DeLLphi-301: Tarlatamab phase 2 trial in small cell lung cancer (SCLC)—Efficacy and safety analyzed by presence of brain metastases

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Key Takeaways

- In this subgroup analysis of the phase 2 DeLLphi-301 study in previously treated SCLC, tarlatamab demonstrated durable anticancer activity regardless of the presence of treated, stable brain metastases at baseline
- The safety profile of tarlatamab in patients with brain metastases was manageable and consistent with the safety profile from the overall study
- CNS tumor shrinkage was observed after radiotherapy in some patients treated with tarlatamab

CNS, central nervous system; **SCLC**, small cell lung cancer.

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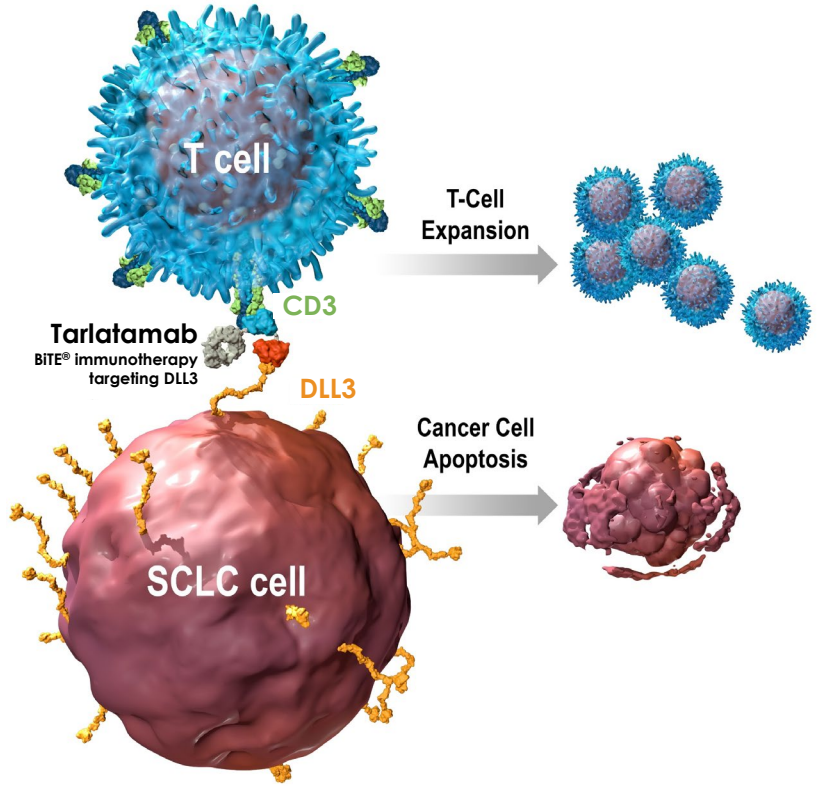
Introduction

- Brain metastases are common in patients with SCLC[1-2]
- Tarlatamab (10 mg Q2W) has shown durable responses and promising survival outcomes in previously treated SCLC; initial report on DeLLphi-301:[3]
  - ORR = 40%
  - mPFS = 4.9 months
  - 9-month OS = 68%; mOS = 14.3 months
- In the phase 1 DeLLphi-300 study, results suggest potential intracranial activity from tarlatamab[4]



- **We present a subgroup analysis of the phase 2 DeLLphi-301 study by the presence or absence of stable brain metastases at baseline**
- **We also explore CNS tumor shrinkage in patients with CNS lesion ≥ 10 mm**

BiTE, bispecific T-cell engager; **CD3,** cluster of differentiation 3; **CNS,** central nervous system; **DLL3,** delta-like ligand 3; **mOS**, median overall survival; **mPFS**, median progression-free survival; **ORR**, objective response rate; **Q2W**, every 2 weeks; **SCLC**, small cell lung cancer.

1. Slotman B, et al. *N Engl J Med.* 2007;357:664–672. 2. Takahashi T, et al. *Lancet Oncol.* 2017;18:663–671. 3. Ahn MJ, et al. *N Engl J Med*. 2023;389:2063–2075. 4. Hummel HD, et al. Oral presentation at ELCC 2024. Prague, CZE; March 20–23, 2024. Abstract 195MO.

