NCCN 2025
Lung Cancer Congress

Managing Small Cell Lung Cancer: Practical Strategies for Primary and Subsequent Systemic Therapy

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NCCN National Comprehensive Cancer Network®

Learning Objectives

1. **Evaluate and apply evidence-based therapeutic strategies** for primary and subsequent treatment of SCLC.
2. **Assess practical considerations, challenges, and strategies** for implementing *tarlatamab* in the community oncology setting.
3. **Identify current and emerging clinical trials and pipeline agents** in SCLC and integrate this knowledge into shared decision-making for eligible patients.

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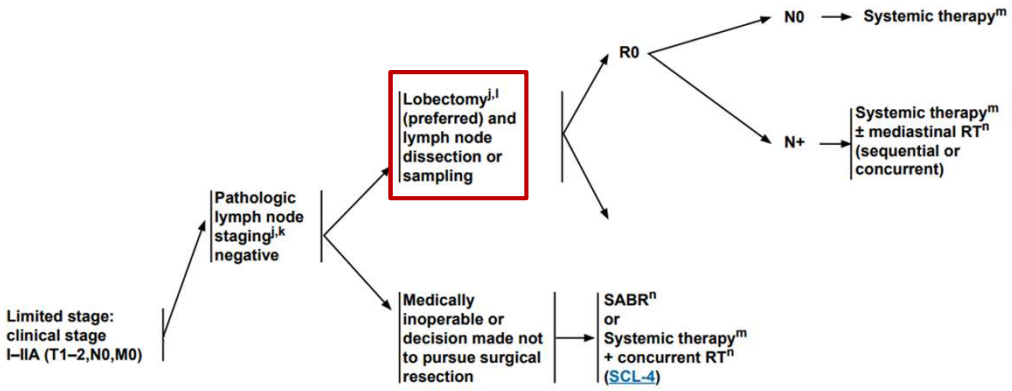
Management of LS SCLC

- ✓ Approval of durvalumab consolidation after definitive chemoradiation

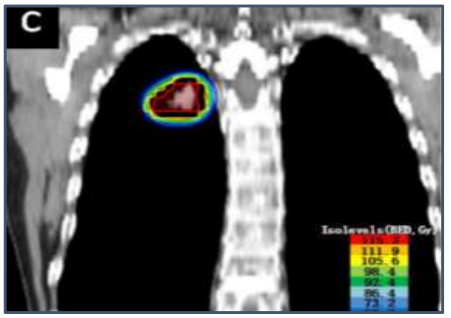
Management of Stage I-IIA SCLC

~5% of SCLC have Stage I-IIA (T1-2aN0) disease

- Patients should have mediastinal LN staging prior to resection
- If surgical candidate and LN (-) → Lobectomy followed by mediastinal lymph node dissection
- If surgery is not an option, consider SABR
- **Adjuvant chemotherapy** is recommended
- Consider adjuvant radiation if LN +



Stage I

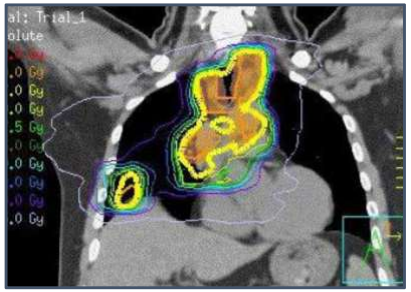


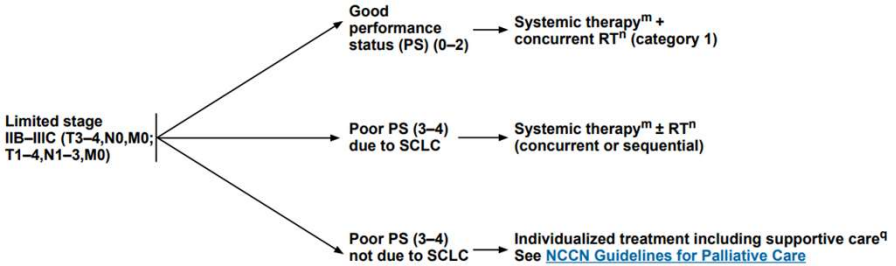
T/M	Subcategory	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

AJCC 8th Edition

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Small Cell Lung Cancer (Version 2.2026). SCL-3.

Stage IIB-IIIC SCLC: ChemoRT Followed by Durvalumab Consolidation





T/M	Subcategory	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

PRINCIPLES OF SYSTEMIC THERAPY

PRIMARY OR ADJUVANT THERAPY FOR LIMITED STAGE SCLC:

Four cycles of cytotoxic chemotherapy are recommended.
Planned cycle length should be every 21–28 days during concurrent RT.
During cytotoxic chemotherapy + RT, Cisplatin/Etoposide is recommended (category 1).
The use of myeloid growth factors is not recommended during concurrent cytotoxic chemotherapy therapy plus RT (category 1 for not using GM-CSF).[1]

Preferred
- Cisplatin 75 mg/m² Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[2]
- Cisplatin 60 mg/m² Day 1 and Etoposide 120 mg/m² Days 1, 2, 3[3]
- Carboplatin area under the curve (AUC) 5–6 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[b,4]
- Consolidation Therapy
  - Durvalumab 1500 mg Day 1 every 28 Days (category 1)[a,5]

Other Recommended
- Cisplatin 25 mg/m² Days 1, 2, 3 and Etoposide 100 mg/m² Days 1, 2, 3[2]

NCCN Guidelines® for Small Cell Lung Cancer (Version 2.2026). SCL-4, SCL-E.
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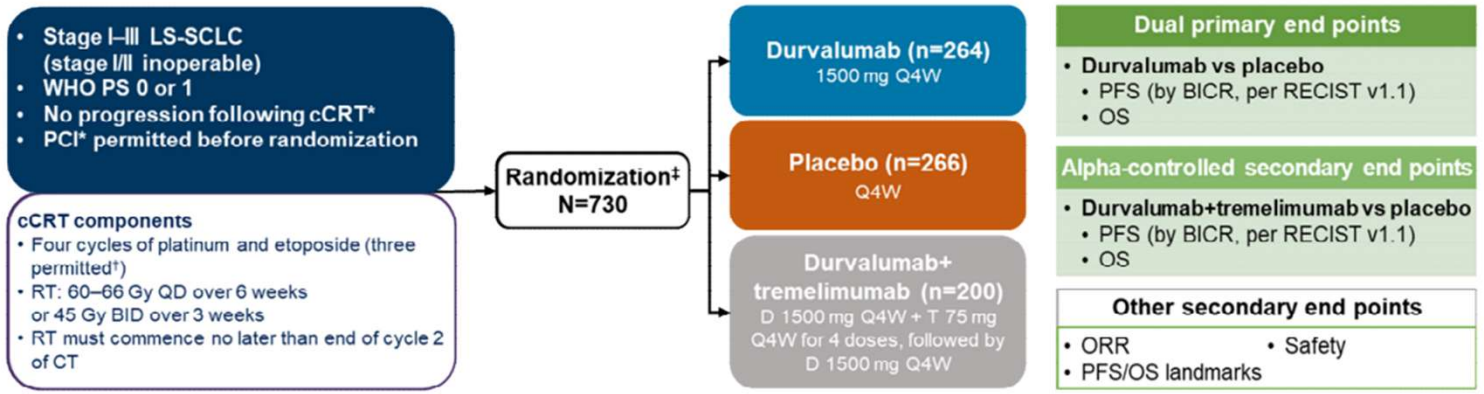
ADRIATIC: Consolidation Durvalumab in LS SCLC

Figure S1. ADRIATIC Study Design and Dual Primary, Alpha-Controlled Secondary, and Other Secondary End Points.



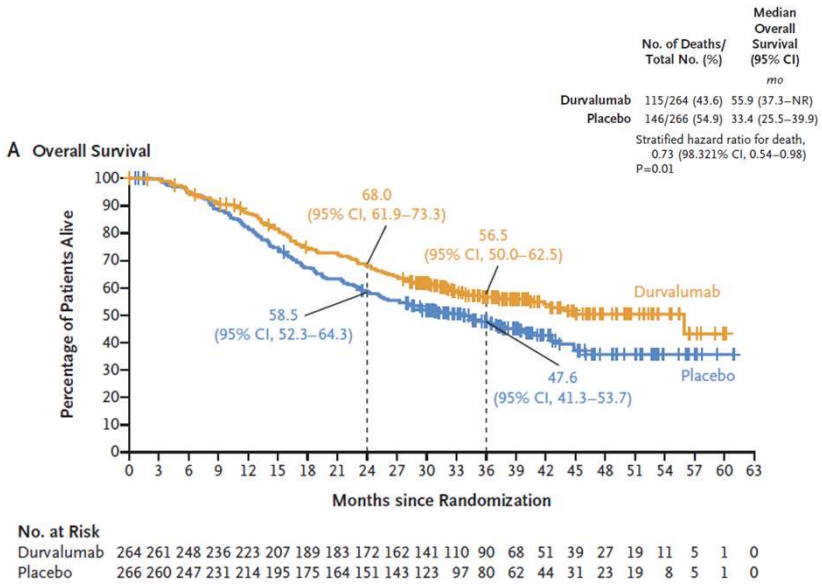
*cCRT and PCI, if received per local standard of care, had to be completed 1–42 days before randomization and treatment start.

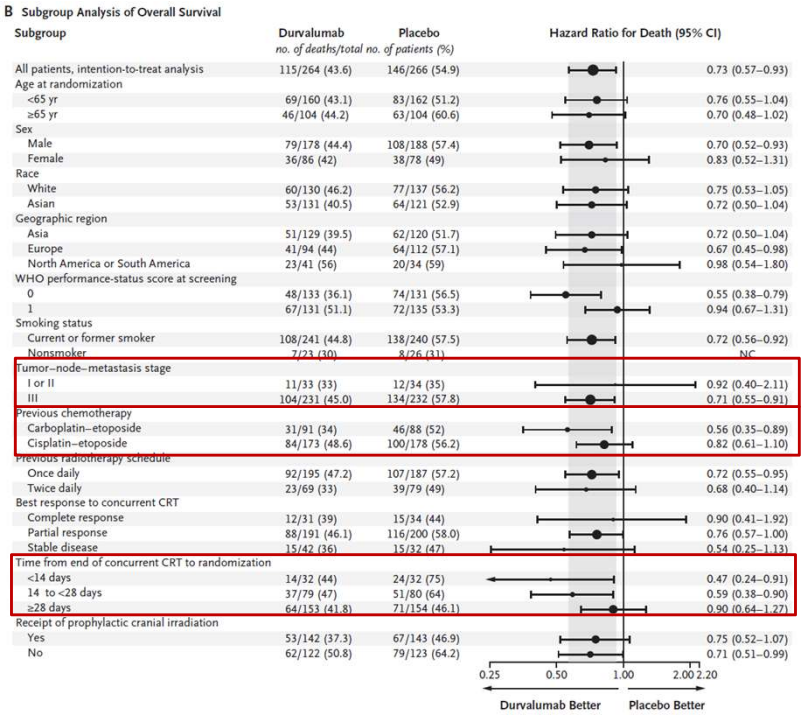
†3 cycles of chemotherapy were permitted if disease control was achieved and no additional benefit was expected from an additional cycle, as determined by the investigator.

‡Randomization stratified by disease stage (I/II vs. III) and receipt of PCI (yes vs. no).

Cheng, Y et al., N Engl J Med 2024;391:1313-1327 DOI: 10.1056/NEJMoa24048

ADRIATIC: OS and Subgroup Analysis





Cheng, Y et al., N Engl J Med 2024;391:1313-1327 DOI: 10.1056/NEJMoa24048

ADRIATIC: Exposure and Adverse Events

Exposure and Safety Summary

		Durvalumab (n=263)	Placebo (n=265)
Number of durvalumab or placebo doses	Median (range)	9.0 (1–26)	9.0 (1–26)
	Mean (standard deviation)	12.9 (9.62)	11.8 (9.22)
Any-grade all-cause AEs, n (%)		248 (94.3)	234 (88.3)
Maximum grade 3/4 AEs		64 (24.3)	64 (24.2)
Serious AEs		78 (29.7)	64 (24.2)
AEs leading to treatment discontinuation		43 (16.3)	28 (10.6)
AEs leading to death		7 (2.7)	5 (1.9)
Treatment-related* AEs leading to death		2 (0.8)‡	0
Any-grade immune-mediated AEs†		84 (31.9)	27 (10.2)
Maximum grade 3/4 immune-mediated AEs		14 (5.3)	4 (1.5)

*Assessed by investigator.
†Defined as an AE of special interest that is associated with drug exposure and consistent with an immune-mediated mechanism of action, where there is no clear alternate etiology, and requiring the use of systemic steroids or other immunosuppressants and/or, for specific endocrine events, endocrine therapy.
‡Causes of death were encephalopathy and pneumonitis.
AEs, adverse events.

