

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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Timeline of the FORESEE Study

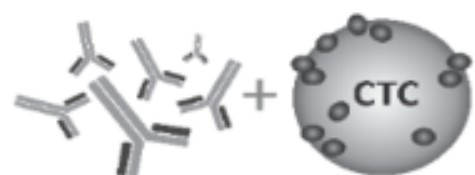


CNSide CSF Diagnostic Platform

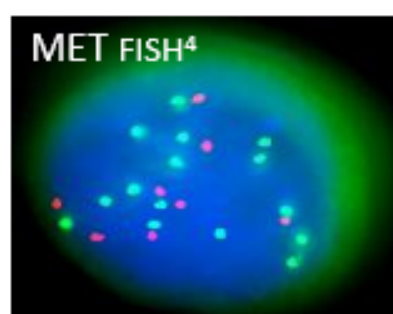
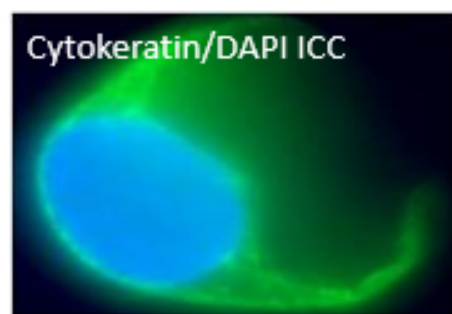
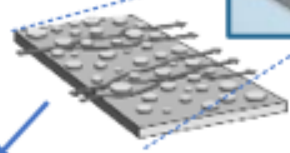
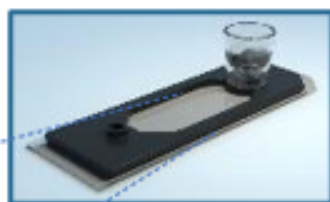
Tumor Cell Detection Workflow

cfDNA Detection Workflow

Antibody Cocktail Tumor Cell Isolation^{1,*}

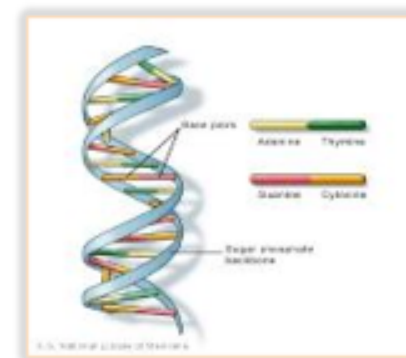


Patented Microfluidic Channel^{2,*}



Collection tube for ambient shipping up to 4 days
^{*}Unique cell capture technology for FISH and protein expression assays

CSF cfDNA Isolation




NGS on CSF cfDNA




¹ Mikolajczyk et al. JCO (2011), ² Dickson et al. Microfluidics (2011)

³ Pecot et al. Cancer Discovery (2011), ⁴ Mayer et al. Cancer Genetics (2011)


Retrospective analyses showing utility (but no prospective study to date)



CNSide helps to
diagnose LMD



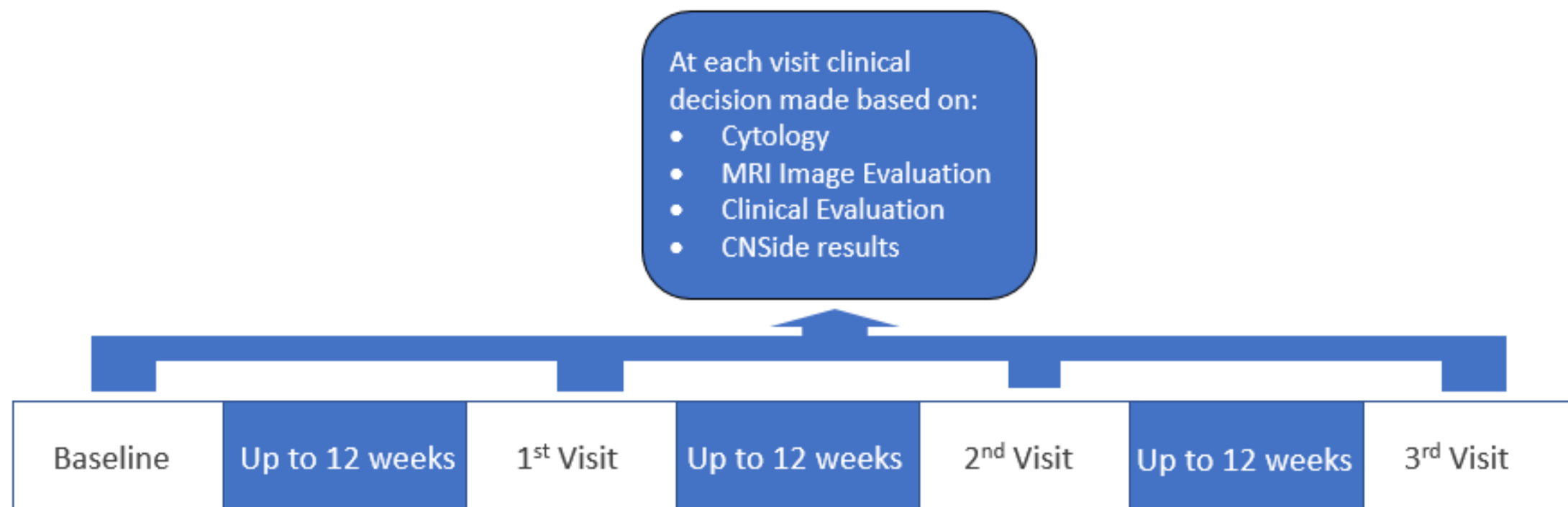
CNSide helps to
determine response to
LMD directed therapy



