VIII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN
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TCE: CARCINOMA MICROCITICO

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Disclosure slide

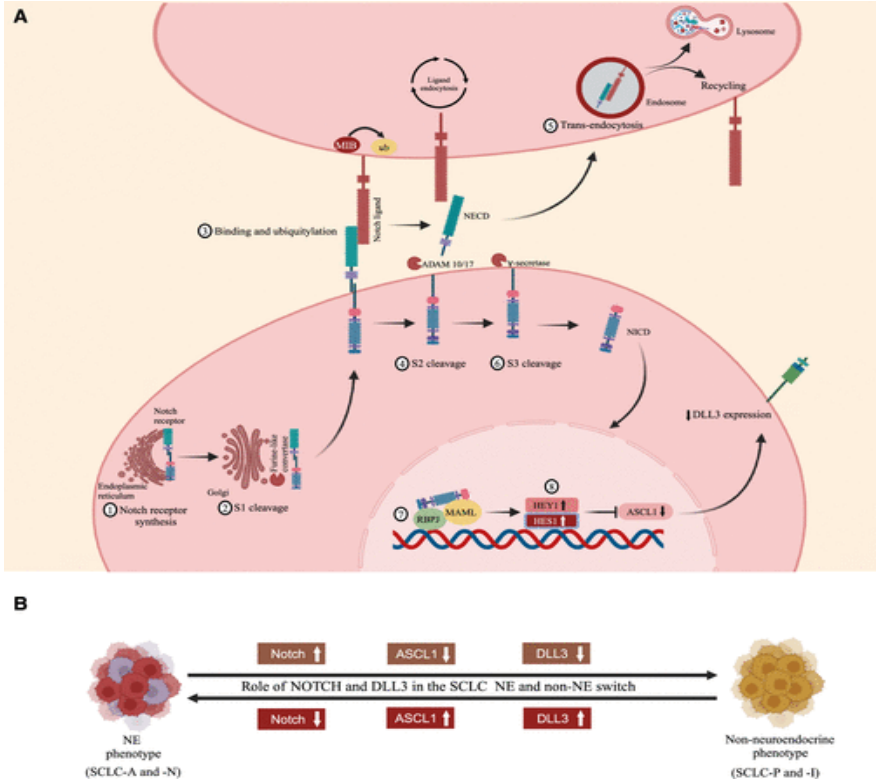
- Speaker, advisory, or travel honoraria from Amgen, Boehringer Ingelheim, Janssen, Pierre Fabre, Takeda, Sanofi, BMS, Astra Zeneca, MSD, Roche, Pfizer, Novartis, and NanoString

- Research support/grants from Janssen, Pfizer, Astra Zeneca, and Roche

Outline

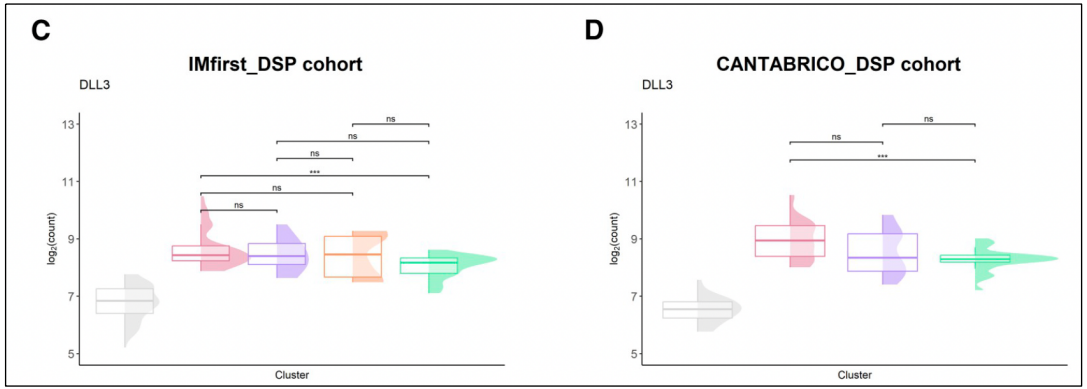
- Introduction to T cell redirection strategies in SCLC
- T cell engagers (TCE) in recurrent SCLC
- T cell engagers (TCE) in 1L SCLC
- Conclusions