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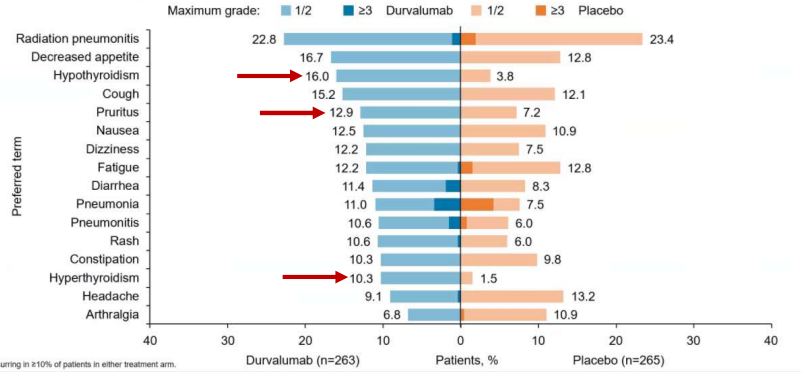
Most Frequent AEs*



*Occurring in ≥10% of patients in either treatment arm.

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Spigel at al., ASCO 2024 proceedings; Cheng, Y et al., N Engl J Med 2024;391:1313-1327 DOI: 10.1056/NEJMoa24048

Other ChemoRT/ICI Studies: Reported

- No benefit with other approaches yet
- Durvalumab consolidation FDA approved Dec 2024
- Durvalumab/Tremelilumab arm of ADRIATIC has not been reported yet

ICI after chemoRT					
ACHILES (NCT03540420)	RP2	1) Atezolizumab x 12 months 2) Observation	212	PD-L1	No PFS,OS benefit
STIMULI (NCT02046733)	RP2	1) Nivolumab/ipilimumab x 4 followed by nivolumab x 12 months 2) Observation	260 (planned) 174 (Final)	PD-1/CTLA-4	No PFS benefit
Concurrent chemoRT/ICI					
NRG-LU005 (NCT03811002)	2/3	1) Chemoradiation/atezolizumab followed by 1 year of atezolizumab 2) Chemoradiation followed by observation	545	PD-L1	No OS benefit

Gronberg H et al., ASCO 2025 proceedings JCO 43, 2025; Peters S et al., Ann Oncol 10.1016/j.annonc.2021.09.011; Higgins KA, et al., 2024 Proceedings, ASTRO .

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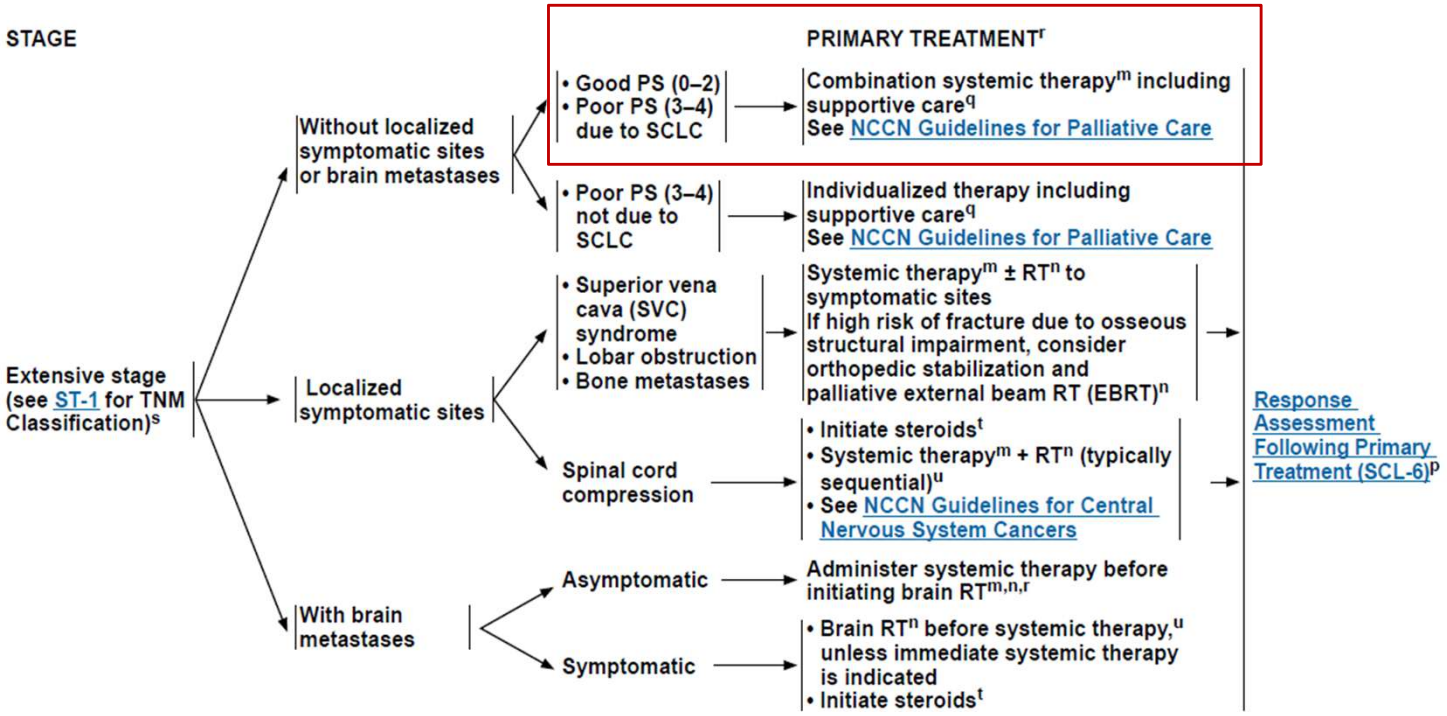
First–Line Management of ES SCLC

- ✓ Approval of lurbinectedin in combination with atezolizumab maintenance

NCCN Algorithm for 1st line ES SCLC



NCCN Guidelines® for Small Cell Lung Cancer (Version 2.2026). SCL-5.

ES SCLC: Initial management

2/3 of SCLC cases at diagnosis
Definition: TNM Stage IV or volume too large to be encompassed in a tolerable RT plan

Standard of Care: PD-L1 plus etoposide/platinum

- 4-6 cycles of EP + PD-L1 followed by PD-L1 maintenance
  - Atezolizumab (IMpower133): FDA approval 2019
  - Durvalumab (CASPIAN): FDA approval 2020
  - **Outcomes**:
    - ORR ~60%
    - OS 12 months
    - mPFS 5.5 months
    - 3 year survival: 17.6% vs 5% (CASPIAN); 16% IMpower133
- PCI and/or post-induction TRT – non consensus

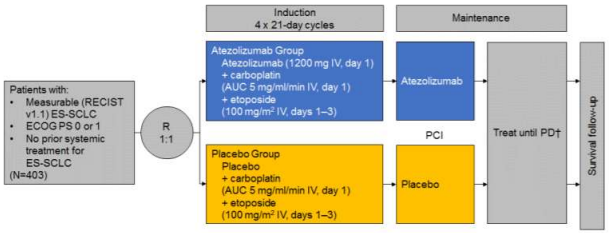
FDA-approved Maintenance

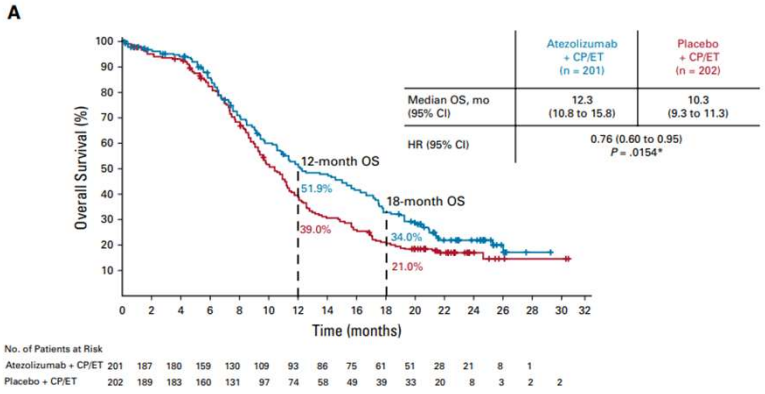
- New Data: lurbinectedin added to atezolizumab maintenance improves survival (Imforte)

Horn L et al., NEJM 2018; , Paz-Ares et al., Lancet Onc 2019

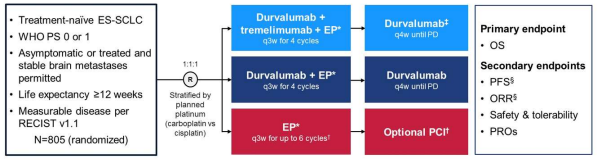
First-line management: Platinum, etoposide plus PD-L1

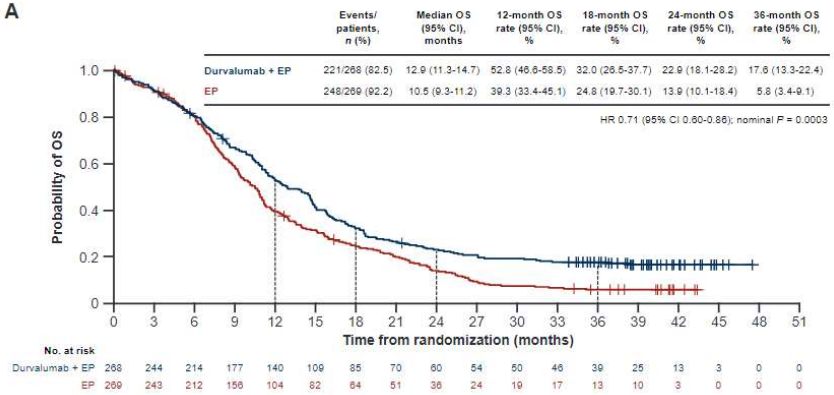
IMpower133





CASPIAN: Durvalumab arm





Liu S et al., WCLC 2018 proceedings, Horn et al., NEJM 2018 10.1056/NEJMoa1809064; Paz-Ares L, et al., Lancet 2019, 10.1016/S0140-6736(19)32222-6, Pas-Arez et al., ESMO Open 2022 doi.org/10.1016/j.esmoop.2022.100408 ; Reck M et al., Lung Cancer 2024; doi: 10.1016/j.lungcan.2024.107924

