Understanding CNS Cancer Differently:

Advancing Precision Diagnosis, Treatment, & Research



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CNSide™

REYOBIQ™ rhenium re 186 obisbemeda injection

The Society for Neuro-Oncology has reviewed and approved this symposium as appropriate for presentation as an Independent Supported Symposium. The symposium constitutes the content and views of the sponsor and is not part of the official SNO Annual Meeting program.

LM Patient Management & A Case-Based Perspective

(the UT Southwestern Experience)

Michael Youssef, MD
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Leptomeningeal disease

- Typically comes to concern with clinical symptoms, such as headaches, focal cranial nerve deficits that may mimic stroke, incontinence, back pain
- Workup typically includes MRI of the brain and/or spine, focused where disease is discovered and symptoms are localizing
- Lumbar puncture remains gold standard for diagnosis, with CSF sampling for standard tests as well as cytology
- Cytology has limited sensitivity
- Need test to diagnose patients earlier, before severe symptoms develop due to increased disease burden, which may be irreversible.

Utility of CTC-TC in patients with suspected LMD

- CNSide developed to provide earlier diagnosis of LM
- One lumbar puncture sample has a sensitivity of 75-92% sensitivity
- CNSide provides a quantitative enumeration which allows for the physician to know “how positive” the patient is, or how severe the LM is at diagnosis[4]

CNSide CSF Assay Platform

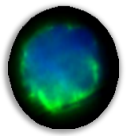
4 Testing Platforms from a Single CSF Draw

CSF Sample Collection



Accurate capture & preservation

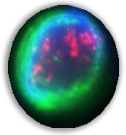
Cellular Assays



Tumor Cell Enumeration (TCE)



ICC*

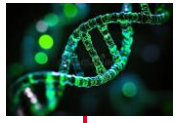


FISH*

Multiplex analysis
Detect & quantify tumor cells
Cellular biomarkers

Molecular Assays

DNA/RNA isolation



NGS Profiling



Detects ctDNA
Variant analysis
Genetic heterogeneity

Patient Testing Cycle

Cancer Patient Presents Signs & Symptoms Suggestive of LM

Tests Performed & Info Gathered
- SoC & CNSide® TCE+ICC+NGS
- Tumor cell count & biomarker detection

Clinical Decision Making
- Diagnosis (LM: + or –) based on TCE
- LM treatment based on ICC, NGS

LM Patient Follow-Up Visit

Tests Performed & Info Gathered
- SoC & CNSide® TCE+ICC
- Tumor cell count & biomarker detection

Clinical Decision Making
- LM treatment based on TCE, ICC
- Continue/Discontinue LM therapy
- Use different LM therapy/monitoring

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Testing conducted in centralized CLIA and CAP accredited lab, Houston TX

* Not commercially available

Slide provided by Cerenome

Clinical Evidence: How does CNSide perform?

Higher diagnostic yield than SoC — validated by growing peer-reviewed evidence base

Diagnostic Performance vs. Standard of Care

MRI Imaging

Sensitivity: 75%

Specificity: 77%

Imaging alone — no molecular or cellular data

CSF Cytology

Sensitivity: 50%

Specificity: 95%

Current SoC — misses ~50% of true LM cases

CNSide TCE

Sensitivity: 92%

Specificity: 95%

Quantitative tumor cells · diagnosis + longitudinal monitoring

+40% yield vs. cytology

Growing Peer-Reviewed Evidence Base

Appel et al., Neuro-Oncology Advances (2024)

Comparative evaluation showed CNSide identified all cytology-positive cases and detected additional cases beyond cytology, supporting higher diagnostic yield

Sweed et al., Arch Pathol Lab Med (2025)

Published validation reported high analytical performance and supports CNSide as a standardized CLIA-based CSF testing approach

Onoichenco et al., Neuro-Oncology Advances (2026)

CSF CTC quantification plus genomics supports the strategic case for richer molecular profiling and clinical decision support

Higher diagnostic yield than SoC + growing peer-reviewed evidence base = **clinically validated CSF oncology platform**

12+ publications & abstracts *supporting diagnostic yield, analytical validity, prognostic value, and molecular utility*

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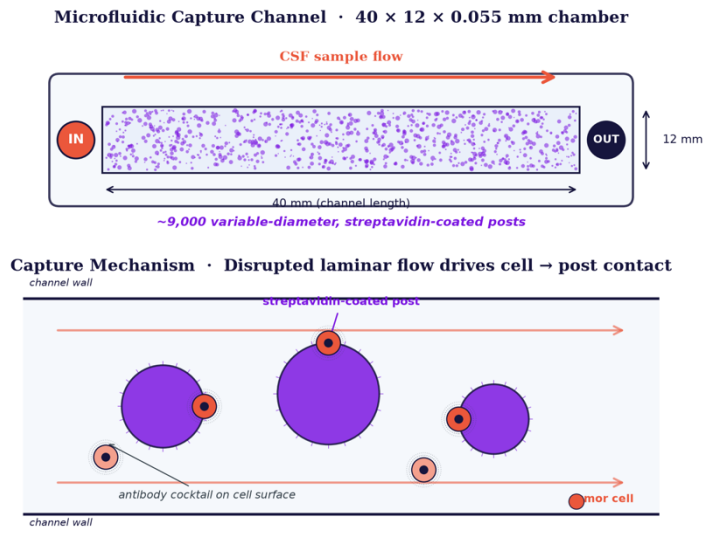
Slide courtesy of Cerenome

How CNSide Captures Tumor Cells

The microfluidic capture channel · antibody-cocktail chemistry · in-channel enumeration

1 · CHIP ANATOMY

Microfluidic capture channel



- 40 × 12 × 0.055 mm rectangular chamber
- ~9,000 variable-diameter posts, randomly placed
- Posts disrupt laminar flow → maximize cell-post contact
- Transparent for direct in-channel microscopy

2 · CAPTURE CHEMISTRY

10-antibody cocktail

Epithelial surface antigens

EpCAM · HER2 · MUC1 · EGFR · TROP-2 · Folate-BP

Mesenchymal / stem-cell antigens

c-MET · N-cadherin · CD318 · MSC antigen

Antibody cocktail is added directly to CSF cells → biotinylated antibodies bind tumor-cell surface antigens → streptavidin-coated posts capture the antibody-cell complex. Captures CK-positive AND CK-negative (post-EMT) tumor cells that EpCAM-only platforms miss.

3 · ENUMERATION & DETECTION

In-channel immunofluorescence

Tumor-cell signature

CK^+ / $CD45^-$ / $DAPI^+$

Detection markers

Cytokeratin (CK)	*Epithelial tumor cells*
CD45	*Excludes leukocytes*
DAPI	*Nuclear stain*
FISH (in-channel)	*Confirms CK^- CTCs; HER2, aneuploidy*

Captures BOTH CK^+ and CK^- tumor cells

Post-EMT (CK^-) cells are missed by EpCAM-only platforms — critical for accurate LM detection.

>80% capture across cell types

10-antibody cocktail vs. <10% EpCAM-alone on non-epithelial (T24) — 8× improvement, p = 0.0001.

In-channel FISH & staining

Sequential staining and FISH performed within the microchannel — no cell-transfer loss.

Source: Pecot CV et al., Cancer Discov 2011;1(7):580–586 · Biocept Target Selector™ / CEE™ microchannel (CNSide predecessor platform).

Slide courtesy of Cerenome

The UTSW experience

- 97 Unique patients
- Diagnosis include: Breast, Lung, GI, H/N, Melanoma, GU cancers, and miscellaneous others
- Test dates: 12/1/2020- 7/14/2023
- Total of 347 samples were obtained and sent
  - **Ommaya Reservoir: 186** (53.6%)—serial monitoring
  - **Lumbar Puncture: 92** (26.5%)—initial and repeat testing in patients not on IT chemotherapy
  - **Unspecified / Missing (NaN): 69** (19.9%)

Patient population

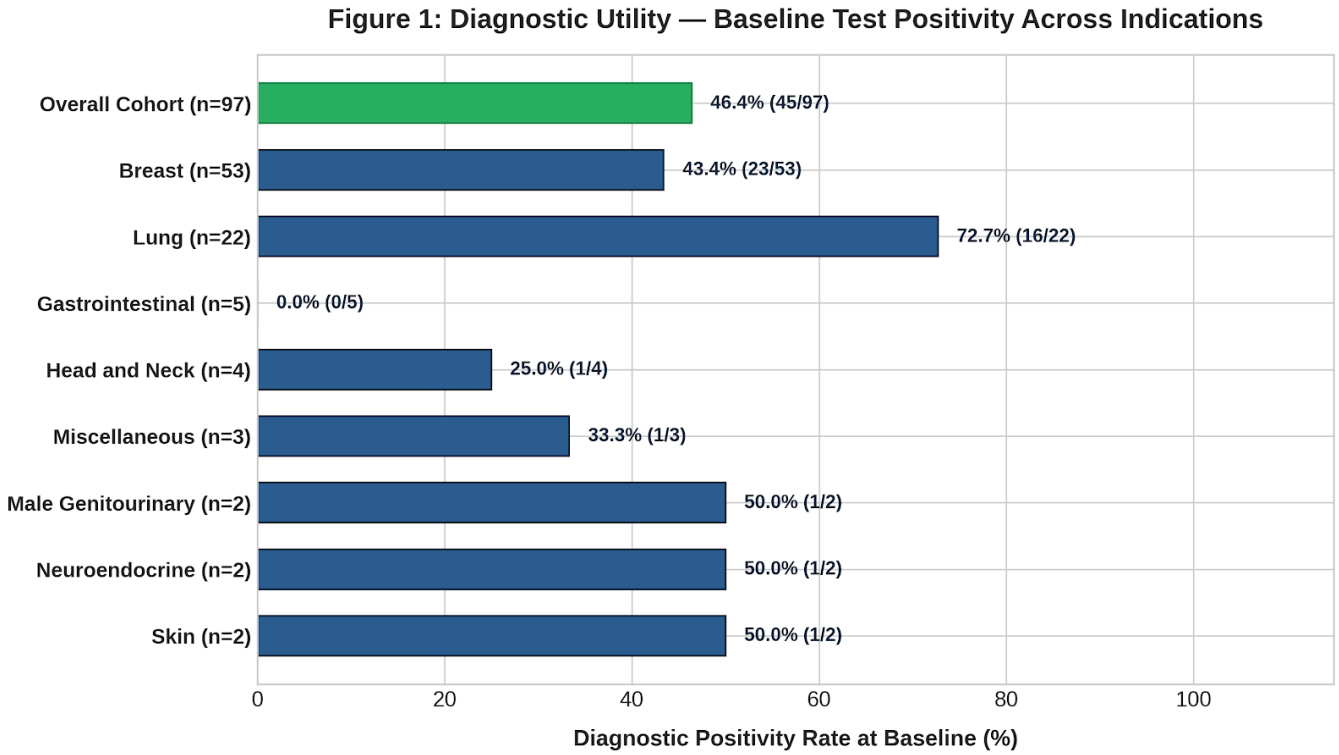
- 97 unique patients
- Age: 27-99
- 28 men, 69 women
  - –Skew towards women due to majority diagnosis being Breast cancer
- 46 patients exclusively negative, 60 patients with AT LEAST one negative
- 50 patients with a positive result
  - –Range of positive: 1 CTC to 131,485 CTCs

Diagnostic Utility

Figure 1: Diagnostic Utility — Baseline Test Positivity Across Indications

Key Highlights:

- **Overall Cohort Baseline Positivity: 46.4%** (45 / 97 unique patients positive at Draw 1)
- **Lung Cancer Positivity: 72.7%** (16 / 22 positive at Draw 1)
- **Breast Cancer Positivity: 43.4%** (23 / 53 positive at Draw 1)



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HER2

- CNSide was able to use FISH technology to detect HER2 mutation in samples
- 23 unique patients tested positive for HER2 FISH
  - 6 experienced the “HER2 Flip”, with samples showing a change from positive to negative, based on treatment

