Tarlatamab Sustained Clinical Benefit and Safety in Previously Treated SCLC: DeLLphi-301 Phase 2 Extended Follow-Up

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SC-AT-AMG 757-00052 0924 Presented at World Conference on Lung Cancer (WCLC) 2024. September 7-10, 2024; San Diego, CA, USA.

SC-AT-NP-00098 10.24

Tarlatamab in Small Cell Lung Cancer (SCLC)

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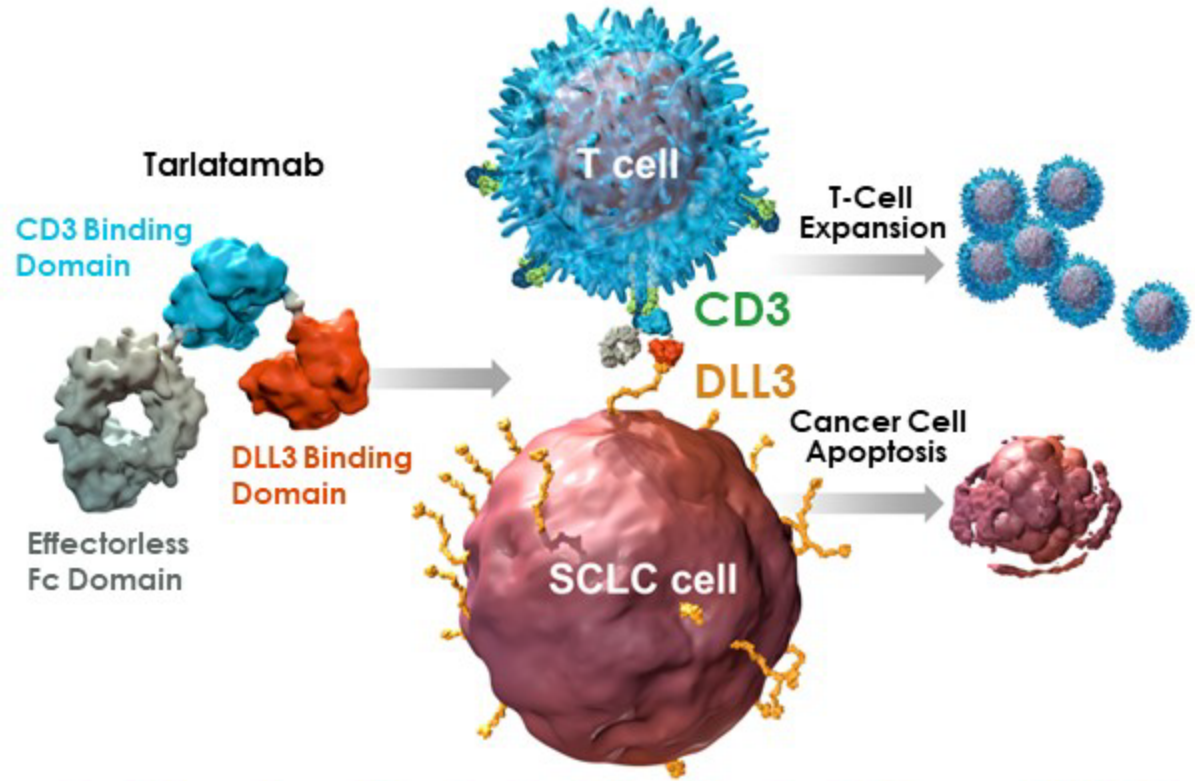
- Tarlatamab is a bispecific T-cell engager (BiTE®) immunotherapy that targets delta-like ligand 3 (DLL3) on SCLC cells and CD3 on T cells, leading to T-cell–mediated cancer cell lysis[1]
- At the primary analysis of the DeLLphi-301 phase 2 study, tarlatamab showed durable responses and a manageable safety profile in patients with previously treated SCLC[2]
- In May 2024, the FDA granted tarlatamab accelerated approval for the treatment of ES-SCLC with disease progression on or after platinum-based chemotherapy[3]



Tarlatamab activates T cells without relying on MHC-I

WE PRESENT EFFICACY AND SAFETY OUTCOMES FROM EXTENDED FOLLOW-UP OF THE DeLLphi-301 STUDY

CD3, cluster of differentiation 3; **ES-SCLC**, extensive-stage small cell lung cancer; **Fc**, fragment crystallizable; **FDA**, US Food and Drug Administration; **MHC-I**, major histocompatibility complex-I.

1. Giffin MJ, et al. *Clin Cancer Res.* 2021;27:1526-1537. **2.** Ahn MJ, et al. *N Engl J Med.* 2023;389:2063-2075. **3.** IMDELLTRA (prescribing information). Amgen Inc., Thousand Oaks, CA. Accessed May 2024 from https://www.pi.amgen.com/-/media/Project/Amgen/Repository/pi-amgen-com/Imdelltra/imdelltra_fpi.pdf.