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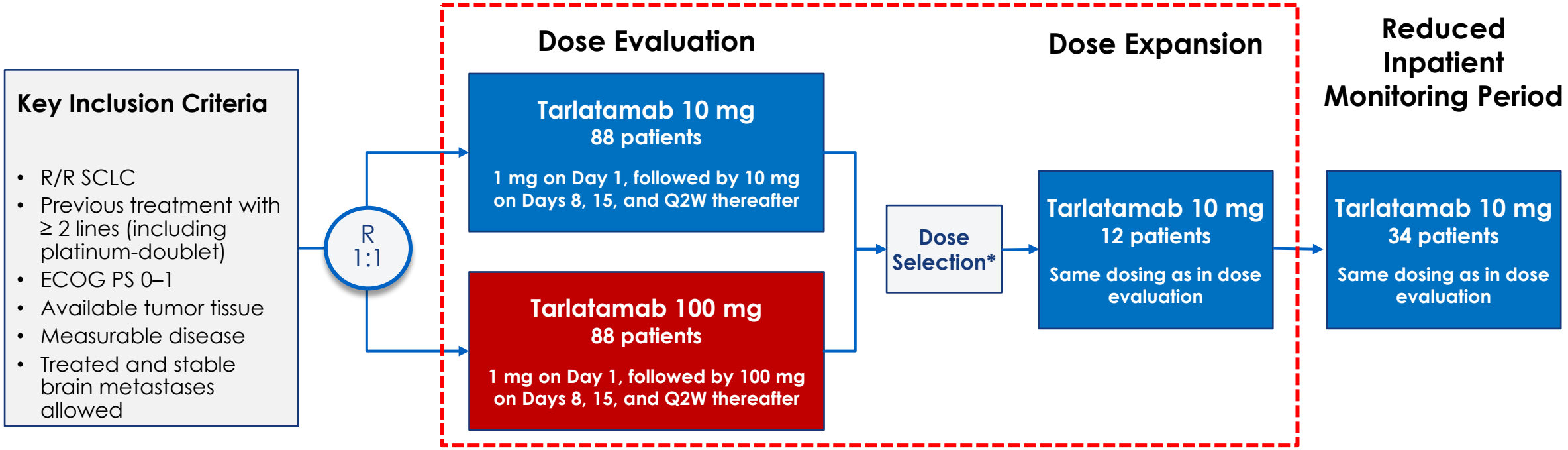
Phase 2 DeLLphi-301 Study Design



Primary Endpoint: ORR per RECIST v1.1 by BICR, TEAEs, tarlatamab serum concentrations

Secondary Endpoints: DOR, DCR, PFS per RECIST v1.1 by BICR, OS

Subgroup Analysis: Efficacy by BICR and safety, by presence or absence of baseline brain metastases

Post-hoc Analysis: Intracranial activity

NCT05060016. Post-enrollment, brain imaging was performed if clinically indicated. *Once 30 patients per dose level had the opportunity to confirm an objective response after the first post-treatment scan or up to 13 weeks of follow-up, whichever occurred first. **BICR**, blinded independent central review; **DCR**, disease control rate; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **R**, randomization; **RECIST**, Response Evaluation Criteria in Solid Tumors; **R/R SCLC**, relapsed/refractory small cell lung cancer; **TEAE**, treatment-emergent adverse event.
Ahn MJ, et al. *N Engl J Med*. 2023;389:2063-2075.

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Patient Baseline Clinical Characteristics

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 100)†	
	Yes (n = 23)	No (n = 77)
ECOG PS 0 / 1, n (%)	4 (17) / 19 (83)	22 (29) / 55 (71)
Median prior lines of therapy, n (range)	2 (2–5)	2 (1–6)
Prior anti-PD-(L)1 treatment, n (%)	19 (83)	55 (71)
DLL3 expression (> 0% of tumor cells), x/X (%)	21/22 (95)	59/61 (97)

Median follow-up period: 10.6 months‡

*Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383.
†The intention-to-treat analysis set consists of all patients who were randomized and enrolled according to assigned treatment dose levels. ‡OS data yet to mature.
DLL3, delta-like ligand 3; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PD-(L)1**, programmed cell death 1 protein/programmed cell death ligand-1 protein; **Q2W**, every 2 weeks.

