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LBA100

Detailed safety analysis of DeLLphi-304: The first phase III study to evaluate tarlatamab versus chemotherapy for previously treated small cell lung cancer

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Background

Tarlatamab, a bispecific T-cell engager targeting DLL3, significantly improved overall survival for patients (pts) with previously treated SCLC in DeLLphi-304. Top-line safety results aligned with prior data; additional analyses were conducted to further characterize adverse events (AEs).

Methods

Pts were randomized to tarlatamab or chemotherapy (CTx: topotecan, lurbinectedin, or amrubicin). Tarlatamab-treated pts underwent 48-h or 6–8-h monitoring. Analyses evaluated treatment-related adverse events (TRAEs), cytopenias, infection, cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and dysgeusia.

Results

Tarlatamab was associated with fewer hematological toxicities and infections (Table). Grade ≥3 TRAEs with tarlatamab declined over time (17% in month 1; 9% in months 1–3; 12% beyond), while rates with CTx remained >38%. CRS was the most common tarlatamab TRAE, occurring in 56% of pts. Descriptive comparisons (not formally tested as predictive for CRS) showed CRS rates of 53% vs 58% in pts with ECOG status 0 vs 1-2; 63% vs 53% in pts with vs without liver metastases; 57% vs 56% in pts with vs without brain metastases, 59% vs 51% in pts with vs without prior PD-(L)1 use, and 62% vs 51% in those with high vs low tumor burden. Hospitalization for any grade CRS on C1D1/D8 was comparable between the 48-h (n = 209) and 6-8-h (n = 43) cohorts (7.7% vs 7.0%). Neurologic TRAEs occurred in 45% of tarlatamab treated pts. Dysgeusia was the most common (23%), occurring with a median time to onset of 28 days and median duration among resolved cases of 126 days; none required tarlatamab discontinuation. ICANS occurred infrequently (15 pts; 6%), was mostly grade 1-2, and 14 pts (93%) also experienced CRS.

Conclusions

In the DeLLphi-304 trial, tarlatamab demonstrated a predictable and manageable safety profile in 2L SCLC, with no new safety signals identified.Table: LBA100

Treatment-related adverse events

TRAE	Tarlatamab (n = 252)		CTx (n = 244)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Anemia	19.8%	2.0%	61.5%	27.9%
Neutropenia	7.5%	4.4%	29.5%	22.1%
Thrombocytopenia	3.2%	0.4%	23.8%	11.8%
Infection	6.3%	1.2%	15.2%	8.6%

Clinical trial identification

NCT05740566.

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