Detailed Breakdown of HER2 Conversions

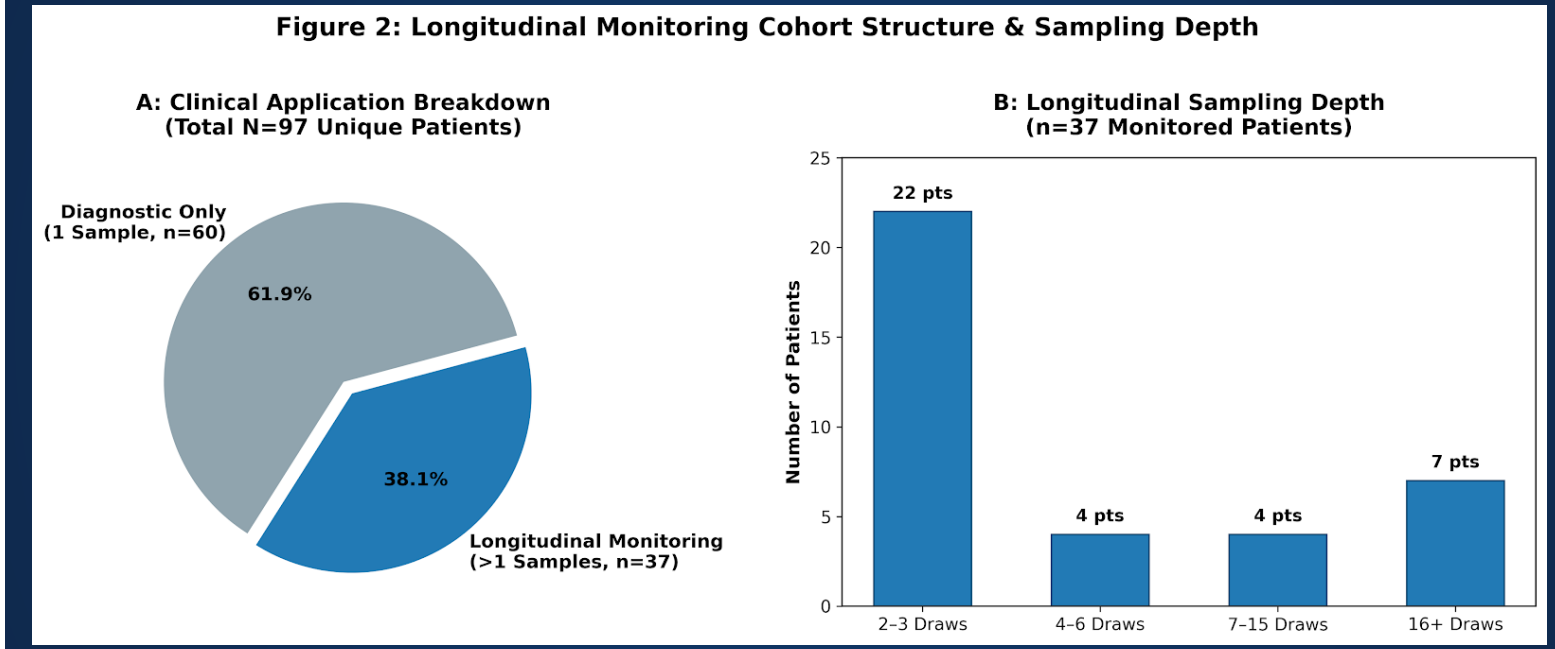
Initials	Primary Diagnosis	HER2 Transition Sequence	Conversion Type
BM	Breast Cancer	Draw 1–2: Not Detected → Draw 3: Detected	Negative to Positive
MP	Breast Cancer	Draw 1: Not Detected → Draw 2: Detected	Negative to Positive
MC	Breast Cancer	Draw 1: Not Detected → Draw 2: Detected	Negative to Positive
KD	Breast Cancer	Draw 1: Detected → Draw 2: Not Detected	Positive to Negative
IV	Breast Cancer	Toggled: Draw 1 Detected → Draw 2 Not Detected → Draw 3–5 Detected → Draw 6–22 Not Detected → Draw 23 Detected → Draw 24+ Not Detected	Both (Fluctuated)
JE	Breast Cancer	Draw 1 Detected → Draws 2–20 Not Detected → Draw 21 Detected → Draws 22+ Not Detected	Both (Fluctuated)

Treatment monitoring

- Testing for CTCs provides a quantitative method for treatment monitoring
- Notably CTCs will rise prior to changes on imaging or changes in cytology, indicating a change in therapy is warranted

Figure 2: Longitudinal Monitoring Cohort Structure & Sampling Depth

- *Demonstrates the dual utilization of the test for single diagnostic checks vs. serial monitoring.*
- **38.1% of Patients (*n*=37)** underwent serial longitudinal monitoring (>1 draw).
- **Deep Serial Tracking: 11** of these monitored patients underwent ≥7**sequential samples** (4 patients with 7–15 draws and 7patients with 16+draws), demonstrating strong utility for long-term clinical management.



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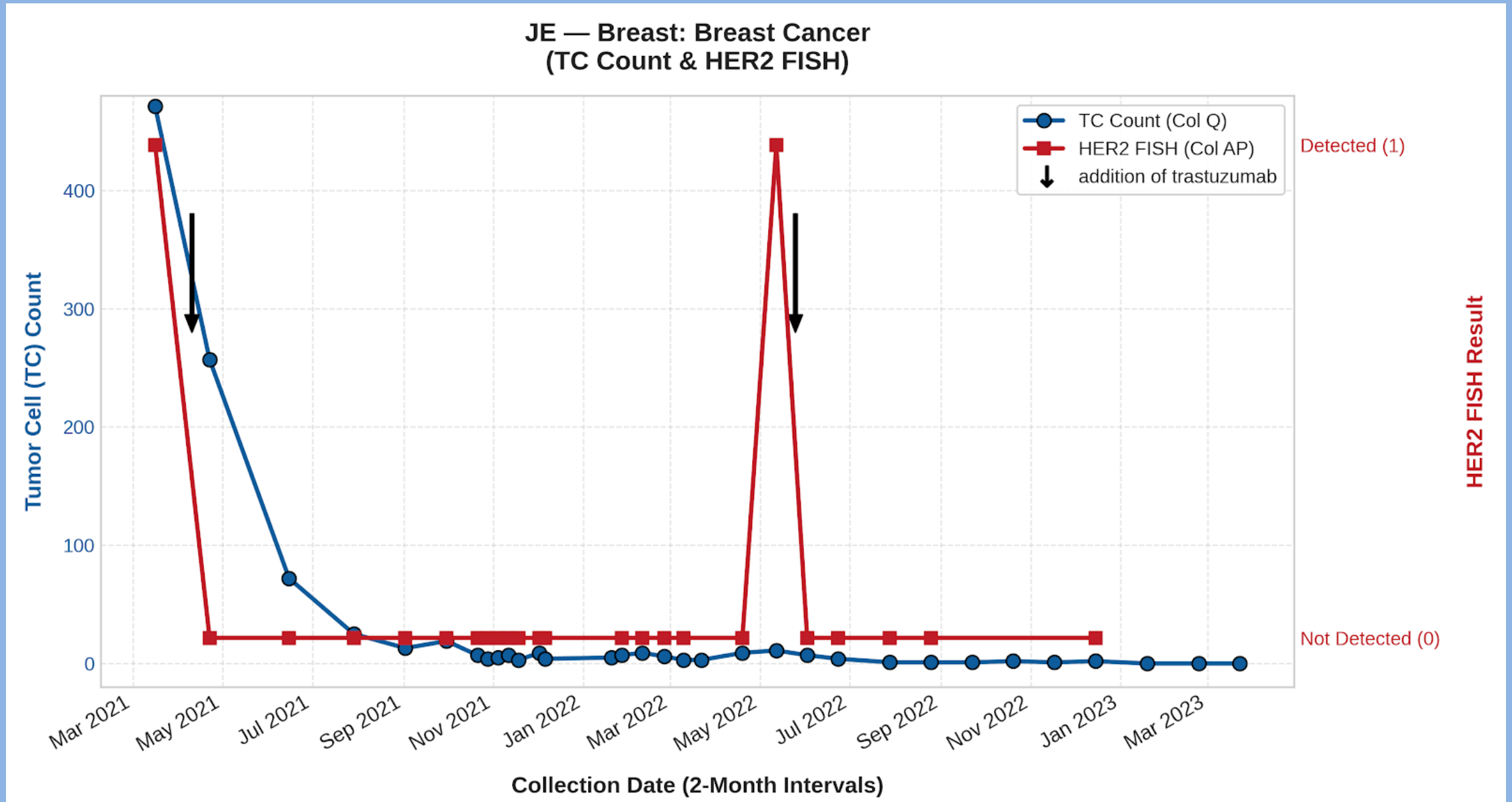
Patient Case

- Patient JE—32yo F with metastatic breast cancer, ER/PR/HER2 negative
- Diagnosed with both breast cancer and LMD in 12/2020. Received WBRT and had Ommaya reservoir placement at OSH (Northwestern)
- Presented to UTSW in 3/2021 to establish care
- Plan of care: start intrathecal chemotherapy with IT topotecan twice weekly
- Shortly after beginning IT chemotherapy, CNSide revealed HER2 mutation in CSF not seen in systemic disease. Started IT trastuzumab


JE — Breast: Breast Cancer
(TC Count & HER2 FISH)
TC Count (Col Q)
HER2 FISH (Col AP)
addition of trastuzumab
Tumor Cell (TC) Count
0
100
200
300
400
Detected (1)
Not Detected (0)
HER2 FISH Result
Mar 2021
May 2021
Jul 2021
Sep 2021
Nov 2021
Jan 2022
Mar 2022
May 2022
Jul 2022
Sep 2022
Nov 2022
Jan 2023
Mar 2023
Collection Date (2-Month Intervals)

Results by draw

Notable results:

- Initially with high CTC count prior to therapy
- Addition of trastuzumab resulted in dramatic decrease in CTC
- Cessation of trastuzumab resulted in elevated CTCs (5/2022)
- Patient is currently on IT topotecan and trastuzumab once monthly with NED systemically

Collection Date	Draw #	CTC Count (TC Count)	HER2 FISH Result
2021-03-16	1	471	DETECTED
2021-04-22	2	257	NOT DETECTED
2021-06-15	3	72	NOT DETECTED
2021-07-29	4	25	NOT DETECTED
2021-09-02	5	13	NOT DETECTED
2021-09-30	6	19	NOT DETECTED
2021-10-21--2022-03-22	7-19	Single digits (avg 4)	NOT DETECTED
2022-04-19	20	9	NOT DETECTED
2022-05-12	**21**	**11**	**DETECTED**
2022-06-02	22	7	NOT DETECTED
2022-06-23	23	4	NOT DETECTED
2022-07-28	24	1	NOT DETECTED
2022-08-25	25	1	NOT DETECTED
2022-09-22	26	1	Result could not be determined 1
2022-10-20	27	2	Result could not be determined 1
2022-11-17	28	1	Result could not be determined 1
2022-12-15	29	2	NOT DETECTED
2023-01-19	30	0	Result could not be determined 1
2023-02-23	31	0	Result could not be determined 1
2023-03-23	32	0	Result could not be determined 1

