Intracranial Efficacy of Tarlatamab Versus Chemotherapy (CTx) as Second-Line (2L) Treatment for Small Cell Lung Cancer (SCLC): DeLLphi-304 Phase 3 Post Hoc Analysis

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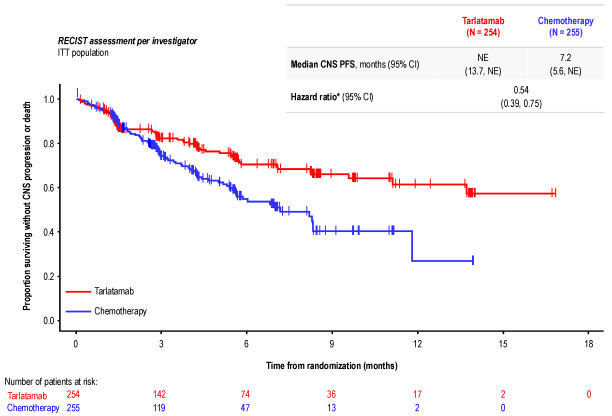
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BACKGROUND

- Patients with SCLC and brain metastases face a particularly poor prognosis with 2L chemotherapy (median overall survival of ~4.5–6.6 months across real-world and clinical trial settings)[1-4]
- In the phase 3 randomized DeLLphi-304 trial, when compared with standard chemotherapy, tarlatamab demonstrated superior median overall survival (13.6 vs 8.3 months; HR, 0.60; $p < 0.001$) and median progression-free survival (4.2 vs 3.7 months; HR, 0.71; RMST $p = 0.002$) among patients with SCLC whose disease had progressed during or after platinum-based chemotherapy[5]
  - This survival benefit with tarlatamab was observed in the prespecified subgroup of patients with a history of brain metastases per investigator

Here we report DeLLphi-304 post hoc analyses detailing intracranial efficacy of tarlatamab versus chemotherapy by BICR per mRANO-BM[6]

Tarlatamab delayed time to CNS progression or death in all patients



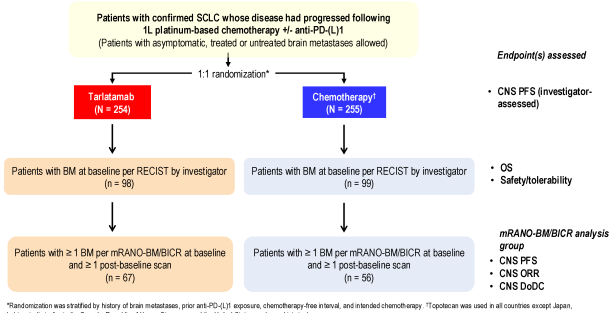
	Tarlatamab (N = 254)	Chemotherapy (N = 255)
Median CNS PFS, months (95% CI)	NE (13.7, NE)	7.2 (5.6, NE)
Hazard ratio* (95% CI)	0.54 (0.39, 0.75)	

Patients in the tarlatamab group had a 46% lower risk of CNS disease progression or death compared to those in the chemotherapy group

*Hazard ratio and 95% CI were estimated using a stratified Cox proportional hazards model.

METHODS

Post hoc analysis of intracranial efficacy in the DeLLphi-304 trial



*Randomization was stratified by history of brain metastases, prior anti-PD-(L)1 exposure, chemotherapy-free interval, and intended chemotherapy. †Topotecan was used in all countries except Japan, lurbinectedin in Australia, Canada, Republic of Korea, Singapore and the United States, and amrubicin in Japan.

RESULTS

*Baseline patient and disease characteristics**

	Tarlatamab (n = 67)	Chemotherapy (n = 56)
Median age, years (range)	64.0 (20–86)	63.5 (26–84)
Male / Female, %	75 / 25	70 / 30
Race		
Asian / Black / White, %	31 / 0 / 67†	41 / 2 / 55†
Smoking history		
Current or former smokers / Never smokers, %	90 / 10	93 / 7
ECOG performance status, 0 / 1 / 2, %	25 / 75 / 0	37 / 61 / 2‡
Prior anti-PD-(L)1 therapy, %	66	79
Prior therapy for brain metastases, %		
Radiotherapy and/or Surgery / No treatment	75 / 25	71 / 29
Median time from prior brain radiotherapy to randomization, days (range)	37.0 (7–634)	36.5 (8–650)
Patients with CNS lesion(s) ≥ 10 mm in diameter, n	16	13
DLL3 expression, %, (n / n‡§)	100 (56 / 56)	89 (42 / 47)

*The CNS full analysis set (cFAS) is a subset of the intention-to-treat analysis set comprising patients who had at least two brain scans (one at baseline and one post-baseline) and were identified per modified RANO-BM by BICR as having at least one brain lesion at baseline. †1% of patients in the tarlatamab group were classified as belonging to the 'Others' category and 2% in the chemotherapy group had missing or unwilling to disclose entries. ‡After screening, the ECOG performance-status score declined to 2 in one patient before the administration of treatment (baseline). §n = number of patients with DLL3 expression, n1 = number of patients with available DLL3 results.