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DeLLphi-301 Study Design

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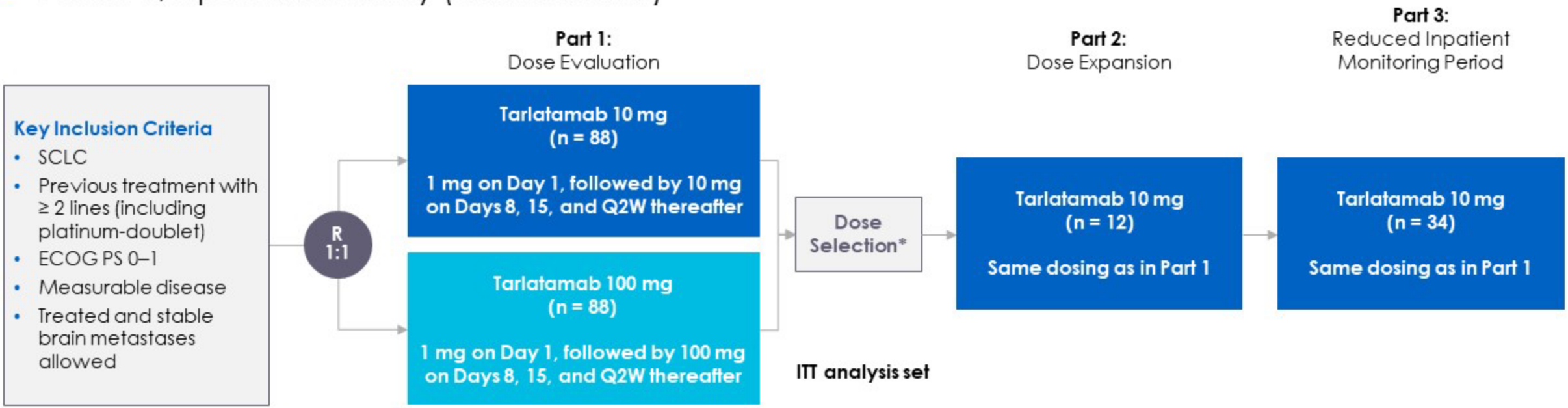
- Phase 2, open-label study (NCT05060016)



PRIMARY ENDPOINT: ORR per RECIST 1.1 by BICR

SECONDARY ENDPOINTS INCLUDED: DOR, DCR, PFS per RECIST 1.1 by BICR, OS, TEAEs, TARLATAMAB SERUM CONCENTRATIONS

Data cutoff was January 12, 2024 for all efficacy and safety outcomes, except for OS. For OS, the data cutoff was May 16, 2024 to obtain mature OS data with a median follow-up of 20.7 months.

*Once 30 patients per dose level had the opportunity to confirm an objective response after the first post-treatment scan or ≥ 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; **ITT**, intention-to-treat; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **R**, randomization; **RECIST**, Response Evaluation Criteria in Solid Tumors; **SCLC**, small cell lung cancer; **TEAE**, treatment-emergent adverse event.

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Baseline Characteristics

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	Parts 1 + 2 Tarlatamab 10 mg (n = 100)	Part 3 Tarlatamab 10 mg (n = 34)
Median age, years (range)	64 (35–82)	66 (49–80)
Male, %	72	71
Asian/Black or African American/White,*%	41 / 0 / 58	6 / 3 / 91
Patients who ever smoked/patients who never smoked, %	92 / 8	97 / 3
ECOG performance status: 0/1, %	26 / 74	29 / 71
Prior lines of therapy, median (range)	2 (1–6)†	2 (2–6)
2 prior lines of therapy, %	65	65
≥ 3 prior lines of therapy, %	33	35
Prior anti–PD-(L)1 treatment, %	74	82
< 90 days to progression after first-line platinum therapy,‡%	28	21
Brain/liver metastases, %	23 / 39	12 / 35
DLL3 expression (> 0%), n/N evaluable (%)	80 / 83 (96)	15 / 16 (94)

Data cutoff, January 12, 2024. Median follow-up was 16.6 months. *No patients of American Indian, Alaska Native, Native Hawaiian, or other Pacific Islander race were enrolled.
†Two patients were treated with one prior line of therapy. ‡Platinum sensitivity was calculated as end of first-line platinum therapy to date of first progression.
DLL3, delta-like ligand 3; **ECOG**, Eastern Cooperative Oncology Group; **PD-(L)1**, programmed cell death (ligand) 1 protein.

