Repeated Intraventricular Rhenium-186 Obisbemeda (186RNL) in Leptomeningeal Metastases: Interim Dosimetry, Safety, and CSF Tumor Cell Response From the ReSPECT-LM Multiple-Dose Study

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1 BACKGROUND

- Leptomeningeal metastases (LM) involve the cerebrospinal fluid (CSF) and leptomeningeal surfaces and have limited treatment options.
- REYOBIQ™ (Rhenium-186 obisbemeda; 186RNL) is a nanoliposomal β-emitter (Re-186 half-life 89.2 h) given into the ventricular CSF via an Ommaya reservoir.
- In the single-dose ReSPECT-LM study, the MFD was 66 mCi and the recommended Phase 2 dose 44 mCi; with absorbed doses ranging from 28–272 Gy to the cranial subarachnoid.
- Fractionation may allow higher cumulative dose. These findings motivated evaluation of repeated administration.
- Here, we report initial treatment exposure, safety, dose-to-dose dosimetry, and longitudinal CSF tumor-cell findings from the ongoing multiple-dose study (NCT07098806).

2 METHODS

Patients and treatment

- Adults with LM Type 1 or Type 2A-C from any solid tumor; KPS ≥ 70.
- 186RNL 13.2, 26.4 or 44.1 mCi per dose, 3 doses every 56, 28 or 14 d (8 cohorts); Cohorts 1a, 1b and 2a enrolled to date.
- Escalation: 1a and 2a open in parallel; the next shorter interval opens after 3 evaluable patients complete the 28-day DLT window; 3a opens after 3 patients in 2a receive Dose 2 without DLT. 1 of 3 with DLT: expand by 3; ≥2 with DLT: combination not tolerable. RP2D favors the highest dose at the shortest interval with the lowest TRAEs.

Dosimetry

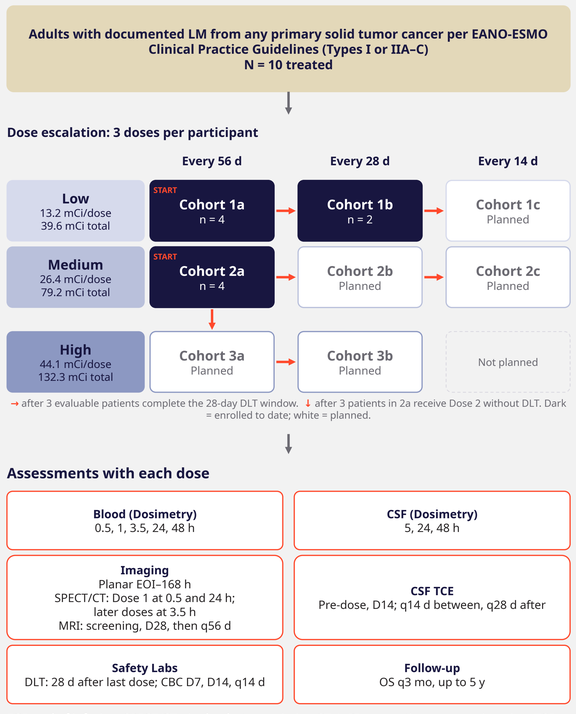
- LM compartment dose (mean absorbed dose to the CSF space) from serial CSF samples (5, 24, 48 h): D (Gy) = 7.126 × ∫C(t)dt; CSF mass 120 g (F) / 140 g (M); lower (A) and upper (B) bounds.
- Red marrow from blood activity × 0.3 (self-dose, upper bound); organ and target dose from planar and SPECT/CT imaging to 168 h.
- Dose-to-dose reproducibility: within-patient coefficient of variation (CV) of Gy/mCi and CSF effective half-life across doses.

Response, safety, and feasibility

- CSF tumor cell enumeration (TCE, CNSide; tumor cells/mL) pre-dose and Day 14 after each dose, every 14 d between doses, and every 28 d in follow-up. Response: ≥50% reduction from baseline (protocol); ≥80% exploratory. Radiographic and clinical response per RANO-LM.
- AEs per CTCAE v5.0; hematologic nadir after each dose. Feasibility: on-schedule dosing, delays, Ommaya complications, collections in window.
- Descriptive statistics; no formal between-cohort comparisons.