DLL3 is a surface target for neuroendocrine neoplasms

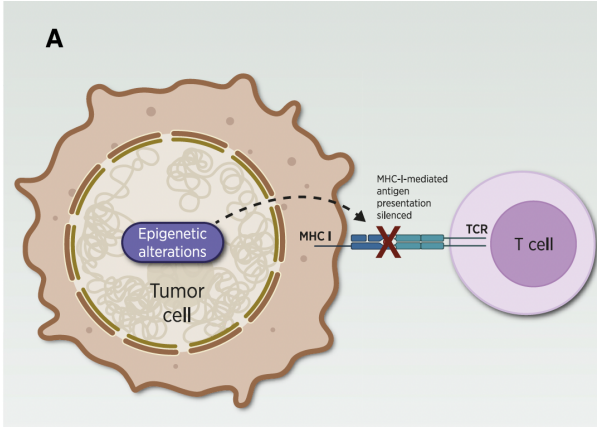


Aijaz et al. ASCO Educational Book 2025

Why DLL3xCD3 TCEs are effective in SCLC



Peressini et al. (Zugazagoitia) Clin Cancer Res 2024



Zugazagoitia et al. Clin Cancer Res 2024

Outline

- Introduction to T cell redirection strategies in SCLC
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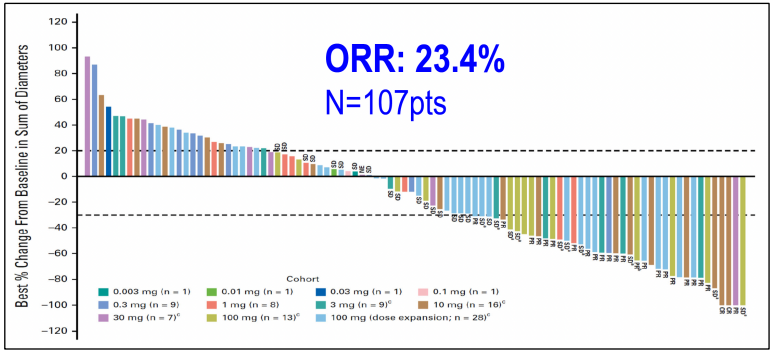
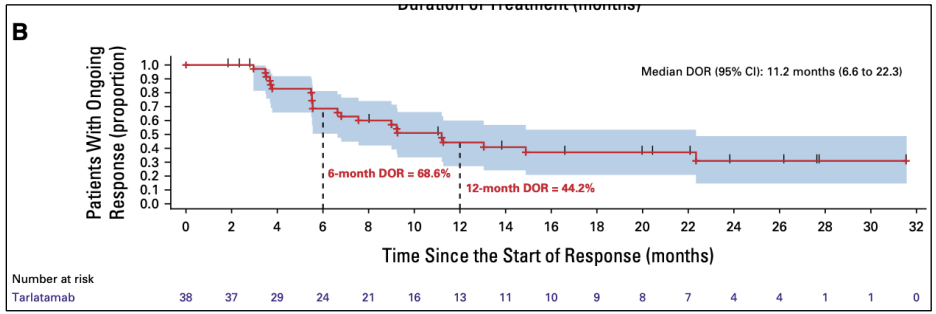
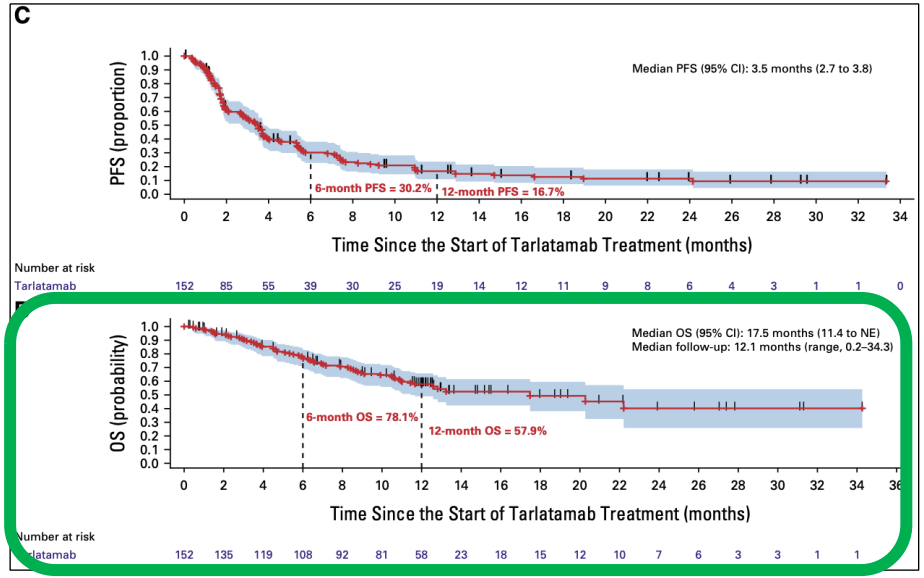
- Conclusions

Sustained clinical efficacy of tarlatamab (>10 mg) in relapsed SCLC (DeLLphi-300)