Key 1st line ICI Studies in ES SCLC of PD-1/PD-L1

Study	IMpower133 [31,32]		CASPIAN [39,40]		CAPSTONE-1 [41]		ASTRUM-005 [46]		RATIONALE-312 [49]		EXTENTORCH [50]	
	Atezolizumab group	Placebo group	Durvalumab group	CE group	Adebrelimab group	Placebo group	Serplulimab group	Placebo group	Tislelizumab group	Placebo group	Toripalimab group	Placebo group
Setting	First-line		First-line		First-line		First-line		First-line		First-line	
Experimental drug	Atezolizumab		Durvalumab		Adebrelimab		Serplulimab		Tislelizumab		Toripalimab	
randomization	1:1		1:1:1		1:1		2:1		1:1		1:1	
Population	403		805		462		585		457		442	
Sites and countries	106 sites in 21 countries		209 sites in 23 countries		47 sites in China		114 sites in 6 countries		China		China	
Percentage of Asians (%)	17		14.5		100		68.5		100		100	
Primary endpoint	PFS & OS		OS		OS		OS		OS		PFS & OS	
Chemotherapy cycle	Four		Four or six		Four or six		Four		Four		Four or six	
Median follow-up	22.9		39.4		13.5		12.3		14.2		11.8	
Stratification factors	sex, ECOG PS (0/1), brain metastases		planned platinum (carboplatin or cisplatin)		hepatic metastases, brain metastases, LDH (normal vs. elevated)		PD-L1 expression levels, brain metastases, age (< 65 vs. ≥ 65)		ECOG PS (0/1), planned platinum (carboplatin or cisplatin), brain metastases		Gender, ECOG PS (0/1)	
median age	64 (28–90)	64 (26–87)	62 (58–68)	63 (57–68)	62 (55–66)	62 (56–67)	63 (28–76)	62 (31–83)	63 (31–78)	62 (34–78)	62 (27–80)	63 (30–77)
Brain metastasis	8.5 %	8.9 %	10 %	10 %	2.2 %	2.2 %	12.9 %	14.3 %	0.4 %	1.7 %	1.3 %	1.8 %
Hepatic metastases	38.3 %	35.6 %	40 %	39 %	31.7 %	31.7 %	25.4 %	26.0 %	28.2 %	25.7 %	26.9 %	22.8 %
Sum of maximum diameter [a]	113 (12–325)	105 (15–353)	NA	NA	NA	NA	117.7 (13.8–323.7)	120.5 (14.5–269.6)	NA	NA	NA	NA
Median OS **months**	12.3	10.3	12.9	10.5	15.3	12.8	15.4	10.9	15.5	13.5	14.6	13.3
HR	HR = 0.70, 95 % CI; 0.54–0.91		HR = 0.71, 95 % CI: 0.60–0.86		HR = 0.72, 95 % CI: 0.58–0.59		HR = 0.63, 95 % CI: 0.49–0.82		HR = 0.75, 95 % CI: 0.61–0.93		HR = 0.798, 95 % CI: 0.65–0.98	
P-value	0.007		0.0003		0.0017		<0.001		0.0040		0.0327	
Median PFS **months**	5.2	4.3	5.1	5.4	5.8	5.6	5.8	4.3	4.7	4.3	5.8	5.6
HR	HR = 0.77, 95 % CI: 0.62–0.96		HR = 0.80, 95 % CI: 0.66–0.96		HR = 0.67, 95 % CI: 0.54–0.83		HR = 0.47, 95 % CI: 0.38–0.59		HR = 0.64, 95 % CI: 0.52–0.78		HR = 0.667, 95 % CI: 0.54–0.82	
P-value	0.02		/		<0.0001		<0.001		<0.0001		0.0002	
24 (18) −month OS, %	34	21	22.9	13.9	31.3	17.2	43.1	7.9	33.2	22.4	NA	NA
DOR, months	4.2	3.9	5.1	5.1	5.6	4.6	5.6	3.2	4.3	3.7	NA	NA
ORR, %	60.2	64.4	68	58	70.4	65.9	80.2	70.4	68.3	61.7	NA	NA
ESMO-MCBS	Grade 3		Grade 3		Grade 2		Grade 4		Grade 2		Grade 2	

ES SCLC – Select first-line studies of additional combinations

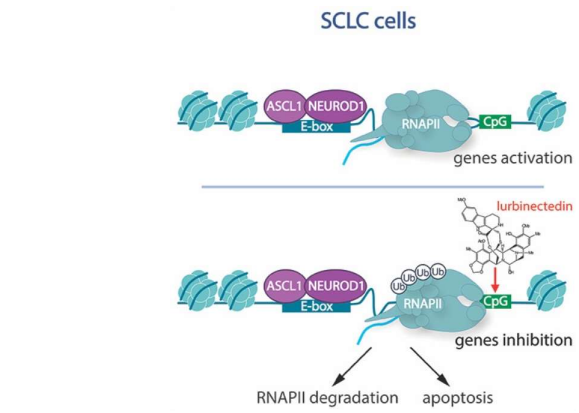
Study	Phase	Clinical Setting	Treatment arms	1ºEP	Results/notes
CASPIAN NCT05091567	III	ES SCLC therapy naive	Pbo/Pbo vs Durva + **Treme (CTLA-4)**	OS/PFS	No improvement over durvalumab
SKYSCRAPER-2 NCT03043872	III	ES SCLC therapy naive	CE + atezo/pbo vs CE + atezo plus **tiragolumab (TIGIT)**	IA OS IA PFS	Negative study
KEYVIBE-008 NCT05224141	III	ES SCLC therapy naive	CE + pembro/pbo vs CE + pembro plus **vibostolimab (TIGIT)**	OS	Discontinue due to futility
Anti-FucGM1 NCT05091567	RPII	ES SCLC therapy naive	CE + nivo vs CE + nivo + **BMS-986012**	Safety, PFS	Interim Analysis – no PFS improvement
Positive					
SWOG1929 NCT04334941	RPII	Maintenance after chemoIO in SLFN11 (+) SCLC	Atezo vs Atezo + **Talazoparib**	PFS	Met primary endpoint of improved PFS Biomarker-based study
IMforte	RP3	Maintenance after chemoIO	Atezo vs AtezoLurbinectedin	OS, PFS	Met primary endpoints

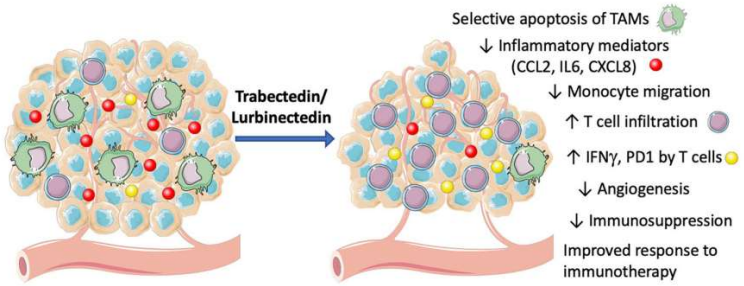
Goldman et al., doi.org/10.1016/S1470-2045(20)30539-8; Rudin et al. JCO 2024 DOI: https://doi.org/10.1200/JCO.23.01363; Press release @ bit.ly/3WFtg1W; Karim et al., JTO 2024 doi: 10.1016/j.jtho.2024.10.021; Kalinka et al., 2024, Ann Oncol 2024;35(suppl):Abstr 1786O ESMO proceedings, ASCO 2025 proceedings

Lurbinectedin: mechanism

- Selective inhibitor of oncogenic transcription
- Specific effects on ASCL1 and NEUROD1, two dominant transcriptional regulators in SCLC

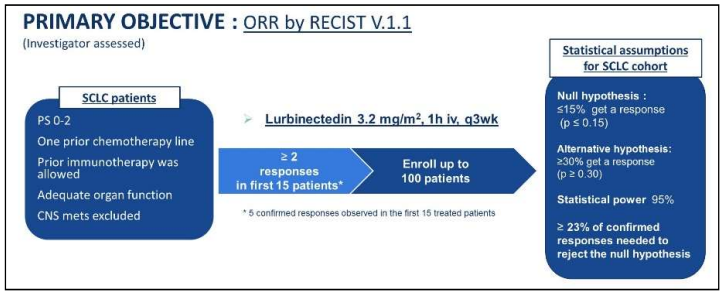
Also impacts the tumor microenvironment
- Including selective apoptosis of TAM
- Decreased monocyte migration
- Increases T-cell infiltration

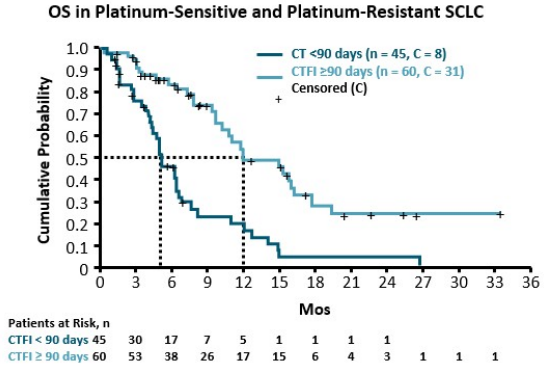




Costanzo, et al., EMBO J 2022; 12;e14841 DOI: 10.15252/emmm.202114841
Allavena, P et al., Front. Oncol., 01 March 2022; //doi.org/10.3389/fonc.2022.851790

Lurbinectedin: Single arm Ph2 in relapsed SCLC





	Basket phase 2 study SCLC cohort Lurbinectedin (n = 83)		ATLANTIS phase 3 study Topotecan subgroup (n = 98)	
	IA	IRC	IA	IRC
ORR, % (95 % CI)	41.0 (30.3–52.3)	33.7 (23.7–44.9)	25.5 (17.2–35.3)	25.5 (17.2–35.3)
DoR (months), median (95 % CI)	5.3 (3.5–5.9)	5.1 (4.8–5.9)	3.9 (3.0–5.7)	4.3 (3.0–5.6)
PFS (months), median (95 % CI)	4.0 (2.6–4.7)	3.7 (2.6–4.6)	4.2 (3.0–4.8)	4.1 (2.9–4.7)
OS (months), median (95 % CI)	10.2 (7.6–12.0)		7.6 (6.1–10.3)	
% events	74 (89.2 %)		80 (81.6 %)	
Censored	9 (10.8 %)		18 (18.4 %)	

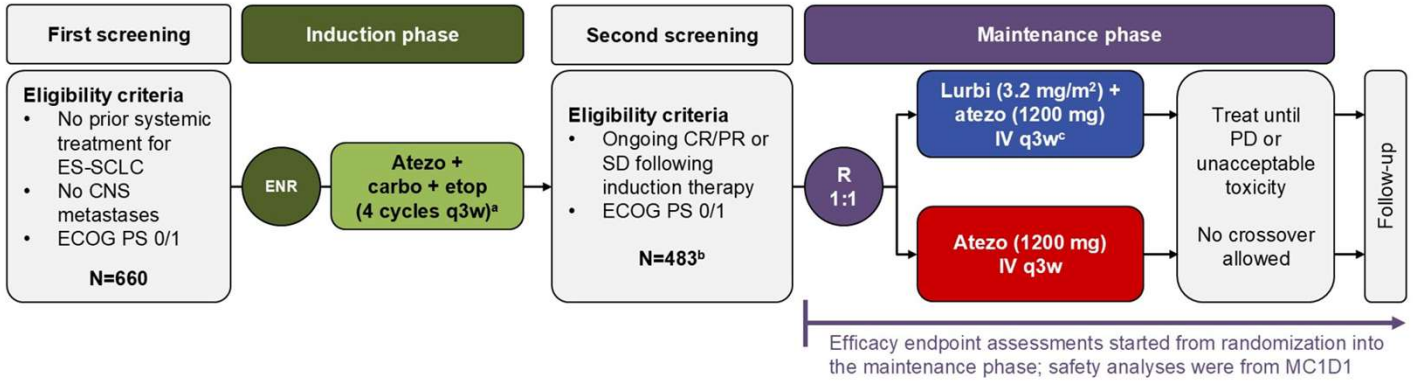
Abbreviations: CI, confidence interval; DoR, duration of response; IA, investigator assessment; IRC, Independent Review Committee; ORR, overall response rate; PFS, progression free survival; OS, overall survival.

- June 2020, lurbinectedin received accelerated FDA approval for relapsed SCLC
- Full approval will require confirmation by the Phase 3 LAGOON Study which compared lurbinectedin to irinotecan (or investigator's choice)

Trigo. Lancet Oncol. 2020;21:645; Peters S, Lung Cancer 2024

IMforte: Phase 3 Study of Maintenance Lurbinectedin in Combination With Atezolizumab Compared With Atezolizumab

IMforte study design



Stratification factors for randomization
- ECOG PS (0/1)
- LDH (≤ULN/>ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

Primary endpoints
IRF-PFS and OS

Secondary endpoints included
INV-PFS, ORR, DOR, and safety

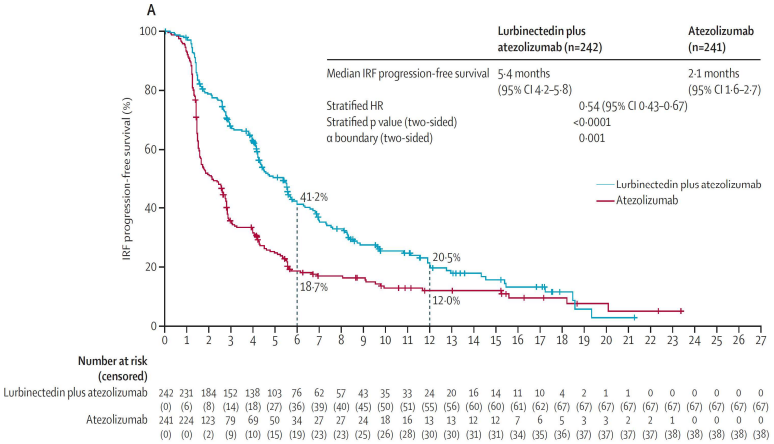
Last patient randomized: April 30, 2024
Clinical cutoff: July 29, 2024

ClinicalTrials.gov ID: NCT05091567.
[a] Administered per standard dose. [b] 73% of patients continued from induction to maintenance. [c] With **prophylactic granulocyte colony-stimulating factor** and anti-emetics.
atezo, atezolizumab; BL, baseline; carbo, carboplatin; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; ENR, enrollment; etop, etoposide; INV-PFS, investigator-assessed PFS; IRF-PFS, independent review facility-assessed PFS; IV, intravenously; LDH, lactate dehydrogenase; lurbi, lurbinectedin; MC1D1, maintenance Cycle 1 Day 1; PCI, prophylactic cranial irradiation; q3w, every 3 weeks; R, randomization; ULN, upper limit of normal; Y/N, yes/no.