CNSide helps to inform
specific LMD therapy
selection

- No prospective data in controlled setting to confirm clinical utility observed from retrospective analysis
- Need to understand clinical performance of tumor cell detection of CNSide compared to current gold standard, CSF cytology

FORESEE Trial: Trial Schema



- 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

FORESEE Trial: End Points

- Primary end point
 - Evaluate if CNSide results contribute to a clinical decision (Target: 20% of decisions)
- Secondary end points
 - Evaluate tumor cell detection by CNSide as a therapy response monitoring tool
 - Sensitivity, Specificity, NPV and PPV of CNSide compared to CSF cytology

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Clinical Utility Trial

Clinical Utility Trial designs are a common trial design for Molecular Diagnostic tests

Title	NCT#	Primary End Point	Type of Test
BESPOKE Study of ctDNA Guided Immunotherapy	04761783	Percent of Melanoma, - NSCLC and Colorectal patients who have their immunotherapy treatment regimen changed due to the SIGNATERA ctDNA test result	Patient tailored gene panel to detect cfDNA from the blood
Treatment Decision Impact of OncotypeDx in HR+, N- Breast Cancer Patients (SWITCH)	01446185	Impact of OncotypeDx Recurrent Score on treatment decisions	21-gene test that predicts recurrence of early-stage breast cancer
Study of the Clinical Utility of PSMA Imaging in the Evaluation of Men With Prostate Cancer	02825875	Changes to clinical management of patients with prostate cancer after Physician reviews a PET/CT scan of PSMA	PSMA Imaging by PET/CT
Prospective Clinical Utility Study to Assess the Impact of Decipher on Treatment Decisions after Surgery (PRO-IMPACT)	02080689	Number of participants for which the Urologist changed the patient's treatment plan based on Decipher test results	Next Generation Sequencing of tumor tissue
Decision Impact Study of PreciseDx Breast (PDxBRUTILITY)	06309615	Proportion of Physicians who utilized PBxBR results in their management of patients with invasive breast cancer (target: 20%)	Combination of Artificial Intelligent grading of histology and clinical data that predicts recurrence in early-stage breast cancer patients

FORESEE Trial: Physician Questionnaire

Impact of CNSide results on clinical management of LMD was assessed via a questionnaire

Baseline:

1. Was the patient diagnosed with LM prior to Baseline visit (yes, no)
 - a. If no, is the patient diagnosed with LM at the Baseline visit (yes, no)
 - b. 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:

