# CSF Tumor Cell (CSF-TC) Detection, Quantification and Biomarker Assessment Helps in Clinical Management of Breast Cancer and Non-Small Cell Lung Cancer Patients Having Leptomeningeal Disease (FORESEE Study, NCT05414123)

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BIOM-04

## Background

+ A multi-center clinical utility study assessing the impact of the CNSide® CSF assay platform on disease management of patients with leptomeningeal disease.
+ The study enrolled 39 patients with breast (21 patients) or non-small cell lung cancer (18 patients) with a suspected or confirmed diagnosis of LM.
+ Primary endpoint assessed how CNSide® test results influenced clinical decision making.
+ Secondary endpoints assessed CNSide® vs the gold standard of LM diagnosis, CSF cytology, and its use for personalization of treatment selection based on tumor molecular phenotype.

## Introduction

+ Current standard of care methods to diagnose or assess treatment response of LM (Clinical Evaluation, MRI and Cytology) have limited sensitivity and specificity and are poorly quantifiable.
+ This creates challenges for physicians to manage LM or determine the best course of treatment.
+ The FORESEE Study was a multi-center, prospective clinical trial evaluating a novel diagnostic platform, CNSide, that aimed to overcome these challenges.
+ CNSide can detect and quantify tumor cells in the CSF from patients with breast cancer or NSCLC having a suspicious or confirmed LM.

## Platform

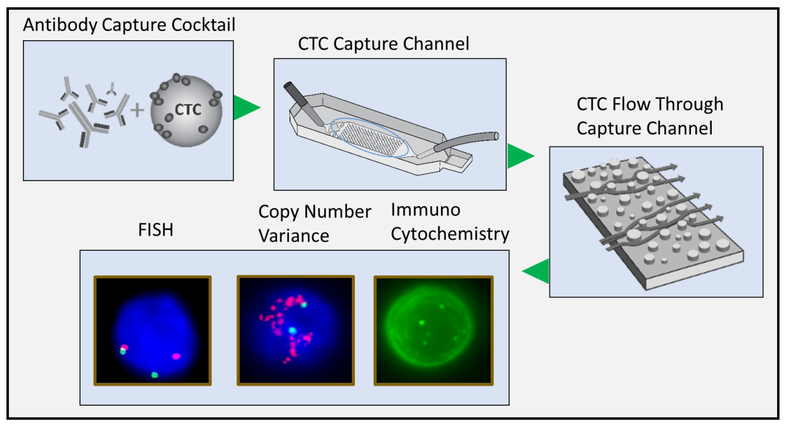
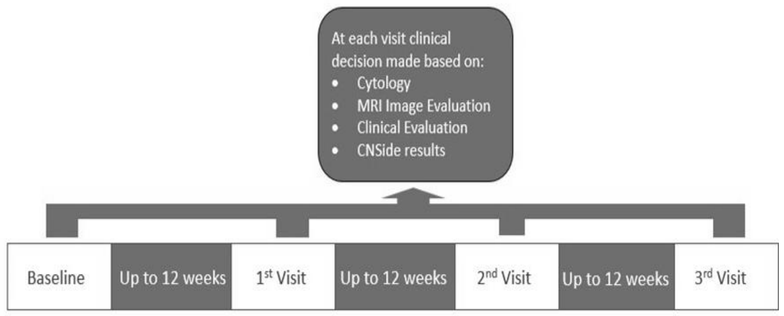



**Figure 1.** CNSide workflow demonstrating usage of a 10-antibody cocktail for cell capture, followed by biotinylation and passage through a microfluidic device for immobilization and FISH and ICC analysis.

## Methods




+ At each visit, CNSide's contribution to a clinical decision was evaluated via a Questionnaire
+ Treatment decisions were at Physician discretion
+ Enrollment goal: 20 patients with breast cancer, 20 with NSCLC

**Primary End Point:**
+ Evaluate if CNSide results contribute to a clinical decision (target: 20% of decisions)

**Secondary End Point:**
+ Evaluate tumor cell detection by CNSide as a therapy response monitoring tool
+ Sensitivity, Specificity, NPV, and PPV of CNSide compared to CSF cytology

### Physician Questionnaire:

Baseline

1. Was the patient diagnosed with LM prior to Baseline visit (yes, no)
   - If no, is the patient diagnosed with LM at the Baseline visit (yes, no)
   - If yes, what is the status of the LM tumor at this visit (no change, progression, resolution)
2. Did CNSide contribute to this assessment? (yes, no)
3. Did CNSide inform the specific drug selected for treatment (yes, no)

Subsequent visits

1. What is the status of the LM tumor? (no change, progression, resolution)
2. Did CNSide contribute to this assessment? (yes, no)
3. Did CNSide inform the specific drug selected for treatment? (yes, no)