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Efficacy Summary

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 100)†	
	Yes (n = 23)	No (n = 77)
ORR, % (95% CI)	52 (31–73)	38 (27–49)
Median DOR, months (range)	NE (3–12+)	NE (2–12+)
DOR probability at 12 months, KM estimate, % (95% CI)	55 (22–78)	50 (29–68)
Median PFS, months (95% CI)	6.7 (3–NE)	4.0 (3–6)
Median OS‡, months (95% CI)	14.3 (14–NE)	NE (9–NE)

Tarlatamab demonstrated durable response with promising survival regardless of the presence of treated, stable brain metastases at baseline

Data cutoff, June 27, 2023. Median follow-up: 10.6 months. *Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383. †The intention-to-treat analysis set consists of all patients who were randomized and enrolled according to assigned treatment dose levels. ‡OS data yet to mature. **CI,** confidence interval; **DOR**, duration of response; **KM**, Kaplan-Meier; **NE**, not estimable; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks.

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Treatment-Related Adverse Events (TRAEs)

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 99)†	
	Yes (n = 22)	No (n = 77)
TRAEs, n (%)	21 (95)	71 (92)
Grade ≥3	8 (36)	25 (32)
Fatal (grade 5)§	0	0
Leading to dose interruption and / or reduction of tarlatamab	3 (14)	11 (14)
Leading to discontinuation of tarlatamab	1 (5)	3 (4)
TRAEs of interest		
CRS‡	12 (55)	39 (51)
Grade ≥3	0	0
Leading to discontinuation of tarlatamab	0	0
ICANS and associated neurological events§	3 (14)	5 (6)
Grade ≥3	0	0
Leading to discontinuation of tarlatamab	0	1 (1)

*Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383.
†The safety analysis includes all patients who received ≥ 1 dose of tarlatamab. One patient in the tarlatamab 10 mg group did not receive tarlatamab. Coded using MedDRA version 26.1. CRS and ICANS events were graded using American Society for Transplantation and Cellular Therapy 2019 Consensus Grading. ‡CRS based on AMQ narrow search. §ICANS and associated neurological events based on 61 selected preferred terms with AMQ broad search. §One patient (1%) in the tarlatamab 10 mg group died during part 3 from respiratory failure assessed by the investigator to be related to the trial treatment; contributing factors include baseline chronic obstructive pulmonary disease requiring supplemental oxygen, baseline compromised functional reserve, concurrent Grade 3 CRS and pneumonitis after cycle 1 day 1 treatment, and a decision against escalation to ICU-level care. This patient did not have brain metastases at baseline screening. **AMQ**, Amgen MedDRA query; **CRS**, cytokine release syndrome; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **MedDRA**, Medical Dictionary for Regulatory Activities; **Q2W**, every 2 weeks; **TRAE**, treatment-related adverse event.