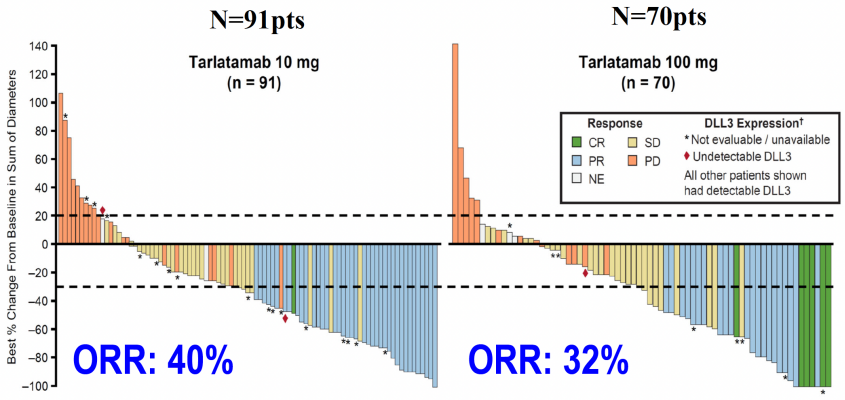




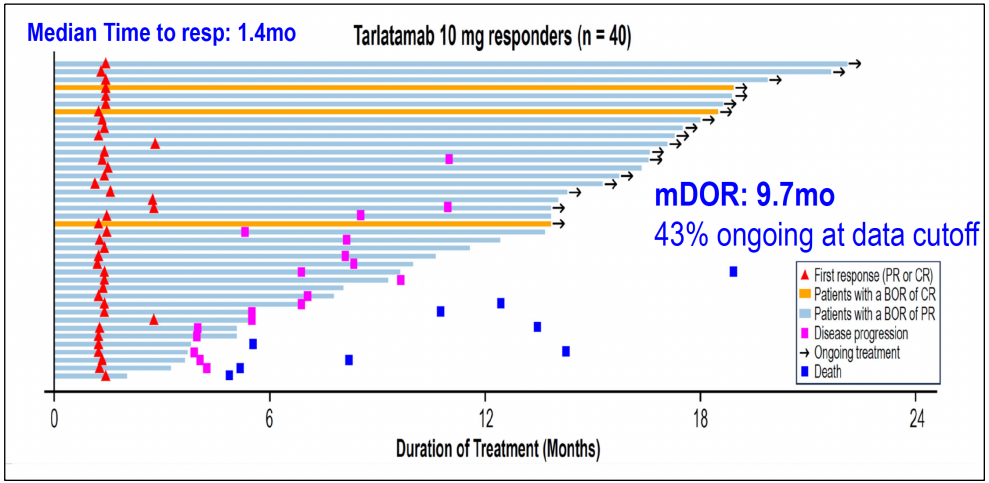


Paz-Ares et al. J Clin Oncol 2023
Paz-Ares et al. J Clin Oncol 2024

Confirmed deep and durable responses with tarlatamab in DeLLphi-301 trial

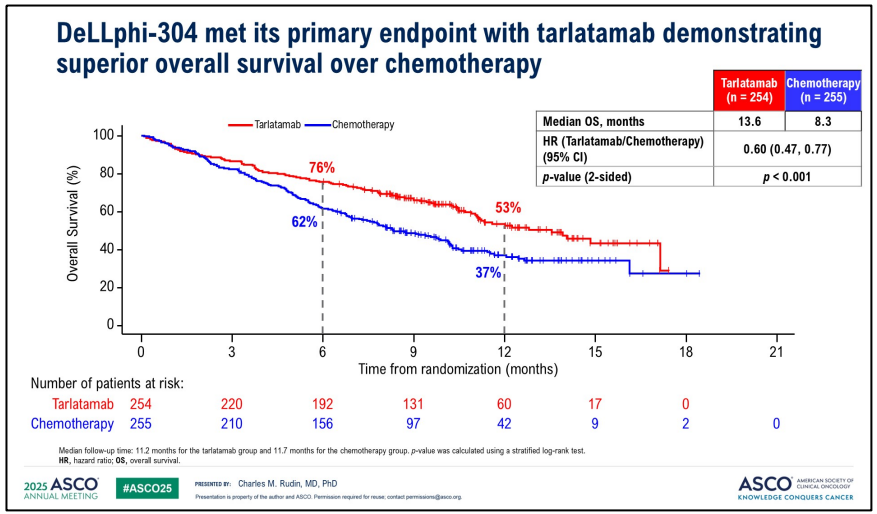


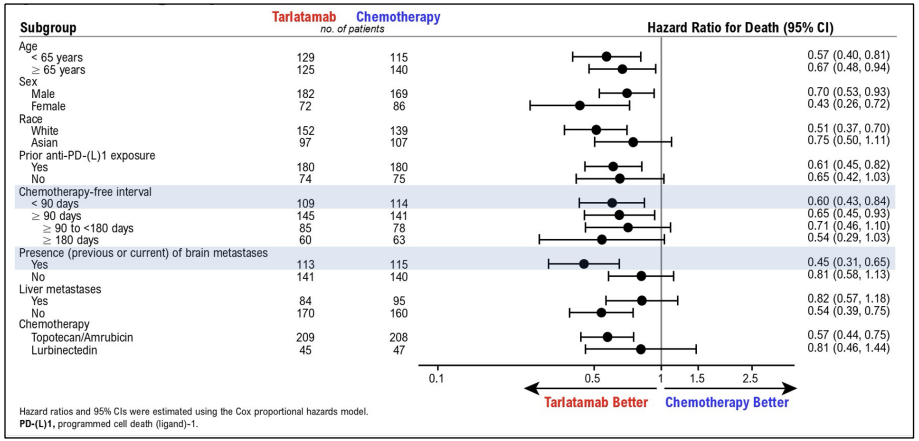
Ahn et al. (Paz-Ares) NEJM 2023



Sands et al. WCLC 2024

Robust OS benefit with tarlatamab in a global phase III clinical trial setting

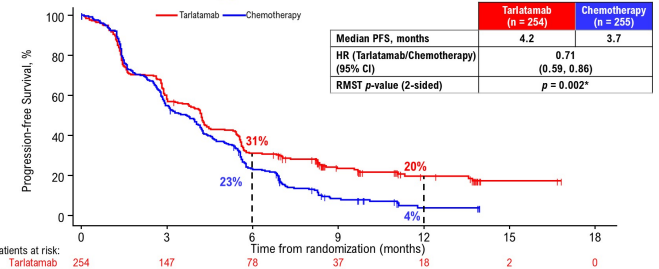




Rudin et al. ASCO 2025
Mountzios et al. NEJM 2025

More modest benefit with tarlatamab in terms of RR or PFS

Progression-free survival was significantly longer with tarlatamab vs chemotherapy



