EP13.24: Safety of Tarlatamab and Thoracic Radiotherapy: A Multi-Institution, Real-World Experience

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INTRODUCTION

Tarlatamab, a Delta-like ligand (DLL3)/CD3-targeted bispecfic T cell engager, recently received recent FDA approval for the treatment of patients with extensive-stage small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

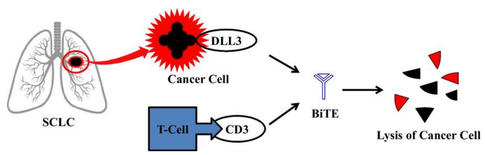


Figure 1. Mechanism of action of Tarlatamab. Adapted from Goyal et al. (2024)[1]

The DeLLphi-304 trial[2,3,4] demonstrated a significant improvement in overall survival with the receipt of tarlatamab compared to physician's choice chemotherapy. It is currently poorly understood whether administration of thoracic radiotherapy (TRT) with tarlatamab carries an increased risk of toxicity, specifically cytokine release syndrome (CRS) and radiation pneumonitis (RP), as radiation therapy within 21 days of tarlatamab administration was exclusionary on the DeLLphi-304 trial.

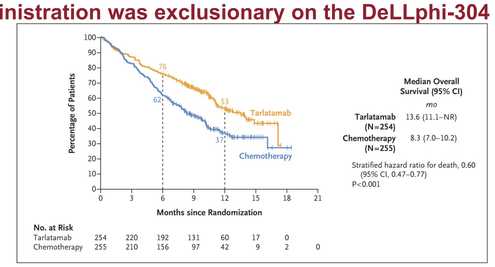


Figure 2. Kaplan-Meier overall survival from the DeLLphi-304 trial. Adapted from Mountzios et al. (2025)[4]

METHODS

A retrospective, multi-institution cohort of patients with metastatic small cell or neuroendocrine lung cancers treated with tarlatamab was assembled.

Thoracic radiation was defined as any radiotherapy to the chest, including lung, mediastinal, chest wall, or thoracic spine radiation. Peritarlatamab thoracic radiation was defined as treatment <u>within three months of tarlatamab receipt</u>.

Baseline characteristics, treatment records, and toxicity including development of CRS and pneumonitis were collected. Radiation and clinical records along with imaging data were reviewed for the development of radiation pneumonitis in the peritarlatamab cohort.

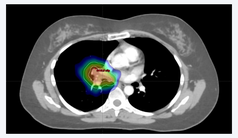
CONCLUSIONS AND FUTURE DIRECTIONS

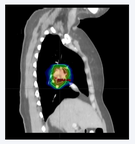
Conclusions

- In patients who received thoracic radiation within three months of tarlatamab, rates of radiation pneumonitis were low
- The rate of cytokine release syndrome (CRS) and treatments for CRS in patients who received tarlatamab were similar between those with a recent history of thoracic radiation and those without

Future Directions

- There were no major safety signals with peri-tarlatamab thoracic radiation. Combining thoracic radiation with tarlatamab warrants further studies in prospective trials





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3. Dowlati, A. et al. Sustained clinical benefit and intracranial activity of tarlatamab in previously treated small cell lung cancer: DeLLphi-300 trial update. *J. Clin. Oncol.* **42**, 3392–3399 (2024).
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RESULTS

Baseline Characteristics

	Cohort n = 140
Diagnosis	De novo SCLC: 121 (86%) Carcinoid: 8 (6%) Transformed SCLC: 5 (4%) Combined histology: 4 (3%) Large cell neuroendocrine: 2 (1%)
Age (Median)	64.5 (range: 18-84)
Sex	Male: 71 (51%) Female: 69 (49%)
ECOG Performance Status (Median)	1 (range: 0-2)
Smoking history	Former: 93 (66%) Current: 29 (21%) Never: 18 (13%)
Prior lines of systemic therapy (Median)	1 (range: 0 – 8)

Figure 3. Baseline characteristics of the multi-institutional cohort of patients who received tarlatamab between June 2024 and August 2025

Progression Free Survival

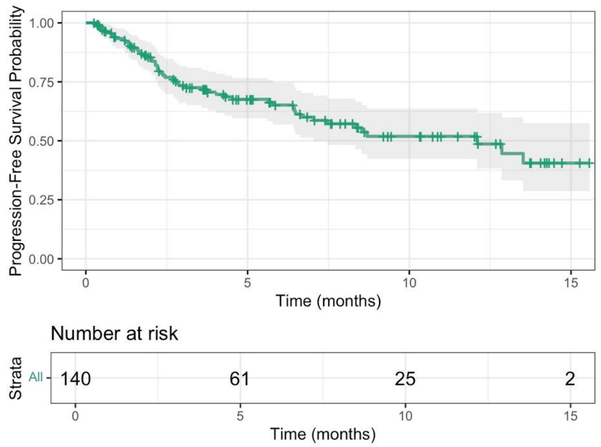

Figure 4. Progression Free Survival of the multi-institutional cohort. With a median follow up of 8.4 months the median PFS was 11.7 months

Thoracic Radiation (TRT) and Tarlatamab

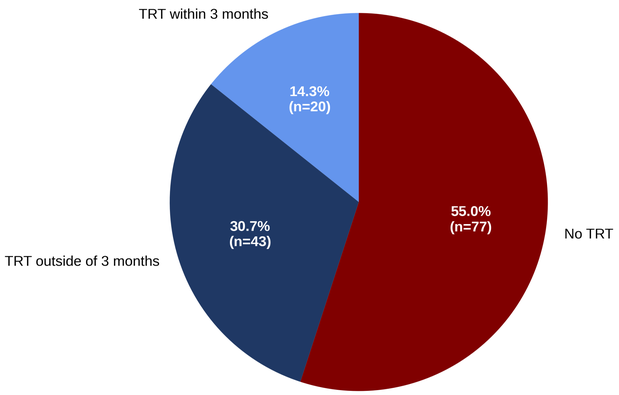

Figure 5. Thoracic radiation and Tarlatamab. A total of 63 patients had history of thoracic radiation. 20 patients received radiation within three months of tarlatamab (i.e. peri-tarlatamab). Of these patients, 16 received radiation prior to tarlatamab, 3 concurrently, and 1 after discontinuing tarlatamab. The median days from radiation end to tarlatamab start in the peri-tarlatamab cohort was 52.5 days.

Thoracic Radiation and Risks of Radiation Pneumonitis and Cytokine Release Syndrome (CRS) with Tarlatamab

	TRT within 3 months prior to tarlatamab start n = 16	No TRT within 3 months prior to tarlatamab start n = 124	P value
Grade 2+ Radiation Pneumonitis	20%	n/a	n/a
Any grade CRS	43.8%	55.6%	p= 0.43
CRS requiring tocilizumab	37.5%	29.0%	p = 0.56
CRS requiring steroids	37.5%	26.6%	p = 0.38
Supplemental Oxygen Support	31.3%	16.1%	p = 0.16

Figure 6. Risks of cytokine release syndrome and radiation pneumonitis with TRT and tarlatamab. There was no significant difference in CRS occurrence, tocilizumab initiation, dexamethasone initiation, or use of supplemental oxygen between the TRT and no TRT cohorts

Disclosure

- No disclosures