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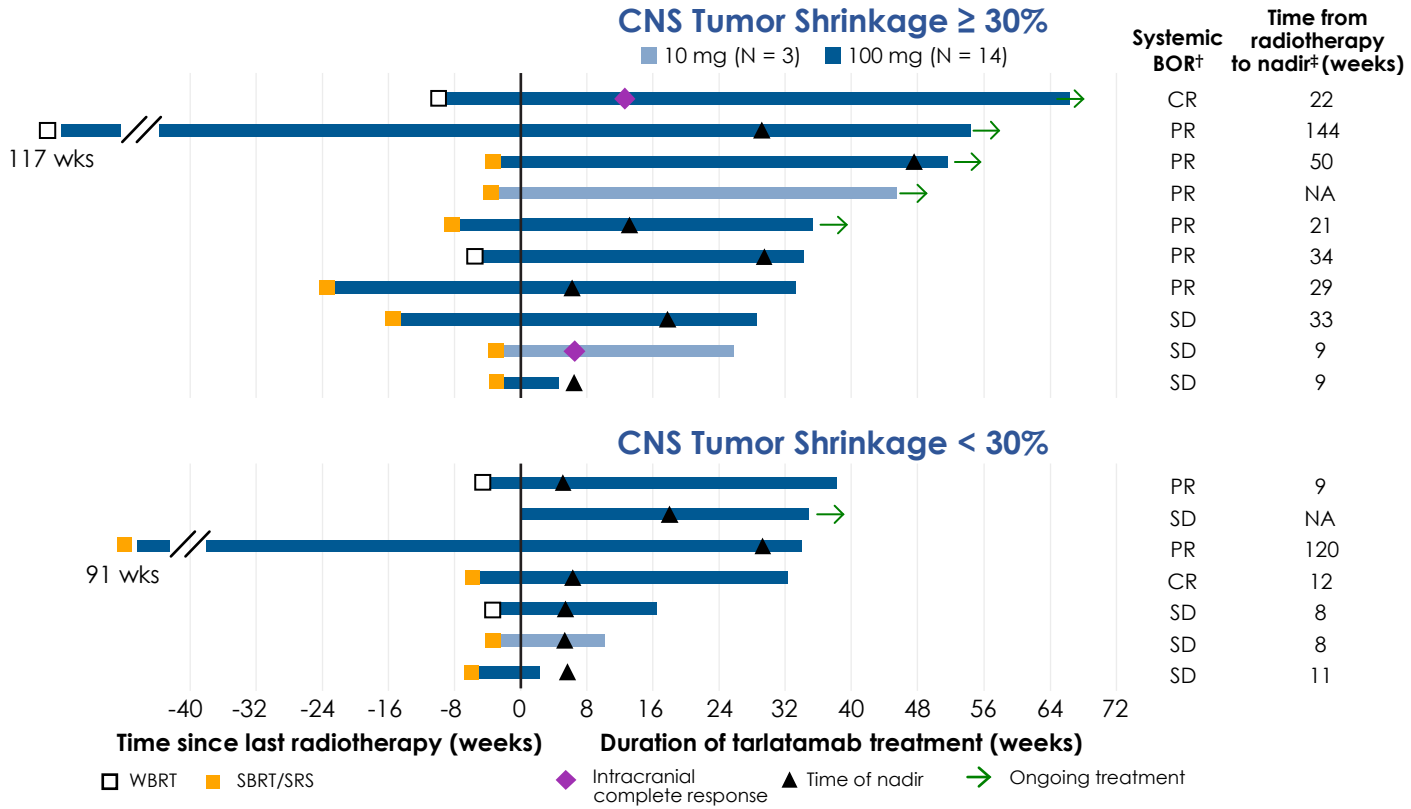
Intracranial Activity*

Tarlatamab 10 mg (n = 3) or 100 mg (n = 14) Q2W with baseline CNS lesion ≥ 10 mm

- **mRANO BM§ analyses (N = 17)**
  - CNS tumor shrinkage ≥ 30% in 10 of 17 patients (59%)
  - Intracranial disease control in 94% (16 of 17) patients (95% CI, 71.3–99.9)
  - Median duration of intracranial disease control was NE (range, 2.6–13.9+ months)
  - CNS disease progression per modified RANO-BM occurred in 3 of 17 patients (18%)



CNS tumor shrinkage was observed in patients with previously treated brain metastases

*The CNS measurable analysis set included patients who had ≥ 2 brain scans (baseline and post-baseline) and were identified per modified RANO-BM by BICR as having ≥ 1 brain lesion ≥ 10 mm at baseline. †Systemic BOR was determined using RECIST v1.1 by BICR. ‡Minimum percentage change from baseline (smallest SLD) before disease progression. Median follow-up: 11.8 months. §mRANO BM represents RANO BM criteria with the following modifications: (1) corticosteroid data and clinical status were not incorporated into imaging reads; (2) diffusion weighted imaging MRI sequences were not required but were made available to the independent reviewer if received. **BICR**, blinded independent central review; **BOR**, best overall response; **CNS**, central nervous system; **CR**, complete response; **mRANO BM**, modified response assessment in neuro-oncology criteria for brain metastases; **MRI**, magnetic resonance imaging; **NA**, not available; **NE**, not estimable; **PR**, partial response; **RECIST**, Response Evaluation Criteria in Solid Tumors; **RT,** radiotherapy; **SBRT**, stereotactic body radiation therapy; **SD**, stable disease; **SLD**, sum of longest diameter; **SRS**, stereotactic radiosurgery; **WBRT**, whole brain radiation therapy.

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Limitations

- Interpretation of intracranial results may be confounded by prior radiotherapy
- Sample sizes for patients with brain metastases ≥ 10 mm at baseline were small
- Only patients with confirmed brain metastases at baseline had mandated surveillance CNS imaging

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Conclusions

- Tarlatamab 10 mg Q2W demonstrated a favorable benefit-risk profile in patients with previously treated SCLC irrespective of the presence of treated and stable brain metastases (BM) at baseline
  - ORR was 52% in patients with BM (n = 23) and 38% in patients without BM (n = 77)
  - In patients with BM, median PFS was 6.7 months and median OS was 14.3 months
  - The safety profile of tarlatamab in patients with BM was manageable and consistent with the overall safety profile from the tarlatamab program
- CNS tumor shrinkage was observed after radiotherapy in some patients treated with tarlatamab

Results support further study of tarlatamab in patients with previously treated SCLC irrespective of the presence of brain metastases at baseline

CNS, central nervous system; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **SCLC**, small-cell lung cancer.