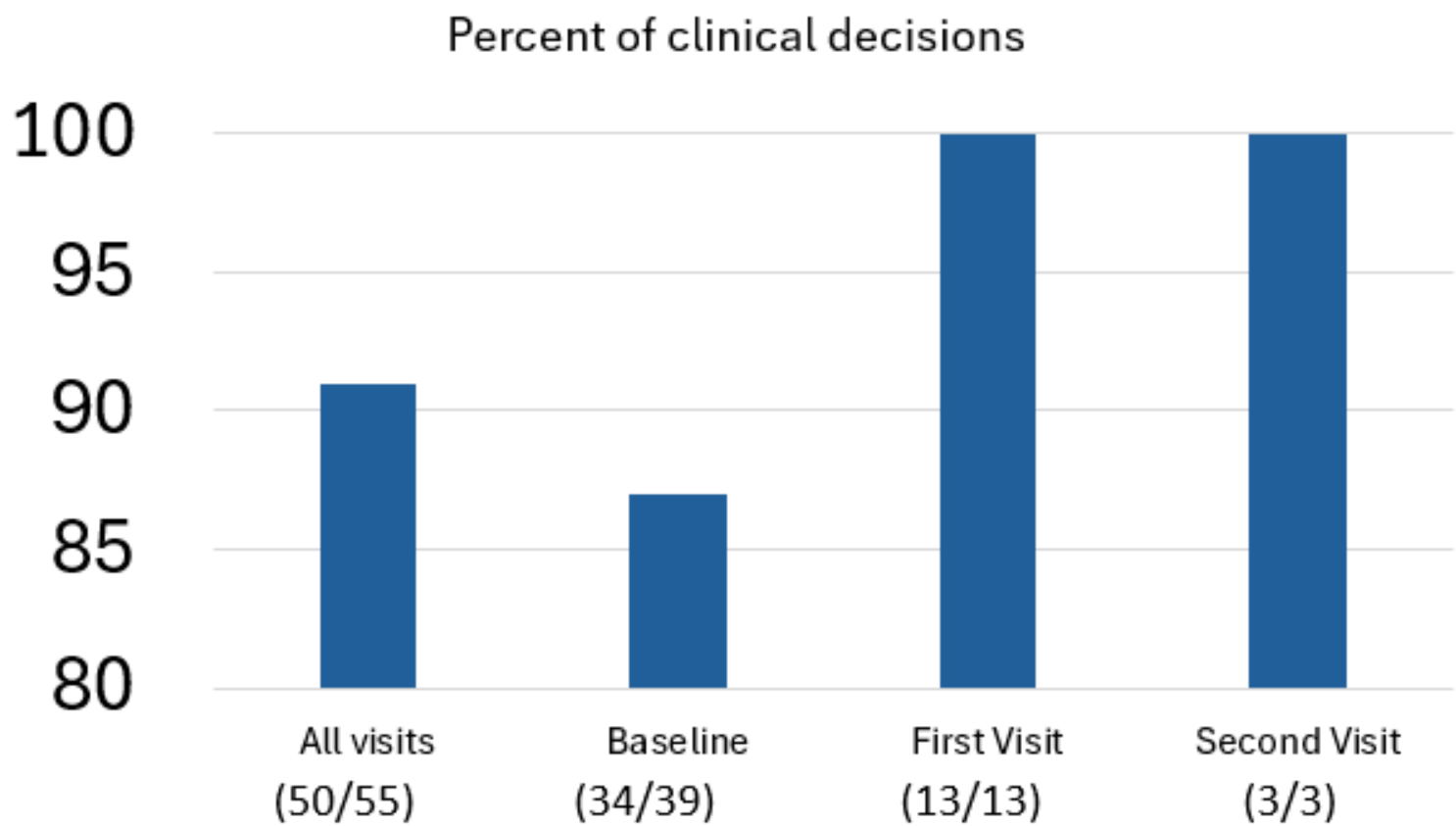
1. What is the status of the LM tumor (No Change, Progression, Resolution)
2. Did CNSide contribute to this assessment? (yes, no)
3. Did CNSide inform the specific drug selected for treatment? (yes, no)

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 patients (N=21 breast cancer, N=18 NSCLC)