PRESENTED BY: Luis Paz-Ares, MD, PhD

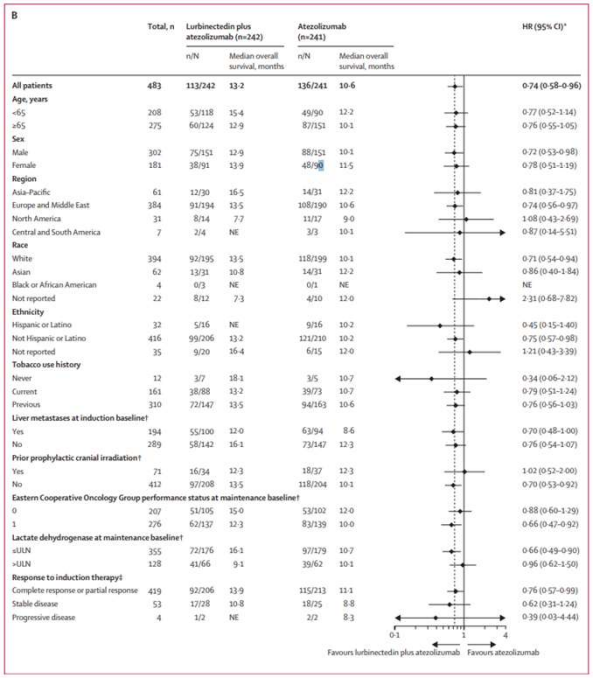
IMforte ASCO 2025
Abstract 8006

IMforte: lurbinectedin added to atezolizumab maintenance improves mPFS and mOS



Paz-Ares et al., Lancet 2025, /doi.org/10.1016/S0140-6736(25)01011-6

IMforte: subgroup analysis OS and AEs



B	Total, n	Lurbinectedin plus atezolizumab (n=242)		Atezolizumab (n=241)		HR (95% CI)*
		n/N	Median overall survival, months	n/N	Median overall survival, months	
All patients	483	113/242	13·2	136/241	10·6	0·74 (0·58–0·96)
Age, years						
<65	208	53/118	15·4	49/90	12·2	0·77 (0·52–1·14)
≥65	275	60/124	12·9	87/151	10·1	0·76 (0·55–1·05)
Sex						
Male	302	75/151	12·9	88/151	10·1	0·72 (0·53–0·98)
Female	181	38/91	13·9	48/90	11·5	0·78 (0·51–1·19)
Region						
Asia-Pacific	61	12/30	16·5	14/31	12·2	0·81 (0·37–1·75)
Europe and Middle East	384	91/194	13·5	108/190	10·6	0·74 (0·56–0·97)
North America	31	8/14	7·7	11/17	9·0	1·08 (0·43–2·69)
Central and South America	7	2/4	NE	3/3	10·1	0·87 (0·14–5·51)
Race						
White	394	92/195	13·5	118/199	10·1	0·71 (0·54–0·94)
Asian	62	13/31	10·8	14/31	12·2	0·86 (0·40–1·84)
Black or African American	4	0/3	NE	0/1	NE	NE
Not reported	22	8/12	7·3	4/10	12·0	2·31 (0·68–7·82)
Ethnicity						
Hispanic or Latino	32	5/16	NE	9/16	10·2	0·45 (0·15–1·40)
Not Hispanic or Latino	416	99/206	13·2	121/210	10·2	0·75 (0·57–0·98)
Not reported	35	9/20	16·4	6/15	12·0	1·21 (0·43–3·39)
Tobacco use history						
Never	12	3/7	18·1	3/5	10·7	0·34 (0·06–2·12)
Current	161	38/88	13·2	39/73	10·7	0·79 (0·51–1·24)
Previous	310	72/147	13·5	94/163	10·6	0·76 (0·56–1·03)
Liver metastases at induction baseline†						
Yes	194	55/100	12·0	63/94	8·6	0·70 (0·48–1·00)
No	289	58/142	16·1	73/147	12·3	0·76 (0·54–1·07)
Prior prophylactic cranial irradiation†						
Yes	71	16/34	12·3	18/37	12·3	1·02 (0·52–2·00)
No	412	97/208	13·5	118/204	10·1	0·70 (0·53–0·92)
Eastern Cooperative Oncology Group performance status at maintenance baseline†						
0	207	51/105	15·0	53/102	12·0	0·88 (0·60–1·29)
1	276	62/137	12·3	83/139	10·0	0·66 (0·47–0·92)
Lactate dehydrogenase at maintenance baseline†						
≤ULN	355	72/176	16·1	97/179	10·7	0·66 (0·49–0·90)
>ULN	128	41/66	9·1	39/62	10·1	0·96 (0·62–1·50)
Response to induction therapy‡						
Complete response or partial response	419	92/206	13·9	115/213	11·1	0·76 (0·57–0·99)
Stable disease	53	17/28	10·8	18/25	8·8	0·62 (0·31–1·24)
Progressive disease	4	1/2	NE	2/2	8·3	0·39 (0·03–4·44)

0·1 1 4

Favours lurbinectedin plus atezolizumab Favours atezolizumab

	Lurbinectedin plus atezolizumab (n=242)	Atezolizumab (n=240)
Patients with ≥1 adverse event	235 (97%)	194 (81%)
Treatment-related adverse events	202 (83%)	96 (40%)
Grade 3–4 adverse events	92 (38%)	53 (22%)
Treatment-related grade 3–4 adverse events	62 (26%)	14 (6%)
Grade 5 adverse events	12 (5%)	6 (3%)
Treatment-related grade 5 adverse events	2 (1%)	1 (<1%)
Serious adverse events	75 (31%)	41 (17%)
Treatment-related serious adverse events	28 (12%)	9 (4%)
Adverse events leading to treatment discontinuation of any study drug	15 (6%)	8 (3%)
Adverse events leading to dose interruption/ modification of any study drug	92 (38%)	33 (14%)
Adverse events of special interest for lurbinectedin	93 (38%)	62 (26%)
Grade 3–4	18 (7%)	12 (5%)
Grade 5	7 (3%)	4 (2%)
Serious	28 (12%)	16 (7%)
Adverse events of special interest for atezolizumab	76 (31%)	54 (23%)
Grade 3–4	15 (6%)	8 (3%)
Grade 5	0	0
Serious	10 (4%)	5 (2%)
Requiring corticosteroids	40 (17%)	18 (8%)

Data are n (%).

Table 2: **Adverse events during the maintenance phase (safety analysis set; n=482)**

Paz-Ares et al., Lancet 2025, /doi.org/10.1016/S0140-6736(25)01011-6

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Management of Relapsed SCLC

- ✓ Approval of tarlatamab after platinum-based chemotherapy

Relapsed SCLC

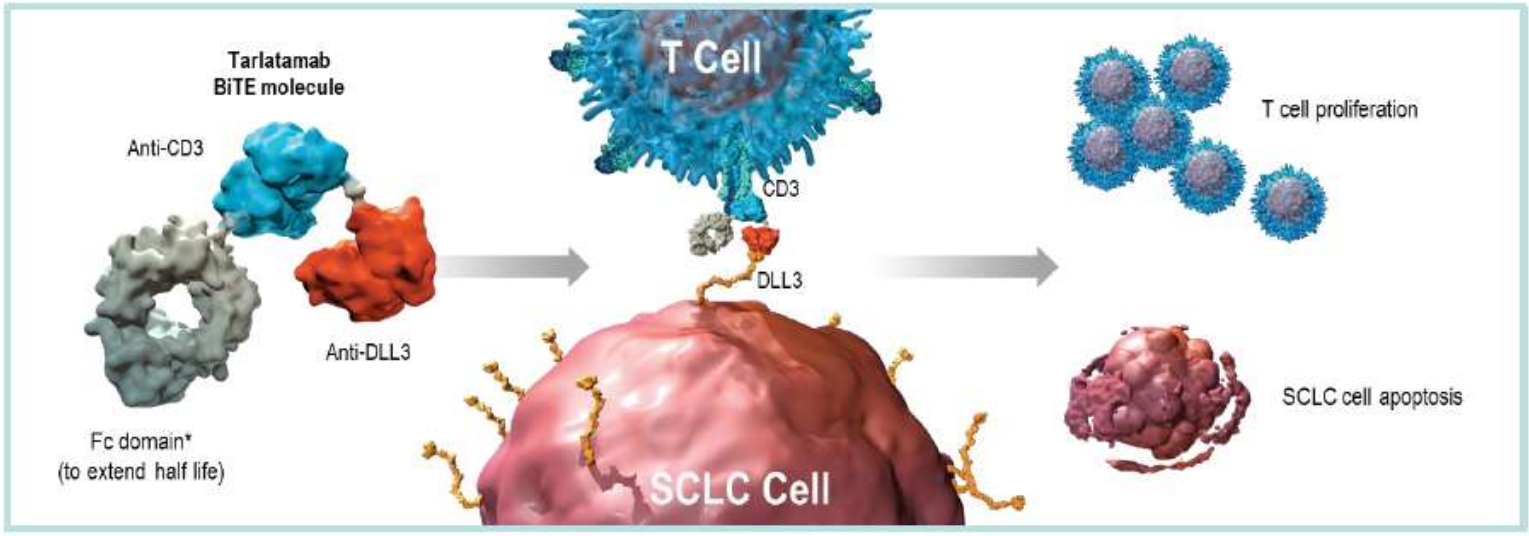
- The majority of patients diagnosed with SCLC will relapse
- Historically survival was 4-6 months with 2nd line therapy

SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)[g] Consider dose reduction or growth factor support for patients with PS 2
Preferred
• Tarlatamab-dlle[i,27] (category 1)
• Clinical trial enrollment
• Irinotecan[f,25,26]
• Lurbinectedin (if not previously used)[20,21]
• If prolonged disease free time, re-treatment with platinum-based doublet with or without immunotherapy[15-19]
• Topotecan Oral (PO) or Intravenous (IV)[17,22-25]
Other Recommended
• CAV (Cyclophosphamide/Doxorubicin/Vincristine)[22]
• Docetaxel[36]
• Gemcitabine[37,38,39]
• Nivolumab[n] or Pembrolizumab (if not previously treated with an ICI)[d,28-31]
• Oral Etoposide[40,41]
• Paclitaxel[32,33]
• Temozolomide[34,35]

NCCN Guidelines® for Small Cell Lung Cancer (Version 2.2026). SCL-E, 3 of 6.

Tarlatamab: a DLL3-CD3 Bispecific T-Cell Engager

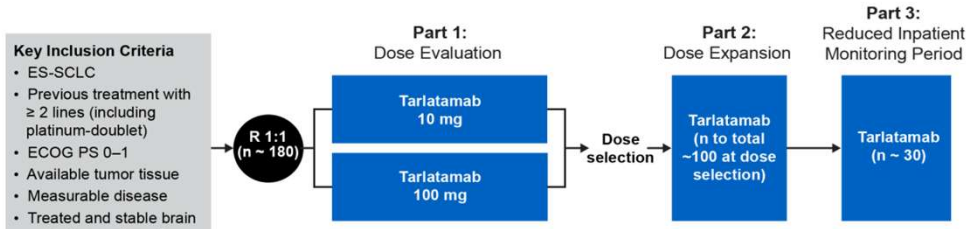
- DLL3 is highly expressed on SCLC and HGNEC
- Tarlatamab is a half-life extended bispecific T-cell engager that binds DLL3 and CD3
- **Phase 1 study 107 patients**, ORR 23.4% in heavily-pretreated patients with SCLC
  - mDOR 12.3 months, mOS 13.2 months



Paz Ares et al., JCO 2023; DOI: 10.1200/JCO.22.0282

DeLLphi-301: Ph2 study of tarlatamab in relapsed SCLC

Figure S1. Study Design



Endpoints

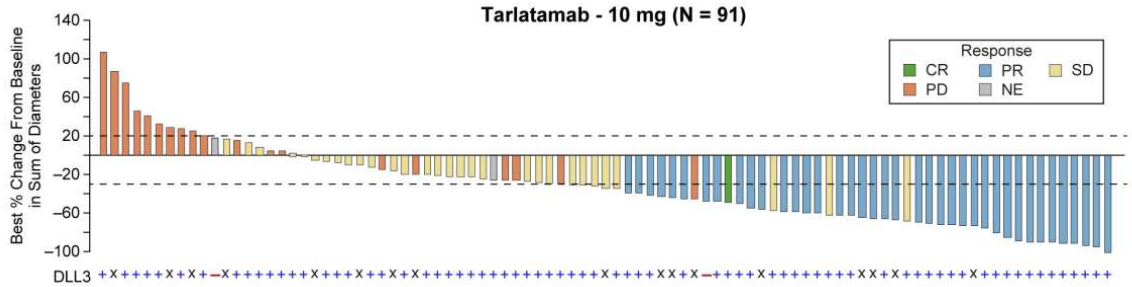
Primary: Objective response rate per RECIST v1.1 by BICR, incidence of adverse events, serum concentrations of tarlatamab

Secondary: Duration of response, disease control rate, duration of disease control, progression-free survival as per RECIST v1.1 by BICR, overall survival; and incidence of anti-tarlatamab antibody formation

BICR: blinded independent central review; ECOG PS: Eastern Cooperative Oncology Group performance status scale; ES-SCLC: extensive stage-small cell lung cancer; R: randomization; RECIST: Response Evaluation Criteria in Solid Tumors.