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Tarlatamab Anti-Cancer Activity

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Outcome	Part 1 + 2 Tarlatamab 10 mg (N = 100)
Objective response rate, n (%) (95% CI for %)	40 (40) (30.3–50.3)
Complete response	3 (3)
Partial response	37 (37)
Stable disease	30 (30)
Progressive disease	20 (20)
Not evaluable / no post-baseline scan*	10 (10)
Disease control rate, n (%) (95% CI for %)	70 (70) (60.0–78.8)

TARLATAMAB 10 mg DEMONSTRATED ANTI-CANCER ACTIVITY IN HEAVILY PRETREATED SCLC, WITH AN ORR OF 40%

Data cutoff, January 12, 2024. Median follow-up was 16.6 months. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety substudy and was not included in this response analysis. *Patients who were not evaluable or did not have post-baseline scans were considered non-responders for the response analysis.

CI, confidence interval; **ITT**, intention-to-treat; **ORR**, objective response rate; **SCLC**, small cell lung cancer.

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Duration of Response and Time on Treatment

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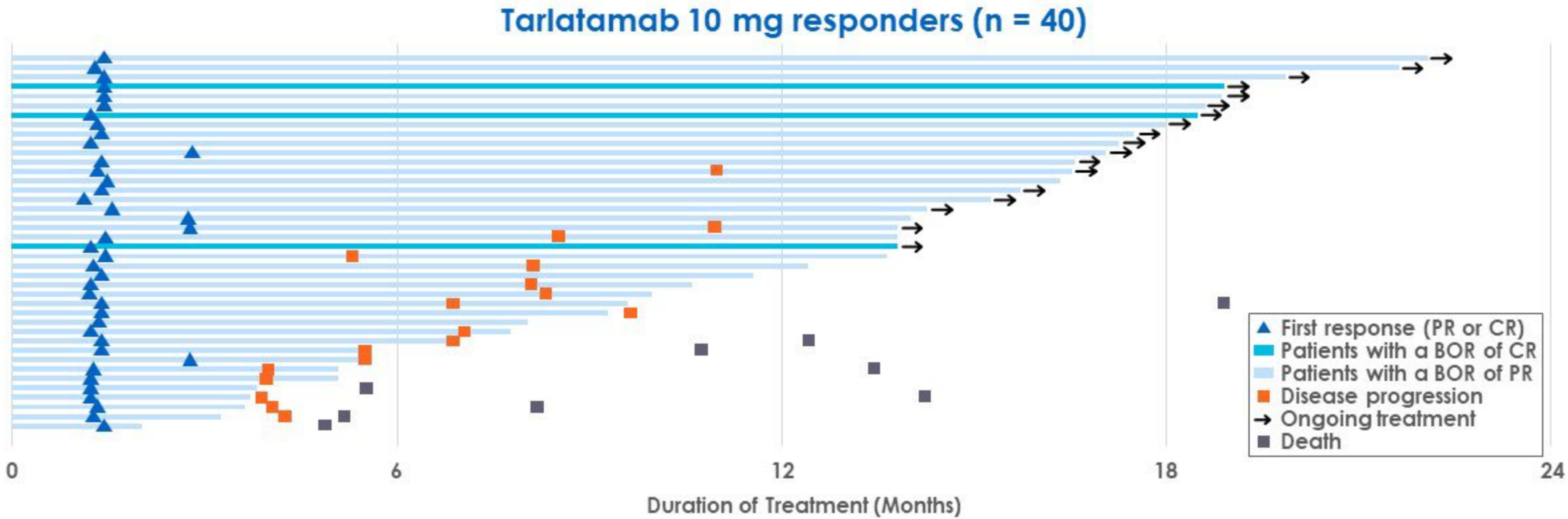

- **MEDIAN TIME TO RESPONSE WAS 1.4 MONTHS (IQR, 1.3–1.4)**
- **MEDIAN DOR WAS 9.7 MONTHS (95% CI, 6.9–NE) WITH 17/40 (43%) OF RESPONSES ONGOING AT DATA CUTOFF**

Data cutoff was January 12, 2024. Median follow up for DOR was 15.1 months. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety sub-study and was not included in this response analysis.
BOR, best overall response; **CR**, complete response; **DOR**, duration of response; **ITT**, intention-to-treat; **IQR**, interquartile range; **NE**, not estimable; **PR**, partial response.

