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Updates in Treatment of Patients with SCLC

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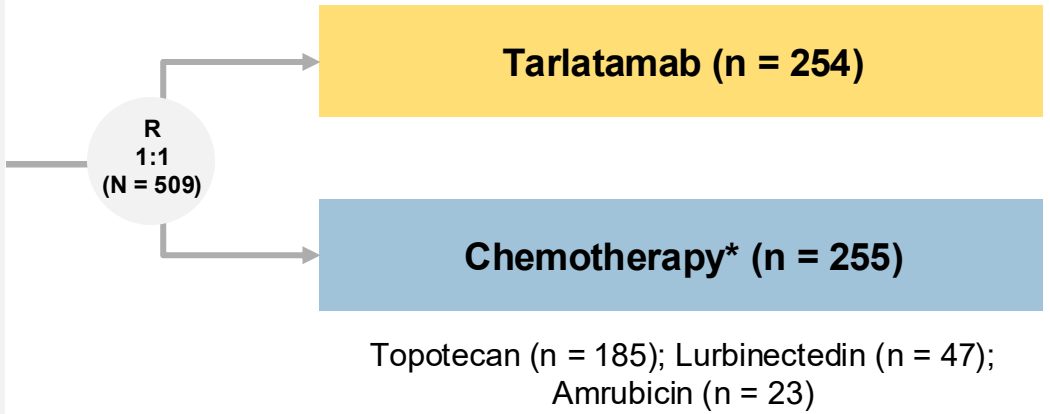
Phase 3 DeLLphi-304 study (NCT05740566)

Key inclusion criteria

- Histologically or cytologically confirmed SCLC
- Progression after 1L platinum-based chemotherapy +/- anti-PD-(L)1
- ECOG PS 0 or 1
- Asymptomatic, treated or untreated brain metastases

Randomization stratified by

- Prior anti-PD-(L)1 exposure (yes/no)
- Chemotherapy-free interval (< 90 days vs ≥ 90 to < 180 days vs ≥ 180 days)
- Presence of (previous/current) brain metastases (yes/no)
- Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)



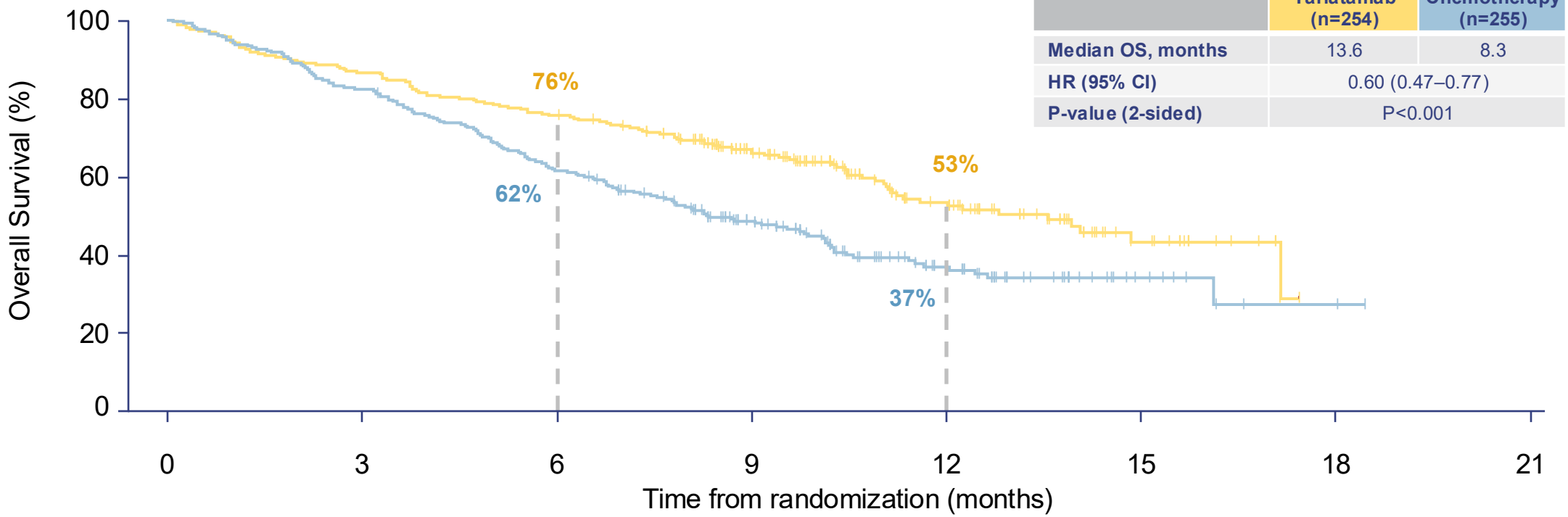
Primary Endpoint: Overall survival
Key Secondary Endpoints: Progression-free survival, patient-reported outcomes
Other Secondary Endpoints: Objective response, disease control, duration of response, safety