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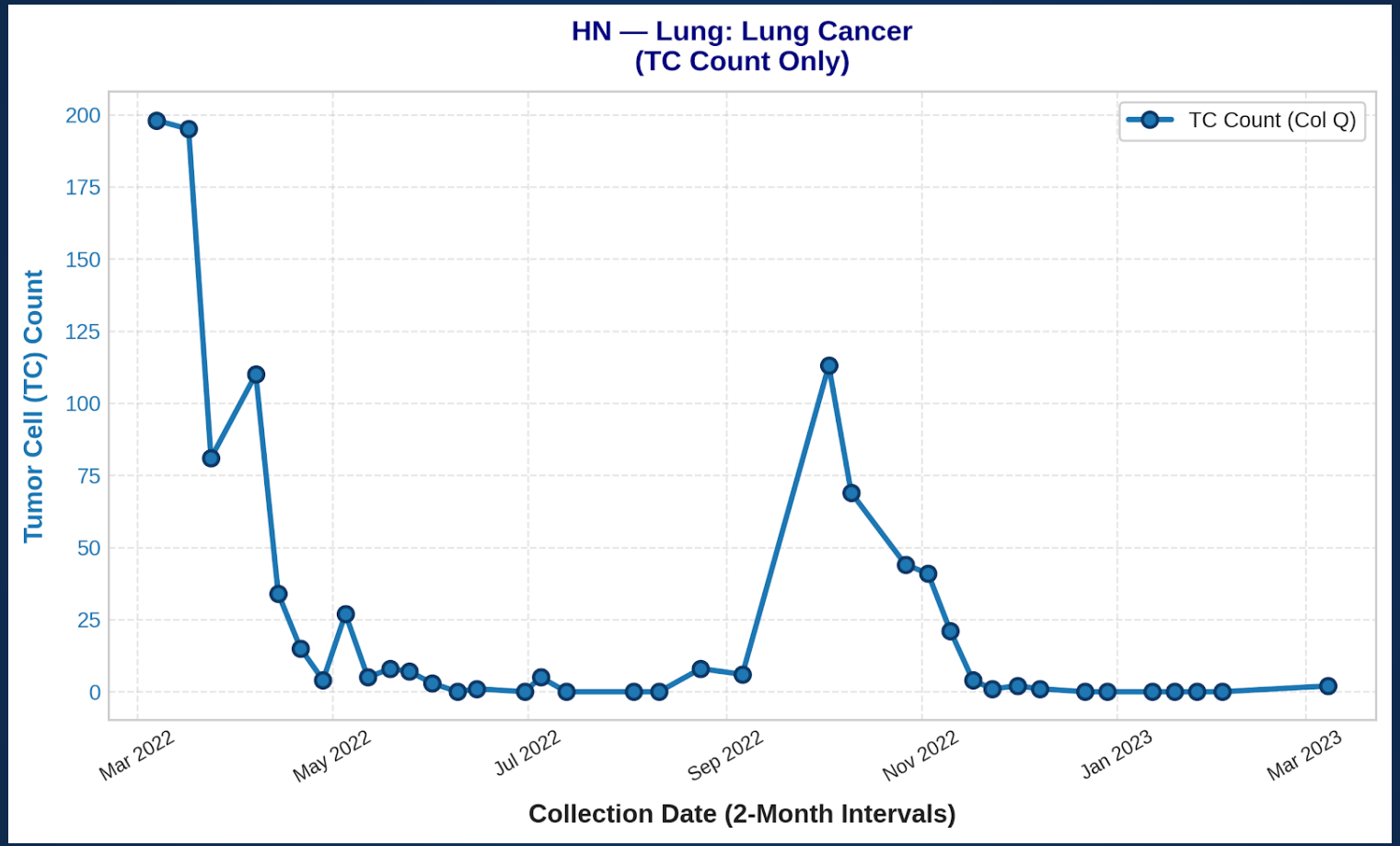
Patient Case

- Patient HN—48yo M w/ lung cancer (NSCLC). Treated with osimertinib but developed LMD
  - First CNSide test NGS showed: ALK (L1196M); ALK (F1174V); EGFR (T790M); MET (CNV) DETECTED
- Patient at time of dx was on osimirtinib 160mg daily for brain metastasis
- Started on IT topotecan and systemic lorlatinib

Patient HN

Notable events:

- Started IT chemotherapy in 3/2022
- Started Lortatinib in 4/2022
- Developed Brain abscess and all therapies held from 9/2022-10/2022
- Lorlatinib restarted 10/22 and IT chemotherapy restarted 11/22
- Pt expired due to progression of disease in 6/2024



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Experience post-CNSide

- CNSide became unavailable in 7/2023
- With CNSide:
  - Patients were diagnosed earlier
  - CSF was able to be cleared
  - Several patients with >2-year survival (3 currently still alive and dx in 2021)
- Post CNSide:
  - Fewer patients with LMD diagnosed and started on treatment
  - Unknown if CSF cleared (some patients cytology NEVER positive and they were diagnosed via imaging and clinical symptoms alone)
  - Currently no patients dx from 8/2023-12/2025 still alive

Conclusion

- Use of CTC testing allows for:
  - –Earlier diagnosis of LMD when cytology may be negative
  - –Therapeutic drug monitoring for rapid monitoring and treatment changes when necessary
  - –Quantitative marker of disease and response to therapy.

- CTC enumeration represents a crucial role in the diagnosis and management of LMD

2026 SOCIETY FOR NEURO-ONCOLOGY ANNUAL MEETING

Intraventricular rhenium-186 obisbemeda for leptomeningeal metastases

The ReSPECT-LM and ReSPECT-LMM studies

Single-dose results and the multidose interim analysis

Andrew J. Brenner, MD, PhD

Mays Cancer Center at UT Health San Antonio



UT Health San Antonio

Cerenome-supported satellite symposium / Philadelphia, November 14, 2026

Disclosures and investigational use

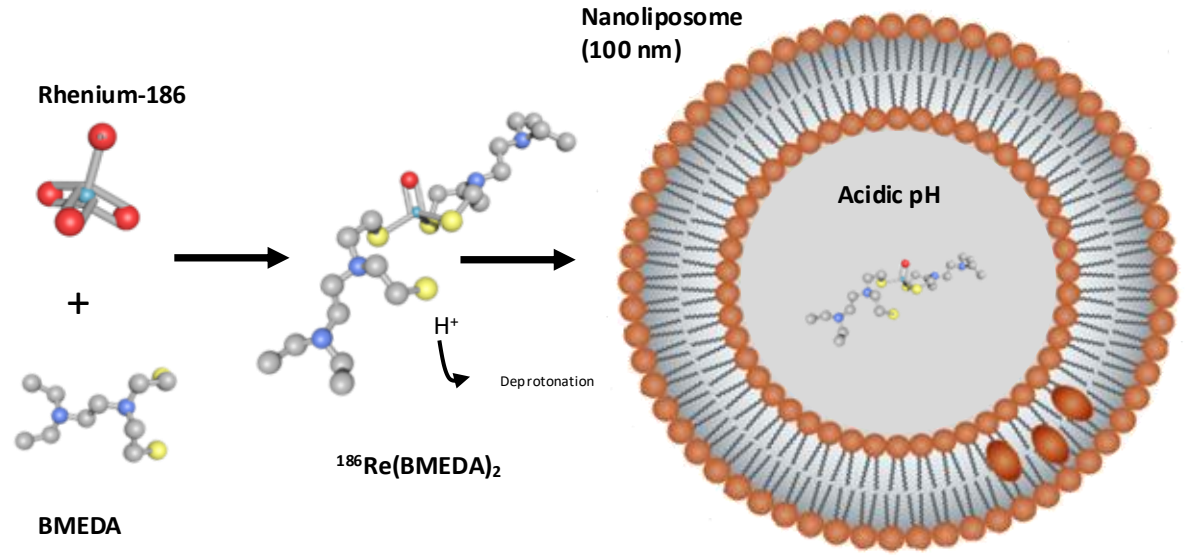
Financial relationship	Entity
Consulting and scientific leadership	Cerenome (formerly Plus Therapeutics); Gilead
Research support	Cerenome and Gilead
Speakers bureau	Pfizer
Equity interests	Cerenome and NanoTx

Rhenium-186 obisbemeda is investigational.

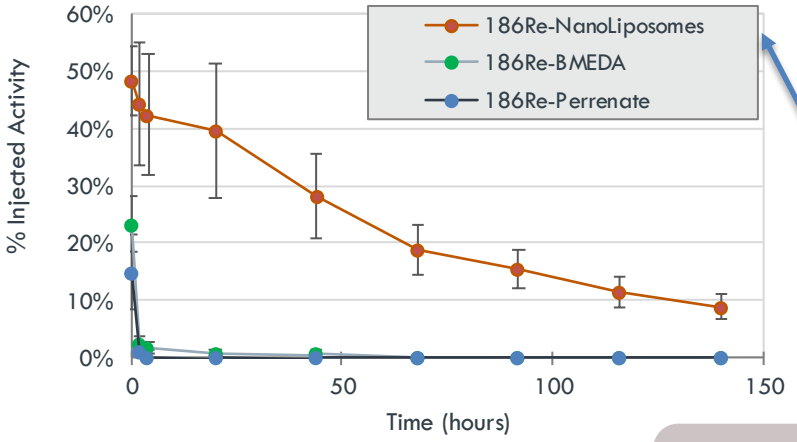
The FDA has not approved it for any indication. Cerenome supports this symposium.

Andrew J. Brenner, MD, PhD. Financial disclosures, November 2026.

Rhenium Obisbemeda (186RNL)

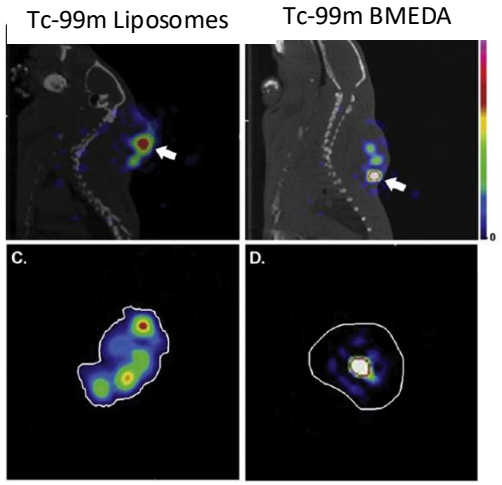


Improved Tumor Retention



Nanoliposomes improve retention and distribution of ^{186}RNL

Improved Drug Distribution



1. **Rhenium-186:** Emits tumor-destroying radiation over short distances while sparing healthy tissue
2. **BMEDA:** Small molecule that chelates to rhenium and is loaded into the nanoliposome where it's irreversibly trapped
3. **Nanoliposome:** Carries the trapped BMEDA-chelated ^{186}Re to tumor

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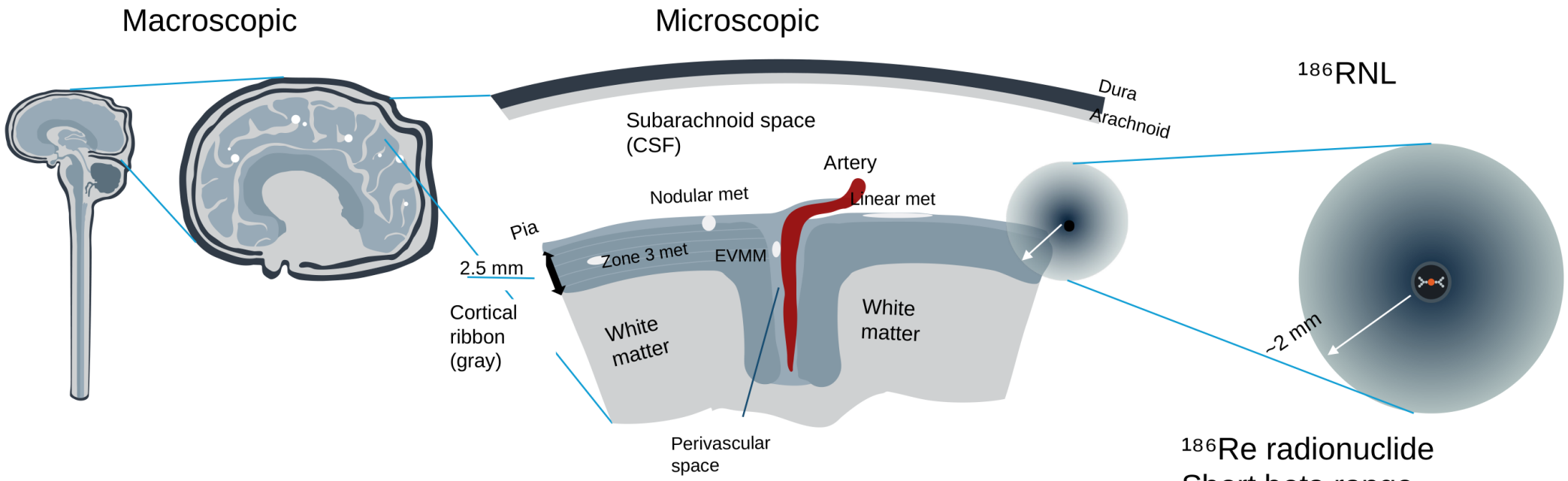
Isotope Physics Meets Disease Anatomy



CSF space

Nodular and linear metastases

Target compartment: CSF and cortical gray matter

Anatomic diagram: investigator-supplied ReSPECT-LM presentation, NMN 2025, slide 5; redrawn labels retained.