	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median PFS, months	4.2	3.7
HR (Tarlatamab/Chemotherapy) (95% CI)	0.71 (0.59, 0.86)	
RMST *p*-value (2-sided)	*p* = 0.002*	

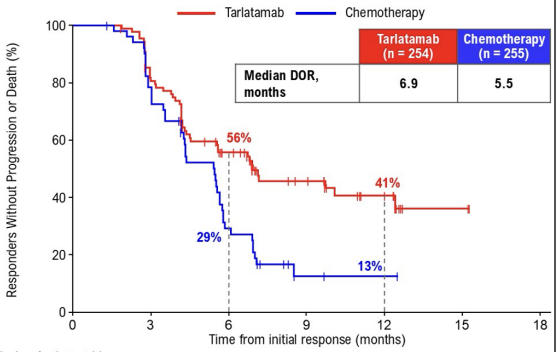
Median follow-up time: 11.0 months for the tarlatamab and the chemotherapy group. *The restricted mean PFS time in the tarlatamab and the chemotherapy group was 5.3 months and 4.3 months at 12 months respectively, resulting in statistically significant improvement of the tarlatamab group over the chemotherapy group.
HR: hazard ratio; **PFS**, progression-free survival.

2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Charles M. Rudin, MD, PhD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Best overall response*†, n (%)		
Complete response	3 (1)	0 (0)
Partial response	86 (34)	52 (20)
Stable disease	84 (33)	112 (44)
Progressive disease	56 (22)	50 (20)
Not evaluable/no post-baseline scan	25 (10)	41 (16)
Objective response rate‡, % (95% CI)	35 (29–41)	20 (16–26)
Median duration of response, months	6.9	5.5
Median time to objective response, months	1.5	1.4
Ongoing response at data cutoff, n§ (%)	42 (47)	8 (15)

Duration of response



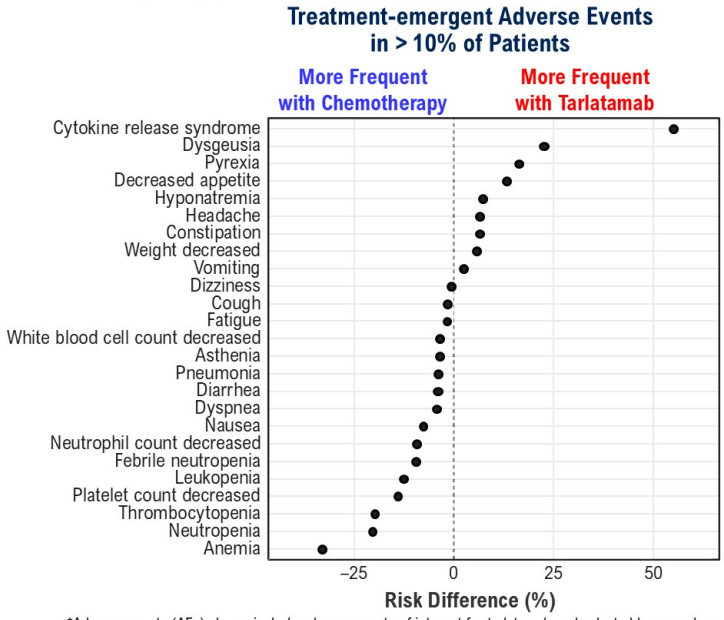
	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median DOR, months	6.9	5.5

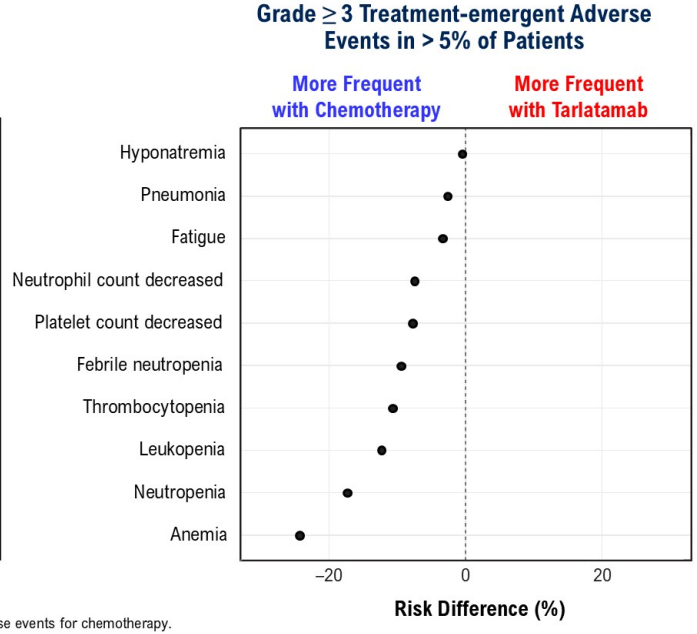
*Assessment of disease response was based on RECIST 1.1 guidelines. Confirmation of complete response and partial response was required no fewer than 4 weeks after initial documentation of complete response or partial response. †Investigator-assessed response in the intention-to-treat analysis set; ‡Odds ratios and *p* value not shown as the difference in ORR between the 2 arms was not formally tested. §Percentage of total number of responders.
DOR, duration of response; **IRECIST**, Response Evaluation Criteria in Solid Tumors.

