Tarlatamab for Patients With Small Cell Lung Cancer: 6–8-Hour Outpatient vs 48-Hour Inpatient Monitoring in Cycle 1

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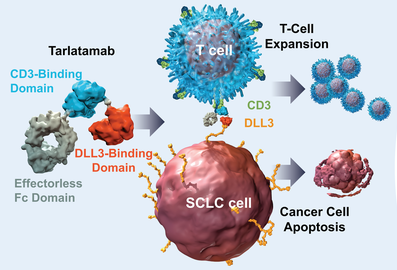
DeLLphi 300

Background

- Tarlatamab, a bispecific T-cell engager (BiTE®) immunotherapy, targets DLL3 on the surface of SCLC cells and CD3 on T cells.[1]

Figure 1. Tarlatamab Directs T Cells to DLL3-Expressing SCLC Cells[2]



- Evidence has shown that tarlatamab has a manageable safety profile at the approved dose of 10 mg IV Q2W.[1,3]
- Initial clinical trials required 48–72-hour inpatient monitoring following cycle 1 tarlatamab administrations given the potential risk of cytokine release syndrome (CRS).[1,3]

Objective

To report safety outcomes in patients treated with tarlatamab 10 mg IV Q2W followed by either 6–8-hour outpatient or 48-hour inpatient monitoring in cycle 1 in the phase 1 DeLLphi-300 study.

Conclusions

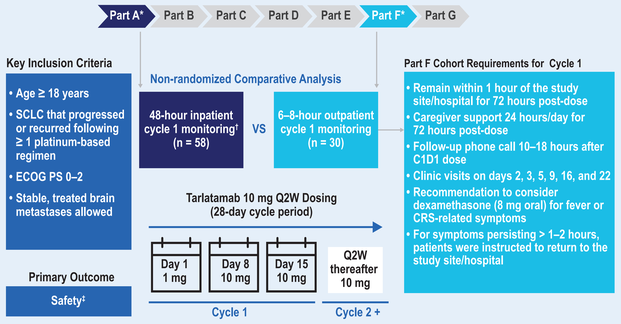
- **In this non-randomized comparative analysis, patients treated with tarlatamab 10 mg IV Q2W and monitored for 6–8 hours in the outpatient setting in cycle 1 exhibited a similar safety profile to patients that received 48-hour inpatient monitoring in cycle 1.**
  - Additional measures in cycle 1 for the outpatient monitoring group included having patients remain within 1 hour of the study site/hospital and having caregiver support 24 hours/day for 72 hours following tarlatamab administrations.
- **There were no major differences in cycle 1 safety outcomes with tarlatamab treatment between the 6–8-hour outpatient and 48-hour inpatient monitoring group:**
  - **CRS events** occurred primarily with the first or second dose given in cycle 1.
    - Outpatient 6–8-hour monitoring did not lead to a higher incidence or greater severity of CRS events vs 48-hour inpatient monitoring (all grade CRS: 60% vs 62%; grade 3–4 CRS: 0% vs 3%).
  - **ICANS** with cycle 1 dosing was rare (3%) and similar for both groups.
  - The rate of **hospitalization or ER visits for all AEs** in cycle 1 was similar between the 6–8-hour outpatient vs 48-hour inpatient groups (27% vs 34%).

Future Directions

Ongoing phase 3 studies (DeLLphi-304 in 2L SCLC, DeLLphi-305 in ES-SCLC 1L maintenance, and DeLLphi-306 in LS-SCLC) include patients monitored with a shortened outpatient monitoring period and will provide further insight for clinical practice.

Trial Design

Figure 2. DeLLphi-300 Phase 1 Trial (NCT03319940)



Data cutoff was August 23, 2024.

*Only Parts A and F were included in this comparative study as they met the following criteria: 1) tarlatamab 10 mg IV Q2W with one-step dosing and 2) 6–8-hour outpatient monitoring or 48-hour inpatient monitoring. †One patient received 72-hour inpatient monitoring during cycle 1. ‡AEs were classified using CTCAE version 4.0 and CRS was graded using Lee et al. 2014.[4]

Patients

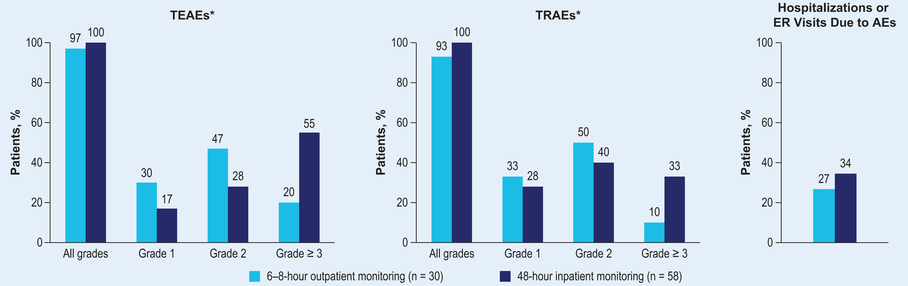
Table 1. Demographics and Baseline Characteristics

	6–8-Hour Outpatient Monitoring (n = 30)	48-Hour Inpatient Monitoring* (n = 58)
Median age, years (range)	66 (46–78)	66 (43–80)
Male, %	43	55
White / Asian / Black or African American / Other,† %	90 / 3 / 7 / 0	78 / 10 / 2 / 10
Patients who ever smoked / patients who never smoked, %	93 / 3‡	84 / 16
ECOG PS 0 / 1 / 2, %	40 / 60 / 0	35 / 60 / 5
Prior lines of therapy, median (range)	2 (1–5)	2 (1–6)
Prior anti–PD-(L)1 treatment, %	83	85
Brain / liver metastases, %	20 / 50	36 / 48

*One patient received 72-hour inpatient monitoring. †There were no people of American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, or multiple races in this study. ‡Prior smoking history for one patient was missing.