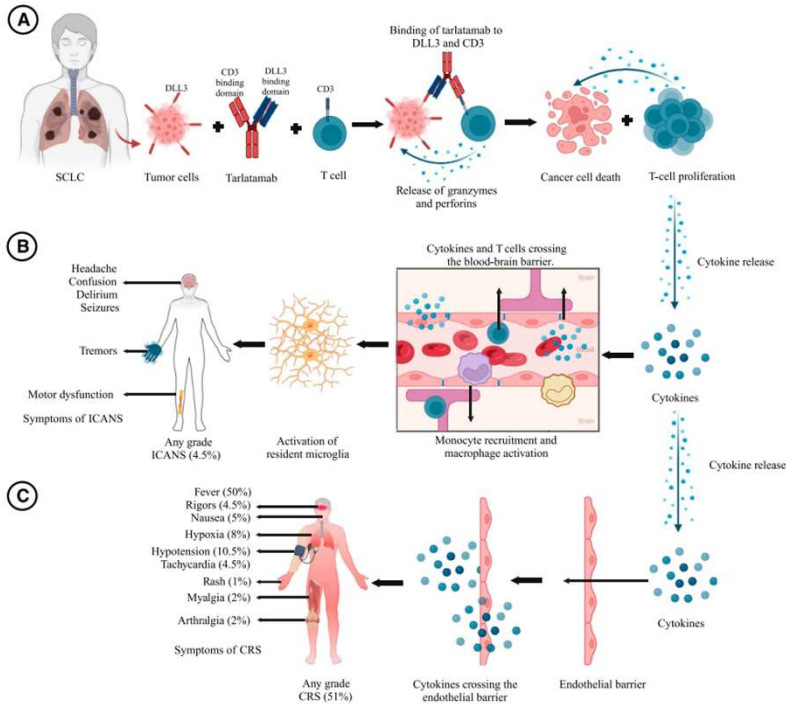
	Tarlatamab 10 mg (N = 100)	Tarlatamab 100 mg (N = 88)
Best overall response – n (%)		
Confirmed complete response	0 (0.0)	0 (0.0)
Confirmed partial response	43 (43.0)	31 (35.2)
Stable disease	32 (32.0)	25 (28.4)
Progressive disease	16 (16.0)	13 (14.8)
Not evaluable	1 (1.0)	2 (2.3)
Death before post-baseline scan	6 (6.0)	14 (15.9)
No post-baseline scan	2 (2.0)	3 (3.4)
Objective response rate – % (97.5% CI[a])	43.0 (31.9, 54.7)	35.2 (24.1, 47.6)
Disease control rate – % (95% CI[a])	75.0 (65.3, 83.1)	63.6 (52.7, 73.6)

Note: The widths of the confidence intervals have not been adjusted for multiplicity. Thus, the confidence intervals should not be used to reject or not reject treatment effects.
Not evaluable, death before post-baseline scan and no post-baseline scan are considered non-responders for response analysis.
[a]Exact confidence intervals were calculated using the Clopper Pearson method.
CI, confidence interval; N, number of patients in the analysis set; n, number of patients with observed data.



Ahn NEJM 2023 DOI: 10.1056/NEJMoa2307980

Tarlatamab: CRS and ICANS mechanism and manifestations



The potential for Cytokine Release Syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), mandated additional monitoring

Aijaz et al., 2025 ASCO Educational Book, DOI: 10.1200/EDBK-25-472794

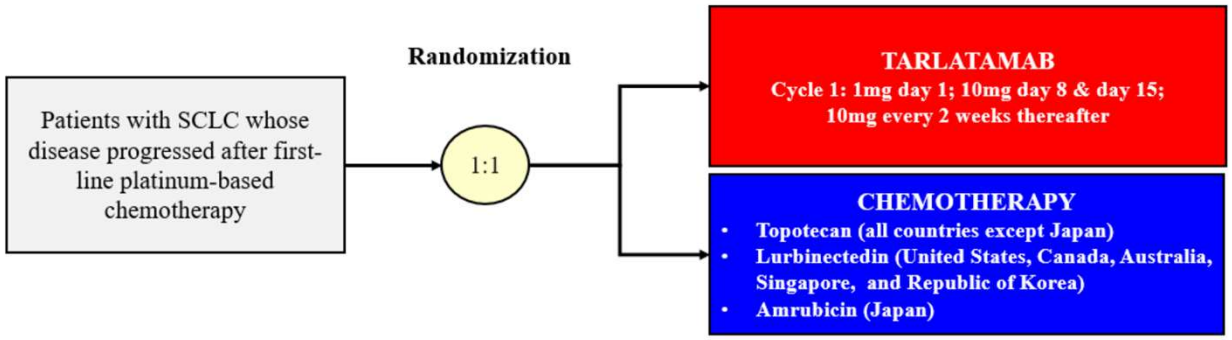
DeLLphi-301: CRS and ICANS

Adverse Events	Tarlatamab, 10 mg		Tarlatamab, 100 mg
	Parts 1 and 2 (N=99)	Part 3, Reduced Monitoring (N=34)	Part 1 (N=87)
	number of patients (percent)		
Events during treatment period			
According to severity			
Any grade	96 (97)	34 (100)	87 (100)
Grade ≥2	86 (87)	33 (97)	83 (95)
Grade ≥3	57 (58)	22 (65)	56 (64)
Grade ≥4	16 (16)	7 (21)	13 (15)
Fatal	3 (3)	4 (12)	5 (6)
Serious adverse event	58 (59)	14 (41)	62 (71)
Event leading to dose interruption, dose reduction, or both	31 (31)	5 (15)	39 (45)
Event leading to tarlatamab discontinuation	7 (7)	3 (9)	6 (7)
Events of interest during treatment period			
Cytokine-release syndrome†			
Overall	49 (49)	19 (56)	53 (61)
Grade ≥3 severity	0	1 (3)	5 (6)
Serious	26 (26)	5 (15)	32 (37)
Leading to tarlatamab discontinuation	0	0	1 (1)
Fatal	0	0	0
ICANS and associated neurologic events‡			
Overall	7 (7)	4 (12)	24 (28)
Grade ≥3 severity	0	0	4 (5)
Serious	2 (2)	2 (6)	11 (13)
Leading to tarlatamab discontinuation	1 (1)	0	1 (1)
Fatal	0	0	0
Neutropenia			
Overall	18 (18)	5 (15)	14 (16)
Grade ≥3 severity	6 (6)	2 (6)	9 (10)
Serious	2 (2)	0	3 (3)
Leading to tarlatamab discontinuation	0	0	0
Fatal	0	0	0

Ahn NEJM 2023 DOI: 10.1056/NEJMoa2307980

DeLLphi-304: RP3 Study of Tarlatamab vs TPC

Figure S1. Study Design



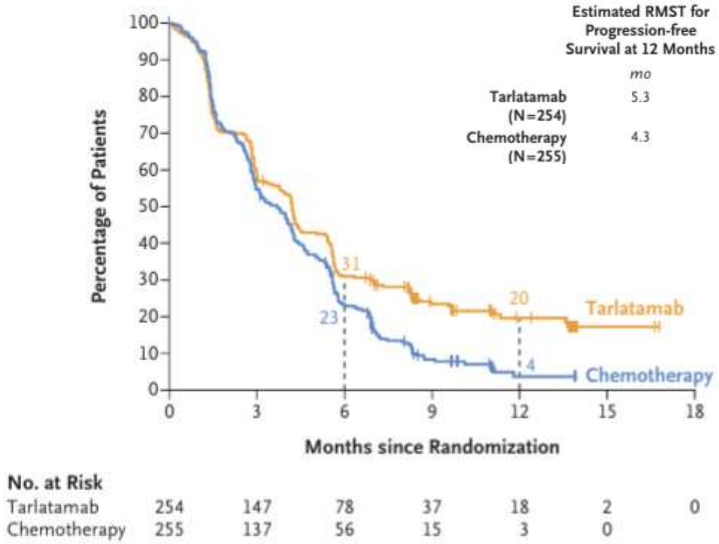
Topotecan: 185 (73%)
Lurbinectedin: 47 (18%)
Amrubicin: 23 (9%)

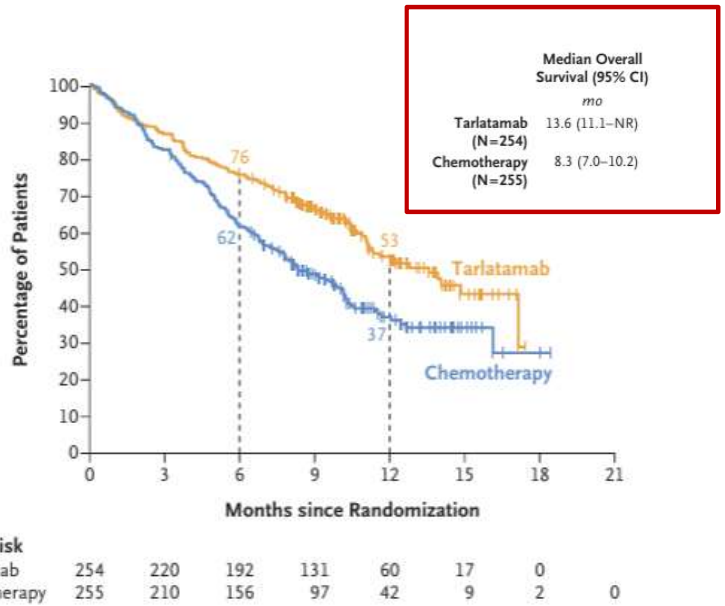
Stratification Factors: 1) Prior anti-PD-1 or anti PD-L1 (yes vs no); 2) Chemotherapy-free interval (<90 days, ≥90 to < 180 days, ≥180 days; 3) Presence (previous or current) of brain metastases (yes vs no); 4) Chemotherapy (topotecan/amrubicin vs lurbinectedin)

Primary endpoint: Overall survival
Key secondary endpoints: Progression-free survival, patient-reported outcomes
Secondary endpoints: Objective response, duration of response, disease control, safety and tolerability

Rudin et al., 2025 ASCO Proceedings; Mountzios, G et al., N Engl J Med 2025;393:349-61. DOI: 10.1056/NEJMoa2502099

DeLLphi-304: mPFS and mOS



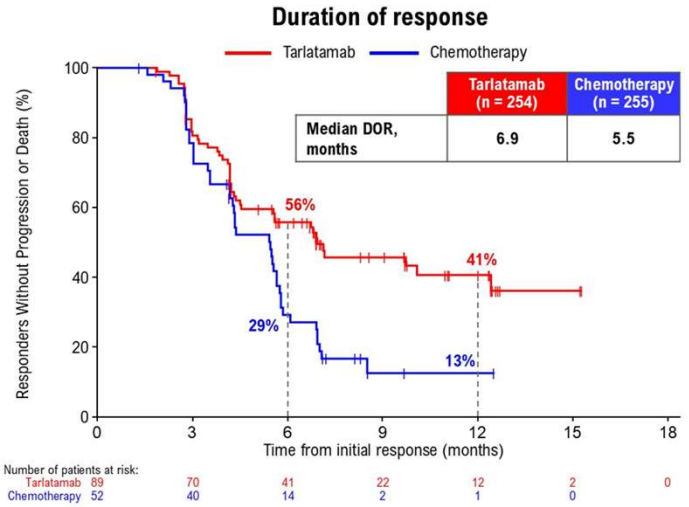


Mountzios, G et al., N Engl J Med 2025;393:349-61. DOI: 10.1056/NEJMoa2502099

DeLLphi-304: Responses and DOR

Tarlatamab was associated with more frequent and more durable responses

	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)