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Sustained Disease Control*

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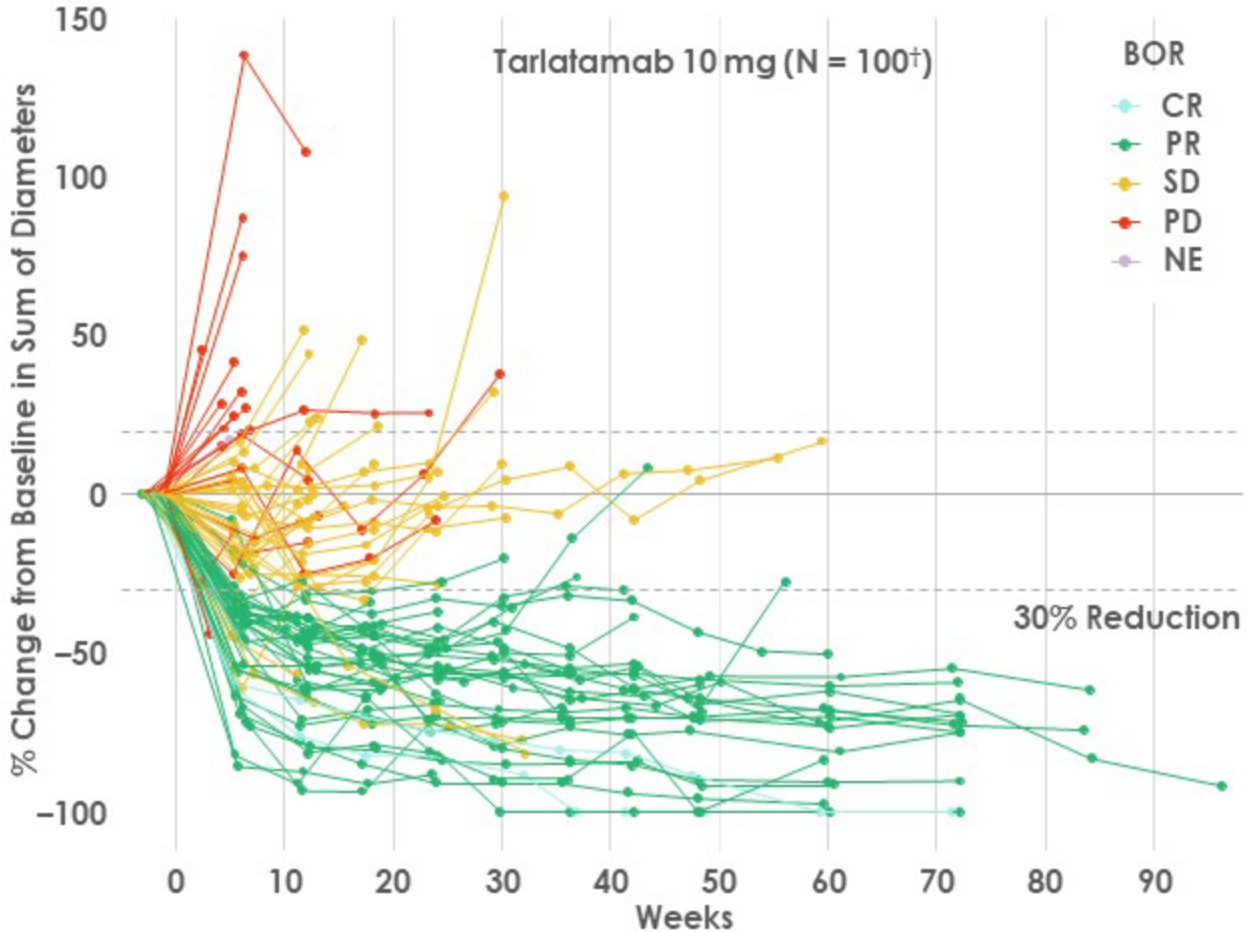

- Tumor shrinkage was seen in 72% of patients
- The median duration of disease control was 6.9 months (95% CI, 5.4–8.6)

26 PATIENTS (26%; 3 CR, 20 PR, 3 SD) HAD SUSTAINED DISEASE CONTROL ≥ 52 WEEKS

Data cutoff, January 12, 2024. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety substudy and was not included in this response analysis.
*Sustained disease control was defined as disease control (CR, PR, or SD) with time on treatment ≥ 52 weeks.
†Seven patients did not have a postbaseline scan.
BOR, best overall response; **CR**, complete response; **ITT**, intention-to-treat; **NE**, not evaluable; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease.

