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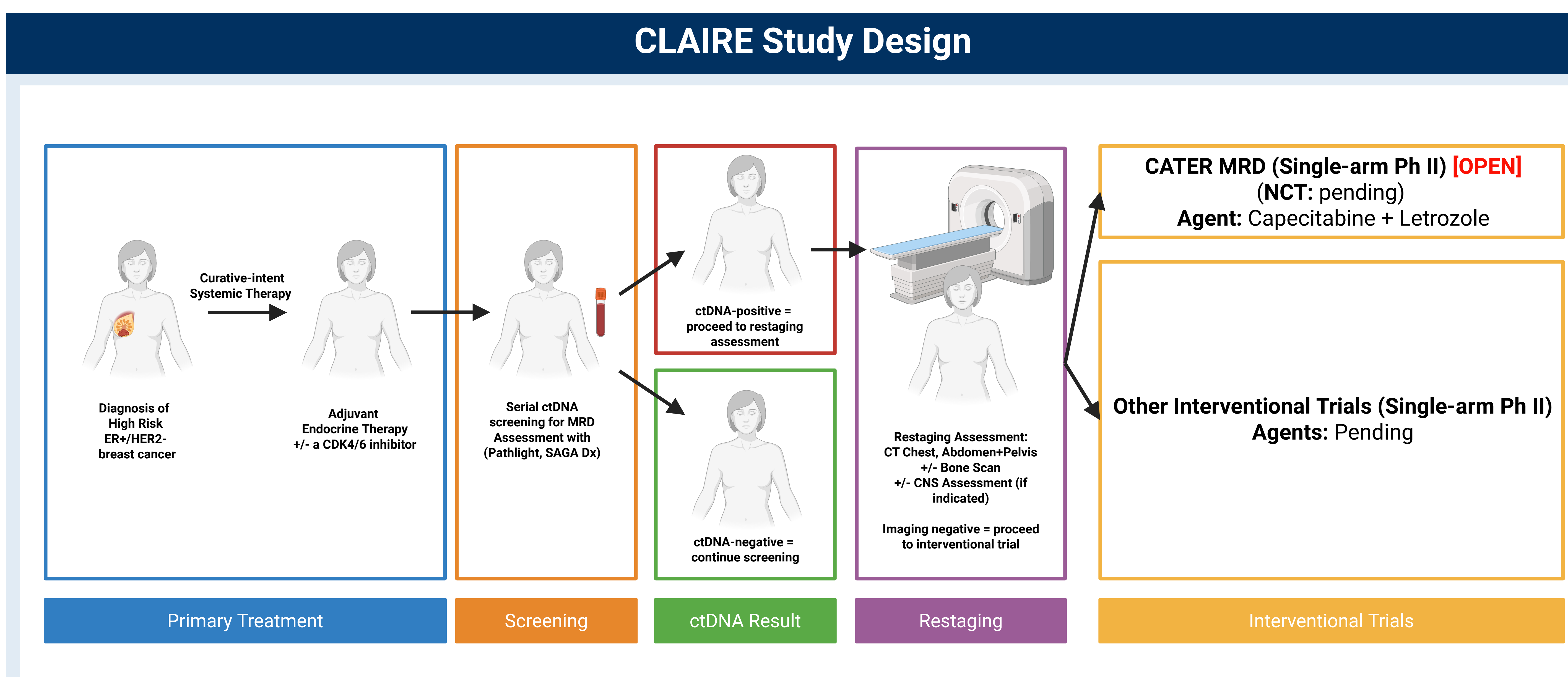
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## INTRODUCTION