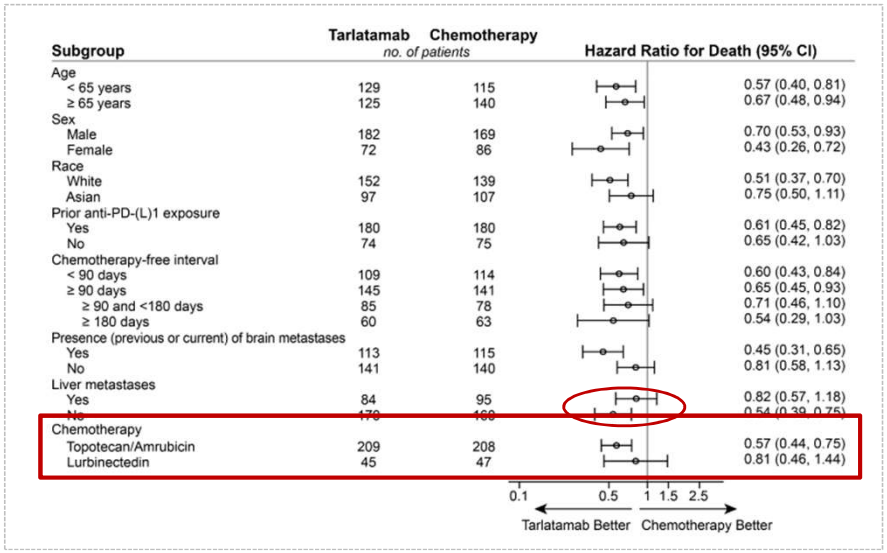


Rudin et al., 2025 ASCO Proceedings; Mountzios, G et al., N Engl J Med 2025;393:349-61. DOI: 10.1056/NEJMoa2502099

DeLLphi-304: Responses and Subgroup Analysis

Table 2. Treatment Response (Intention-to-Treat Population).*

Variable	Tarlatamab (N=254)	Chemotherapy (N=255)
Best overall response — no. (%)†		
Confirmed complete response‡	3 (1)	0
Confirmed partial response‡	86 (34)	52 (20)
Stable disease	84 (33)	112 (44)
Progressive disease	56 (22)	50 (20)
Not able to be evaluated	1 (<1)	1 (<1)
No postbaseline scan	24 (9)	40 (16)
Objective response§		
Percentage of patients (95% CI)¶	35 (29–41)	20 (16–26)
Risk ratio, tarlatamab vs. chemotherapy (95% CI)‖	1.73 (1.29–2.33)	—
Duration of response (95% CI) — mo		
Median	6.9 (4.5–12.4)	5.5 (4.2–5.7)
25th percentile	3.8 (3.0–4.2)	3.0 (2.8–4.2)
75th percentile	NR (12.4–NR)	6.9 (5.7–NR)
Kaplan–Meier estimate of duration of response (95% CI) — %		
At 6 mo	56 (45–66)	29 (17–42)
At 12 mo	41 (29–52)	13 (4–25)
Median time to response (IQR) — mo	1.5 (1.4–1.6)	1.4 (1.3–2.2)
Ongoing response at data cutoff — no./total no. (%)	42/89 (47)	8/52 (15)



Mountzios, G et al., N Engl J Med 2025;393:349-61. DOI: 10.1056/NEJMoa2502099

DeLLphi-304: Toxicities

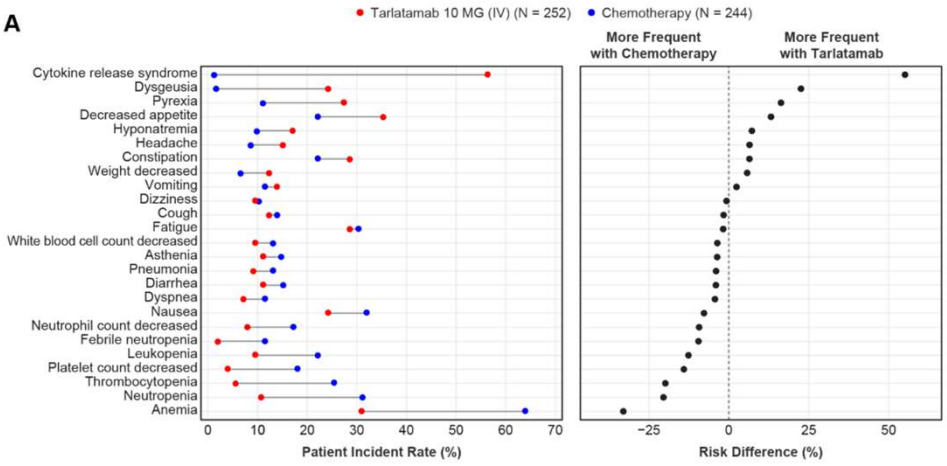


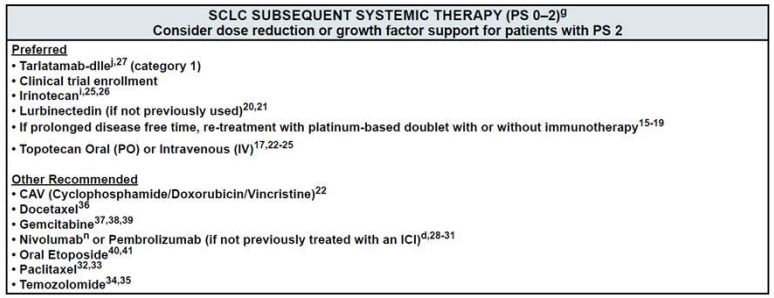
Table 3. Adverse Events (Safety Population).*

Event	Tarlatamab (N=252)	Chemotherapy (N=244)
	no. of patients (%)	
Any adverse event, regardless of relationship to treatment	249 (99)	243 (100)
Adverse event of grade 3 or higher	136 (54)	195 (80)
Serious adverse event	129 (51)	125 (51)
Adverse event resulting in dose interruption, dose reduction, or both†	94 (37)	159 (65)
Adverse event resulting in discontinuation of trial treatment	13 (5)	30 (12)
Adverse event resulting in death	20 (8)	21 (9)
Adverse event related to treatment, as assessed by the investigator	235 (93)	223 (91)
Adverse event of grade 3 or higher	67 (27)	152 (62)
Serious adverse event	70 (28)	75 (31)
Adverse event resulting in dose interruption, dose reduction, or both†	48 (19)	134 (55)
Adverse event resulting in discontinuation of trial treatment	7 (3)	15 (6)
Adverse event resulting in death	1 (<1)	4 (2)
Adverse event of any grade reported in ≥10% of the patients in either group		
Cytokine release syndrome	142 (56)	3 (1)‡
Dysgeusia	61 (24)	4 (2)

Mountzios, G et al., N Engl J Med 2025;393:349-61. DOI: 10.1056/NEJMoa2502099

FDA-approved agents for relapsed disease

Study	N	ORR (%)	mDOR (mo)	mPFS (mo)	mOS (mo)
Topotecan (1997)	101	21.7	7.6	2.8	5.4
Lurbinectedin (Ph2)	105	35.2	5.3	3.5	9.3
Tarlatamab (10mg)	100 34	40%	> 6 mo (in 59%)	4.9	68% at 9mo
Tarlatamab (10mg) vs TPC – Ph 3	509	35%	6.9 mos	5.3 vs. 4.3 (HR 0.71)	13.6 vs. 8.3 mos (HR 0.6)



SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)[g]
Consider dose reduction or growth factor support for patients with PS 2

Preferred
- Tarlatamab-dlle[i,27] (category 1)
- Clinical trial enrollment
- Irinotecan[i,25,26]
- Lurbinectedin (if not previously used)[20,21]
- If prolonged disease free time, re-treatment with platinum-based doublet with or without immunotherapy[15-19]
- Topotecan Oral (PO) or Intravenous (IV)[17,22-25]

Other Recommended
- CAV (Cyclophosphamide/Doxorubicin/Vincristine)[22]
- Docetaxel[36]
- Gemcitabine[37,38,39]
- Nivolumab[n] or Pembrolizumab (if not previously treated with an ICI)[d,28-31]
- Oral Etoposide[40,41]
- Paclitaxel[32,33]
- Temozolomide[34,35]

NCCN Guidelines® for Small Cell Lung Cancer (Version 2.2026). SCL-E, 3 of 6.
© 2025 National Comprehensive Cancer Network, Inc. Available at: NCCN.org.

Ardizzoni et al, JCO 1997; Trigo et al., Peters. et al, Lung Cancer J 2024; Ahn MJ et al., NEJM 2023, NCCN SCLC 2026

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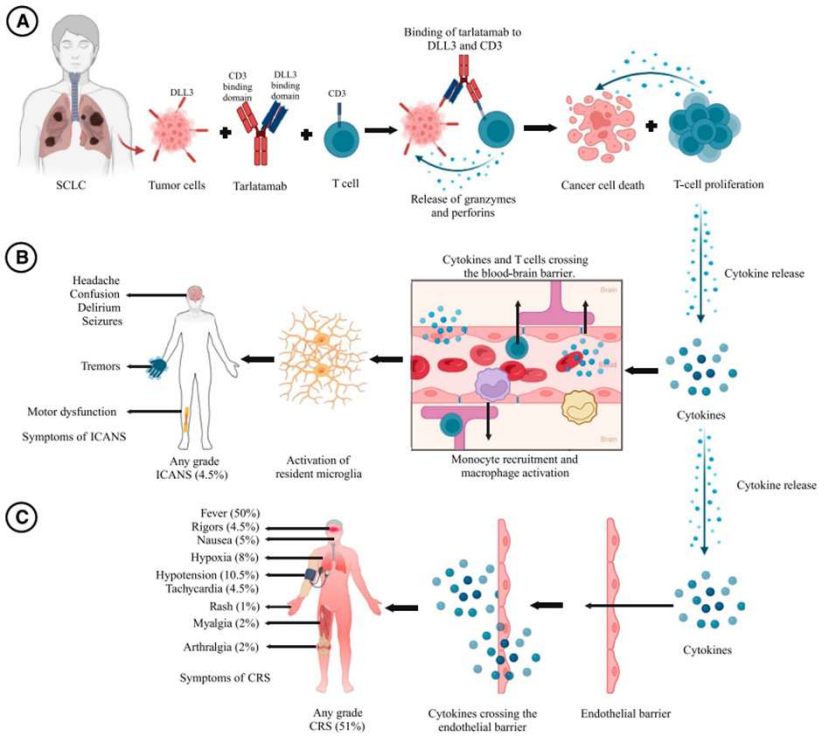
Practical considerations, challenges, and strategies for implementing tarlatamab in the community oncology setting

- ✓ Management of CRS and ICANS

Bispecific T-cell Engagers: CRS and ICANS mechanism and manifestations



Two unique toxicities of tarlatamab, CRS and ICANS, mandated intensive monitoring on study.

