SAGA DIAGNOSTICS

Pathlight™
Molecular Residual Disease

Clinical Validation of Pathlight™: **TRACER** (c**T**dna evaluation in ea**R**ly bre**A**st can**CER**)

Ultrasensitive Detection and Monitoring of Circulating Tumor DNA Using Structural Variants in Early-Stage Breast Cancer[1]

Breaking barriers in clinical performance for breast cancer

There is a critical need for molecular residual disease (MRD) testing that is both ultra-sensitive and ultra-specific, to enable long-term cancer surveillance and risk-aligned treatment decisions. Pathlight is a first-of-its-kind, multi-cancer MRD platform, initially indicated for early breast cancer, that uses structural variants (SVs) as biomarkers, instead of single nucleotide variants (SNVs). SVs are tumor- and patient-specific and often reflect founding events in tumorigenesis, making them stable and informative biomarkers for tracking disease.

The TRACER (cTdna evaluation in eaRly breAst canCER) study, published in Clinical Cancer Research in January 2025, assessed Pathlight's clinical validity in early-stage breast cancer patients and is the first published validation of an SV-based ctDNA detection and monitoring assay.[1] The study demonstrated Pathlight's best-in-class clinical performance, including 100% sensitivity, 100% specificity and a 94% baseline detection rate in estrogen receptor-positive (ER+) breast cancer.

Study overview

Patient selection

100 patients with Stage I–III early breast cancer (ER+, HER2+, TNBC) who received standard of care neoadjuvant and adjuvant therapy and underwent serial blood collection.*

Test validation

Tumor-informed SV fingerprints developed from whole genome sequencing (WGS) of tumor tissue collected at diagnosis or surgery. SVs orthogonally validated using multiplex dPCR.

Serial testing

SV-based ctDNA assays conducted from diagnosis to postoperative clinical recurrence, with a median follow-up of 3.3 years from the time of baseline blood collection. 568 total ctDNA time points assessed.

Key findings

96%
ctDNA detection rate at baseline across all stages and subtypes (94% ER+, 97% HER2+, 96% TNBC)

13.7
month median lead time from positive ctDNA test to distant recurrence (up to 5.3 years)

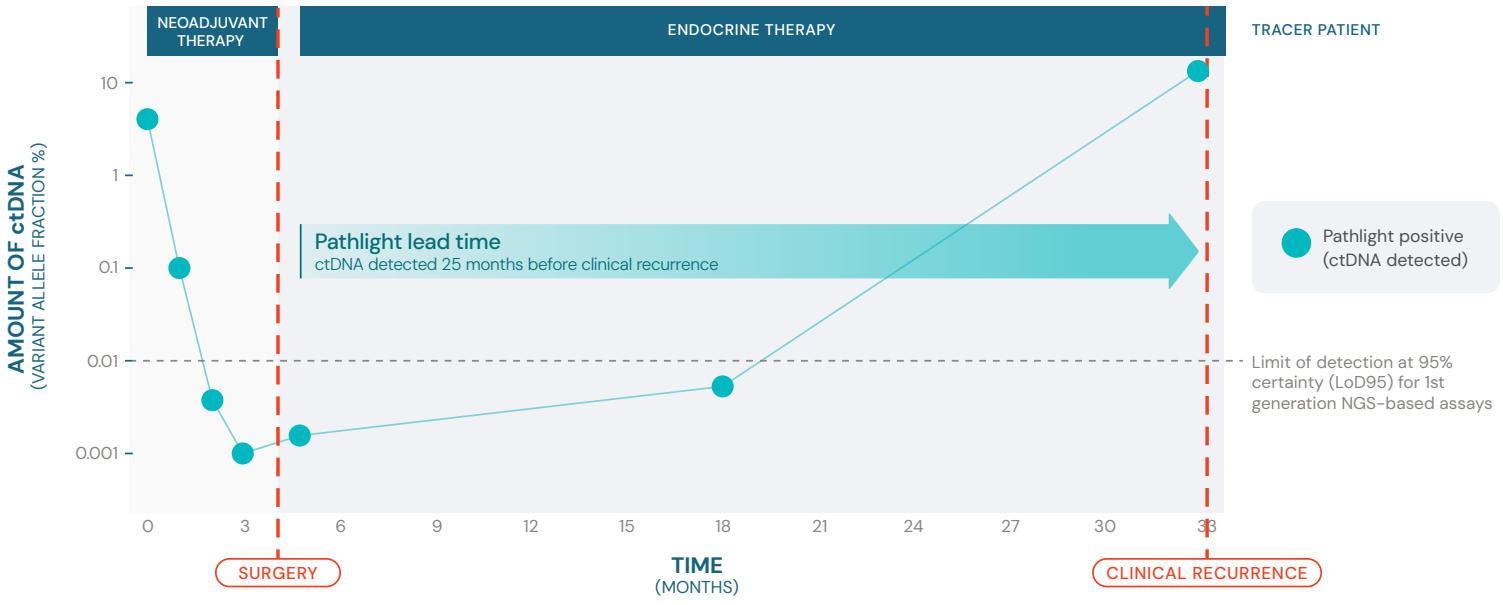
100%
specificity across all timepoints (61/61)

100%
sensitivity for distant recurrence (17/17)

Best-in-class MRD testing for early-stage and ER+ breast cancer

Pathlight's unparalleled sensitivity offers the potential to detect MRD earlier. A 94% baseline detection rate for ER+ breast cancer suggests clinical advantages over first-generation ctDNA assays.

Detection of ctDNA in a participant from the TRACER study and association with clinical outcome



*Patients were enrolled in serial blood collection through the Liquid Biopsy Evaluation and Repository Development at Princess Margaret (LIBERATE) cohort

Improving the Standard of Cancer Care

Pathlight overcomes one of the toughest challenges in oncology – sensitive, specific, and earlier detection of MRD and recurrence by focusing on large scale genomic alterations, referred to as SVs, and detecting these SVs by dPCR. SVs are often early drivers of tumorigenesis across cancer types and are frequently amplified. They are specific to each patient and tumor, thereby enabling exceptional specificity and sensitivity. The SVs selected for Pathlight tests enable accurate and precise detection of MRD over time – potentially increasing the chances for successful treatment and recovery.

Limitations of targeting SNVs

Prone to NGS errors
Contributes to MRD false positives, impacting sensitivity and specificity

Limited sensitivity
Affects baseline detection rates and shortens lead times across tumor types

Loss over time
More susceptible to therapy selection pressure and loss over time due to clonal variation

Benefits of targeting SVs

Unique to each patient's tumor

Highly sensitive
<1ppm detection limit

More stable over time
(less susceptible to therapy selection pressure)

Present across all breast cancer subtypes in the TRACER study

Personalized test development

3–4 weeks

for tumor fingerprint development and initial blood test*

Routine blood tests

3–5 days

for MRD blood test results*

*Following receipt of lab samples

References

1. Elliott MJ, Howarth K, Main S, et al. Ultrasensitive detection and monitoring of circulating tumor DNA using structural variants in early-stage breast cancer. *Clin Cancer Res*. Published online January 7, 2025. doi:10.1158/1078-0432.CCR-24-3472

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