3 STUDY DESIGN

Figure 1. Study design



EOI, end of infusion; SPECT/CT, single-photon emission CT; MRI, magnetic resonance imaging; TCE, tumor cell enumeration; DLT, dose-limiting toxicity; CBC, complete blood count; OS, overall survival.

6 PLAIN LANGUAGE SUMMARY

Leptomeningeal metastases are cancer cells in the fluid around the brain and spine. In this study, 10 people received a radioactive drug, 186RNL, in up to 4 smaller doses through a small port into that fluid. Patients received more total drug than the highest safe single dose, the drug stayed in the spinal fluid for a similar time with each dose, and radiation to the bone marrow was low.

4 RESULTS · Exposure and Cumulative Dose

Exposure

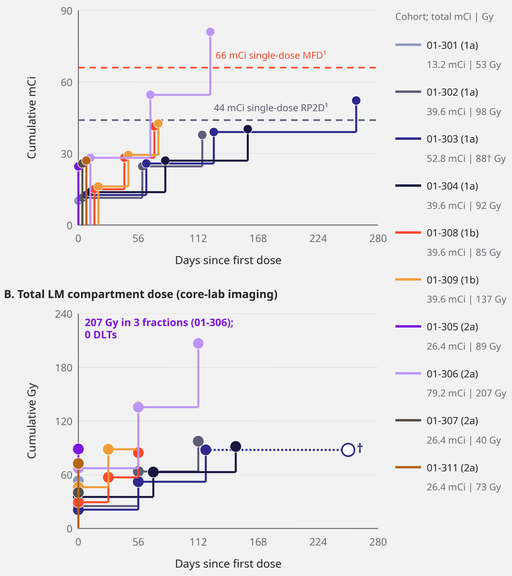
10	79.2 mCi	0
patients treated	max cumulative dose administered (vs 66 mCi single-dose MFD[1])	DLTs to date

Table 1. Baseline characteristics

Characteristic	13.2 mCi (n = 6)	26.4 mCi (n = 4)	Total (N = 10)
Age, median (range), y	57.5 (47–70)	61.5 (40–74)	58.5 (40–74)
Female, n (%)	5 (83)	3 (75)	8 (80)
KPS, median (range)	90 (80–100)	85 (80–90)	90 (80–100)
Primary tumor, n (%)			
Breast	2 (33)	1 (25)	3 (30)
Non-small cell lung	1 (17)	0	1 (10)
Melanoma	2 (33)[b]	2 (50)	4 (40)[b]
Other (ovarian, neuroendocrine)	1 (17)	1 (25)	2 (20)
EANO-ESMO LM type, n (%)[a]			
IA	0	1 (25)	1 (10)
IB	0	1 (25)	1 (10)
IIA	3 (50)	1 (25)	4 (40)
IIB	1 (17)	0	1 (10)
IIC	2 (33)	1 (25)	3 (30)
Prior LM therapy, n (%)	6 (100)[c]	3 (75)[c]	9 (90)[c]
Concurrent systemic tx, n (%)	1 (17)[d]	2 (50)[d]	3 (30)[d]

SNO data compilation 31 Oct 2026. [b]Includes 01-308 (choroidal melanoma). [c]Radiation: 01-301 to 01-305, 01-308; chemotherapy: 01-306 (systemic), 01-311 (intrathecal); both + radiation: 01-309; none: 01-307. [d]01-305 trastuzumab deruxtecan; 01-309, 01-311 agents not specified. [e]I, positive CSF cytology; II, clinical and MRI findings without positive cytology; A, linear; B, nodular; C, linear and nodular enhancement.

Figure 2. Cumulative activity and LM compartment dose per patient



Each step is one administration. A: nominal activity (13.2 or 26.4 mCi per dose); measured activity was within 6% of nominal; 01-303 Dose 4 (day 252) given under compassionate use (14.4 mCi delivered). B: total LM compartment dose per administration from core-lab planar imaging (fixed CSF mass 120 g F / 140 g M), summed. †Open marker: 01-303 Dose 4 (compassionate use—dosimetry not measured).