Aijaz et al., 2025 ASCO Educational Book, DOI: 10.1200/EDBK-25-472794

CRS evaluation and experience in DeLLphi-301,-304

Table 2
ASTCT CRS Consensus Grading

CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever*	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C
		With		
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
		And/or[†]		
Hypoxia	None	Requiring low-flow nasal cannula[‡] or blow-by	Requiring high-flow nasal cannula[‡], facemask, nonrebreather mask, or Venturi mask	Requiring positive pressure (eg, CPAP, BiPAP, intubation and mechanical ventilation)

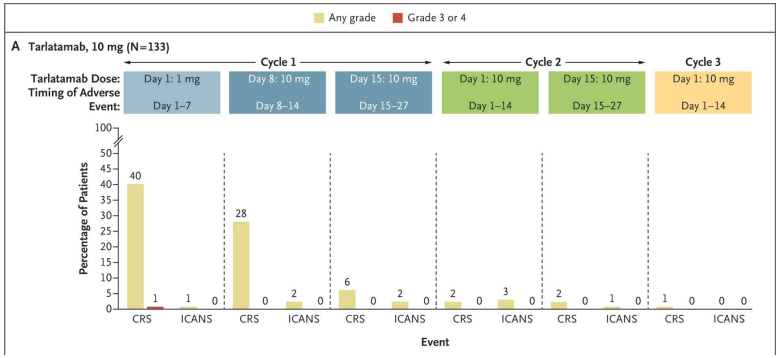


TABLE S5. PATIENT INCIDENCE OF CRS AND INTERVENTION UTILIZATION

	All Tarlatamab (N=252) n (%)
All treatment-emergent CRS events	142 (56.3)
Grade ≥ 2	35 (13.9)
Grade ≥ 3	3 (1.2)
Grade ≥ 4	0 (0.0)
Serious adverse events	43 (17.1)
Leading to dose interruption of tarlatamab	4 (1.6)
Leading to discontinuation of tarlatamab	1 (0.4)
Fatal adverse events	0 (0.0)
Utilization of CRS interventions	54 (21.4)
Tocilizumab use	9 (3.6)
Corticosteroids use	41 (16.3)
Vasopressor use	1 (0.4)
IV fluid use	15 (6.0)
Supplemental oxygen use	19 (7.5)
High-flow (> 6 L/Min) oxygen	1 (0.4)

Lee DW et al., doi: 10.1016/j.bbmt.2018.12.758; Ahn et al., NEJM 2023; Mountzios, G et al., DOI: 10.1056/NEJMoa2502099

ICANS evaluation and experience in DeLLphi-304

Table 6
ASTCT ICANS Consensus Grading for Adults

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score*	7-9	3-6	0-2	0 (patient is unarousable and unable to perform ICE)
Depressed level of consciousness†	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse. Stupor or coma
Seizure	N/A	N/A	Any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min); or Repetitive clinical or electrical seizures without return to baseline in between
Motor findings‡	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Elevated ICP/ cerebral edema	N/A	N/A	Focal/local edema on neuroimaging§	Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; or papilledema; or Cushing's triad

ICE

- **Orientation:** orientation to year, month, city, hospital: 4 points
- **Naming:** ability to name 3 objects (eg, point to clock, pen, button): 3 points
- **Following commands:** ability to follow simple commands (eg, "Show me 2 fingers" or "Close your eyes and stick out your tongue"): 1 point
- **Writing:** ability to write a standard sentence (eg, "Our national bird is the bald eagle"): 1 point
- **Attention:** ability to count backwards from 100 by 10: 1 point

TABLE S7. PATIENT INCIDENCE OF ICANS

	Tarlatamab N=252 n (%)
Treatment emergent ICANS events	15 (6.0)
Grade ≥ 2	8 (3.2)
Grade ≥ 3	1 (0.4)
Grade ≥ 4	1 (0.4)
Serious adverse events	9 (3.6)
Leading to dose interruption of tarlatamab	2 (0.8)
Leading to discontinuation of tarlatamab	1 (0.4)
Fatal adverse events	1 (0.4)

ICANS adverse events are based on ICANS preferred term only. Adverse events are coded using

Lee DW et al., Biol Blood Marrow Transplant. 2019 Apr;25(4):625-638. doi: 10.1016/j.bbmt.2018.12.758; Mountzios, G et al., DOI: 10.1056/NEJMoa2502099.

Tarlatamab: FDA-recommended monitoring protocol

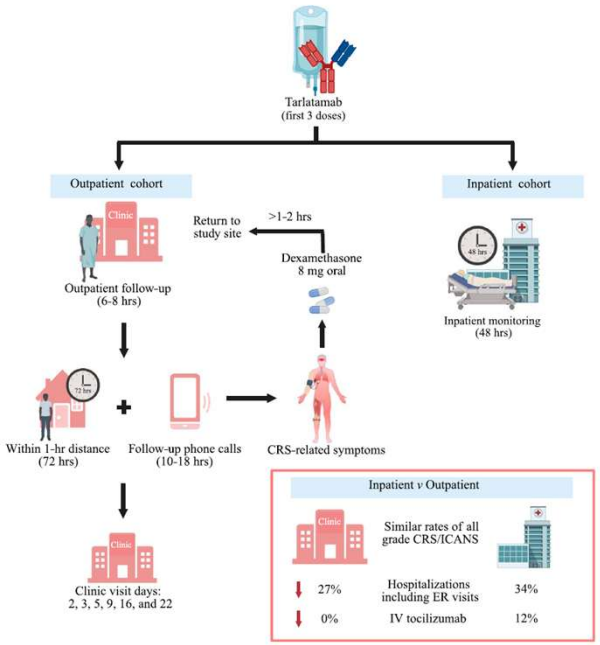
Table 1. Recommended Dosage and Schedule of IMDELLTRA

Dosing Schedule	Day	Dose of IMDELLTRA	Administration Instructions	Recommended Monitoring
Step-up Dosing Schedule Cycle 1	Day 1[a]	Step-up dose[a] 1 mg	Administer IMDELLTRA as a 1-hour intravenous infusion in an appropriate healthcare setting.	Monitor patients from the start of the IMDELLTRA infusion for 22 to 24 hours on Cycle 1 Day 1 and Cycle 1 Day 8 in an appropriate healthcare setting. Recommend that patients remain within 1-hour of an appropriate healthcare setting for a total of 48 hours from start of the infusion with IMDELLTRA, accompanied by a caregiver.
	Day 8[a]	10 mg[a]		
	Day 15	10 mg		Observe patients for 6-8 hours post IMDELLTRA infusion[b].
Cycle 2	Day 1 and 15	10 mg		Observe patients for 6-8 hours post IMDELLTRA infusion[b].
Cycles 3 and 4	Day 1 and 15	10 mg		Observe patients for 3-4 hours post IMDELLTRA infusion [b].
Cycle 5 and subsequent infusions	Day 1 and 15	10 mg		Observe patients for 2 hours post IMDELLTRA infusion [b].

Aijaz et al., 2025 ASCO Educational Book, DOI: 10.1200/EDBK-25-472794; FDA label (fda.gov/drugsatfda_docs/label/2024/761344s000lbl.pdf)

Tarlatamab: toxicity monitoring, inpatient vs outpatient

DeLLphi-300 (FIH)



Aijaz et al., 2025 ASCO Educational Book, DOI: 10.1200/EDBK-25-472794

Adopt strategies employed by our Heme Malignancies colleagues

- Consider IP/OP unit - at JHH for HM
- Standardized CRS/ICANS mitigation/management protocols

- **NCT06957314** – A study of Hospital-at-Home for people receiving tarlatamab (MSKCC)
- **DeLLphi-305** (1st-line maintenance) and **DeLLphi-306** (consolidation for LS SCLC) are evaluating a shortened outpatient monitoring period after dosing

Integrate remote patient monitoring, wearable devices

Current Practice:
Tertiary centers serve as a referral center for community practices – for D1, D8, and typically the first few cycles (C2 ~ 6 hours, C3-4 3-4 hours)

Financial considerations:
~$31,500 (USD) for the first cycle
~$30,000 (USD) for each additional cycle thereafter
Median cost for treatment > $165K

JOHNS HOPKINS
UNIVERSITY

Current and emerging clinical trials and pipeline agents in SCLC

- ✓ T-cell engagers
- ✓ ADCs

Tarlatamab: ongoing studies

The road ahead: Tarlatamab

Is earlier tarlatamab better (e.g. first-line ES-SCLC, or LS-SCLC)?

DeLLphi trial #	Phase	Indication	Design	Recruiting?	Trial ID
303	1b	1L ES-SCLC	Tarlatamab + standard therapy	N	NCT05037847
305	3	1L ES-SCLC maintenance	Tarlatamab + durva vs. durva alone	Y	NCT06502977
306	3	LS-SCLC post-chemoRT	Tarlatamab vs. placebo	Y	NCT06117774
310	1b	1L ES-SCLC maintenance	Tarlatamab + YL201 + atezo or durva	Y	NCT06898957

Is tarlatamab more effective in combination?

DeLLphi trial #	Phase	Indication	Design	Recruiting?	Trial ID
302	1b	2L+ SCLC	Tarlatamab + anti-PD-1 therapy	Y	NCT04184050
305	3	1L ES-SCLC maintenance	Tarlatamab + durva vs. durva alone	Y	NCT06502977
310	1b	2L SCLC	Tarlatamab + YL201	Y	NCT06898957
		1L ES-SCLC maintenance	Tarlatamab + YL201 + atezo or durva		

2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Catherine B. Meador, MD, PhD

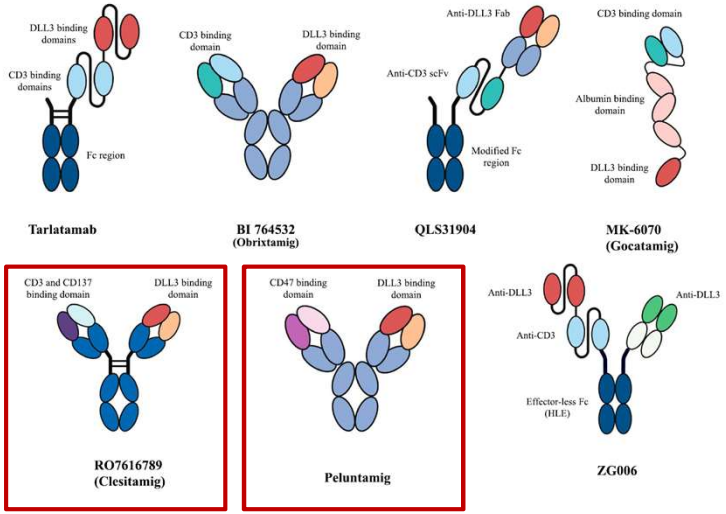
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Meador C., 2025 ASCO Proceedings

DLL3- targeted engagers in development

DLL3-targeting bispecifics/trispecifics in clinical development

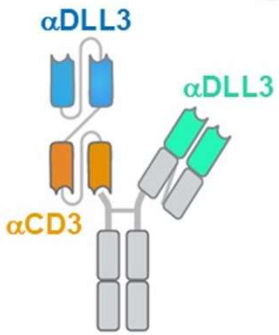
Project	Description	Company	Status
Imdelltra	DLL3 TCE	Amgen	AA for 2nd-line SCLC based on 40% ORR in Dellphi-301
Alveltamig (ZG006)	DLL3 x DLL3 TCE	Suzhou Zelgen	China ph2 data in 3rd-line SCLC presented at ASCO 2025: ORR 63% & 58% with 10mg Q2W & 30mg Q2W respectively
Obrixtamig (BI 764532)	DLL3 TCE	Boehringer Ingelheim	Ph2 Dareon-5 in 3rd-line SCLC & 2nd-line neuroendocrine tumours, completes Oct 2026
Gocatamig (MK-6070)	DLL3 TCE*	Merck & Co (via Harpoon)	Ph1/2 data in 2nd-line solid tumours at ESMO 2023: ORR 35% across tumour types; ifinatamab-dxd combo trials ongoing
Peluntamig (PT217)	DLL3 x CD47 MAb	Phanes Therapeutics	Ph1/2 Skybridge in 2nd-line SCLC & NETs, completes Dec 2027
RO7616789	DLL3 x 4-1BB TCE	Roche	Ph1 in 2nd-line SCLC & NETs, completed Mar 2025
QLS31904	DLL3 TCE	Qilu	China ph1 in 2nd-line solid tumours, completed Sep 2024, status unknown



https://www.oncologypipeline.com/apexonco/dll3-goes-trispecific

Trispecific T-Cell engager (ZG006): DLL3x2 /CD3

- Randomized Phase 2 study – dose optimization, 10mg q2W and 30mg q2 W
- ES SCLC with progression after platinum-based CT
- Primary EP: ORR



	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)

Toxicities:

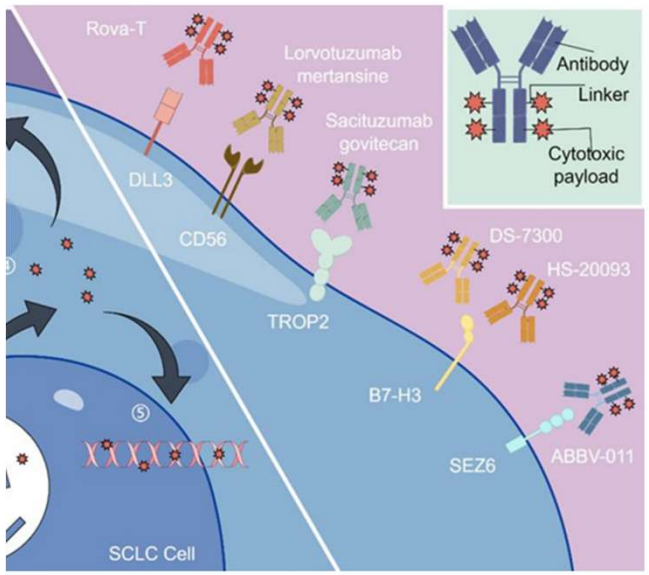
Priming dose of 1mg used
CRS : 41.7 %(10mg), 75% (30mg)
Most were G1-2