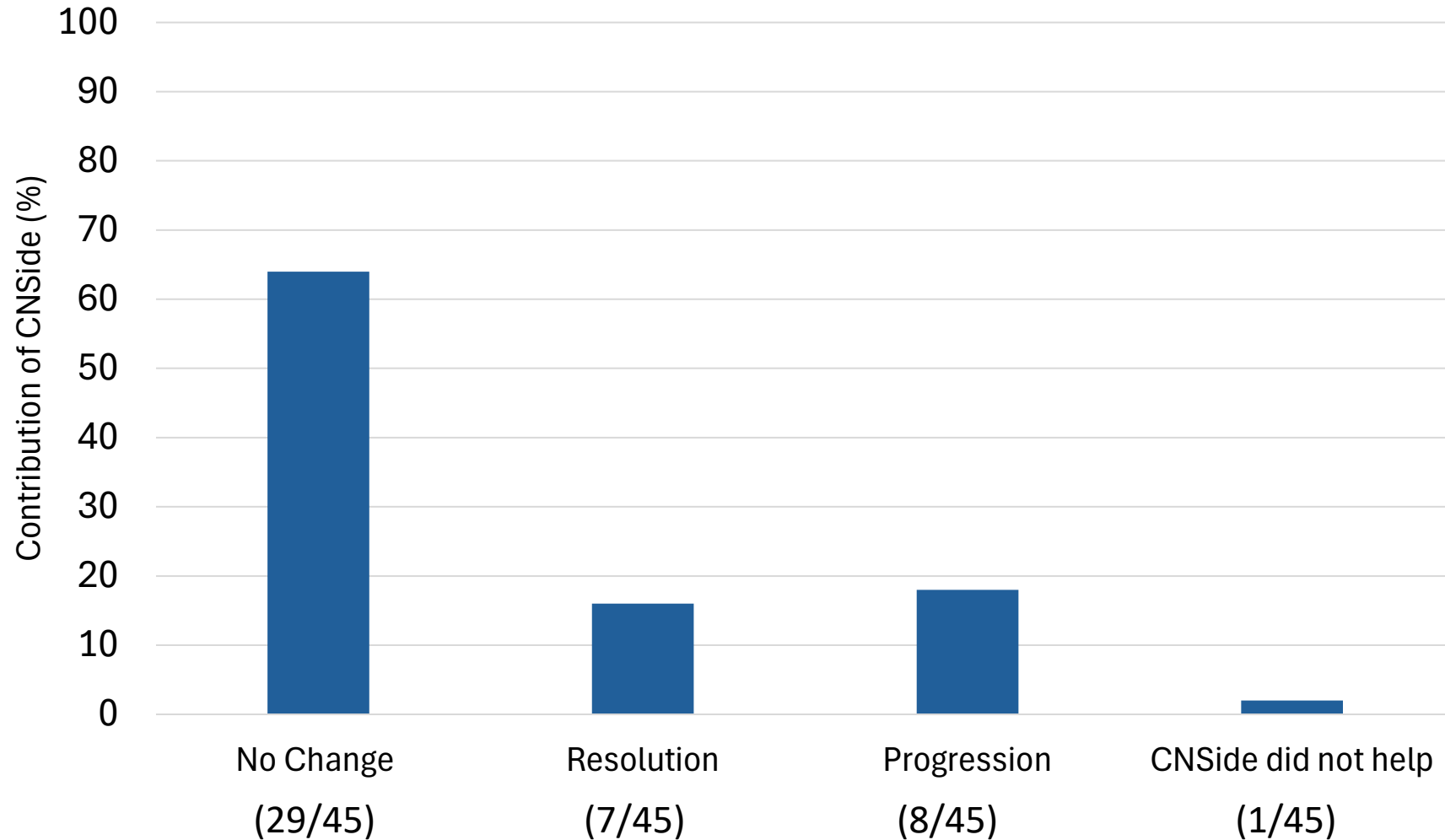
Take Home #1: CNSide helped make clinical decisions in LMD patients