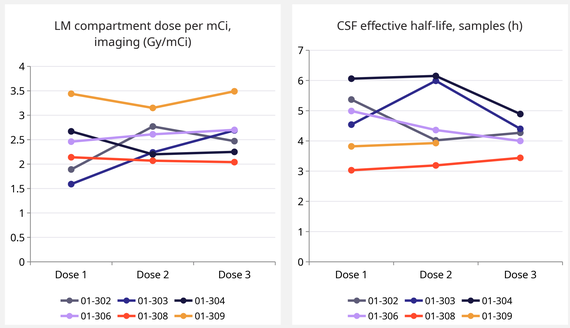
4 RESULTS · Dosimetry and Reproducibility

Table 2. Dosimetry by organ, per administration

Organ / region	13.2 mCi Gy | Gy/mCi	26.4 mCi Gy | Gy/mCi
Target		
CSF, Ventricular	4.3–5.3 | 0.32–0.40	9.6–11.7 | 0.36–0.44
Cranial, Subarachnoid	39.1 ± 13.7 | 2.92	71.7 ± 12.7 | 2.65
Spinal, Subarachnoid	23.5 ± 15.5 | 1.75	53.9 ± 24.4 | 1.99
Normal organs		
Red marrow (blood, upper)	0.029 ± 0.031 | 0.002	0.105 ± 0.170 | 0.004
Liver	1.27 ± 0.67 | 0.095	2.21 ± 1.25 | 0.081
Spleen	0.68 ± 0.53 | 0.051	1.32 ± 1.18 | 0.049
Kidneys	0.43 ± 0.34 | 0.032	0.74 ± 0.35 | 0.027
Whole body	0.16 ± 0.08 | 0.012	0.38 ± 0.20 | 0.014
Kinetics		
CSF T½ eff, 5–24 h (h)	4.72 ± 1.31	5.22 ± 2.54
Blood peak, % IA per L	0.82 ± 0.62	1.42 ± 1.98
Ventricular CSF-to-marrow ratio, median	158	222

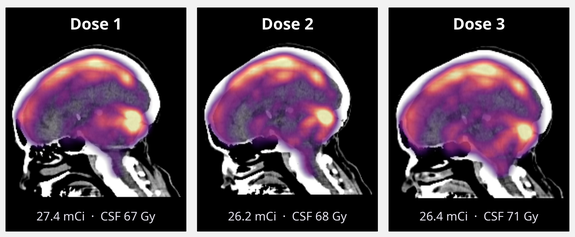
Mean ± SD unless noted. CSF, Ventricular: Ommaya (ventricular) CSF samples at 5, 24 and 48 h; range of means: lower bound holds the concentration from end of infusion to 5 h at the 5-h value; upper bound back-extrapolates the 5–24 h clearance to end of infusion (SD 2.7–3.3 Gy at 13.2 mCi, 5.4–6.0 Gy at 26.4 mCi; 15 and 5 doses); CSF-to-marrow ratio uses the lower bound. Cranial/Spinal, Subarachnoid and organs: core-lab planar imaging (fixed CSF mass 120 g F / 140 g M; 68% intracranial / 32% spinal), 16 and 6 doses (whole body 15 at 13.2 mCi); Blood-based marrow 15 doses at 13.2 mCi. Median marrow dose, all doses: 0.023 Gy (0.010–0.41). IA, injected activity.

Figure 3. Dose-to-dose reproducibility within patients



Left: core-lab planar imaging, total LM compartment dose per mCi (trial-protocol method); 01-302 Dose 3 and 01-304 Doses 2–3 from revised core-lab reports (1 Nov 2026). Right: Ommaya sample-based CSF T½ eff, 5–24 h (database v11). Median within-patient CV (coefficient of variation): Gy/mCi 8% (range 3–26%); T½ 12% (2–18%). 01-303 Dose 4 not shown; 01-309 Dose 3 samples pending.