Summary

Very active agent
ORR: 62.5 and 58.3%
CRS > 40%, most G1/2
Final dose pending

Ai X et al., 2025 ASCO Proceedings, 10.1200/JCO.2025.43.16_suppl.8007; NCT06283719

ADCs in Clinical Development for SCLC



B7-H3

- B7 family of immune checkpoint proteins
- inhibits T-cell activation and promotes immune evasion
- **SCLC expression ~65%**

SEZ6 *(Seizure Related 6 Homolog)*

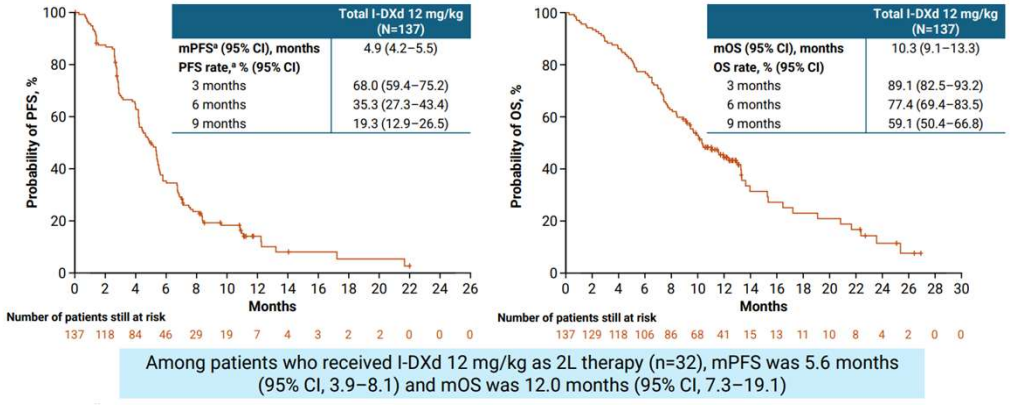
- TM protein on surface of selected neuronal lineage cells
- involved in dendrite formation and regulates neuronal signal transmission
- **Highly expressed in SCLC**
- Molecules: ABBV-011, ABBV-706

TROP-2 *(trophoblast cell-surface antigen 2)*

- TM glycoprotein involved in cell signaling, proliferation, and migration
- **SCLC expression is low**
- Molecules: SHR-A1921, Datopotamab, Sacituzumab

Ifinatamab Deruxtecan (B7-H3 ADC): IDeate-Lung01

- Phase 2 randomized (dose-optimization) study relapsed SCLC
  - 8mg/kg vs 12mg/kg → dose expansion 12mg/kg
  - N = 137 (12mg/kg)
- ES SCLC with progression after platinum-based CT
  - Asymptomatic CNS disease
- Primary EP: ORR by BICR



Among patients who received I-DXd 12 mg/kg as 2L therapy (n=32), mPFS was 5.6 months (95% CI, 3.9–8.1) and mOS was 12.0 months (95% CI, 7.3–19.1)

Ahn MJ et al., WCLC 2025 proceedings, Rudin CM et al., JCO 2025 Phase 3 IDeate-Lung02 trial (NCT06203210)

Results:
ORR 48.2%, mDOR 5.3 mos
mPFS = 4.9 mos
mOS = 10.3 mos
IC responses are observed

Toxicities:
- 36.5% ≥G3 TRAEs
  - Hematologic, GI were MC
- Adjudicated ILD/pneumonitis: 12.4% (2 G5)

SUMMARY
Very promising efficacy in relapsed ES-SCLC

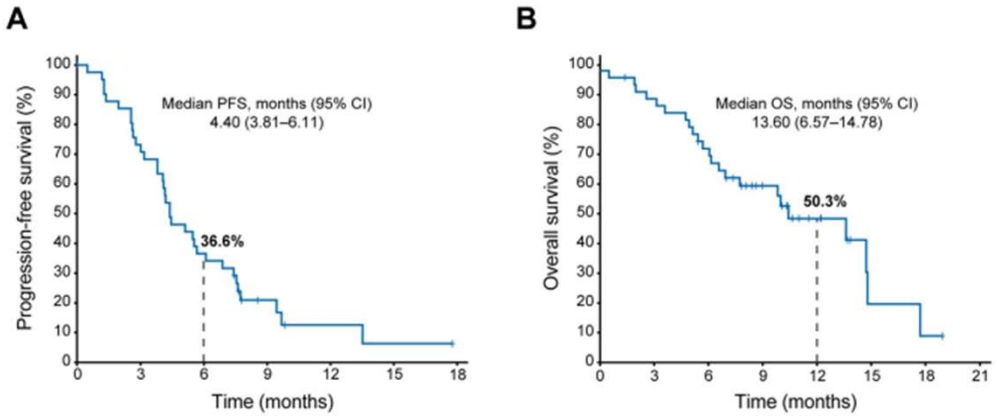
Trials ongoing:
- IDeate-Lung02: RP3 of I-DXd vs TPC
- IDeate-Lung03 (Phase 1b/2) in maintenance

B7-H3 ADCs in SCLC

Drug	Payload	Phase	Dose q3W	N*	ORR	mOS (mo)	mPFS	Notable Toxicities (G3+)	IC activity?
IDXd	Topo-I	2	12 mg/Kg	137	48.2%	11.8	5.5	GI, heme. AESI: pneumonitis	Y
YL201	Topo-I	1/1b	1.6-2.8 mg/kg	72	63.9%		6.3	heme	Y
HS-20093	Topo-I	1	8mg/kg	31	61.3%	9.8	5.9	Cytopenias	
			10mg/kg	22	50.0%	NR	7.3		
MHB088C	SuperTopoi	1/2	1.6mg/kg q2W → 3.0mg/kg	31	61.3%			heme	

Sacituzumab Govitecan (Trop2-ADC): TROPICS-3

- Phase 2 basket study including 43 with relapsed SCLC
- ES SCLC with progression after platinum-based CT
  - No CNS disease
- Primary EP: ORR



Results:
ORR 41.9% (N= 43)
mPFS = 4.4 mos
mOS = 13.6 mos

Toxicities:
- 74.4% had ≥G3 TRAEs
  - Neutropenia and diarrhea
- SAE: 37.2%

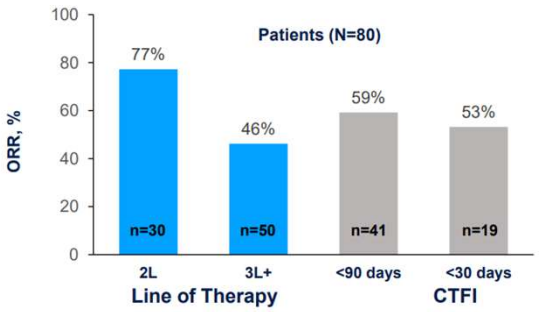
SUMMARY
Promising activity in relapsed ES-SCLC

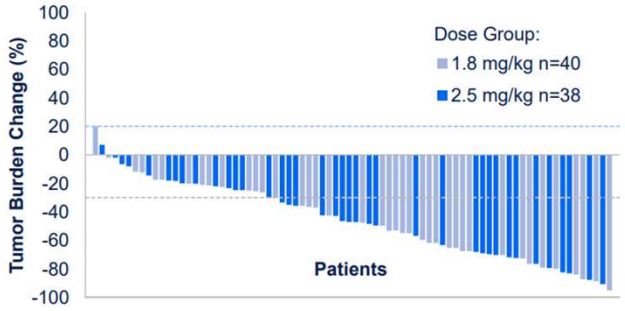
Trials to watch:
- EVOKE-SCLC-04: Ph 3, SG vs SOC in relapsed ES-SCLC
- PESGA: Ph2, 1st-line ES-SCLC (added to maintenance)

Dowlati, et al., J Thorac Oncol. 2025;20:799-808

ABBV-706 (SEZ6-ADC): Phase 1 and dose optimization

- Phase 1 study and dose optimization
  - 1.8 and 2.5mg/kg doses assessed
  - Topo1 payload
- ES SCLC with progression after platinum-based CT
  - Asymptomatic CNS disease
- Primary EPs: safety, tolerability, PK, RP2D





Results:
ORR = 46% (N= 80)
mPFS = 5.7 mos
mDOR = 5.6 mos

Toxicities:
- 63% had ≥G3 TRAEs
  - hematological
- ILD adjudicated in 7 patients, 4 with ≥ G3

SUMMARY
Promising activity in relapsed ES-SCLC, 1.8mg/kg to move forward

Byers et al., WCLC 2025 proceedings

Conclusions

- In 2025 treatment options for SCLC have improved at all stages
- LS SCLC – patients who undergo definitive chemoradiotherapy should receive up to 2 years of consolidation durvalumab
- ES SCLC –adding maintenance lurbinectedin to atezolizumab after at least SD after chemo-PD-L1 induction results in improvement in OS
  - Consider for patients who did not present with brain metastases and who have a good PS after chemoIO
- Tarlatamab is the SOC for patients with relapsed SCLC after platinum-based therapy
  - though, not widely available yet due to monitoring requirements
- Many new agents are in the pipeline including additional DLL3-targeted T-cell engagers, ADC, and targeted agents (not discussed, PARPi, antiangiogetic agents, epigenetic modifier)

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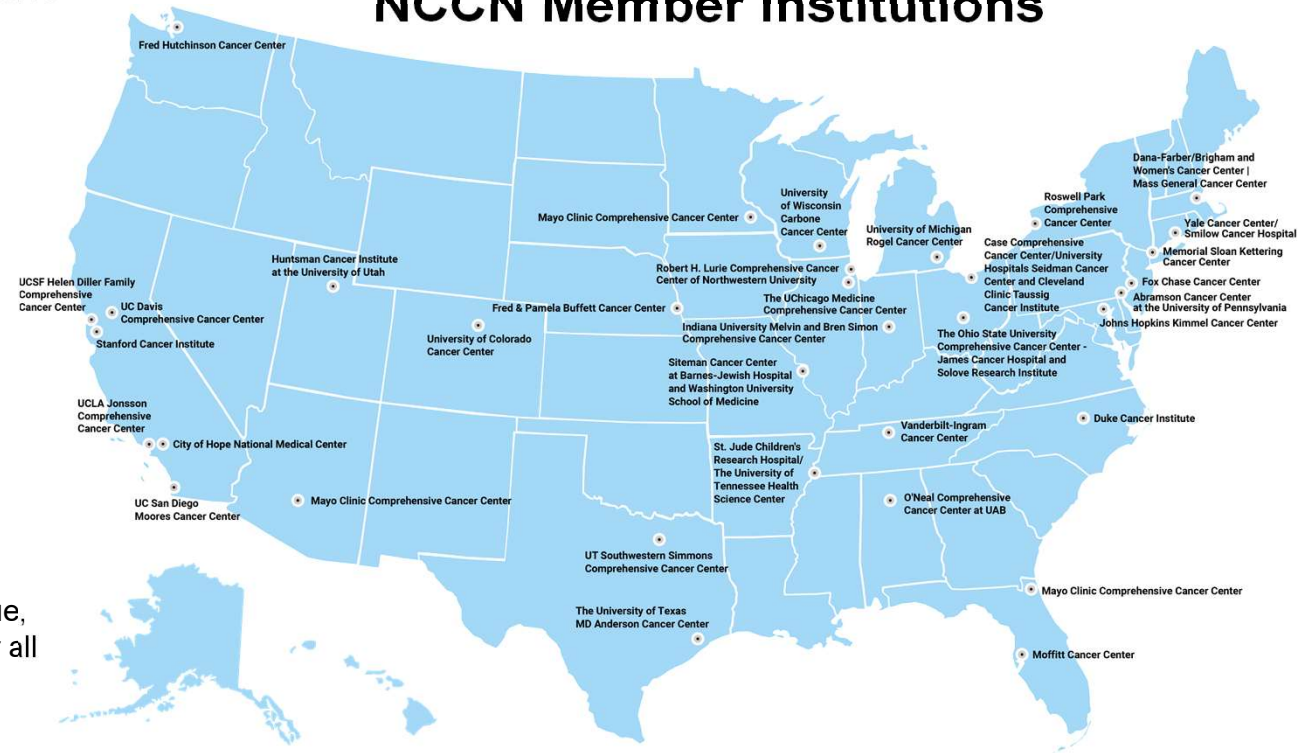

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