Rudin et al. ASCO 2025
Mountzios et al. NEJM 2025

Lower incidence of severe AEs with tarlatamab than chemotherapy

Patients treated with tarlatamab experienced lower incidence of high-grade AEs





*Adverse events (AEs) shown include adverse events of interest for tarlatamab and selected known adverse events for chemotherapy.

Rudin et al. ASCO 2025
Mountzios et al. NEJM 2025

Other T cell redirection strategies against DLL3 in clinical development for SCLC

The road ahead: Other DLL3-targeted agents

Agent	MOA	Targets	Phase	Indication	Sponsor	Recruiting?
BI 764532	BiTE	DLL3/CD3	1-2	SCLC/NEC	Boehringer	Y
PT217	BiTE	DLL3/CD47	1	SCLC/NEC	Phanes	Y
QLS31904	BiTE	DLL3/CD3	1	SCLC/NEC	Qilu	
HPN328	TriTE	DLL3/CD3/albumin	1-2	SCLC/NEC	Harpoon	Y
RO7616789	TriTE	DLL3/CD3/CD137	1	SCLC/NEC	Roche	N
ZG006	TriTE	DLL3/DLL3/CD3	1-2	SCLC/NEC	Zejing	Y
LB2102	CAR-T	DLL3	1	ES-SCLC LC-NEC	Legend	Y
DLL3-CAR-NK-92	CAR-NK	DLL3	1	SCLC/NEC	Academic*	Y

PRESENTED BY: Catherine B. Meador, MD, PhD

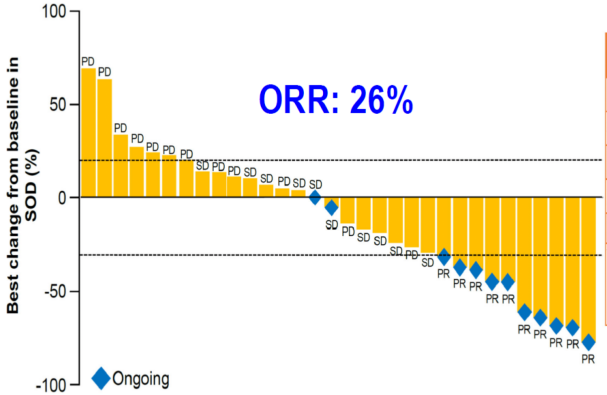
* Tianjin Medical University Cancer Institute

Meador CB. ASCO 2025

Clinical efficacy of other DLL3-CD3 TCEs in recurrent SCLC

Obrixtamig

Efficacy in patients with SCLC (doses≥90μg/Kg)



n, (%)	SCLC (n=39)*	LCNEC (n=5)*
PR	10 (26)	3 (60)
SD	10 (26)	2 (40)
PD	12 (31)	0
DCR	20 (51)	5 (100)
NE†	7 (18)	0

*Efficacy population: ≥1 post-baseline tumor assessment or permanently discontinued prior to tumor assessment; responses evaluated per RECIST v1.1 criteria; †Discontinued prior to tumor assessment

M.Wermke et al, WCLC202

Wermke et al. WCLC 2024

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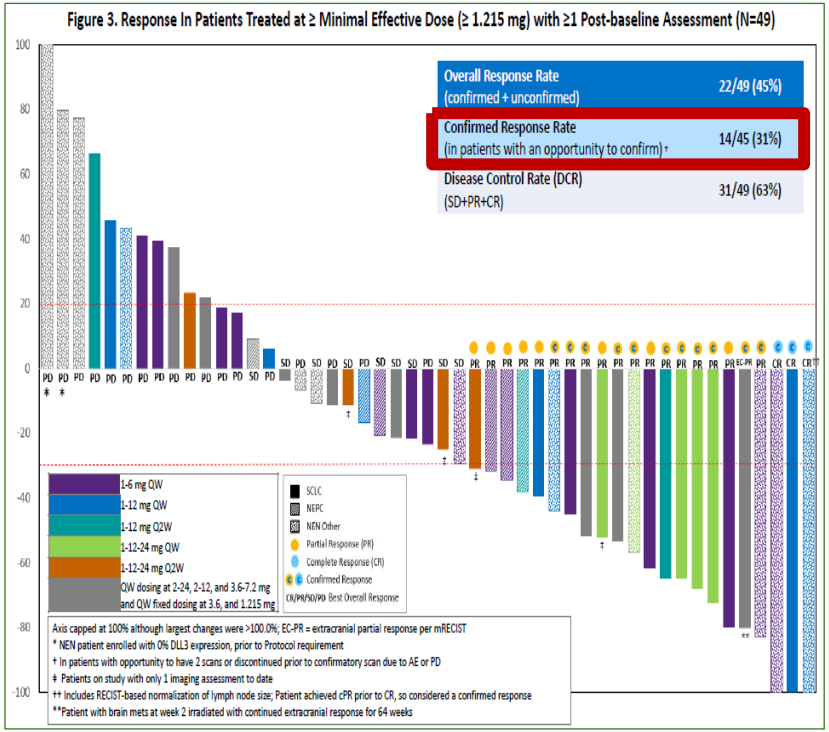
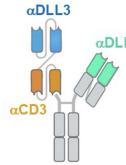


Choudhury et al. ESMO 2023

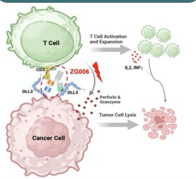
Aveltamig (ZG006), a tri-specific T cell engager (TRI-TCE), in recurrent SCLC