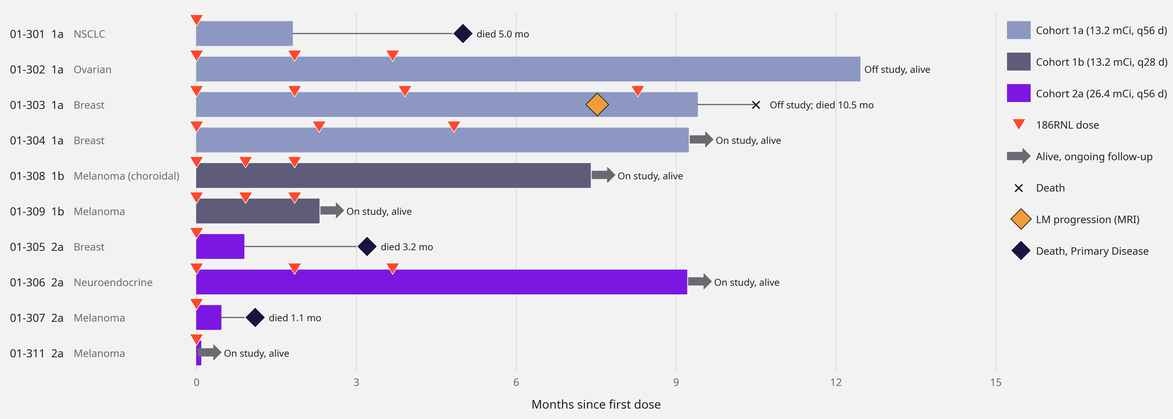
Figure 4. 24 h SPECT/CT after each dose, 01-306 (Cohort 2a)



Sagittal MIP (maximum intensity projection) fused to CT. Activity covers the cerebral convexities and posterior fossa and extends into the cervical spinal canal, with a similar pattern after each dose. Activity: core-lab measured. CSF: core-lab total CSF dose. Qualitative display; Re-186 SPECT quantitation pending.

4 RESULTS · Treatment Course

Figure 5. Swimmer plot: dosing and follow-up for each patient



Bars end at the last CNSide sample or end of study; 01-303 fourth dose (8.3 mo) given under compassionate use. Thin line = off-study follow-up to death (01-301, 01-303, 01-305, 01-307). 01-302 off study at 12.5 mo without progression; alive at last contact 22 Sep 2026.

4 RESULTS · Safety

Table 3. Summary of safety

Patients, n (%)	13.2 mCi (n = 6)	26.4 mCi (n = 4)	Total (N = 10)
Any TEAE	6 (100)	4 (100)	10 (100)
Grade ≥3 TRAE	1 (17)[b]	0	1 (10)[b]
Serious AE	1 (17)[c]	0	1 (10)[c]
Dose-limiting toxicity	0	0	0
AE leading to discontinuation	0	0	0
Most common TEAEs (≥40% overall)			
Nausea	4 (67)	2 (50)	6 (60)
Headache	2 (33)	2 (50)	4 (40)
Lymphocyte count decreased	2 (33)	2 (50)	4 (40)
WBC decreased	3 (50)	1 (25)	4 (40)

[b]01-302 grade 3 nausea, definitely related—resolved in 5 days. [c]01-303 shortness of breath, unrelated. TEAE, treatment-emergent AE; TRAE, treatment-related AE. CTCAE v5.0.