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Progression-Free Survival

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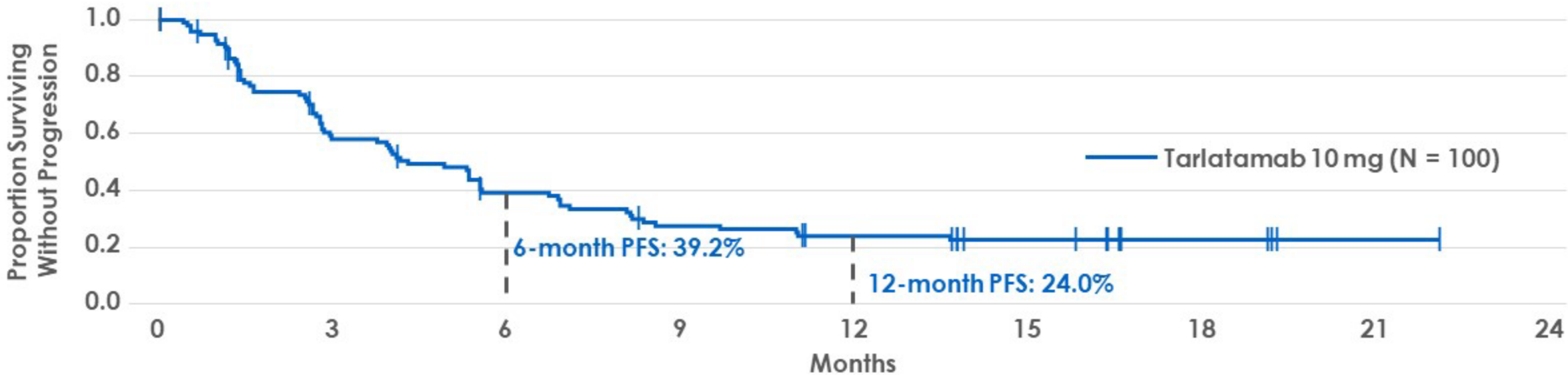

Number of Patients at Risk:

Tarlatamab 10 mg	100	53	34	23	18	13	4	1	0

MEDIAN PFS WAS 4.3 MONTHS (95% CI, 2.9–5.6)

Data cutoff, January 12, 2024. Median follow-up for PFS was 16.4 months. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety substudy and was not included in this response analysis.
ITT, intention-to-treat; **PFS**, progression-free survival.

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Overall Survival

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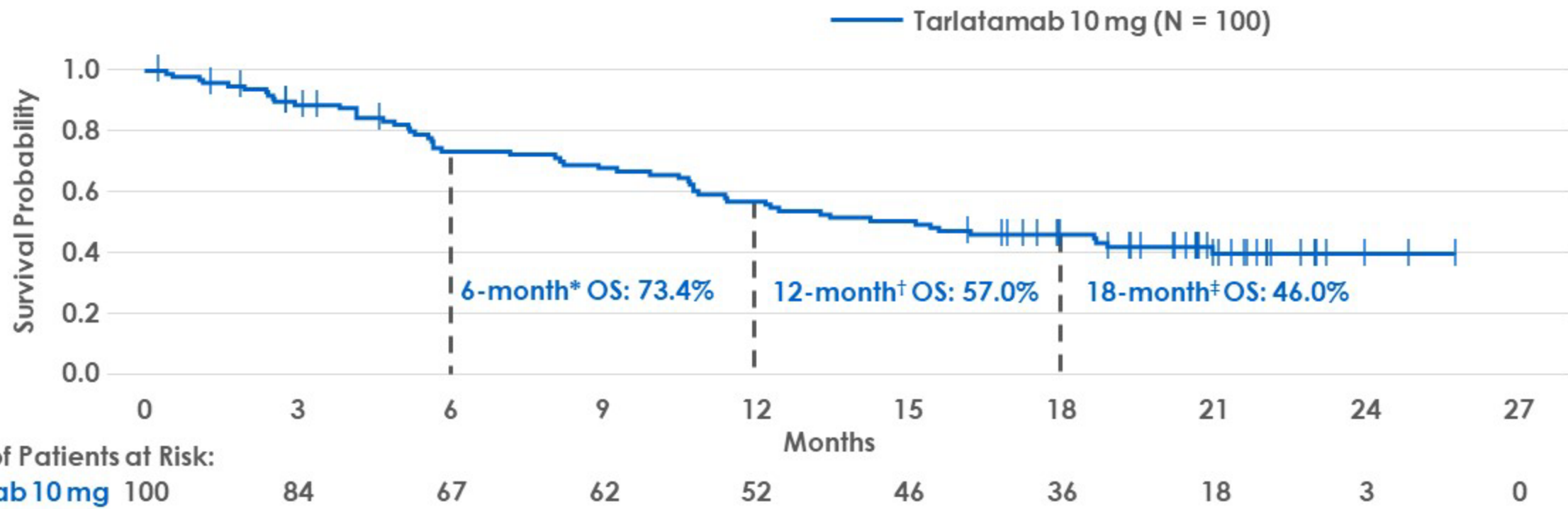

MEDIAN OS WAS 15.2 MONTHS (95% CI, 10.8–NE)

Median follow-up for OS was 20.7 months. Data cutoff, May 16, 2024. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in ITT analysis. Part 3 was a safety substudy and was not included in this response analysis. *95% CI, 63.2–81.2. †95% CI, 46.3–66.3. ‡95% CI, 35.6–55.8. Progression-free interval after first line platinum treatment is defined as days from the last first line platinum treatment to disease progression or start of second line treatment, whichever is earlier.
ITT, intention-to-treat; **NE**, not estimable; **OS**, overall survival.