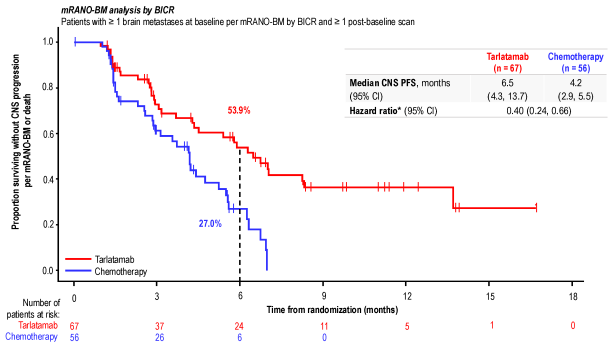
Tarlatamab improved efficacy outcomes vs chemotherapy in patients with brain metastases

	Tarlatamab (n = 67)	Chemotherapy (n = 56)
Best overall CNS response*, n (%)		
Complete response (95% CI)	10 (14.9) (7.4, 25.7)	3 (5.4) (1.1, 14.9)
Non-CR/Non-PD	42 (62.7)	37 (66.1)
Progressive disease	13 (19.4)	16 (28.6)
Not evaluable	2 (3.0)	0
Median duration of CNS complete response, months (range) (95% CI)	NE (1.3+, 13.6+) (2.9, NE)	3.6 (1.3+, 4.2) (3.1, NE)
CNS disease control rate, n (%) (95% CI)	52 (77.6) (65.8, 86.9)	40 (71.4) (57.8, 82.7)
Median duration of CNS disease control, months (range) (95% CI)	8.2 (1.2+, 16.7+) (6.3, NE)	5.2 (1.2+, 7.0) (4.2, 6.2)
CNS tumor shrinkage of ≥ 30%†, n / N1	56.3% (9 / 16)	38.5% (5 / 13)
Ongoing CNS response at data cutoff, n (%)	5 (50.0)	0

Tarlatamab was associated with a better intracranial complete response rate, duration of intracranial complete response, and duration of intracranial disease control compared to chemotherapy

At the data-cutoff date of January 29, 2025, the median study follow-up was 11.4 months (tarlatamab) and 11.5 months (chemotherapy). + denotes censored data.
*As most patients (> 70%) had received prior treatment for CNS disease, specified outcomes were CR, non-CR/non-PD, and PD.
†Assessed in patients with ≥ 1 lesion that was ≥ 10 mm in diameter.

Tarlatamab delayed CNS progression or death in patients with brain metastases

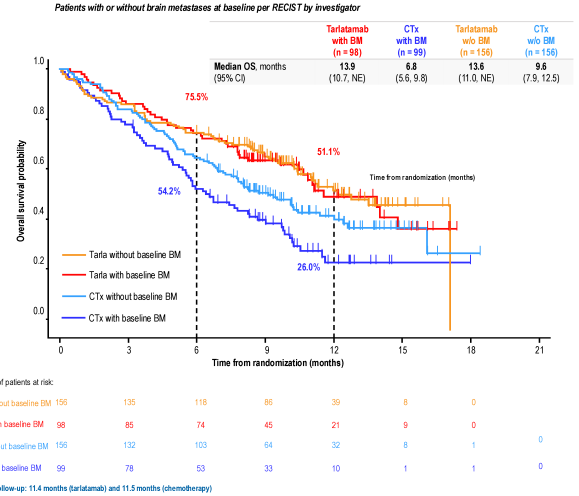


	Tarlatamab (n = 67)	Chemotherapy (n = 56)
Median CNS PFS, months (95% CI)	6.5 (4.3, 13.7)	4.2 (2.9, 5.5)
Hazard ratio* (95% CI)	0.40 (0.24, 0.66)	

Among patients with brain metastases, treatment with tarlatamab reduced the risk of CNS disease progression or death by 60% compared to chemotherapy

*Hazard ratio and 95% CI were estimated using an unstratified Cox proportional hazards model.

Tarlatamab improved overall survival vs chemotherapy regardless of the presence of brain metastases



Treatment with tarlatamab reduced the risk of death by 49% in patients with brain metastases vs chemotherapy (HR 0.51 [95% CI: 0.34, 0.74])

*Hazard ratio and 95% CI were estimated using an unstratified Cox proportional hazards model. †Hazard ratio for death for tarlatamab versus chemotherapy in patients with brain metastases at baseline.