*Topotecan was used in all countries except Japan, lurbinectedin in Australia, Canada, Republic of Korea, Singapore and the United States, and amrubicin in Japan.
1L, first-line; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-(L)1, programmed death (ligand)-1; R, randomization; SCLC, small cell lung cancer.

ClinicalTrials.gov, NCT05740566 (accessed July 2025);
Rudin C, et al. ASCO 2025; abstract LBA8008; Mountzios G, et al. N Engl J Med 2025; Online ahead of print.

DeLLphi-304

Primary endpoint: overall survival



	Tarlatamab (n=254)	Chemotherapy (n=255)
Median OS, months	13.6	8.3
HR (95% CI)	0.60 (0.47–0.77)	
P-value (2-sided)	P<0.001	

Number of patients at risk:

Tarlatamab	254	220	192	131	60	17	0
Chemotherapy	255	210	156	97	42	9	2	0

Tarlatamab demonstrated superior OS vs chemotherapy

Data cut-off: 29 January 2025; median follow-up: 11.2 months for tarlatamab group and 11.7 months for the chemotherapy group.

Rudin C, et al. ASCO 2025; abstract LBA8008; Mountzios G, et al. N Engl J Med 2025; Online ahead of print.

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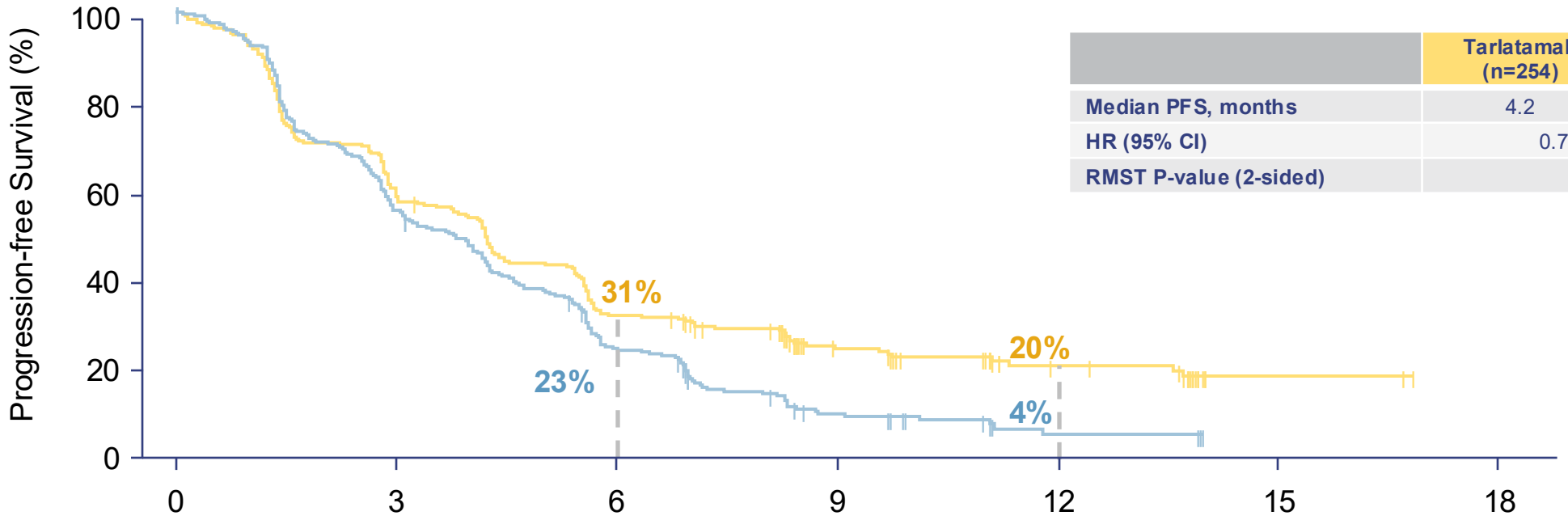
Progression-free survival