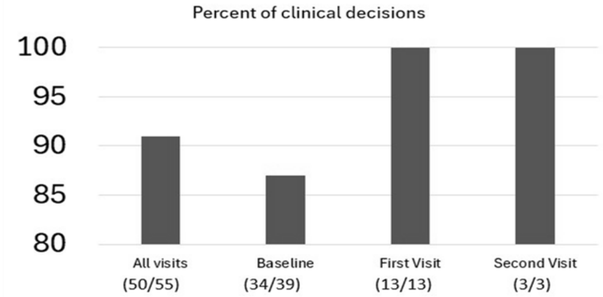
### Patient Demographics (n=39 pts*, n=55 decision points)

| | Breast Cancer (N=21) | NSCLC (N=18) |
|---|---|---|
| Age Range | 58 years | 58 years |
| Gender | F (N=21) | F (N=9), M (N=9) |
| Parenchymal brain metastasis diagnosed prior to enrollment | 52% (11/21) Positive, 43% (9/21 Negative, 5% (1/21) Unknown | 56% (10/18) Positive, 44% (8/18) Negative |
| LMD Diagnosed prior to trial enrollment (by investigator assessment) | 81% (17/21) Positive, 14% (3/21) Negative, 5% (1/21) Unknown | 61% (11/18) Positive, 39% (7/18) Negative |
| Primary HER2 status | 19% (4/21) Positive, 76% (16/21) Negative, 5% (1/21) Unknown | Not Applicable |
| Primary HER2-/ER-/PR- | 9% (2/21) | Not Applicable |
| Primary ER+ | 76% (16/21) Positive, 19% (4/21) Negative, 5% (1/21) Unknown | Not Applicable |
| Primary PR+ | 67% (14/21) Positive, 24% (5/21) Negative, 10% (2/21) Unknown | Not Applicable |
| Number of Questionnaires completed (N=55 total; 29 BC and 26 NSCLC) | 72% (21/29) Baseline, 24% (7/29) First Visit, 3% (1/29) Second Visit | 69% (18/26) Baseline, 33% (6/26) First Visit, 8% (2/26) Second Visit |
| Number of patients with Baseline Visit | 21 | 18 |
| Number of Patients with Baseline + First Visit | 7 | 6 |
| Number of Patients with Baseline + First Visit + Second Visit | 1 | 2 |

*N=40 patients enrolled; data was entered for N=39 9N=21 breast cancer, N=18 NSCLC)

## Results

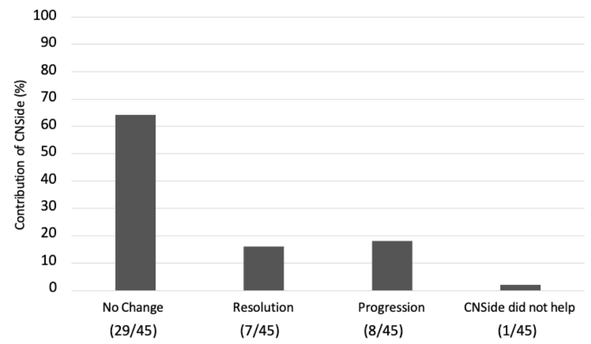
### Take Home #1: CNSide helped make clinical decisions in LMD patients




### Take Home #2: CNSide helped to diagnose LMD

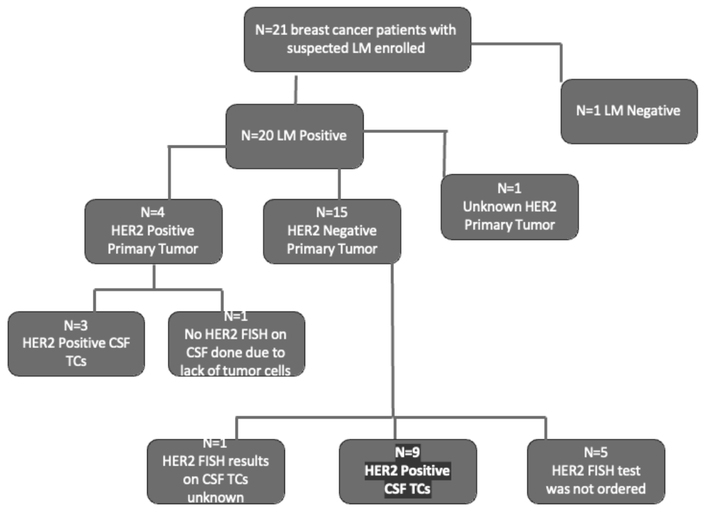
+ N=10 patients not diagnosed with LMD prior to trial enrollment
  - These patients were deemed LMD positive or negative after the Baseline visit based on Investigator assessment
+ LMD Positive Patients (N=7)
  - Cytology Positive, CNSide Positive: N=2
  - Cytology Negative, CNSide Positive: N=5
+ LMD Negative Patients (N=3)
  - All three patients were Cytology Negative and CNSide Negative
  - Investigators noted on the questionnaire that CNSide helped to rule out LMD

### Take Home #3: CNSide helped to evaluate the status of the LMD tumor (45 questionnaires)*




*N=35 patients

### Primary vs LM HER Status ('HER2 Flip')




## Conclusions

+ FORESEE study met primary end point
+ CNSide helped to make a clinical decision in 91% (50/55) of decisions
+ CNSide helped to inform therapy selection in 24% (13/55) of decisions
+ Compared to cytology in matched samples, CNSide more than doubled the sensitivity of tumor cell detection in the CSF
+ 60% of systemically her2 negative cancers showed her2 positivity in the CSF (matched primary and LMD)

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