Real-World Safety and Outcomes of Tarlatamab in Extensive-Stage Small Cell Lung Cancer

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Background:
Tarlatamab, a bispecific delta-like ligand 3–directed T-cell engager, has become a standard treatment option for relapsed or refractory small cell lung cancer (SCLC) following first-line platinum-based chemotherapy. Real-world outcome data for tarlatamab remain scarce.

Methods:
We conducted a retrospective cohort study using the TriNetX Global Research Network, which aggregates de-identified electronic health record data from more than 160 healthcare organizations worldwide. We identified adults diagnosed with lung cancer between November 1, 2020, and November 1, 2025, who received platinum-based chemotherapy prior to tarlatamab. Primary endpoints included the 15-day incidence of cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), tocilizumab use, and mortality. Secondary endpoints included 6-month mortality, receipt of subsequent systemic therapy, and development of new cytopenias or hyponatremia.

Results:
A total of 336 patients met inclusion criteria. The median age was 65 years (range 21–88); 52% were male and 78% were White (table 1). Brain metastases were present in 47%. Comorbidities were common, including COPD (50%), ischemic heart disease (40%), diabetes (27%), chronic kidney disease (17%), and cirrhosis (5%). Nearly all patients received prior etoposide (99%), and many had prior immunotherapy exposure (atezolizumab 59%; durvalumab 24%); 26% received lurbinectedin.

Within 15 days of tarlatamab initiation, ICANS occurred in 53 patients (15.8%), CRS in 116 patients (34.5%), and tocilizumab was administered in 95 patients (28.3%); no deaths occurred during this period (table 2). At 6 months, 117 patients had died (34.8%), and only 27 patients (8%) received subsequent systemic therapy, most commonly platinum agents, irinotecan, or

topotecan. New onset hyponatremia and cytopenias occurred in 35.6% and 21.3% of patients, respectively.

Conclusions:
Tarlatamab demonstrated a safety profile and clinical outcomes comparable to those reported in the DeLLphi-304 trial. The limited use of subsequent therapies after progression underscores the critical need for improved post-tarlatamab treatment options in extensive-stage SCLC.

Table 1. Baseline Characteristics

Characteristics	**n (%)**
Mean ± SD age, years	65.7 ± 9.81
Male sex	176 (52%)
Race / Ethnicity	
White	262 (78%)
Black or African American	29 (9%)
Asian	13 (4%)
Brain metastases	158 (47%)
Prior treatments	
Carboplatin	311 (93%)
Cisplatin	63 (19%)
Etoposide	334 (99%)
Atezolizumab	199 (59%)
Durvalumab	81 (24%)
Lurbinectedin	89 (26%)
Irinotecan	13 (5%)
Topotecan	13 (4%)
Paclitaxel	17 (5%)
Comorbidities	
Hypertension	225 (67%)
Chronic obstructive pulmonary disease	169 (50%)
Ischemic heart disease	135 (40%)
Diabetes	92 (27%)
Chronic kidney disease	58 (17%)
Liver cirrhosis	17 (5%)

Table 2. Clinical Outcomes

	Patients with outcomes, n (%)	Patients at risk (n)
15 days outcome		
CRS	116 (34.5)	336
ICANS	53 (15.8)	336
Tocilizumab use	95 (28.3)	336
Death	0 (0)	336
6 months outcome		
New hyponatremia	31 (35.6)	87
New cytopenia	19 (21.3)	89
Next line therapies	27 (8.0)	336
Carboplatin/cisplatin	14 (4.2)	336
Irinotecan	14 (4.2)	336
Topotecan	12 (3.6)	336
Death	117 (34.8)	336