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Overall Survival

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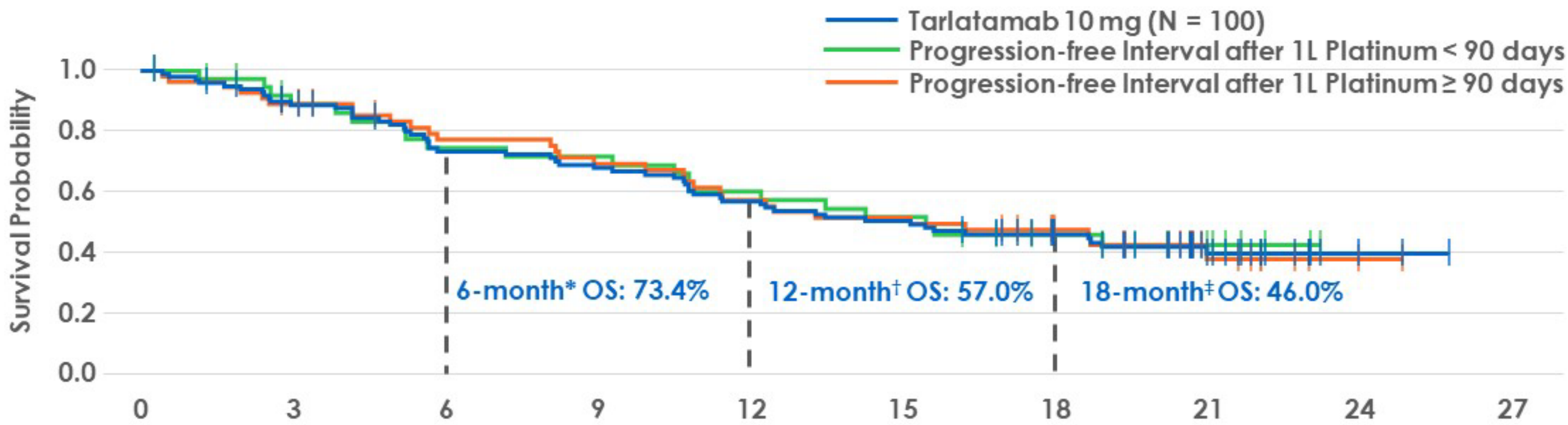

Number of Patients at Risk:										
Tarlatamab 10 mg	100	84	67	62	52	46	36	18	3	0
< 90 days	39	31	26	25	21	18	13	7	0	
≥ 90 days	55	48	39	35	29	26	21	9	2	0

OS WAS SIMILAR REGARDLESS OF PROGRESSION-FREE INTERVAL AFTER 1L PLATINUM TREATMENT (< 90 d vs ≥ 90 d)

Median follow-up for OS was 20.7 months. Data cutoff, May 16, 2024. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in ITT analysis. Part 3 was a safety substudy and was not included in this response analysis. *95% CI, 63.2–81.2. †95% CI, 46.3–66.3. ‡95% CI, 35.6–55.8. Progression-free interval after first line platinum treatment is defined as days from the last first line platinum treatment to disease progression or start of second line treatment, whichever is earlier.
ITT, intention-to-treat; **NE**, not estimable; **OS**, overall survival.