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

Number of patients at risk:

Tarlatamab	254	147	78	37	18	2	0
Chemotherapy	255	137	56	15	3	0	

Tarlatamab demonstrated superior PFS vs chemotherapy

Rudin C, et al. ASCO 2025; abstract LBA8008; Mountzios G, et al. N Engl J Med 2025; Online ahead of print.

DeLLphi-304

Safety summary

	Tarlatamab (n = 252)*	Chemotherapy (n = 244)*
Median duration of treatment, months, (range)	4.2 (< 1–17)	2.5 (< 1–15)
All grade, TEAEs, n (%)	249 (99)	243 (100)
All grade, TRAEs n (%)	235 (93)	223 (91)
Grade ≥ 3 TRAEs, n (%)	67 (27)	152 (62)
Serious TRAEs, n (%)	70 (28)	75 (31)
TRAEs leading to dose interruption and/or dose reduction, n (%)	48 (19)	134 (55)
TRAEs leading to discontinuation, n (%)	7 (3)	15 (6)
Treatment-related grade 5 events†, n (%)	1 (0.4)	4 (2)

Tarlatamab had a favorable safety profile vs chemotherapy

*Safety analysis set (all patients who received at least one dose of study treatment). †The single grade 5 TRAE observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension. Grade 5 TRAEs observed with chemotherapy were attributed to general physical health deterioration (n = 1), pneumonia (n = 1), respiratory tract infection (n = 1), and tumor lysis syndrome (n = 1). ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Rudin C, et al. ASCO 2025; abstract LBA8008; Mountzios G, et al. N Engl J Med 2025; Online ahead of print.

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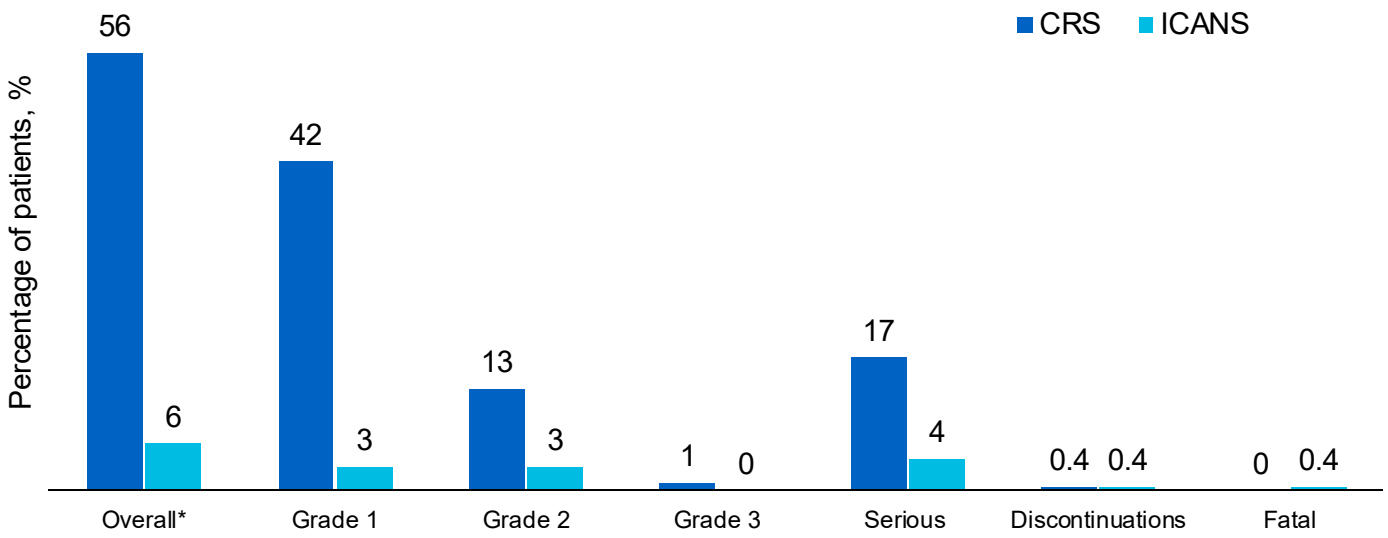
CRS and ICANS