- Standard guidelines do not recommend routine lab or imaging surveillance for distant recurrence after curative-intent therapy in early-stage breast cancer (EBC).<sup>1,2</sup>
- These recommendations rely on decades-old evidence, when early detection (via x-ray/ultrasound) did not improve survival with treatments available at the time.<sup>2,3</sup>
- ≥20% of EBC patients will ultimately relapse with metastatic disease, accounting for >60% of breast cancer-specific deaths due to high prevalence and limitations of current risk-stratification.<sup>4</sup>
- There is a need for individualized secondary adjuvant strategies to identify high-risk patients while avoiding broad overtreatment.
- Circulating tumor DNA (ctDNA) enables detection of clinically occult, impending recurrence with high sensitivity and specificity.<sup>5</sup>
- The Pathlight™ (SAGA Dx) structural variant -based ctDNA assay showed ultrasensitive MRD performance suitable for clinical use.<sup>6</sup>
- Using Pathlight, ctDNA was detected prior to distant recurrence in all evaluable cases, with:<sup>6</sup>
  - 100% sensitivity
  - 100% specificity
  - Median lead time: 595 days (range: 15-1931 days).
- We seek to evaluate the clinical utility of prospective ctDNA monitoring using Pathlight for patients with ER+/HER2- EBC.

## CLAIRE Study Design



**Figure 2. Overview of the CLAIRE ctDNA-Guided Surveillance Program.** After completing curative-intent therapy for high-risk ER+/HER2- early-stage breast cancer, patients enter serial tumor-informed ctDNA monitoring (Pathlight, SAGA Dx) to detect MRD. ctDNA-negative patients continue routine surveillance, whereas ctDNA-positive results trigger reflex restaging assessment. Individuals with radiographic metastases receive standard care; those with molecular recurrence only (ctDNA-positive, imaging-negative) may enroll in MRD-directed trials, including the CATER Phase II study (capecitabine added to endocrine therapy) and additional planned ADC- or combination-based Phase II interventions.

**CLAIRE will prospectively evaluate ctDNA surveillance using an ultrasensitive MRD assay in ER+/HER2- EBC to identify patients for interventional trials and understand the clinical utility of surveillance.**

## STUDY INFORMATION

**Status:** Active and Recruiting

**Sites:**

- Princess Margaret Cancer Centre, Toronto, Canada [\[Open\]](#)

**Clinicaltrials.gov Identifier:** NCT05196087

## ACKNOWLEDGEMENTS

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## ENDPOINTS

### Primary Endpoint:

- The rate of radiographically overt metastatic disease in the setting of ctDNA detection (Pathlight)\*
  - In participants with a previous negative ctDNA test
  - All participants
- The rate of clinically overt, recurrent local or metastatic disease in the absence of ctDNA detection
- The rate of participants without radiographic overt metastatic disease who proceed to systemic therapy in the setting of ctDNA positivity
- \*To account for the cross sectional nature of the study, where participants are enrolled at various stages of follow up, this distinction is required as participants may have initial ctDNA positivity at their initial testing where radiographically overt metastatic disease is already present.

### Secondary Endpoint:

- The rate of adherence to the prescribed screening frequency
- Evaluation of patient reported outcomes (PROs)
- Distant recurrence free survival (DRFS) in those with and without ctDNA detected
- Overall survival (OS) in those with and without ctDNA detected
- Health services utilization for those with negative tests, compared to a historical control

**Exploratory objectives:** Evaluation of features from whole-genome sequencing in those with or without clinical recurrence

## ENROLMENT

### Part A (CLAIRE; Screening Phase):

This study will target enrolment of 300 patients. With an expected cumulative ctDNA positivity rate of 8-15% based on previous data and the population risk, 25-45 patients will be evaluable for the primary endpoints of this trial and the subsequent interventional trials.

### Inclusion Criteria:

- Male or female patients ≥ 18 years of age with histologically confirmed (by local assessment with ASCO/CAP criteria), Hormone receptor (HR)-positive, HER2-negative stage I-III breast cancer
- At elevated risk of recurrence based on clinical pathologic features
- No clinical, pathologic or radiographic evidence of unresectable, recurrent or metastatic disease
- Receiving adjuvant aromatase inhibitor

