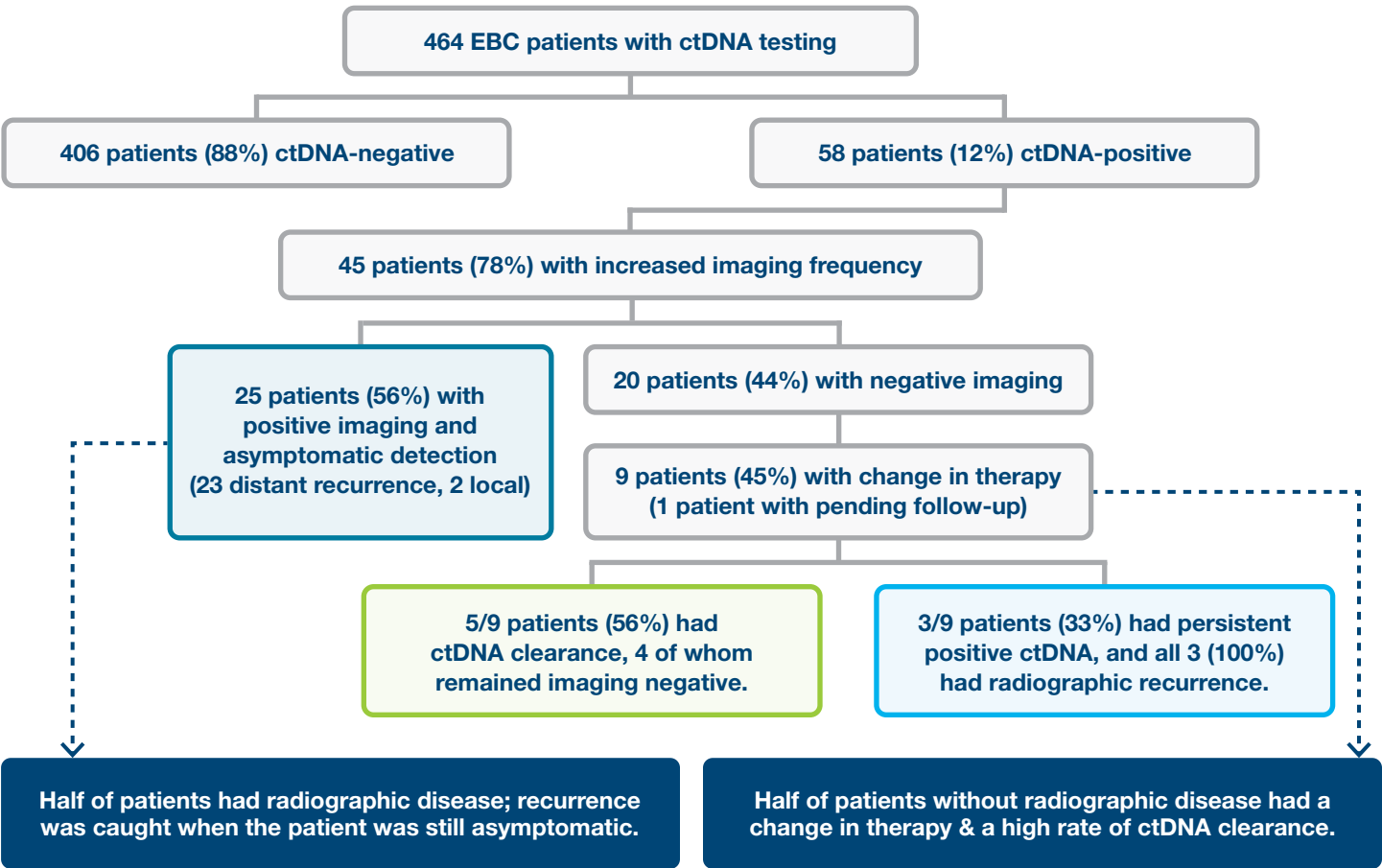


Signatera™ went beyond pCR and delivered insights that identified which patients were at high risk of recurrence after surgery⁷

Patients that were Signatera™-negative prior to NAT had 96.8% 3-year DRFS

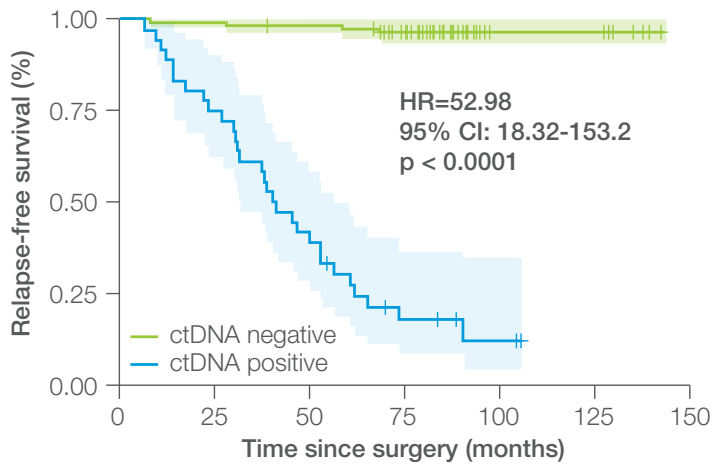
Detecting recurrence before symptoms appear:

In a real-world study of 464 early breast cancer patients, UCLA investigators found that ctDNA positivity prompted increased imaging and enabled detection of recurrence before symptoms emerged. Nearly half of patients with positive ctDNA had a change in therapy, and all patients with persistent ctDNA experienced radiographic recurrence.⁸



Serial Signatera™ monitoring detects recurrence months before radiographic evidence

EBLIS Study: ctDNA status was highly prognostic

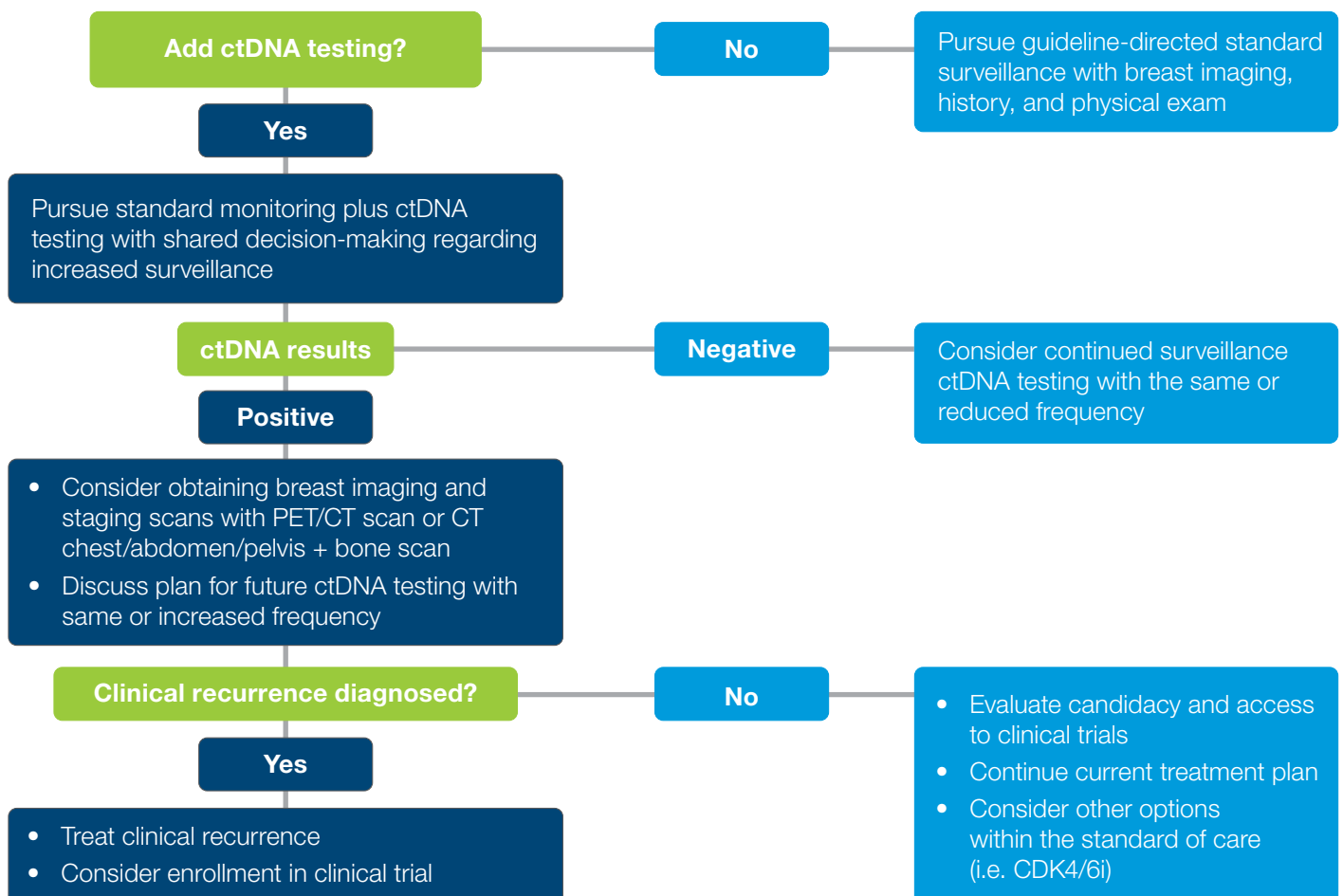


Serial Signatera™ testing identified ctDNA positive patients were **52x** more likely to relapse.¹

10.5 months median lead time over radiographic recurrence (range 0–38 months)¹

What do I do with a patient who has detectable ctDNA?