Treatment-emergent CRS and ICANS with tarlatamab



CRS with first two infusions

Tarlatamab (N = 252)	Minimum required monitoring duration	
	6 - 8 Hours (n = 43)	48 Hours (n = 209)
Treatment emergent CRS, n (%)*	16 (37)	125 (60)
Grade 1	12 (28)	94 (45)
Grade 2	4 (9)	28 (13)
Grade 3	0 (0)	3 (1)
Serious adverse events	3 (7)	39 (19)
Leading to discontinuation of IP	0 (0)	1 (0.5)
Median time to intervention from last tarlatamab dose (hours)	17	27

CRS and ICANS events were consistent with the established safety profile of tarlatamab

*Grade 4 CRS or ICANS events were not observed. A single grade 5 treatment-related adverse event observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension. CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IP, investigational product.

Rudin C, et al. ASCO 2025; abstract LBA8008; Mountzios G, et al. N Engl J Med 2025; Online ahead of print.

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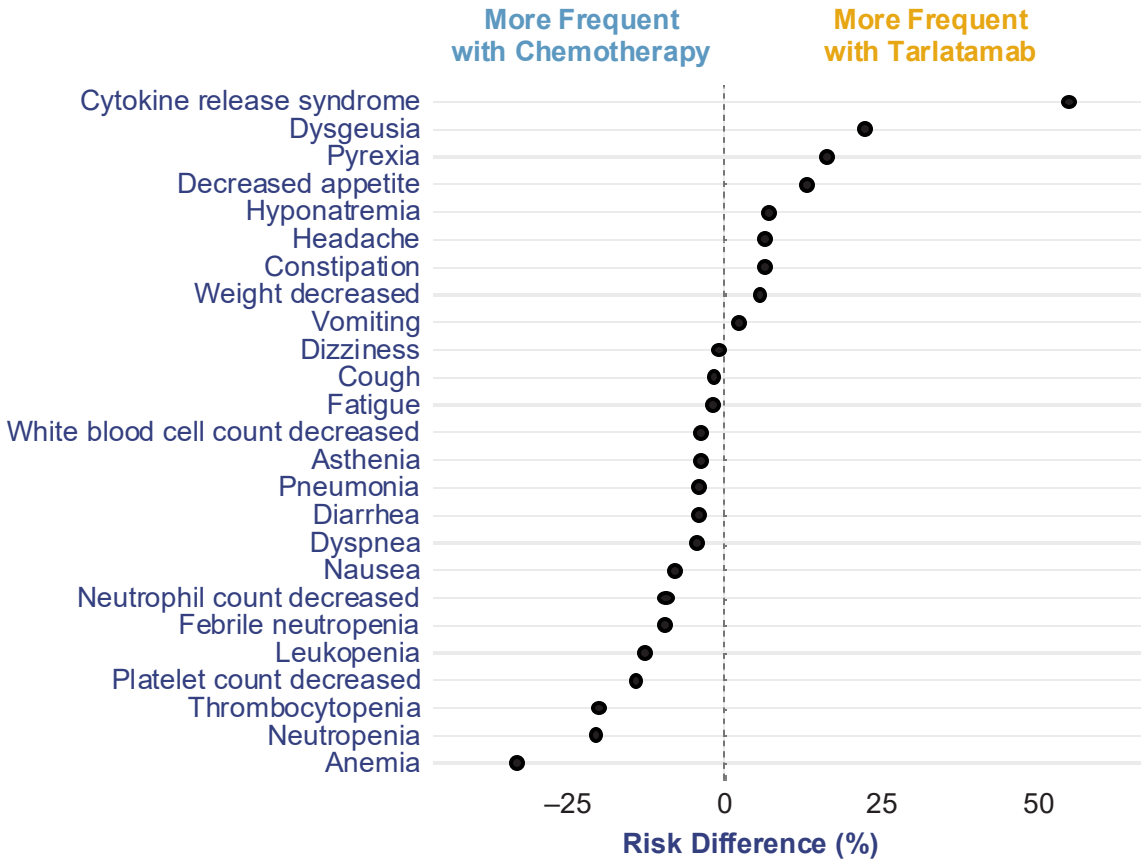
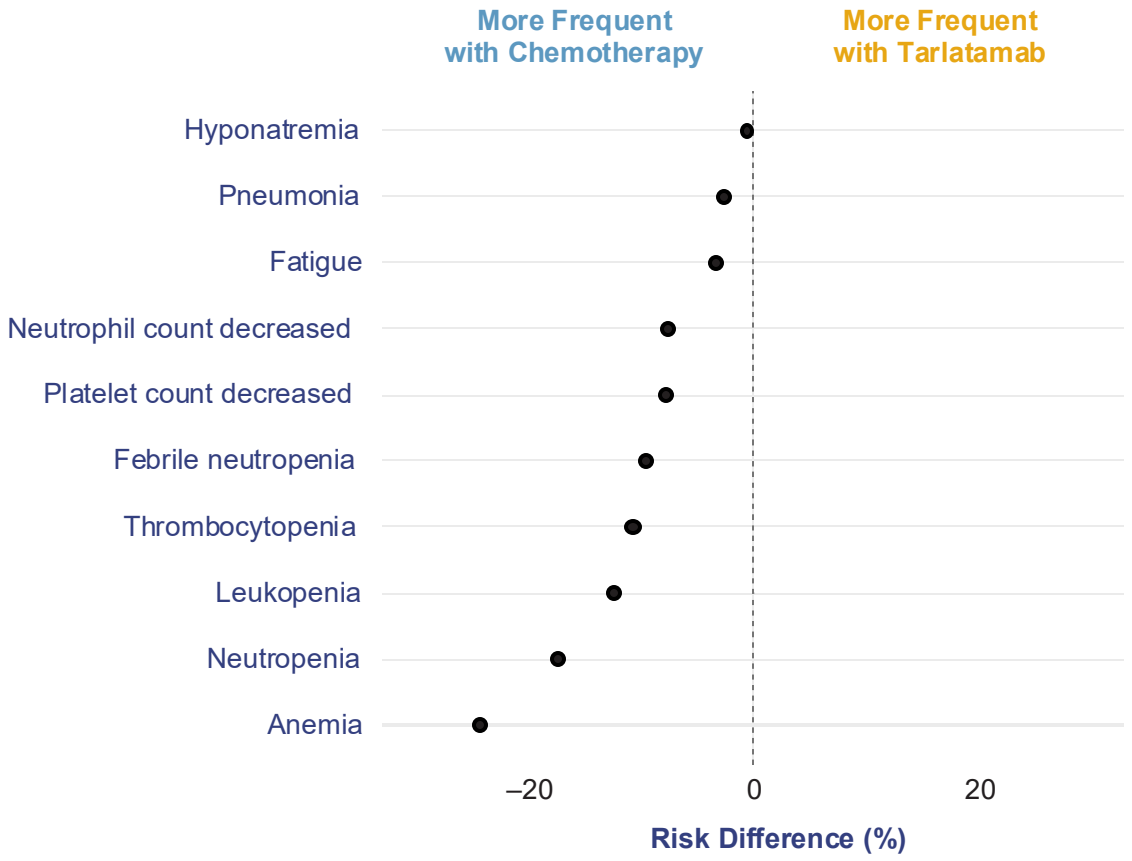
Incidence of high-grade AEs

Treatment-emergent Adverse Events in > 10% of Patients



Grade ≥ 3 Treatment-emergent Adverse Events in > 5% of Patients



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

Rudin C, et al. ASCO 2025; abstract LBA8008; Mountzios G, et al. N Engl J Med 2025; Online ahead of print.