### Exclusion Criteria:

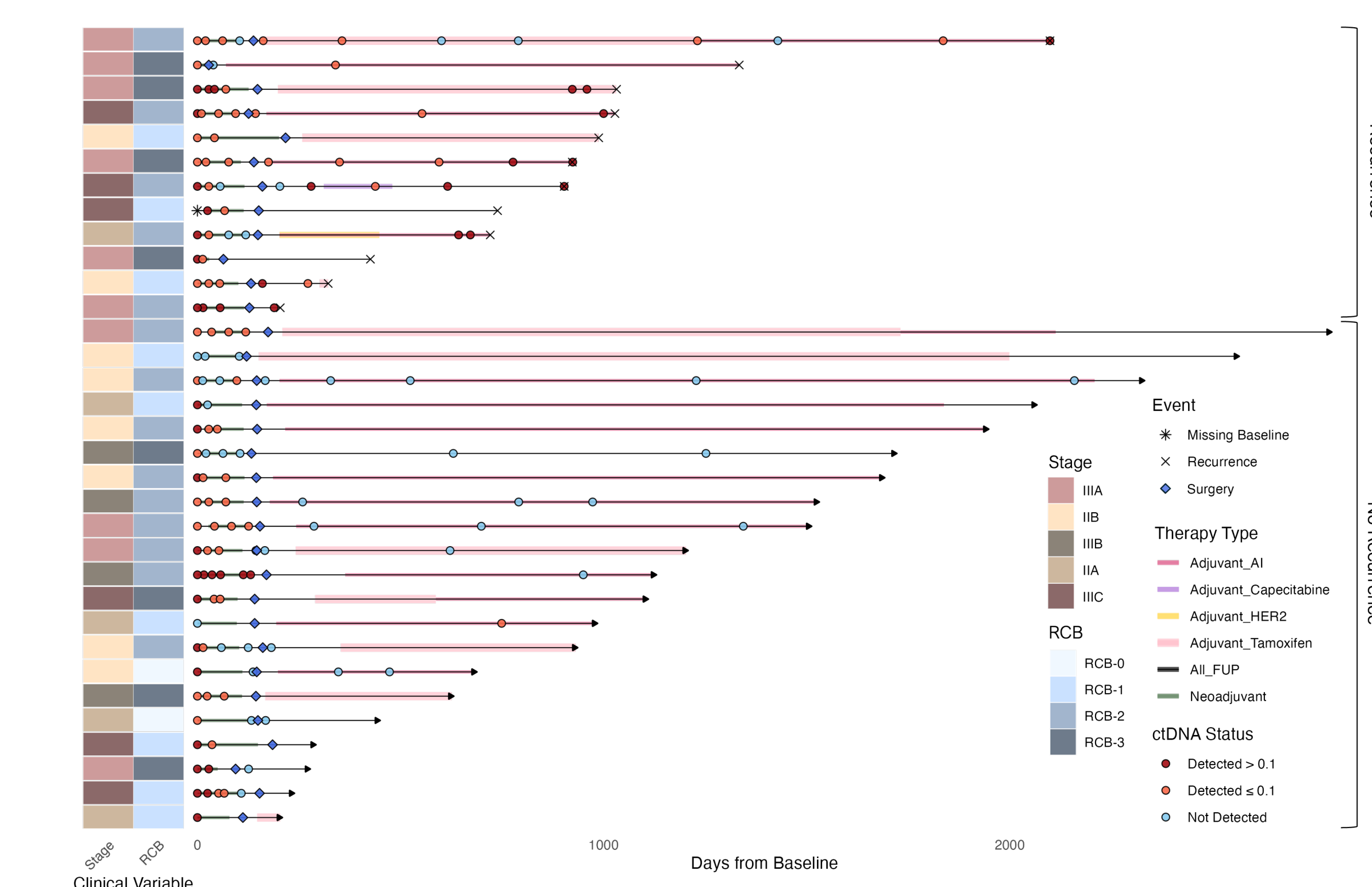
- Other medical comorbidities which would preclude treatment with systemic therapy.
- A lack of diagnostic or surgical tissue available for assay construction.

### Part B (Interventional / Treatment Phase):

### Inclusion Criteria:

- ctDNA+ (Pathlight) with no radiographic evidence of metastatic disease
- No absolute contraindication to study treatment

**Exclusion Criteria:** Study specific



**Figure 1. Disease Course and Time to Distant Recurrence in ER+/HER2- Early-stage Breast Cancer.** Swimmer plot depicting individual trajectories from initial diagnosis through the development of metastatic recurrence as published in Elliott et al., *Clinical Cancer Research* (2025).<sup>6</sup> This visualization highlights the specificity and predictive value of adjuvant ctDNA surveillance in this patient population.