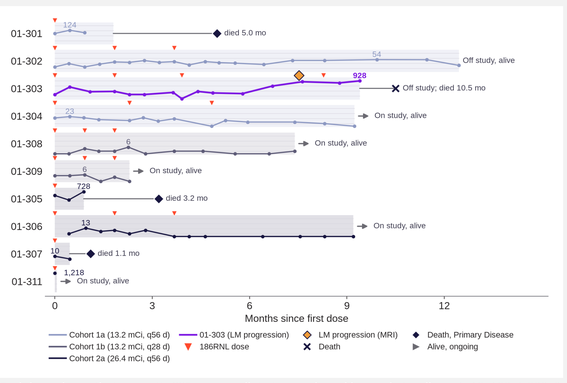
4 RESULTS · CSF Tumor Cell Response

Table 4. CSF tumor cells/mL and LM progression status

Patient	Baseline	Lowest (mo)	Latest (mo)	Samples after D1	LM progression status
Cohort 1a (13.2 mCi, q56 d)					
01-301	29	40 (0.9)	40 (0.9)	2	No
01-302	2	2 (0.9)	4 (12.5)	18	No
01-303	2	0 (3.9)	928 (9.4)	14	Yes
01-304	13	0 (4.8)	0 (9.2)	13	No
Cohort 1b (13.2 mCi, q28 d)					
01-308	0	0 (0.4)	1 (7.4)	11	No
01-309	4	0 (1.4)	0 (2.3)	5	No
Cohort 2a (26.4 mCi, q56 d)					
01-305	128	17 (0.4)	728 (0.9)	2	No
01-306	—[a]	0 (3.7)	0 (9.2)	13	No
01-307	10	3 (0.5)	3 (0.5)	1	No
01-311	1,218	Pending	Pending	0	No

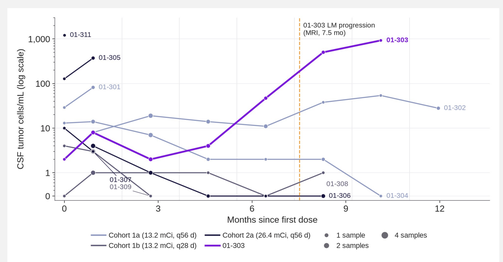
Tumor cells/mL, rounded up; (mo), months since Dose 1. Baseline = last pre-dose sample. Lowest and latest across all CSF samples after Dose 1, including follow-up. Only 01-303 had LM progression (MRI 27 Apr 2026, 7.5 mo); other off-study events and deaths were due to primary-disease progression. Pending, result not yet reported. [a]Failed lab QC, not tested.

Figure 6. CSF tumor cells/mL over each patient's course



Each lane shows that patient's CSF tumor cells/mL on a shared log scale (gridlines 1, 10, 100, 1,000; 0 at lane floor); number = peak value. Timeline as in Figure 5.

Figure 7. Median CSF tumor cells/mL per 8-week window



Baseline = last pre-dose sample; then median per 8-week window (Days 1–56, 57–112, ...); point size = samples in window. CSF sampled ~every 14 d on treatment; 8-week windows consistent with NCCN CSF reassessment every 4–8 weeks. Cohort 1b windows span 2 doses. Values rounded up; 0 at axis base.

5 CONCLUSIONS

- In repeated dosing of 186RNL, a total dose of 79.2 mCi cumulative (3 × 26.4 mCi), has been safe thus far with dose escalation continuing.
- Dosimetry is within the range observed in the single-dose study, with patients receiving approximately 40 Gy from a single 13.2 mCi dose, and a cumulative 85 to 137 Gy after 3 doses at the lowest dose level.
- By 3 and 6 months, no LM progression was documented among evaluable patients (0/5 at each landmark). By nine months, LM progression was documented in 1 of 4 evaluable patients.[a]
- Imaging-based LM compartment dose per mCi was relatively consistent across repeat administrations, and per-administration blood-derived marrow dose estimates were low.
- Further enrollment is needed to define a recommended multiple-dose regimen and characterize clinical activity.

References 1. Brenner A, et al. Neuro-Oncol Adv 2026;8(Suppl 6):CLTR-06. 2. Cerenome. WFNOS/SNO 2025 release.

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Contact: A. Brenner (brenner@uthscsa.edu). ClinicalTrials.gov NCT07098806
Disclosures: A. Brenner, A. Bao and W. Phillips are consultants to Cerenome; E. Daniels and M. Hedrick are employees.

a Evaluability was determined by PI review of available records and progression was documented on or before the landmark, or adequate disease-assessment follow-up established LM status through that landmark. Patients with insufficient follow-up or death from primary disease before the landmark without prior LM progression were excluded.

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