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Trial design: single administration delivery via standard Ommaya reservoir

Dose escalation: 3+3 modified Fibonacci

Primary objective: Safety and tolerability

- Maximum Tolerated Dose (MTD) / Maximum Feasible Dose (MFD) via Ommaya reservoir

Secondary objectives: Efficacy

- Overall Response Rate (ORR)
- Duration of Response (DoR)
- Progression Free Survival (PFS)
- Overall survival (OS)

Other objectives: CSF analyses and PK

- CSF circulating tumor cells (CTCs)
- Pharmacodynamic (PD) markers & dosimetry

Funding: CPRIT

Cohort	Administered Volume (mL)	Administered Activity (mCi)	Administered Concentration (mCi/mL)
1	5	6.6	1.32
2	5	13.2	2.64
3	5	26.4	5.28
4	5	44.10	8.82
5	5	66.14	13.23
6	5	75.0	15.00

➡ ***Trial completed***

Brenner AJ et al. Clin Cancer Res. 2026;32(4 Suppl):PD13-04. Dose schema: investigator-supplied single-dose dataset.

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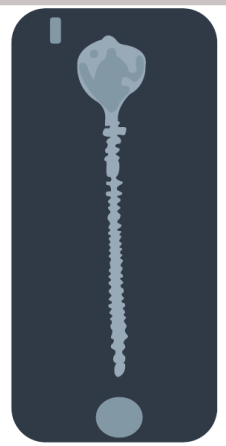
Ommaya administration and serial sampling

Treatment Planning	Drug Infusion	Patient Monitoring
Prior to Treatment	**Day 1**	**Day 2-3**
CSF flow study to confirm no flow obstruction	Single 5-minute injection in outpatient setting	Imaging and PK/PD assessments







Serial CSF and blood samples characterized local clearance and systemic exposure.

Investigator workflow, NMN 2025. Brenner et al. SNO/ASCO 2026, CLTR-06.

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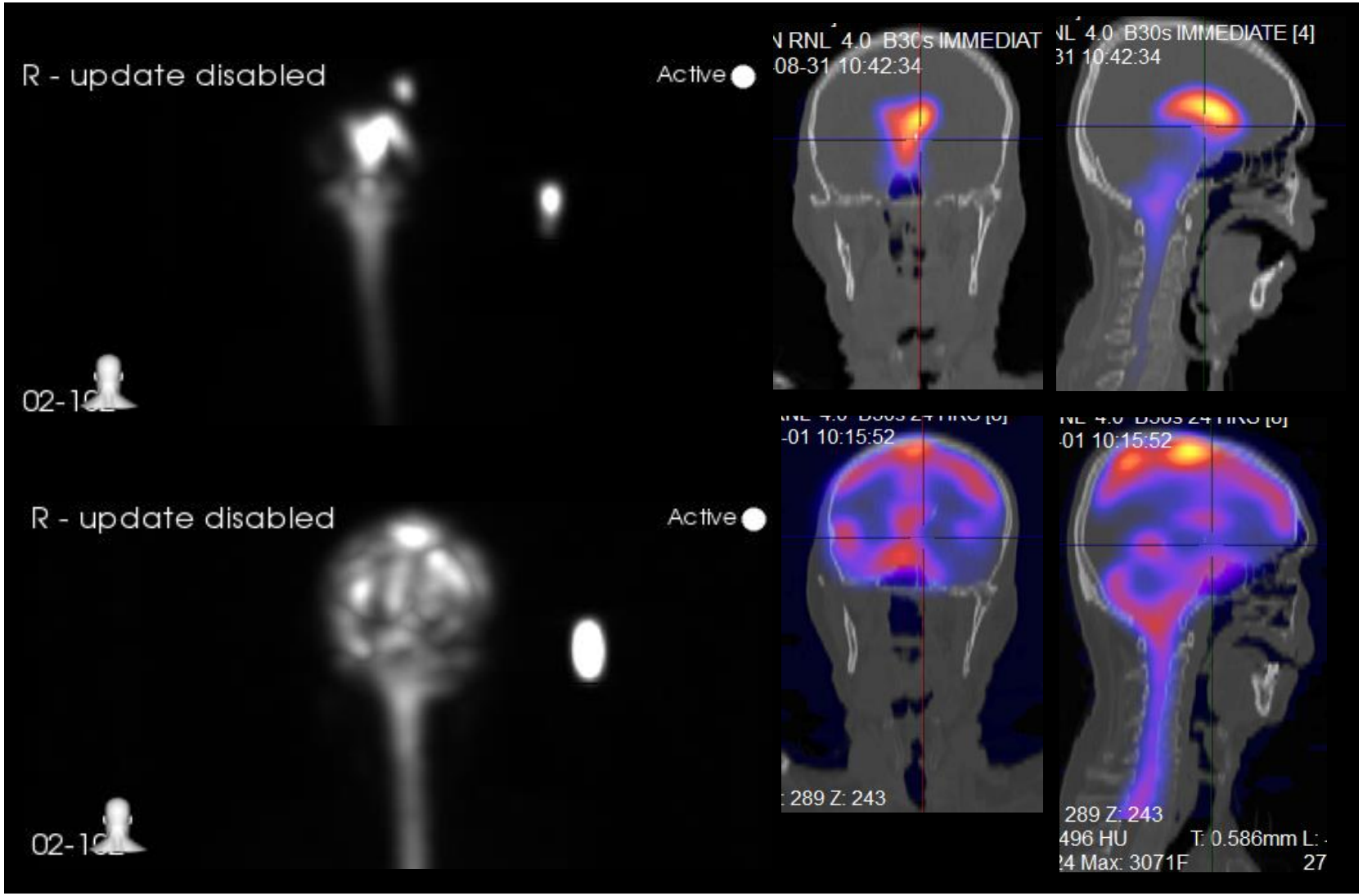
Distribution by 3D SPECT/CT Reconstruction



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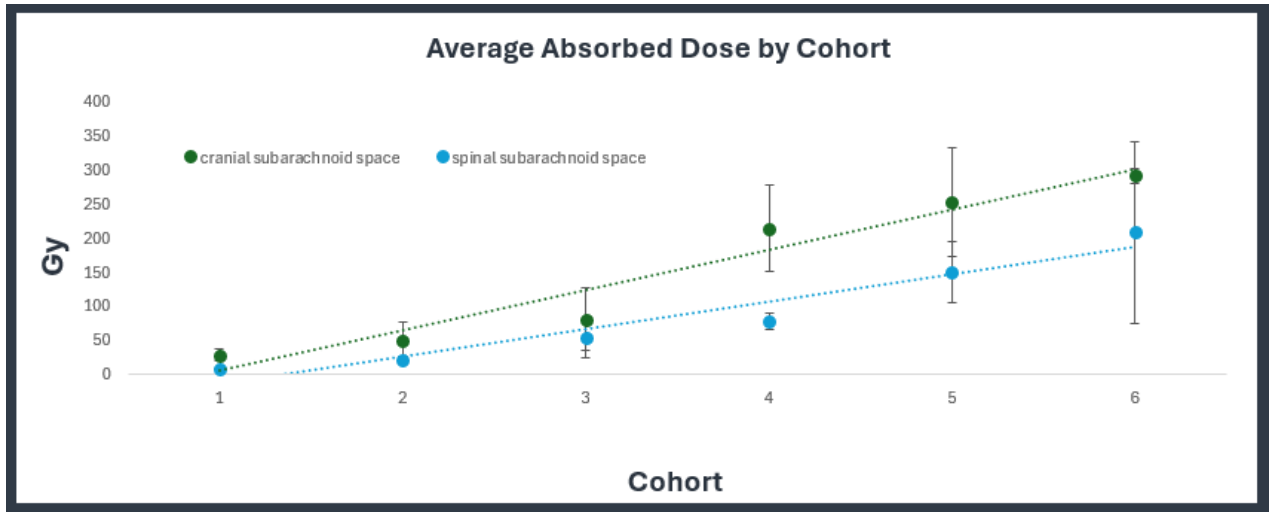
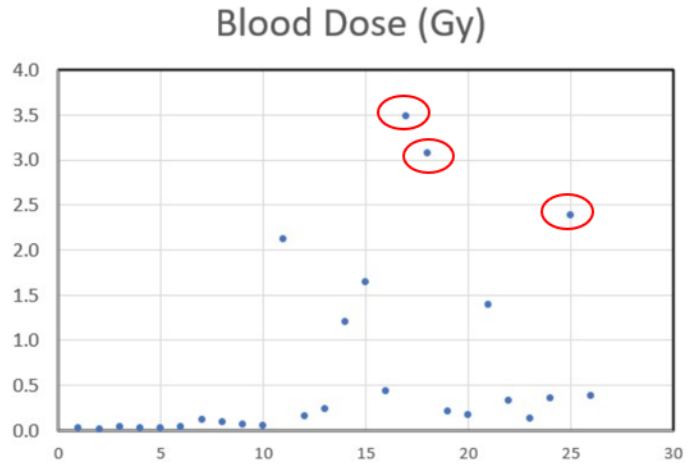
Target dose and blood redistribution explain different effects



Most patients had low blood redistribution; the higher-exposure subgroup had greater count suppression.

Blood redistribution



18 patients: <0.50 Gy
No count changes

7 patients: 1.19–3.47 Gy
Dose-dependent count decreases

Bone marrow: toxicity limit~2–5 Gy

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Cytopenias limited single-dose escalation

Activity	Patients with a DLT	Dose-limiting event
66.1 mCi	1 of 6	Grade 4 thrombocytopenia
75.0 mCi	1 of 3	Grade 4 lymphocytopenia and neutropenia