Overall Safety

Figure 3. Cycle 1 Safety Profile



*Reported as worst grade per patient.

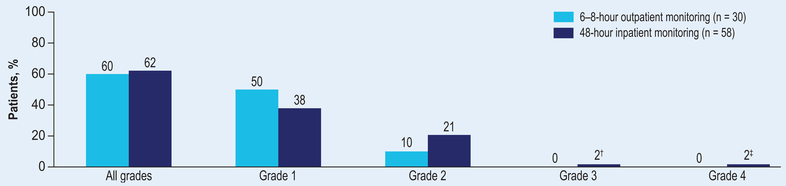
Table 2. TRAEs Occurring in ≥ 25% of Patients (All Cycles)

Preferred Term, n (%)	6–8-Hour Outpatient Monitoring (n = 30)	48-Hour Inpatient Monitoring (n = 58)
CRS	18 (60)	36 (62)
Dysgeusia	14 (47)	25 (43)
Nausea	11 (37)	10 (17)
Asthenia	10 (33)	9 (16)
Decreased appetite	9 (30)	12 (21)
Pyrexia	8 (27)	18 (31)
Fatigue	7 (23)	17 (29)

For overall TEAEs and TRAEs, regardless of cycle, please scan the QR code.

Cycle 1 AE of Interest: CRS

Figure 4. Cycle 1 CRS TRAEs by Grade*



*Reported as worst grade per patient. There were no grade 5 CRS events. †Patient had grade 3 CRS with hypoxia requiring high-flow oxygen and hypotension requiring IV fluids. Potential contribution to this patient's AE may be from concurrent progressive thoracic disease. Upon treatment with corticosteroids and tocilizumab, this grade 3 event resolved within 11 minutes. ‡Patient had grade 4 CRS requiring intervention that was documented as hypotension requiring IV fluids. Potential contribution to this patient's AE may be from concurrent progressive thoracic disease.

Table 3. Onset and Resolution of CRS

	6–8-Hour Outpatient Monitoring	48-Hour Inpatient Monitoring
Median time to onset from last dose, hour (Q1, Q3)	10.6 (7.2, 17.2)	15.1 (8.6, 25.5)
Median time to resolution, days (95% CI)	3.0 (3.0, 4.0)	3.0 (2.0, 3.0)

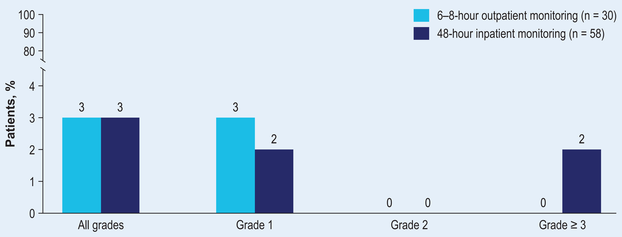
- CRS grading was per Lee et al. 2014.[4]
- In the 6–8-hour outpatient monitoring group, 18 patients (60%) had a total of 25 CRS events, all of which occurred in cycle 1 and all resolved; among the inpatient group, 7 CRS events occurred after cycle 1.
- CRS incidence, median time to onset, and median time to resolution were similar between the groups.
- Tocilizumab was used for CRS management in 0% (0/30) and 12% (7/58) of patients in the 6–8-hour outpatient and 48-hour inpatient monitoring groups, respectively.

72% of CRS events (18/25) after C1D1 and C1D8 did not require hospitalization or an ER visit beyond the monitoring period.

- Eleven of 14 (79%) CRS events following C1D1 were grade 1.
- One patient went to the ER and five patients were hospitalized for CRS following C1D1.
- All CRS events following C1D8 were grade 1.
- One patient went to the ER for CRS following C1D8.

Cycle 1 AE of Interest: ICANS

Figure 5. Cycle 1 ICANS TRAEs by Grade



- In the 6–8-hour outpatient monitoring group, ICANS occurred in 1 patient.
  - One patient had a grade 1 cognitive disorder.
  - Time to onset was 9 days from the first tarlatamab dose and resolved within 2 days.
- In the 48-hour inpatient monitoring group, ICANS occurred in 2 patients.
  - One patient had grade 1 muscular weakness and the other had grade 3 encephalopathy requiring hospitalization.
  - Median time to onset was 14 days (IQR: 12–16) with a median time to resolution of 3 days (IQR: 2–4).

Limitations

- Small size of 6–8-hour outpatient monitoring group.
- Enrollment of groups was not contemporaneous.
- Patients in the 48-hour inpatient monitoring group had more opportunities for direct clinical evaluations while hospitalized that may have led to differences in AE reporting and/or grading compared with patients in the 6–8-hour outpatient monitoring group.

ABBREVIATIONS

1L, first line; **2L**, second line; **AE**, adverse event; **BiTE**, bispecific T-cell engager; **C1D1**, cycle 1 day 1; **C1D8**, cycle 1 day 8; **CD3**, cluster of differentiation 3; **CI**, confidence interval; **CRS**, cytokine release syndrome; **CTCAE**, Common Terminology Criteria for Adverse Events; **DLL3**, delta-like ligand 3; **ECOG PS**, Eastern Cooperative Oncology Group Performance Status; **ER**, emergency room; **ES**, extensive stage; **Fc**, fragment crystallizable; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **IQR**, interquartile range; **IV**, intravenous; **LS**, limited stage; **PD-(L)1**, programmed cell death (ligand) 1; **Q**, quartile; **Q2W**, every 2 weeks; **SCLC**, small cell lung cancer; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related adverse event.

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