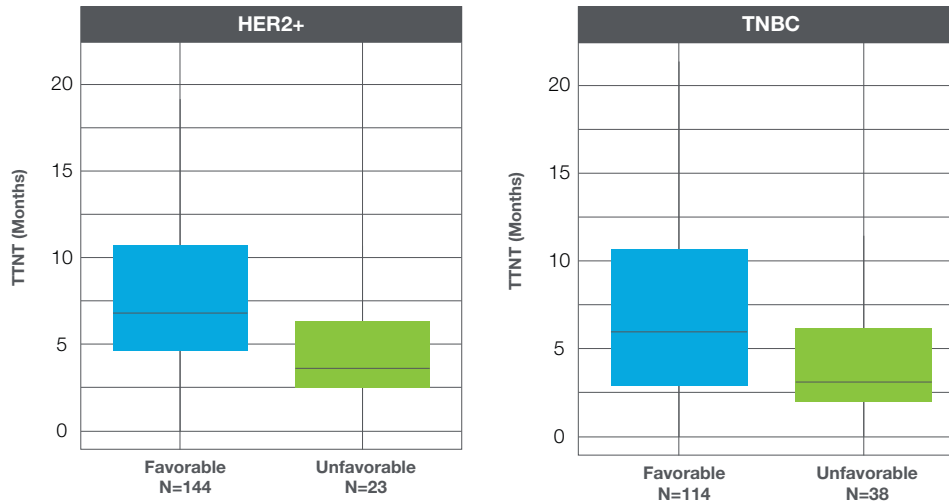
Potential management options for patients with MRD⁸



Signatera™ provides clarity when it matters most

Enhance shared decision-making and guide confident treatment planning.

Patients with favorable ctDNA dynamics demonstrated longer TTNT* across all subtypes⁵



*TTNT = Time to Next Treatment

In a study of 616 mBC patients, Signatera™ predicted which patients would benefit from the treatment⁵

In a multivariate analysis, ctDNA dynamics emerged as the strongest predictor of treatment benefit.

How often should I test?*

Neoadjuvant

Which patients are more likely to recur?

Adjuvant

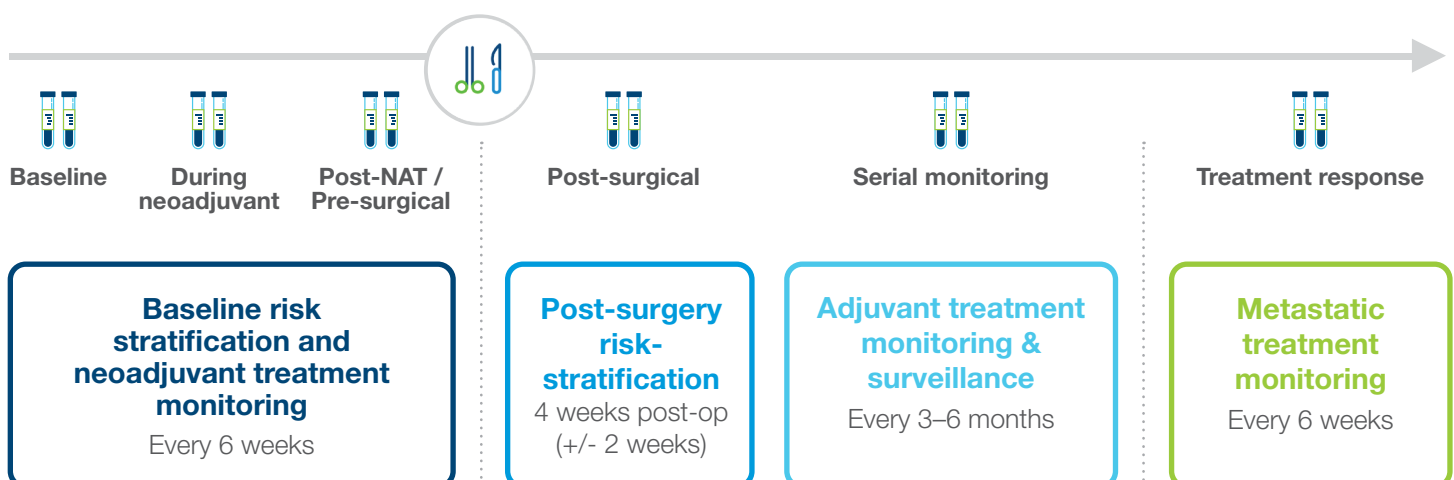
Does my patient need additional therapy?