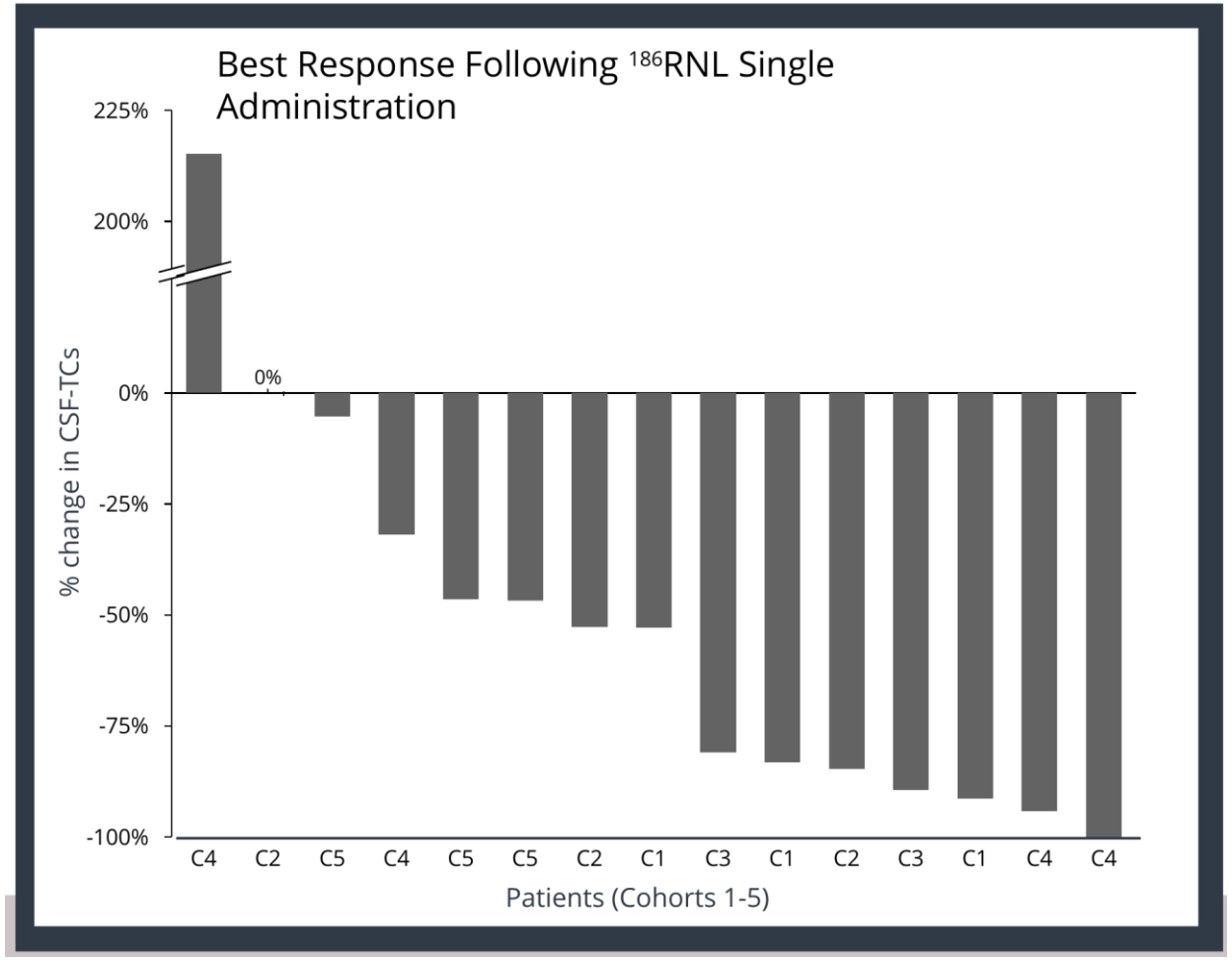
44.1 mCi

Recommended phase 2 activity for a single administration

Headache, vomiting and nausea were common. Most adverse events were grade 1 or 2.

Brenner et al. SNO/ASCO CNS Metastases Conference, 2026, CLTR-06.

CSF tumor-cell counts after a single dose



13 of 15

Patients with a decrease from baseline in CSF tumor cells

7 of 15

Patients with a best observed decline greater than 80%

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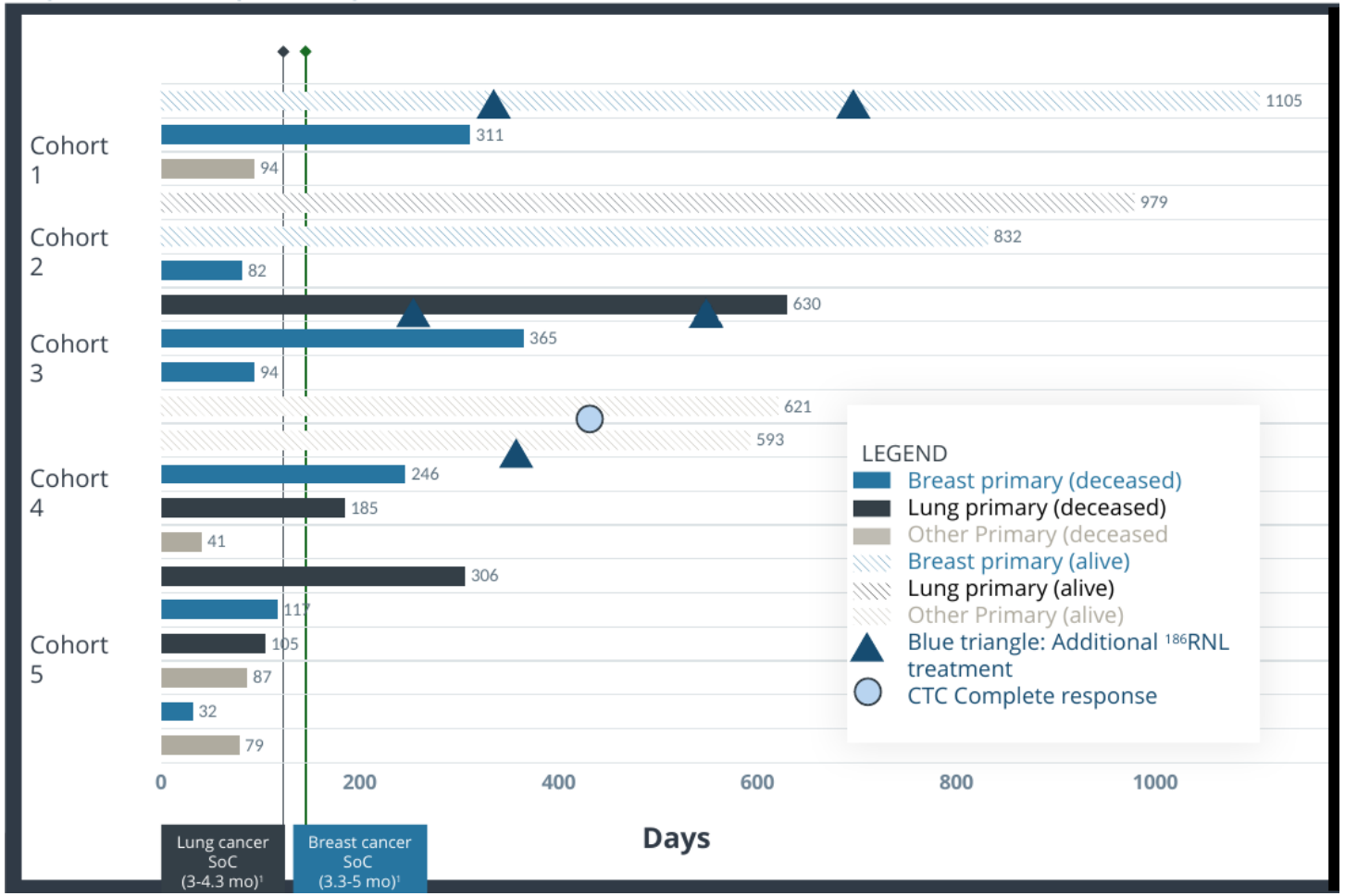
Survival after single administration



9 months

Median overall survival in cohorts 1–4 (n = 16).

The swimmer plot includes 20 patients in cohorts 1–5. Triangles mark additional administrations.

Historical survival markers come from separate populations.

Brenner AJ, NMN 2025, slides 13–14. Brenner et al. SNO/ASCO 2026, CLTR-06.

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MRI and clinical activity through day 112

Assessment	Response or improvement	Stable	Clinical benefit
MRI	5 partial responses	8	13/17 (76%)
Clinical symptoms	2 improved	11	13/15 (87%)

31%

Updated MRI objective response rate
5 of 16 evaluable patients had a CR or PR.

Clinical benefit includes stable disease. The updated MRI ORR uses a separate analysis set.

Brenner et al. Neuro-Oncol Adv. 2025, CTSI-06. Updated MRI ORR from SNO/ASCO 2026, CLTR-06.

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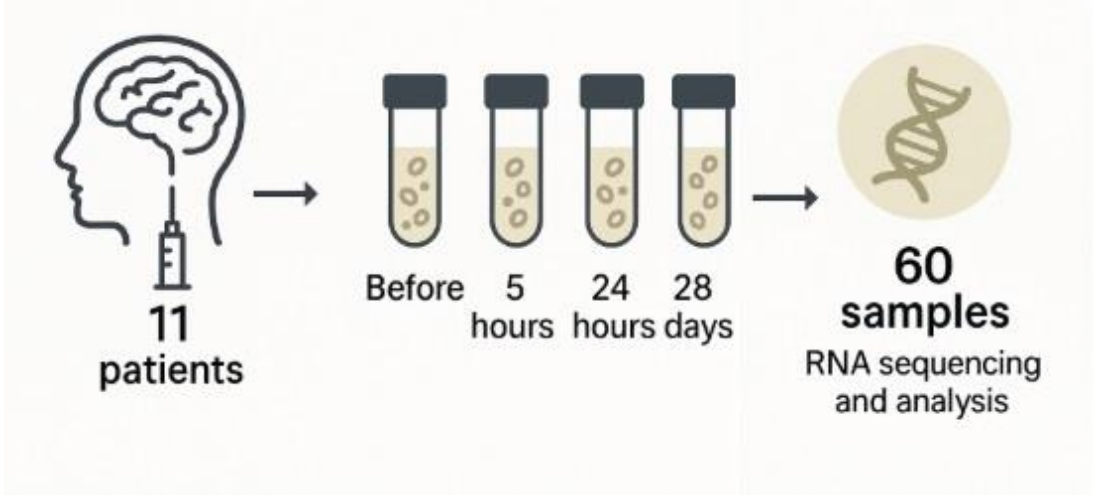
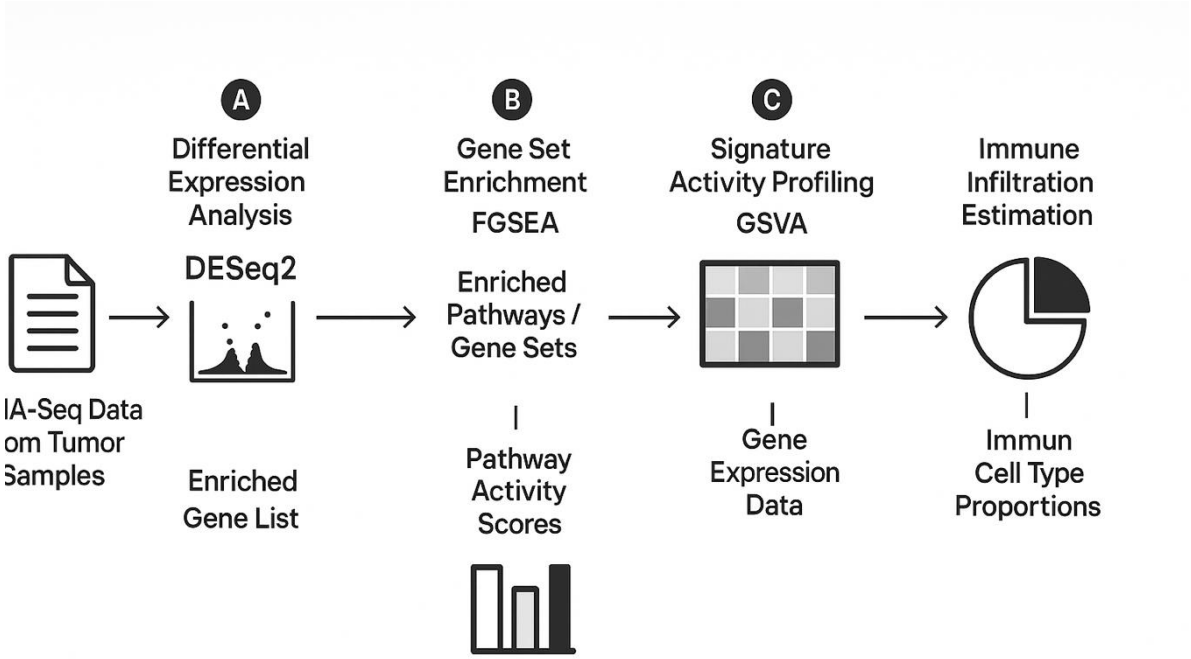
PD Assessment





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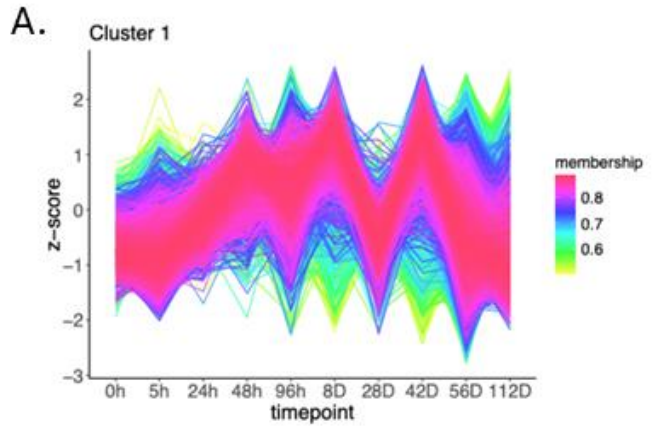
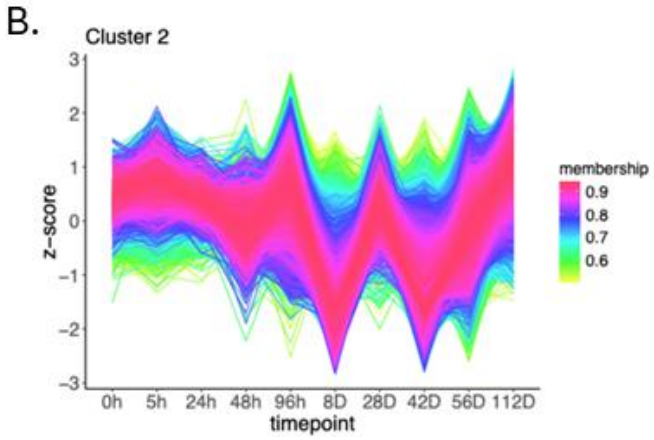
Immune and cell-cycle programs in CSF



Cluster 1 / Immune signaling

Innate immune pathways, cytokine signaling and neutrophil degranulation.