Molecular Design



- 1:2 binding to one CD3 epitope and two distinct DLL3 epitopes (Biparatopic)
- Effector-less Fc as half-life extender

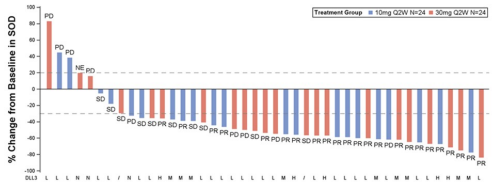
Mechanism of Action



Antitumor Activity as Assessed by IRC

	10 mg Q2W (N=24)	30 mg Q2W (N=24)
BOR		
CR, n (%)	0	0
PR, n (%)	15 (62.5)	14 (58.3)
SD, n (%)	2 (8.3)	2 (8.3)
PD, n (%)	6 (25.0)	6 (25.0)
NE, n (%)	1 (4.2)	2 (8.3)
ORR*, n (%) 95% CI	15 (62.5) (40.6, 81.2)	14 (58.3) (36.6, 77.9)
DCR*, n (%) 95% CI	17 (70.8) (48.9, 87.4)	16 (66.7) (44.7, 84.4)

Best Percentage Changes in Target Lesion Size by Dose Levels in SCLC



N: Negative; L: Low expression; M: Medium expression; H: High expression; /: NA.

CR: Complete Response; PR: Partial Response; SD: Stable Disease; PD: Progressive Disease; BOR: Best Overall Response; *: Non-confirmed

6

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Common Treatment-Related AEs for All Grades

Preferred Term	10 mg Q2W (N=24)	30 mg Q2W (N=24)
Pyrexia	19 (79.2%)	19 (79.2%)
Cytokine Release Syndrome	10 (41.7%)	18 (75.0%)
Anemia	6 (25.0%)	10 (41.7%)
Leukopenia	8 (33.3%)	8 (33.3%)
Decreased Appetite	9 (37.5%)	7 (29.2%)
Hyponatremia	6 (25.0%)	9 (37.5%)
Asthenia	7 (29.2%)	8 (33.3%)
Vomiting	4 (16.7%)	10 (41.7%)
Elevated Aspartate Aminotransferase	9 (37.5%)	4 (16.7%)
Neutropenia	8 (33.3%)	4 (16.7%)
Thrombocytopenia	7 (29.2%)	5 (20.8%)
Hypokalemia	5 (20.8%)	7 (29.2%)
Elevated Alanine Aminotransferase	7 (29.2%)	4 (16.7%)
Rash	4 (16.7%)	6 (25.0%)
Hypoalbuminemia	2 (8.3%)	6 (25.0%)
Proteinuria	3 (12.5%)	5 (20.8%)
Elevated Bilirubin	2 (8.3%)	5 (20.8%)

9

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Ai et al. ASCO 2025

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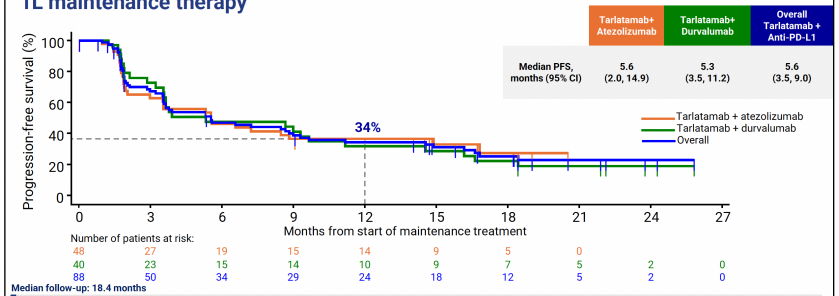
Tarlatamab with a PD-L1 inhibitor as *1LM* demonstrates promising survival outcomes (DeLLphi-303)

Progression free survival with addition of tarlatamab to anti-PD-L1 as 1L maintenance therapy

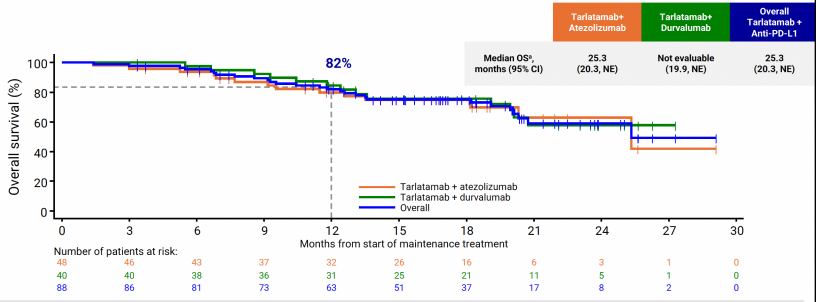


Median follow-up: 18.4 months

Tarlatamab with anti-PD-L1 as 1L maintenance therapy led to a median PFS of 5.6 months (95% CI, 3.5, 9.0).

1L: first-line; **CI:** confidence interval; **PD-L1:** programmed death-ligand 1; **PFS:** progression-free survival.