Surveillance

Is the cancer recurring?

Metastatic

Is it time to switch treatment?



*Based on surveillance guidelines; cadence above is suggested based on utility of other providers in this indication but does not replace clinical judgment or guidance as set forth in your institutions.

A woman with short, wavy blonde hair is shown in profile, looking out a window. She is wearing a light-colored blazer and a necklace. The background shows a cityscape with buildings and a bright sky. A blue circular graphic element is in the bottom right corner.

FEMALE PATIENT WITH STAGE III BREAST CANCER

Why Signatera™?: Postmenopausal accountant and mom of 3 wanted a closer surveillance strategy after definitive treatment

Left breast cancer: cT4N2,
G3 IDC, HR-/HER2+



Completed full course of
neoadjuvant chemotherapy/
HER2 targeted therapy

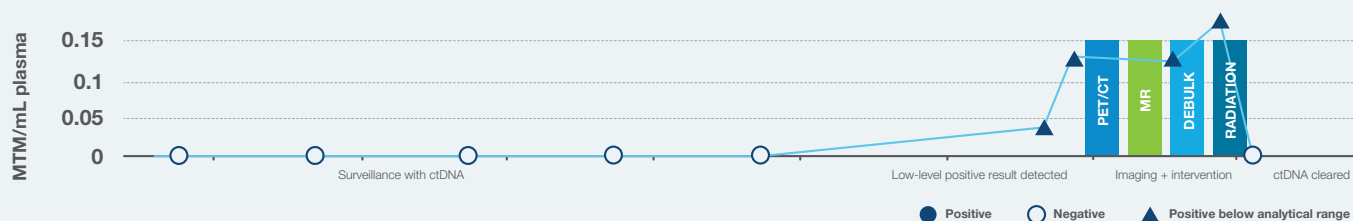


Bilateral mastectomy,
vpTisN0



- **Radiation:** Completed chest wall radiation.
- **Adjuvant therapy:** Started one year of maintenance therapy.
- **Surveillance:** Patient was serially monitored with Signatera™.

Historical results



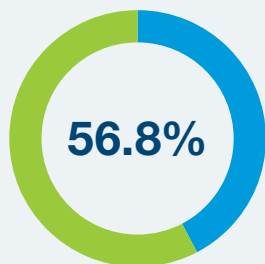
- **ctDNA monitoring:** Serial Signatera™ testing revealed low-level positivity while patient remained asymptomatic.
- **Subsequent PET/CT:** Subtle sclerosis in sternum without hypermetabolic activity
- **Breast MRI:** Bright focus in sternum - unclear whether mets vs. surgical changes
- **Brain MRI:** Left sided intra-axial supratentorial mass measuring 2.8 cm
- **Treatment:** Incomplete debulking of left frontal brain mass followed by brain radiation.
- **Outcome:** ctDNA cleared and patient has remained negative on follow-up.

The patient was relieved to have a tool like Signatera™ to catch her relapse earlier, enabling timely intervention and ultimately allowing her to stay asymptomatic. Patient remains serially ctDNA-negative.

Close the gap: guidelines recommend hereditary testing, but many eligible patients aren't being tested.



■ Eligible tested
■ Eligible untested



Breast cancer patients ≤ 50 years of age and patients with TNBC are eligible for hereditary cancer testing, however only 56.8% are actually receiving it.

Empower™
Hereditary cancer test

Natera Oncology: One sample. Find answers.

Natera can run both Altera™ and Signatera™ at the same time to maximize excised tissue.

Altera™

Support treatment decisions with comprehensive tumor genomic profiling

Empower™

Hereditary cancer testing, made accessible (run on either plasma or saliva)

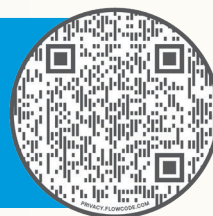
Ordering Signatera™ for patients with breast cancer

- > Can be run at any time point from diagnosis through survivorship, using the core biopsy or surgical resection
- > Medicare coverage for stage II-IV breast cancer across all subtypes receiving neoadjuvant therapy to support real-time assessment of tumor response to treatment, and stage IIb and higher breast cancer to inform treatment decisions in the adjuvant setting and for early detection of recurrence in the surveillance setting



Signatera™ Genome: The only genome-designed MRD assay with Medicare Coverage in the neoadjuvant and surveillance setting for breast cancer.

Learn more at:
**natera.com/
oncology**



References:

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Signatera™ has been developed and its performance characteristics determined by the CLIA-certified laboratory performing the test. The test has not been cleared or approved by the US Food and Drug Administration (FDA). CAP accredited, ISO 13485 certified, and CLIA certified. © 2025 Natera, Inc. All Rights Reserved. SGN_BR_Breast_20251215_NAT-8022653