Cluster 2 / Cell cycle and DNA repair

Mitotic checkpoints, DNA replication and homology-directed repair.

Brenner laboratory, paired and longitudinal CSF RNA-seq analyses, 2025–2026. Unpublished data. Do not reproduce.

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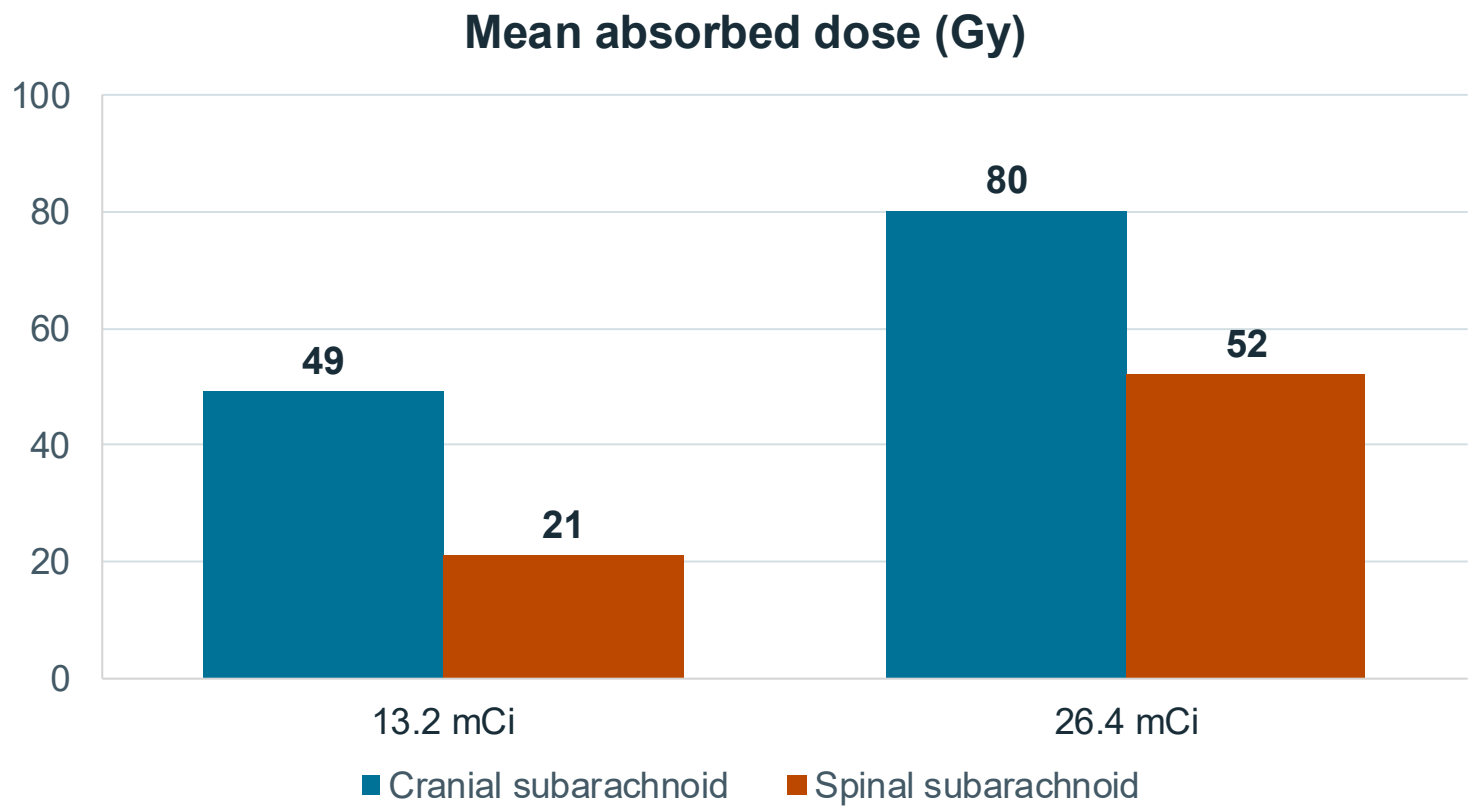
Cranial and spinal subarachnoid dosimetry



Across all single-dose cohorts

28–272 Gy

Range of cranial cohort means

7–205 Gy

Range of spinal cohort means

The chart shows the two activity levels subsequently studied with repeat administration.

Brenner et al. SNO/ASCO 2026, CLTR-06. Single-dose cohort means from the CTNI-40 investigator update.

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Compassionate use prompted a prospective study

Three participants received additional treatment

Observed with compassionate use

Treatments were approximately 8–12 months apart. Survival from first treatment ranged from 19 to at least 36 months.

Question for the next trial

Can we expand the therapeutic index with smaller administrations at defined intervals to increase cumulative exposure while limiting toxicity?

The three patients had already survived long enough to receive retreatment.

Brenner et al. SNO 2026, CTNI-40 interim presentation, slide 7, and SNO/ASCO 2026, CLTR-06.

Multidose trial design and accrual

Three planned administrations per patient, with escalation by activity and interval.

Activity per administration	Every 56 days	Every 28 days	Every 14 days
13.2 mCi	1a (n = 4)	1b (n = 2)	1c (planned)
26.4 mCi	2a (n = 4)	2b (planned)	2c (planned)
44.1 mCi	3a (planned)	3b (planned)	No planned cohort

Eligible patients had solid-tumor LM (EANO–ESMO type I or IIA–C) and KPS ≥70.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

The first 10 patients

Primary cancers

Primary tumor	Patients
Melanoma	4
Breast	3
Non-small cell lung	1
Ovarian	1
Neuroendocrine	1

Clinical characteristics

Median age and performance status

58.5 years (range 40–74)
KPS 90 (range 80–100)

Previous LM treatment

9 of 10 had received LM-directed therapy.

Concurrent treatment

3 of 10 received systemic anticancer therapy.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

Six patients completed all three protocol doses

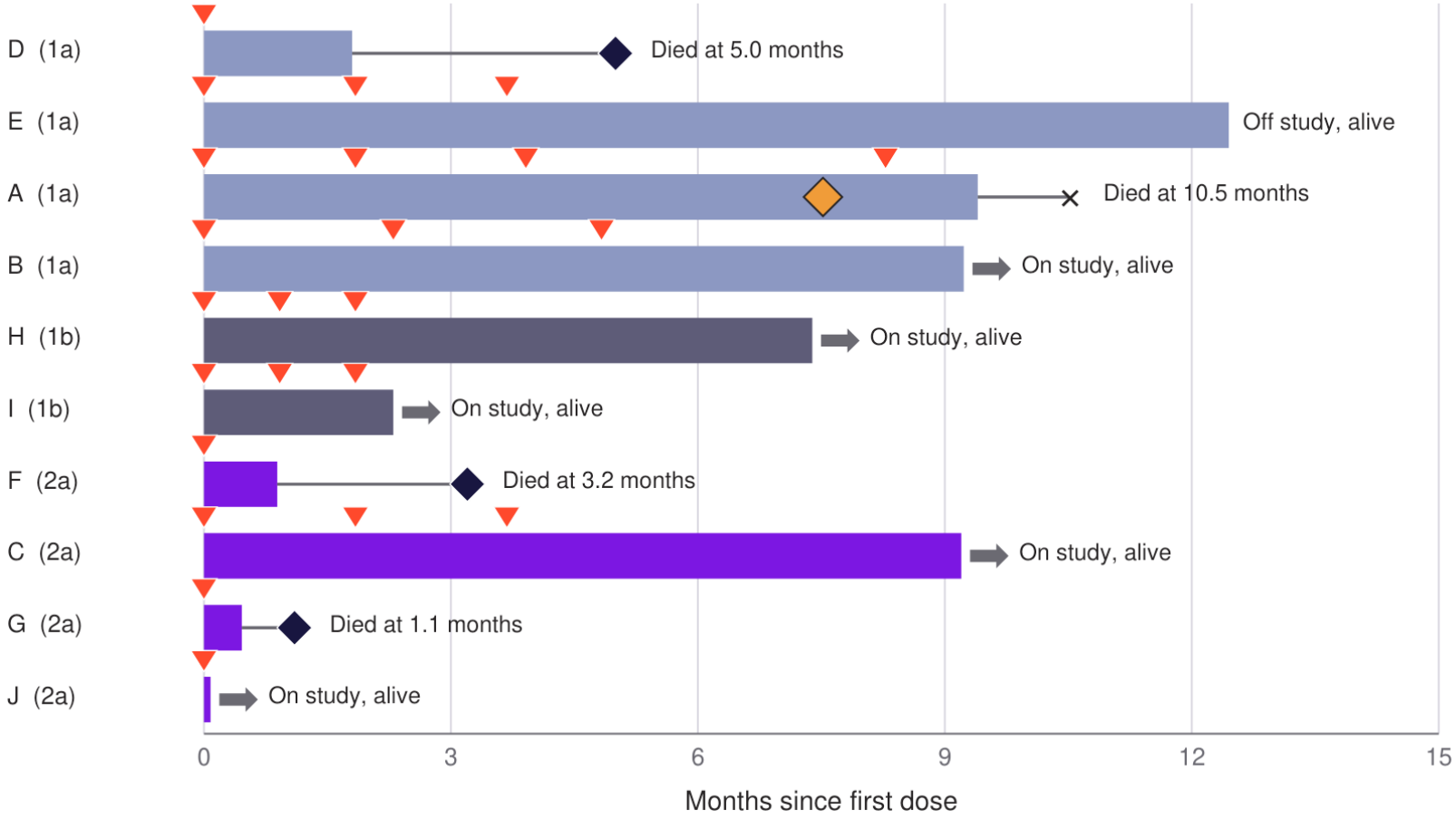
22 protocol administrations across three cohorts

Cohort	Activity and interval	Patients treated	Received all 3 doses
1a	13.2 mCi every 56 days	4	3
1b	13.2 mCi every 28 days	2	2
2a	26.4 mCi every 56 days	4	1
Total		10	6

One additional administration occurred under compassionate use.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

Treatment and follow-up for each patient



Status at cutoff

5 alive on study

1 alive off study

4 deaths

Participant A had MRI progression (orange diamond), followed by a fourth dose under compassionate use.