Take Home #2: CNSide helped to diagnose LMD

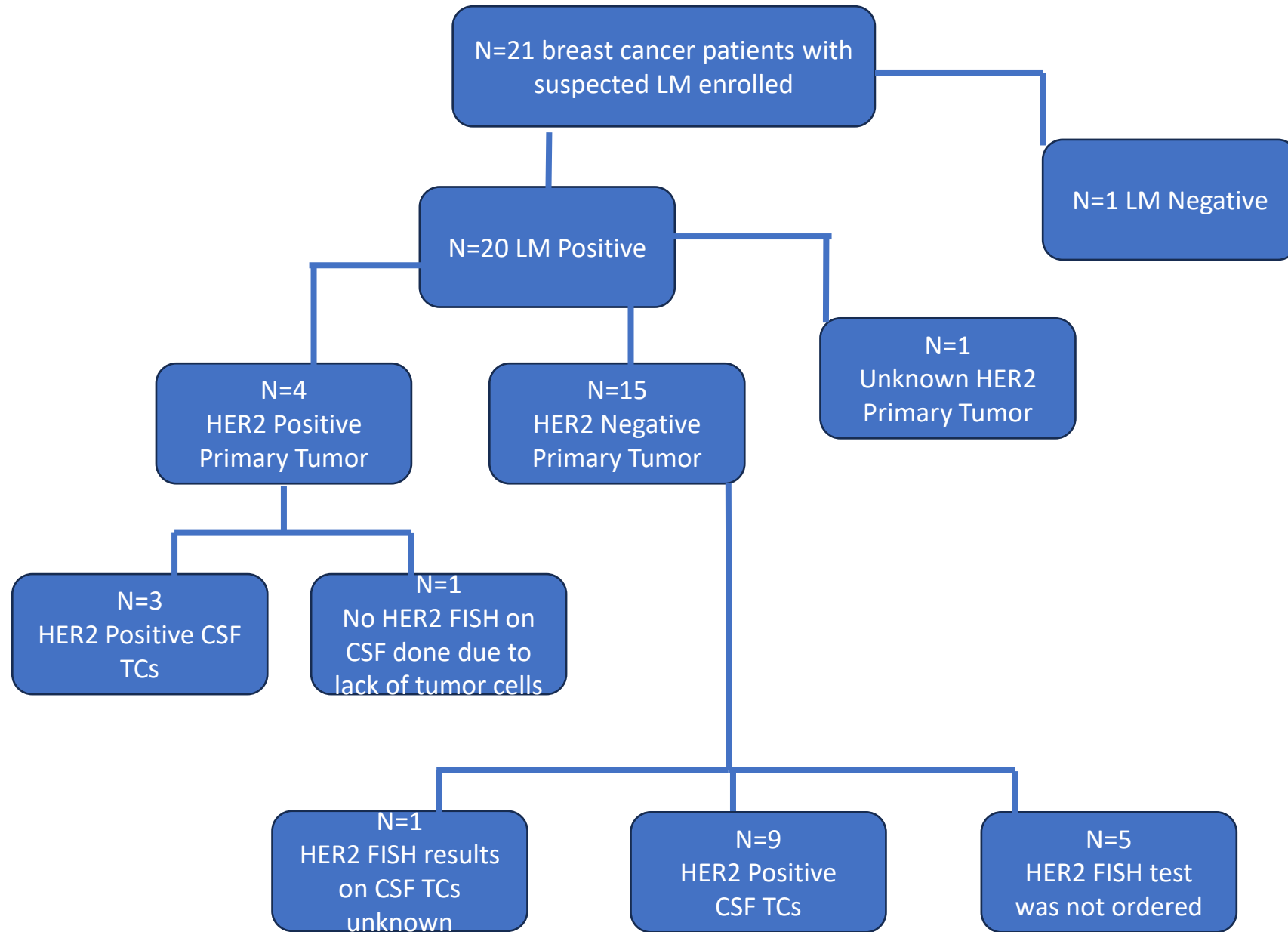
- N=10 patients not diagnosed with LMD prior to trial enrollment
 - These patients were deemed LMD positive or negative after the Baseline visit based on Investigator assessment
- LMD Positive Patients (N=7)
 - Cytology Positive, CNSide Positive: N=2
 - Cytology Negative, CNSide Positive: N=5
- LMD Negative 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)*