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Plain Language Summary

- People with small cell lung cancer (SCLC) often have cancer spread to the brain
- The phase 2 DeLLphi-301 study looked at how well tarlatamab worked and how safe tarlatamab was in people with SCLC who had previously received at least 2 types of lung cancer treatment
- This report looked at study participants in the DeLLphi-301 study with SCLC that had spread to the brain but the cancer in the brain was previously treated and under control
- The results of this report showed:
    - Tarlatamab helped shrink SCLC which was long-lasting for some patients regardless of whether they had cancer spread to the brain
    - The side effects from tarlatamab in this report were similar to those seen when tarlatamab was used in other trials
    - A reduction in the size of cancer in the brain was seen after radiation treatment in some patients treated with tarlatamab, but more research is needed

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Additional Slides

Baseline Clinical Characteristics

Baseline brain metastases:	Tarlatamab 100 mg (n = 88)	
	Yes (n = 32)	No (n = 56)
ECOG PS 0 / 1, n (%)	7 (22) / 25 (78)	17 (30) / 39 (70)
Median prior lines of therapy, n (range)	2 (2–8)	2 (1–6)
Prior anti-PD-(L)1 treatment, n (%)	24 (75)	38 (68)
DLL3 expression (> 0% of tumor cells), x/X (%)	25/25 (100)	46/49 (94)

Median follow-up: 10.6 months

Data cutoff, June 27, 2023. The intention-to-treat analysis set consists of all patients who were randomized and enrolled according to assigned treatment dose levels.
DLL3, delta-like ligand 3; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PD-(L)1**, programmed cell death 1 protein/programmed cell death ligand-1 protein.

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Efficacy Summary

Baseline brain metastases:	Tarlatamab 100 mg (n = 88)	
	Yes (n = 32)	No (n = 56)
ORR, % (95% CI)	41 (24–59)	29 (17–42)
DOR probability at 12 months, KM estimate, % (95% CI)	48 (18–72)	42 (16–66)
Median DOR, months (range)	7 (1+–12+)	8 (3–13+)
Median PFS, months (95% CI)	4 (3–8)	3 (2–4)
Median OS*, months (95% CI)	NE (NE–NE)	NE (9–NE)

ORR was 41% in patients with brain metastases and 29% in patients without brain metastases

*OS data yet to mature.
DOR, duration of response; **KM**, Kaplan-Meier; **NE**, not estimable; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival.

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Treatment-Related Adverse Events (TRAEs)

Baseline brain metastases:	Tarlatamab 100 mg (n = 87)	
	Yes (n = 32)	No (n = 55)
TRAEs, n (%)	31 (97)	52 (95)
Grade ≥3	12 (38)	21 (38)
Leading to dose interruption and / or reduction of tarlatamab	11 (34)	16 (29)
Leading to discontinuation of tarlatamab	0	2 (4)
TRAEs of interest		
CRS*	21 (66)	34 (62)
Grade ≥3	2 (6)	2 (4)
Leading to discontinuation of tarlatamab	0	0
ICANS and associated neurological events†	7 (22)	10 (18)
Grade ≥3	1 (3)	0
Leading to discontinuation of tarlatamab	0	1 (2)

- **No fatal TRAEs were reported**
- **Grade 3 ICANS events occurred in the tarlatamab 100 mg group only, and did not lead to discontinuation in any patient with brain metastases**

The safety analysis includes all patients who received ≥ 1 dose of tarlatamab. One patient in the tarlatamab 100 mg group did not receive tarlatamab. Coded using MedDRA version 26.1. CRS and ICANS events were graded using American Society for Transplantation and Cellular Therapy 2019 criteria. *CRS based on AMQ narrow search. †ICANS and associated neurological events based on selected preferred terms with AMQ broad search. **AMQ**, Amgen MedDRA query; **CRS**, cytokine release syndrome; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **MedDRA**, Medical Dictionary for Regulatory Activities; **TRAE**, treatment-related adverse event.

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