Triangles mark doses. Bars end at the last CSF sample or end of study. Thin lines show off-study follow-up to death.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

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No dose-limiting toxicities reported at cutoff

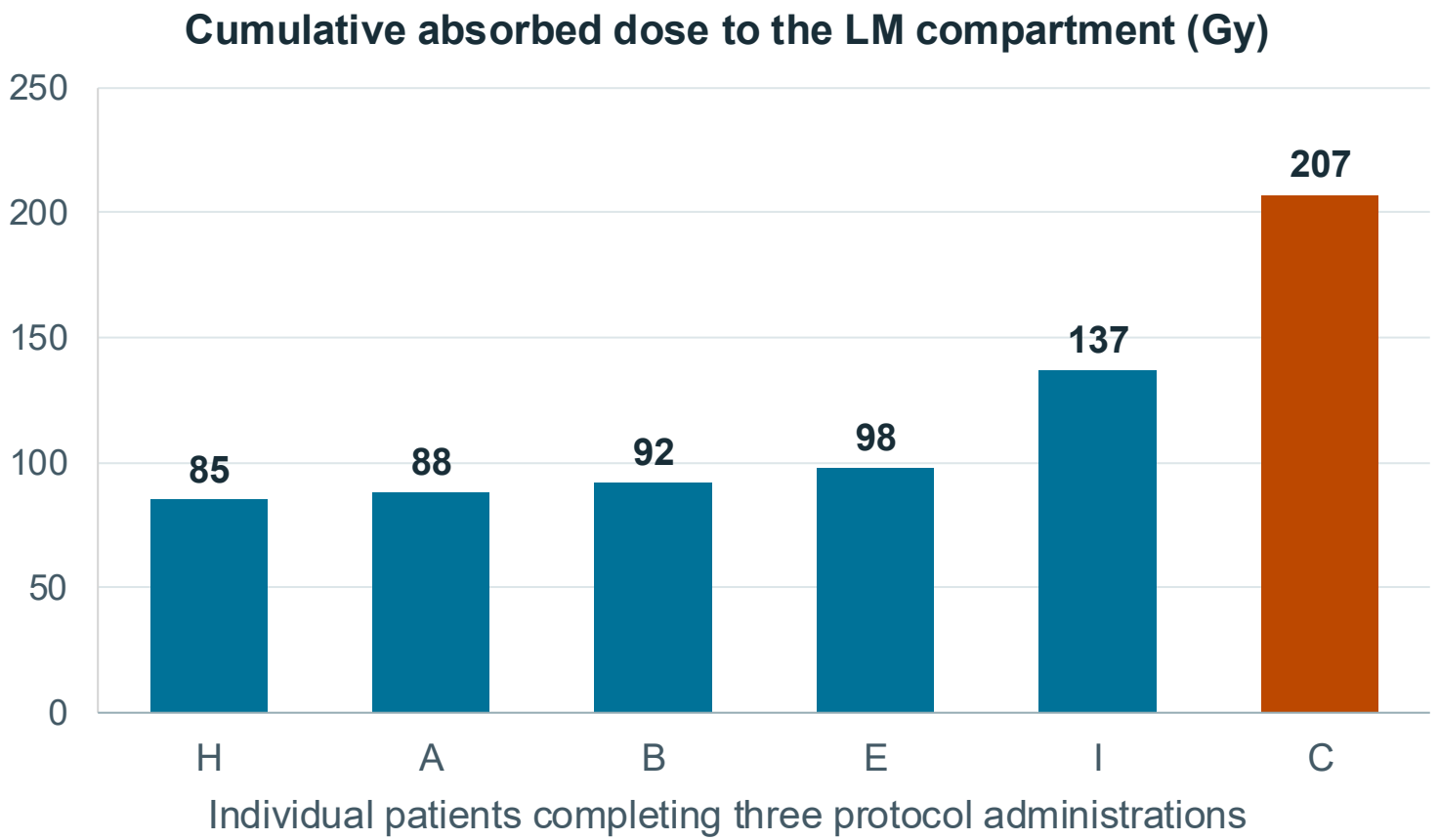
Patients with an event	13.2 mCi (n = 6)	26.4 mCi (n = 4)	Overall (n = 10)
Any treatment-emergent adverse event	6	4	10
Grade ≥3 treatment-related adverse event	1	0	1
Serious adverse event, any cause	1	0	1
Dose-limiting toxicity reported	0	0	0
Discontinued due to an adverse event	0	0	0

Grade 3 treatment-related nausea resolved in five days. The serious event was shortness of breath, assessed as unrelated.

The DLT window extends 28 days after the last dose. Its completion status was unavailable for the full cohort.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

Cumulative absorbed dose over three administrations



13.2 mCi × 3

Five patients received 39.6 mCi nominally. Absorbed doses ranged from 85 to 137 Gy.

26.4 mCi × 3

One patient received 79.2 mCi nominally, with an estimated absorbed dose of 207 Gy.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

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Where the radiation dose was delivered

Estimated absorbed dose per administration (Gy)

Region and measurement method	13.2 mCi	26.4 mCi
Cranial subarachnoid space, imaging	39.1 ± 13.7	71.7 ± 12.7
Spinal subarachnoid space, imaging	23.5 ± 15.5	53.9 ± 24.4
Ventricular CSF, fluid samples	4.3–5.3	9.6–11.7
Red marrow, blood samples	0.029 ± 0.031	0.105 ± 0.170

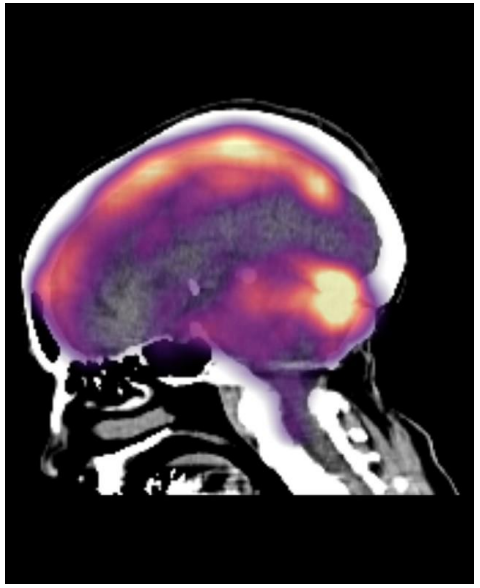
Median blood-derived red-marrow dose was 0.023 Gy per administration (range 0.010–0.41).

Values are means ± SD, except for ventricular CSF, shown as lower and upper model estimates. Imaging included 16 and 6 administrations at 13.2 and 26.4 mCi, respectively.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

Serial SPECT/CT after three administrations

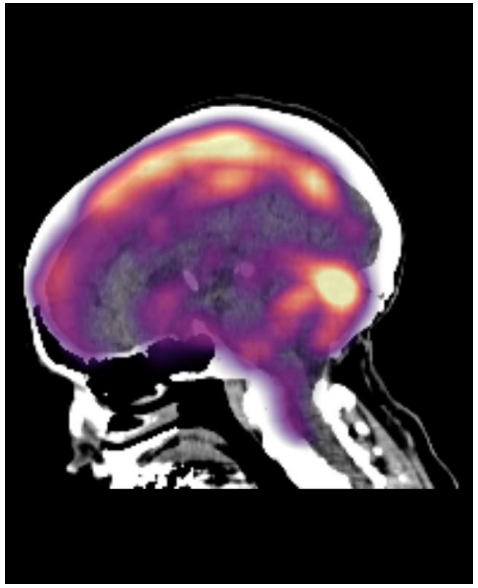
Administration 1



27.4 mCi measured

67 Gy

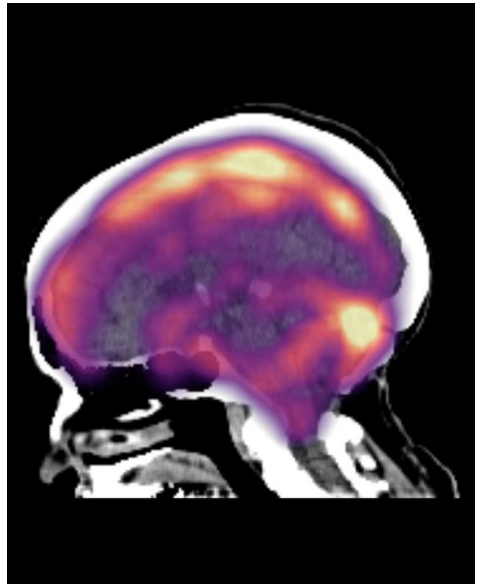
Administration 2



26.2 mCi measured

68 Gy

Administration 3



26.4 mCi measured

71 Gy

Each image shows one nominal 26.4-mCi administration. Gy values give the estimated LM-compartment absorbed dose.

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

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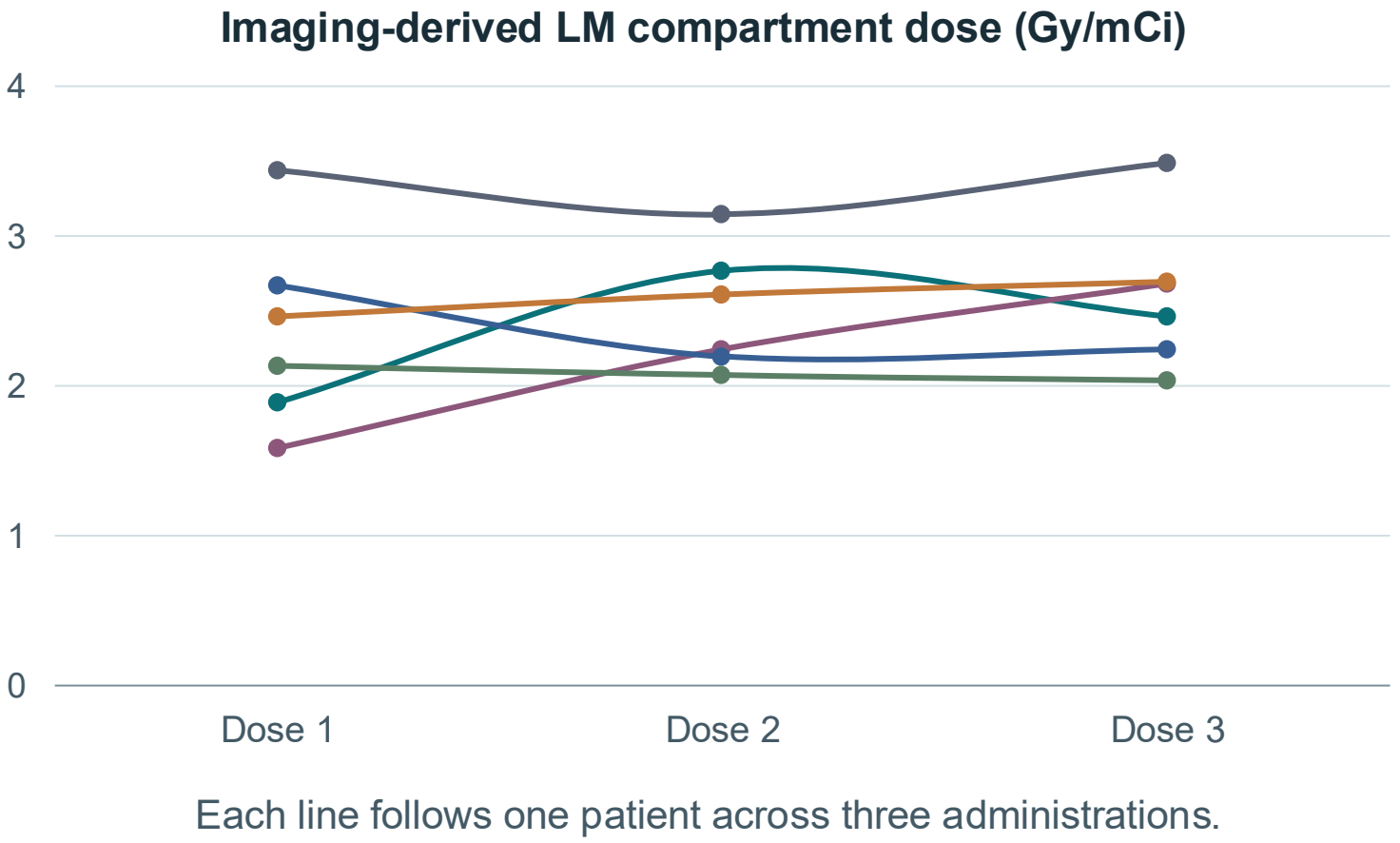
Dose delivery across repeat administrations



Each line follows one patient across three administrations.