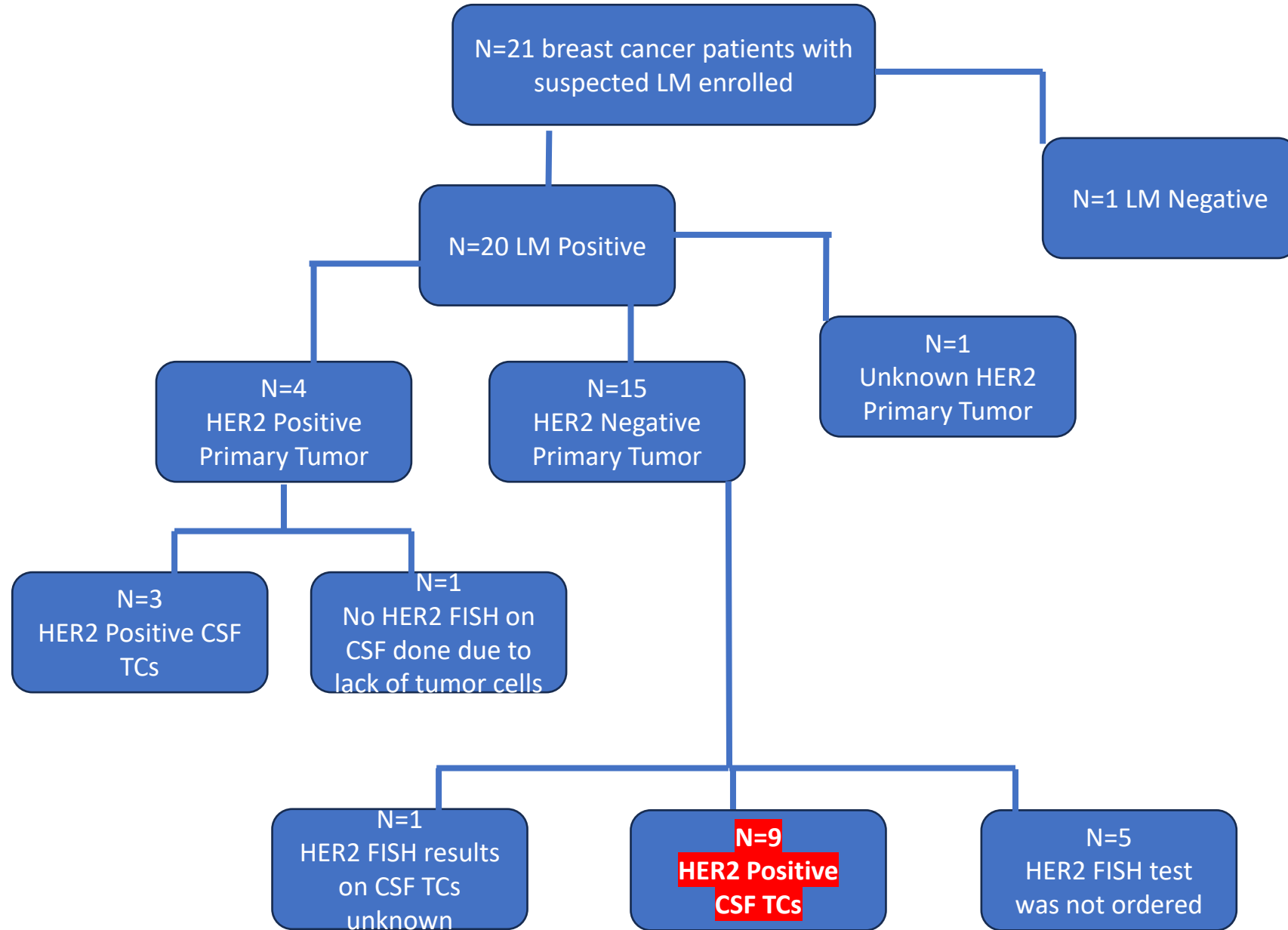


*N=35 pts

Primary vs LM HER status: ('HER2 Flip')



Primary vs LM HER status: ('HER2 Flip')



Conclusions and Next Steps

Preliminary 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)

Next steps

- Working with the sites to obtain mature data to be presented/published in near future

Acknowledgements

- All patients who were enrolled in FORESEE trial
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Appendix

Improved sensitivity of tumor cell detection in LMD patients*with CNSide vs cytology** in matched samples

Cytology		LMD Status		
		Positive	Negative	Total
Cytology (positive or negative)	Positive	13	0	13
	Negative	27	3	30
	Total	40	3	43

Cytology

- Sensitivity: 33%
- Specificity: 100%
- PPV: 100%
- NPV: 10%

CNSide		LMD Status		
		Positive	Negative	Total
CNSide (positive or negative)	Positive	31	0	31
	Negative	9	3	12
	Total	40	3	43

CNSide

- Sensitivity: 78%
- Specificity: 100%
- PPV: 100%
- NPV: 25%

*LMD based on investigator assessment

** Only cytology Positive and Negative results included

Improved tumor cell detection in LMD patients* of CNSide compared to Cytology** in matched samples (N=45)

CNSide

- Detected cells in 80% (36/45) samples of LMD Positive Patients (N=36)
- Did not detect cells in LMD Negative Patients (N=3)

Cytology

- Detected cells in 29% (13/45) samples of LMD Positive Patients (N=36)
- Detected Atypical or Suspicious cells in (4/45) samples of LMD Positive Patients
- Did not detect cells in LMD Negative Patients (N=3)

*LMD based on investigator assessment

**Cytology Atypical and Suspicious for Malignant cells included

Take Home #4: CNSide identified mutations used to make a specific drug selection