Overall survival with addition of tarlatamab to anti-PD-L1 as 1L maintenance therapy



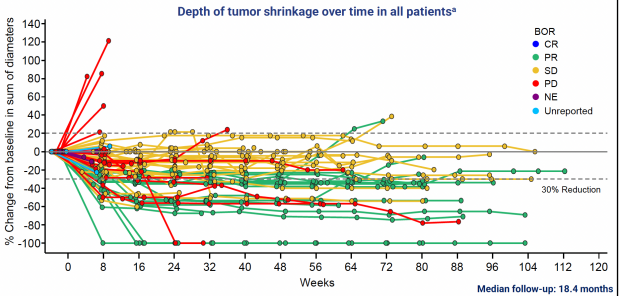
With a median follow-up time of 18.4 months, tarlatamab with anti-PD-L1 as 1L maintenance therapy led to a median OS of 25.3 months (95% CI, 20.3, NE).

[a]The median OS is immature and will continue to evolve with longer follow-up time. **1L:** first-line; **CI:** confidence interval; **NE:** not evaluable; **OS:** overall survival; **PD-L1:** programmed death-ligand 1.

Tarlatamab + anti-PD-L1 in 1L maintenance resulted in disease control in 60% of patients, including 36% with sustained disease control ≥ 52 weeks

From a baseline obtained after completion of 1L chemo-IO:

- Overall ORR: 24% (2 CR, 19 PR); median duration of response: 16.6 months (7.1, NE)
- Overall DCR: 60% (2 CR, 19 PR, 32 SD); median duration of disease control: 14.6 months (95% CI 7.2, 18.4)
- 24% of patients remained on treatment at data cutoff and 36% of patients showed sustained DC ≥ 52 weeks

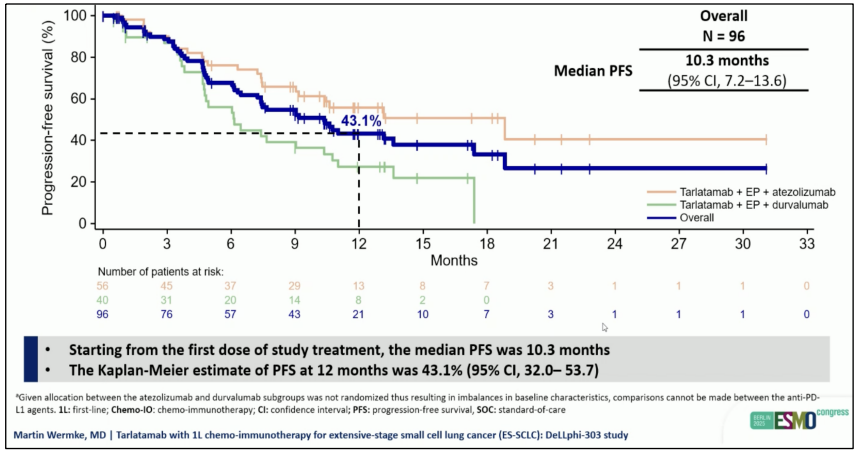


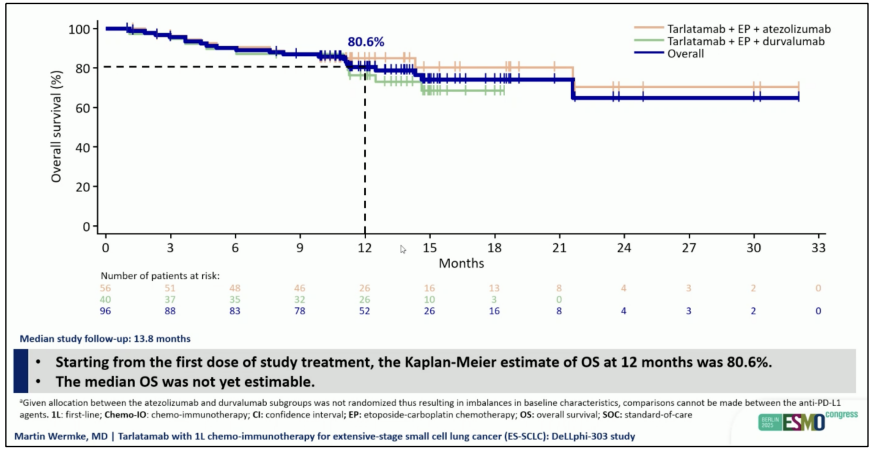
Median follow-up: 18.4 months

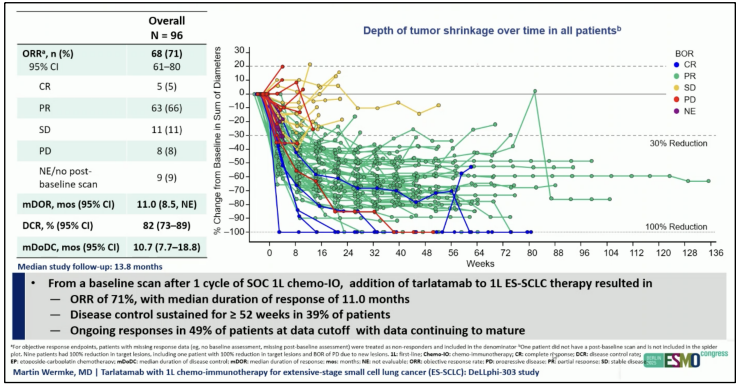
[a]Fifteen patients did not have tumor size information and are not included in the spider plot. This includes two patients with non-target lesions who achieved CR during maintenance therapy with tarlatamab + anti-PD-L1. **1L:** first-line; **BOR:** best overall response; **chemo IO:** chemo-immunotherapy; **CI:** confidence interval; **CR:** complete response; **DC:** disease control; **DCR:** disease control rate; **NE:** not evaluable; **ORR:** objective response rate; **PD:** progressive disease; **PD-L1:** programmed death-ligand 1; **PR:** partial response; **SD:** stable disease.