8%

Median within-patient CV in absorbed dose per mCi (range 3–26%).

12%

Median within-patient CV in effective CSF half-life (range 2–18%).

Brenner et al. SNO 2026, CTNI-40. Multidose interim analysis through October 31, 2026.

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Enrollment and the next dose decision

Recruitment

UT Health San Antonio is recruiting. NYU Langone and Houston Methodist multidose study open. Additional U.S. sites are in activation.

Dose and interval selection

The study will evaluate higher activities and shorter intervals. Cumulative toxicity and dosimetry will inform regimen selection.

Planned phase 2 study

Cerenome is targeting a randomized dose comparison in 2027, contingent on the escalation results and regulatory discussions.

ClinicalTrials.gov NCT07098806. Site listings reviewed November 9, 2026. Cerenome development update, October 27, 2026.

UT Health San Antonio

Single-dose and multidose conclusions

Single administration

The recommended single dose was 44.1 mCi. Grade 4 cytopenias limited escalation at 66 and 75 mCi.

MRI showed an objective response in 5 of 16 evaluable patients (31%).

Repeat administration

Six of 10 patients completed three protocol administrations. No DLT was reported by the interim cutoff.

The median within-patient coefficient of variation in absorbed dose per mCi was 8%. Dose and interval selection is ongoing.

With thanks to the patients and their families, the study teams, Cerenome and CPRIT.

Brenner et al. SNO/ASCO 2026, CLTR-06. Brenner et al. SNO 2026, CTNI-40. Multidose cutoff October 31, 2026.

Thank you

Patients and Caregivers

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Cerenome

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UT Health San Antonio

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FORESEE 2.0: What does a CNSide result mean for your LM patients?

Study overview: a prospective, multicenter observational trial

Priya Kumthekar, MD

Alexandra Gewirtz, MD

Christine Cordova, MD

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The clinical problem

LM care still depends on tests that miss many cases and cannot quantify response

~10%

of patients with metastatic cancer develop LM, most often from NSCLC, breast cancer and melanoma

Months

Median survival after LM diagnosis is measured in months, so every decision point matters

<50%

Sensitivity of a single-sample CSF cytology; MRI is non-specific and hard to quantify

None

of the standard-of-care diagnostics provide a quantitative measure of treatment response

Source: EANO-ESMO LM guideline 2023; Le Rhun 2013; Boire 2019 RANO review

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What FORESEE 1.0 showed

In FORESEE 1.0, CNSide aided 91% of clinical decisions in LM

91%

(53/58) of clinical decisions aided by CNSide, including 87% (34/39) at baseline

75% vs 35%

Sensitivity of CNSide TCE vs cytology in matched CSF samples

N=39

Total evaluable subjects; 55 decision points covered in the study

25%

(14/57) of decisions where FISH/ICC/NGS informed drug selection, including HER2 amplification in patients with HER2-negative primaries

Note: First prospective multicenter study of CNSide clinical utility: 40 enrolled, 39 evaluable (21 breast, 18 NSCLC). Primary endpoint met against a pre-specified 20% threshold.
Source: FORESEE manuscript draft V1 (internal); Kumthekar 2025 (NOA); Kumthekar 2024 (HER2 flip)

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Why FORESEE 2.0

FORESEE 2.0 answers the next clinical question: what does a 'specific' TCE value mean

Still open after FORESEE 1.0	What FORESEE 2.0 will measure
Does baseline TCE, or its change over time, predict outcomes?	Outcome-anchored TCE reporting bands
How does TCE relate to survival?	OS and LM progression-free survival by TCE band and trajectory
How does TCE track with imaging?	Same-visit CSF and MRI pairs read on a structured RANO-LM form
Can TCE inform radiation decisions?	Prospective evidence on avoiding or deferring EBRT, with neurocognition and quality of life

Note: FORESEE 1.0 closed early when its legacy sponsor shut down. Retrospective data support the prognostic value of CSF tumor cellcounts, but no prospectively validated framework exists.
Source: FORESEE manuscript draft V1 (internal); Barbour 2024; Longitudinal CSF TCE (218 patients)

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What the study will deliver

Results aim to give clinicians practical tools for reading and acting on CNSide

Reporting bands

TCE ranges tied to outcome probabilities, such as a "rule-out" band with ≤10% probability of LM diagnosis and bands with 25% / 50% probability of progression or death

Change criterion

A minimum clinically meaningful change in TCE between serial draws

Radiation evidence

How often CNSide supports withholding, deferring or modifying EBRT, and what happens to neurocognition and quality of life

Imaging concordance

Whether TCE changes earlier than, or independently of, MRI, and what discordant results mean

Source: FORESEE 2.0 synopsis draft v0.1; WBRT neurotoxicity review

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Study design

An observational design fits around your standard of care and other LM trials

Observational, no study drug

Prospective, longitudinal, non-interventional diagnostic cohort; not a therapeutic trial

Your treatment decisions

LM treatment is entirely at the treating physician's discretion and is not dictated by the protocol

Co-enrollment allowed

Patients may also join therapeutic LM trials when CSF and MRI schedules are compatible

Established assay

CNSide is commercially available and CLIA-certified, CAP-accredited; TCE captures both EpCAM-positive and EpCAM-negative cells

Any solid-tumor primary

Two cohorts: suspected LM (Cohort A) and confirmed LM (Cohort B)

Multicenter & Sample Size

Targeting 10–20 US sites; target enrollment up to 150 subjects.

Source: FORESEE 2.0 synopsis draft v0.1; Sweed 2024

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Endpoints

Week 12 outcomes in each cohort will anchor the TCE reporting bands

Cohort A – Suspected LM

Primary endpoint: LM diagnosis by SOC criteria (EANO-ESMO: cytology and/or typical MRI with compatible clinical findings) by Week 12

Cohort B – Confirmed LM

Primary endpoint: LM progression-free status at Week 12, by integrated RANO-LM assessment (imaging, neurologic exam, SOC cytology) or death from any cause

Key secondary endpoints

- Week 24 durability of the Week 12 bands
- OS and LM progression-free survival by TCE band and trajectory
- Neurologic function (NANO-LM) over time
- EBRT withheld, deferred or modified, and CNSide's role
- TCE vs RANO-LM imaging agreement and lead time
- Decisions aided by CNSide; TCE vs cytology detection

Source: FORESEE 2.0 synopsis draft v0.1; EANO-ESMO LM guideline 2023; RANO-LM proposal 2017; NANO-LM scorecard 2025

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Who can enroll

Adults with any solid-tumor primary and suspected or confirmed LM can enroll

Key inclusion criteria

- Age ≥18 with a confirmed solid-tumor malignancy (any primary site)
- Suspected LM (Cohort A) or LM confirmed per EANO-ESMO (Cohort B); parenchymal brain metastases and prior cytology of any result allowed
- Serial CSF collection by LP, ventricular reservoir or shunt as part of SOC; a reservoir is not required
- Able to have contrast-enhanced brain and/or spine MRI
- Life expectancy of at least 4 weeks

Key exclusion criteria

- Primary CNS tumor or hematologic malignancy with CNS involvement
- Contraindication to LP with no alternative CSF access route
- Contraindication to gadolinium-enhanced MRI
- Condition making serial CSF collection unsafe

Source: FORESEE 2.0 synopsis draft v0.1; EANO-ESMO LM guideline 2023

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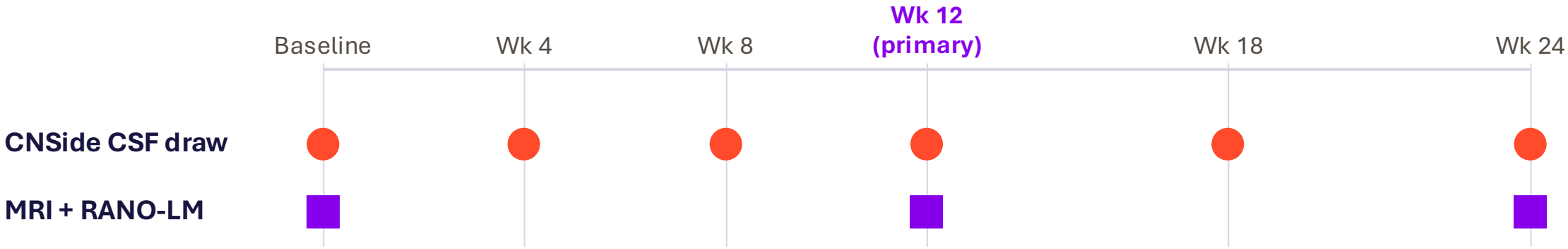
Visit schedule

Six CSF draws and three MRIs over 24 weeks follow NCCN-recommended timing



- CSF every 4 weeks to Week 12, then every 6 weeks
- Every MRI paired with a same-visit CSF draw
- NCCN CNS v1.2026 calls for CSF re-evaluation every 4 to 8 weeks and imaging every 2 to 3 months
- Up to 24 weeks of active assessments per patient, plus survival follow-up
- Visit window ±7 days; MRI within ±10 days of the paired CSF draw

Source: FORESEE 2.0 synopsis draft v0.1; NCCN CNS Cancers v1.2026; FORESEE manuscript draft V1 (internal)

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What participation involves

Each visit adds brief structured assessments to care you already deliver

Every visit

- CNSide TCE; IHC/NGS as clinically indicated
- SOC CSF cytology when performed
- Neurologic exam, NANO-LM, KPS/ECOG
- PROs (EORTC QLQ-C30)
- Clinical decision questionnaire and Radiation Decision CRF
- Treatment record and CSF-collection AEs

Baseline, Weeks 12 and 24

- Brain and/or spine MRI with local read on a structured RANO-LM form
- Brief neurocognitive battery (HVLT-R, Trail Making A/B, COWA)
- Survival status at Weeks 12 and 24

Safety reporting

- Limited to study-specific procedures and SAEs related to CSF collection
- LM progression and death are study outcomes, not reportable AEs
- Long-term survival follow-up every 3 months up to 12 months

Source: FORESEE 2.0 synopsis draft v0.1; NANO-LM scorecard 2025; RANO-LM proposal 2017

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Why participate

Sites receive every CNSide result and help build the evidence for guidelines

Results return to you

All CNSide results (TCE, plus IHC/NGS as ordered) go to the treating physician to use in care

Actionable biomarkers

FORESEE 1.0 found CSF biomarker results informed drug selection in 25% of decisions, including HER2 flips

Low protocol burden

CSF, MRI and neurologic assessments follow your standard-of-care schedule; no study drug

Shape LM practice

Data support guideline inclusion and the payer evidence dossier for CNSide interpretation

Source: FORESEE 2.0 synopsis draft v0.1; Kumthekar 2024 (HER2 flip)

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Enrollment and timeline

Sites go live in FY27, with enrollment expected to complete in FY28

10–20

US sites, activating about 3 per month

~1

patient per site per month expected

24 weeks

of active assessments per patient, plus survival follow-up

Expected primary-tumor mix (from commercial CNSide ordering): breast 48%, lung 30%, other 22%; breast enrollment capped

Program milestones

- **FY27** Protocol locked and sites live
- **FY28** Enrollment complete
- **FY29** Guideline and payer dossier

Note: Final sample size is pending biostatistics review.
Source: FORESEE 2.0 synopsis draft v0.1; Longitudinal CSF TCE (218 patients)

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Join FORESEE 2.0 to help define how CNSide results guide LM care

NEXT STEPS

01	Tell the study team your site is interested	Your site	**Ongoing**
02	Complete the site feasibility questionnaire	Your site	**To Be Provided**
03	Site activation and first patient enrolled	Study team	FY27

Contact: **Eric Daniels, MD (edaniels@cerenome.com)**

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Thank You

Record your
attendance & request
a copy of the recording



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