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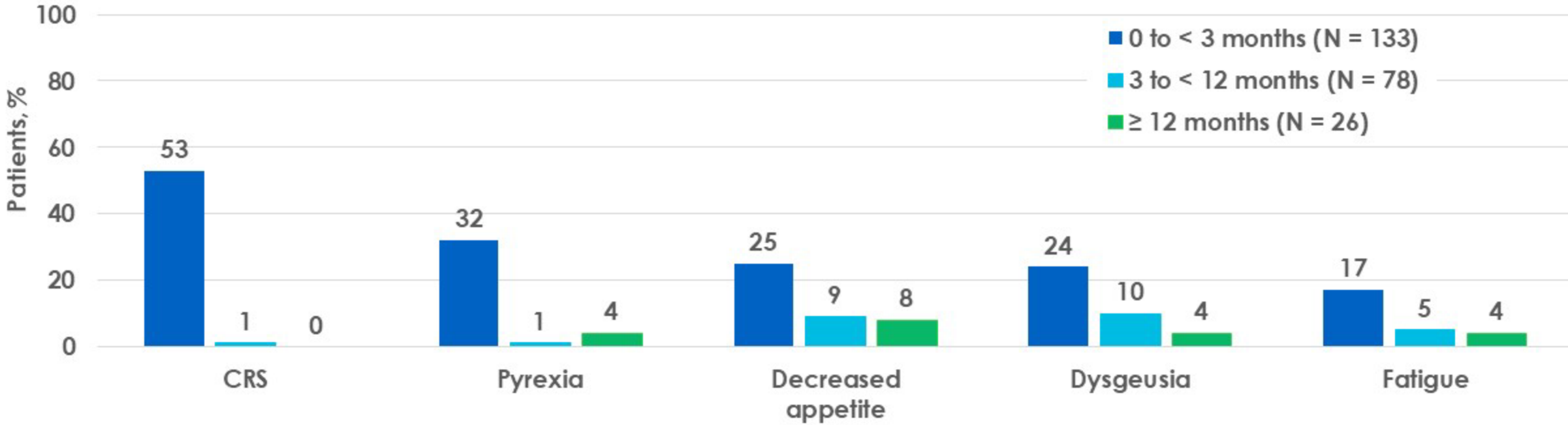
Most Common Tarlatamab-Related AEs over Time



- TRAEs led to dose interruption in 16% and discontinuation in 4% of patients

TARLATAMAB DEMONSTRATED LONG-TERM TOLERABILITY, WITH NO NEW SAFETY CONCERNS

One patient did not receive tarlatamab 10 mg and was not included in the safety analyses. Most common TRAEs refer to TRAEs with overall incidence ≥ 17%. AEs were coded using MedDRA version 26.1. There was one fatal TRAE of respiratory failure, with contributing factors including baseline chronic obstructive pulmonary disease requiring supplemental oxygen, baseline compromised pulmonary functional reserve, concurrent grade 3 CRS and pneumonitis after cycle 1 day 1 treatment, and a decision against escalation to intensive care unit level of care.

AE, adverse event; **CRS**, cytokine release syndrome; **MedDRA**, Medical Dictionary for Regulatory Activities; **TRAE**, tarlatamab-related AE.

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CRS and ICANS* Incidence and Timing

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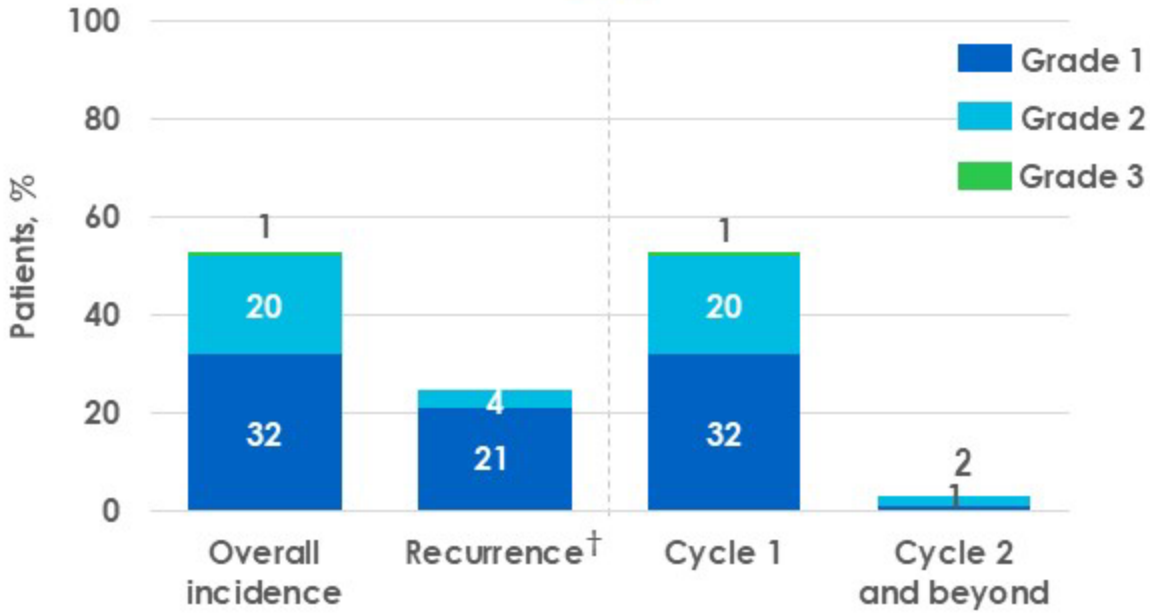
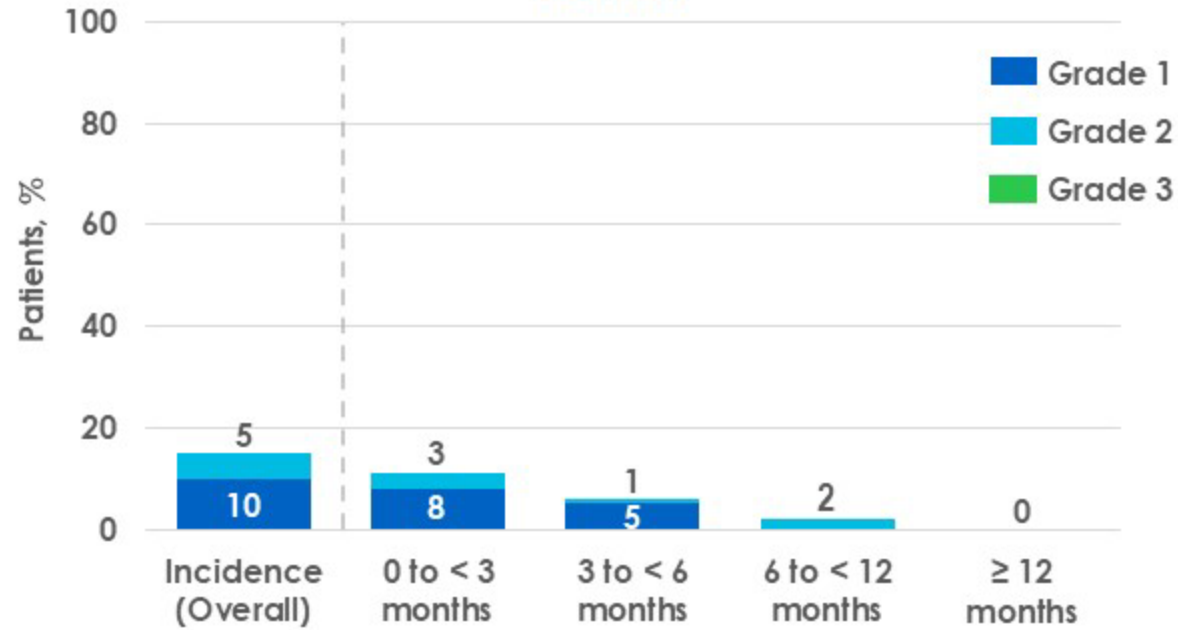
CRS