Paulson et al. WCLC 2025
Paulson et al. Lancet Oncol 2025

Tarlatamab with a PD-L1 inhibitor as *1L* demonstrates promising survival outcomes (DeLLphi-303)

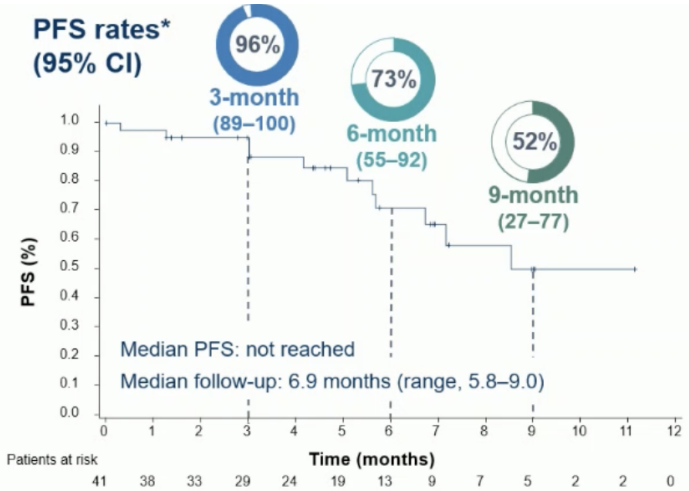






Wermke et al. ESMO 2025

Obrixtamig plus atezolizumab as *1L* demonstrates promising survival outcomes (Dareon-8)



Confirmed ORR†	68%	(95% CI: 49–82)
Confirmed DCR†	89%	(95% CI: 73–96)
Median DoR	7.3 months (95% CI: 4.4–NC)	

Best confirmed response, n (%)	N=28
CR	1 (4)
PR	18 (64)
SD	6 (21)
PD	1 (4)
NE / missing	2 (7)

- Efficacy data from early cohorts demonstrate promising activity, with additional insights expected as data mature at higher dose levels

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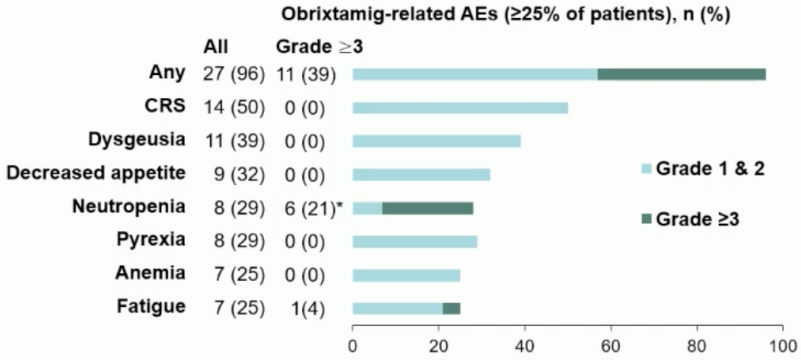
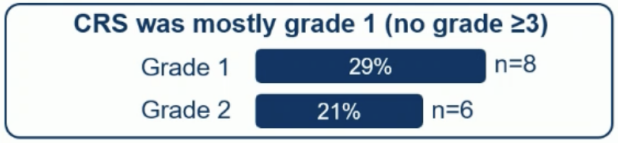
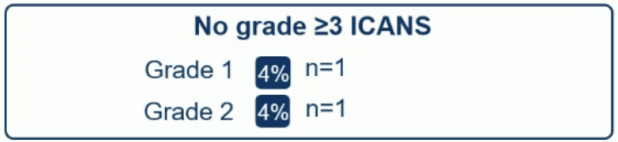
*Per Kaplan–Meier estimates; †Investigator assessed
CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NC, not calculable; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; SoC, standard of care

Peters et al. ESMO 2025

Obrixtamig plus atezolizumab as *1L* has a manageable safety profile (Dareon-8)







- Seven patients (25%) had obrixtamig-related potential neurologic toxicities† including ICANS, with reported preferred terms of muscle spasms (grade 1, 11%), ICANS (grade 1–2, 7%), confusional state (grade 2, 4%), and dizziness (grade 1, 4%)
- Only one case of grade 2 neutropenia was attributed solely to obrixtamig. Primary prophylaxis with G-CSF was not allowed in the dose escalation part of the trial

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*7 of 8 cases of neutropenia were also attributed to chemotherapy; †Generated with a customized MedDRA query of preferred terms to identify potential ICANS and ICANS-like neurotoxicity[1]

1. Wermke M, et al. J Clin Oncol 2025;JCO-25-00363

AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; G-CSF, granulocyte colony-stimulating factor; MedDRA, Medical Dictionary for Regulatory Activities

Peters et al. ESMO 2025

MY TAKE HOME MESSAGES

- Immunotherapy has transformed SCLC.
- Long term survival with PD-1 axis blockade is possible in SCLC.
- The observed survival benefit with 1L DLL3xCD3 TCEs plus an anti-PD-L1 agent is unprecedented, vastly exceeding the associated risks.
- Earlier use of novel IO strategies for LS-SCLC likely to further increase survival.
- The stigma of SCLC as an untreatable deadly disease needs to end.