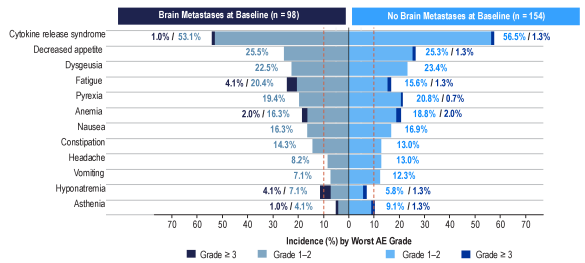
Tarlatamab demonstrated a more tolerable safety profile vs chemotherapy in patients with BM

	Tarlatamab (n = 98)*	Chemotherapy (n = 93)*
Treatment-emergent AE, n (%)		
Grade ≥ 3 AEs	53 (54.1)	81 (87.1)
TEAEs of interest, any grade		
Neurological events (excluding dysgeusia)	45 (45.9)	41 (44.1)
Dysgeusia	23 (23.5)	3 (3.2)
Neutropenia	7 (7.1)	30 (32.3)
Treatment-related AEs, n (%)		
Grade ≥ 3 AE	25 (25.5)	61 (65.6)
Serious AEs	28 (28.6)	33 (35.5)
Leading to dose interruption and/or reduction†	18 (18.4)	51 (54.8)
Leading to discontinuation	2 (2.0)	6 (6.5)
Fatal AEs	0	2 (2.2)

- **Patients treated with tarlatamab had a lower incidence of high-grade and serious AEs, and of dose interruptions and discontinuations due to TRAEs in comparison to those treated with chemotherapy**
- **The incidence of neurological events, excluding dysgeusia, was similar in both groups**

*Safety analysis set includes patients who received at least one dose of treatment. †Dose reduction was only required in the chemotherapy arm.

Tarlatamab demonstrated a similar safety profile in patients with or without brain metastases



- The incidence of neurological events* and dysgeusia TRAEs was similar in patients with or without brain metastases (28%; 23% vs 32%; 23%).
- The incidence of ICANS in patients with brain metastases was 9% (9/98) vs 4% (6/154) in those without brain metastases

Among patients treated with tarlatamab, the incidence and grade of TRAEs were similar among patients with and without brain metastases

*Neurological events include SOC nervous system disorders and SOC psychiatric disorders, excluding dysgeusia. Patient incidence is reported.

LIMITATIONS

- Relatively small cohort of patients with brain metastases
- Exploratory nature of analysis
- Among patients with baseline brain metastases, most patients had received prior CNS-directed therapy; a larger trial including patients with untreated brain metastases is needed to confirm tarlatamab's impact on delaying development and/or progression of CNS disease

CONCLUSIONS

- Tarlatamab improved intracranial efficacy outcomes and delayed CNS disease progression or death compared to chemotherapy in patients with previously treated SCLC and stable, asymptomatic brain metastases
- Tarlatamab improved overall survival in comparison with chemotherapy irrespective of the presence of brain metastases
- Among patients with brain metastases, tarlatamab was better tolerated, with a lower incidence of high-grade and serious adverse events compared to chemotherapy
- The incidence and grade of tarlatamab-related AEs were similar in patients with and without brain metastases

These results further support tarlatamab as the standard of care for SCLC in the second-line setting, including in patients with brain metastases

ABBREVIATIONS

1L, first-line; **2L**, second-line; **AE**, adverse event; **BICR**, blinded independent central review; **BM**, brain metastases; **CI**, confidence interval; **CNS**, central nervous system; **CR**, complete response; **CTx**, chemotherapy; **DLL3**, delta-like ligand 3; **DoDC**, duration of disease control; **ECOG**, Eastern Cooperative Oncology Group; **HR**, hazard ratio; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **ITT**, intention-to-treat; **mRANO-BM**, modified Response Assessment in Neuro-Oncology Brain Metastases; **N1**, number of patients with CNS lesions ≥ 10 mm in diameter; **NE**, not estimable; **ORR**, objective response rate; **OS**, overall survival; **PD**, progressive disease; **PD-(L)1**, programmed death-(ligand)1; **PFS**, progression-free survival; **RECIST**, Response Evaluation Criteria in Solid Tumors; **RMST**, restricted mean PFS time; **SCLC**, small cell lung cancer; **SOC**, system organ class; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related adverse event; **w/o**, without.

Poster presented at the 2026 NCODA International Fall Summit, October 28–30, 2026; Orlando, FL, USA.

DISCLAIMER

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REFERENCES

1. Lambrecht L, et al. *Diagnostics*. 2024;14:1572–1584.
2. Desai A, et al. *Clin Lung Cancer*. 2023;24:689–695.
3. Alx SP, et al. *Lancet Respir Med*. 2023;11:74–86.
4. EU Clinical Trials Register. EudraCT No. 2015-001641-89. https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-001641-89/results Accessed April 28, 2026.
5. Mountzios G, et al. *N Engl J Med*. 2025;393:349–361.
6. Lin NU, et al. *Lancet Oncol*. 2015;16:270–278.

ACKNOWLEDGMENTS

- The authors are grateful to all the patients, their families, other DeLLphi-304 investigators, and site-support staff.
- This study was funded by Amgen Inc.
- Medical writing support for this presentation was funded by Amgen Inc. and was provided by Sukanya Raghuraman, PhD, CMPP of Cactus Life Sciences (part of Cactus Communications), and Liz Leight, PhD of Amgen Inc. Robert Dawson of Cactus Life Sciences (part of Cactus Communications) provided assistance with graphics.

Video Summary:

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