Median time to resolution‡: 3 days (95% CI, 3–4)

ICANS*



Median time to resolution‡: 33 days§ (95% CI, 7–120)

- **CRS PRIMARILY OCCURRED AFTER THE FIRST OR SECOND DOSE IN CYCLE 1, WITH MOST EVENTS OF GRADE 1 OR 2**
- **ICANS* OCCURRED INFREQUENTLY, PRIMARILY WITH EARLY ONSET (< 6 MONTHS) AND ALL EVENTS OF GRADE 1 OR 2**

*ICANS includes associated neurologic events based on a broad search using 61 selected preferred terms from MedDRA version 26.0. †A CRS event is considered a recurrent event if it occurred at a subsequent dose after the first CRS event during cycle 1. ‡Based on Kaplan-Meier estimates. TEAE data are reported. §Based on 22 events.
CI, confidence interval; **CRS**, cytokine release syndrome; **ICANS**, immune effector cell–associated neurotoxicity syndrome; **MedDRA**, Medical Dictionary for Regulatory Activities.

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DeLLphi-301 Conclusions

- With extended follow-up, tarlatamab 10 mg Q2W demonstrated durable response and impressive survival outcomes
  - Median DOR was 9.7 months
  - Median OS was 15.2 months with a Kaplan-Meier estimate for OS at 18 months of 46%
- Tarlatamab demonstrated long-term tolerability with no new safety concerns
- The phase 3 DeLLphi-304 study (NCT05740566) comparing the efficacy and safety of tarlatamab (10 mg Q2W) with standard-of-care chemotherapy is currently in progress

TARLATAMAB DEMONSTRATED DURABLE RESPONSE AND UNPRECEDENTED SURVIVAL OUTCOMES WITH LONG-TERM TOLERABILITY IN PATIENTS WITH PREVIOUSLY TREATED SCLC

DOR, duration of response; **OS**, overall survival; **Q2W**, every 2 weeks; **SCLC**, small cell lung cancer.
Clinicaltrials.gov. NCT05740566. Accessed August 2024 from https://clinicaltrials.gov/study/NCT05740566.

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Acknowledgments

- **The authors thank all patients and their families for their participation in this study, and all investigators**
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- **This study was funded by Amgen Inc. Medical writing support for this presentation was funded by Amgen Inc. and was provided by Lisa Denny, PhD, of ICON plc (Blue Bell, PA) and Liz Leight, PhD, of Amgen Inc.**

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