Real-World Implementation Tarlatamab for Patients With ES-SCLC and Other High-Grade Neuroendocrine Neoplasms

Grade	CRS, No. (%)	ICANS, No. (%)
1	14 (28.6)	8 (16.3)
2	7 (14.3)	6 (12.2)
3	2 (4.1)	3 (6.1)
4	0 (0)	0 (0)

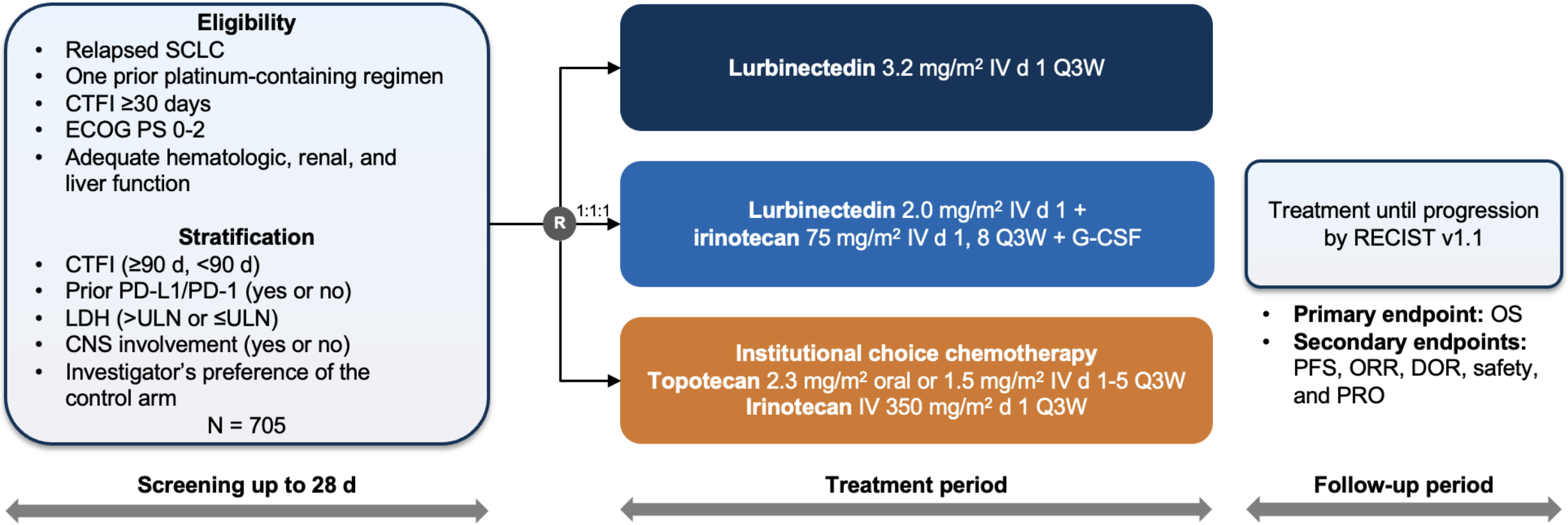
- Median PFS was 3.7 months (95% CI, 2.7 to 5.2)
- Median OS was 7.1 months (95% CI, 4.9 to 9.3)

- 49 patients with SCLC were treated on the outpatient protocol.
- Ten patients required admission from the ICC during the first two cycles because of CRS/ICANS (CRS: 3, ICANS: 4, both: 2, uncontrolled hypertension: 1). CRS/ICANS was observed in 25 patients, two (4.1%) experienced grade 3 CRS, and three (6.1%) experienced grade 3 ICANS.

Carlisle JW, O'Reilly K, Canaslan K, Ji X, Switchenko JM, Steuer CE, Ramalingam SS, Leal T. JCO Oncol Practice 2026

LAGOON Phase 3 trial

The trial did not meet its primary endpoint of OS evaluating lurbinectedin as monotherapy or in combination with irinotecan compared to investigators' choice of topotecan or irinotecan.



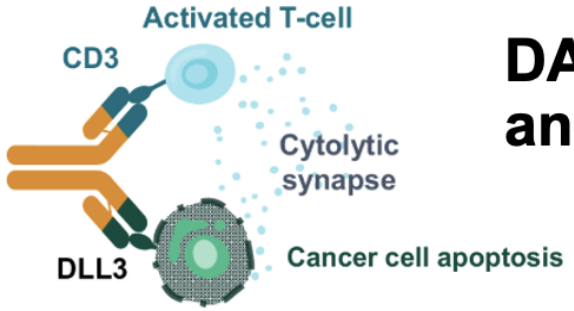
Besse B et al. ASCO 2023. Abstract TPS8613.

1L chemoimmunotherapy for ES-SCLC

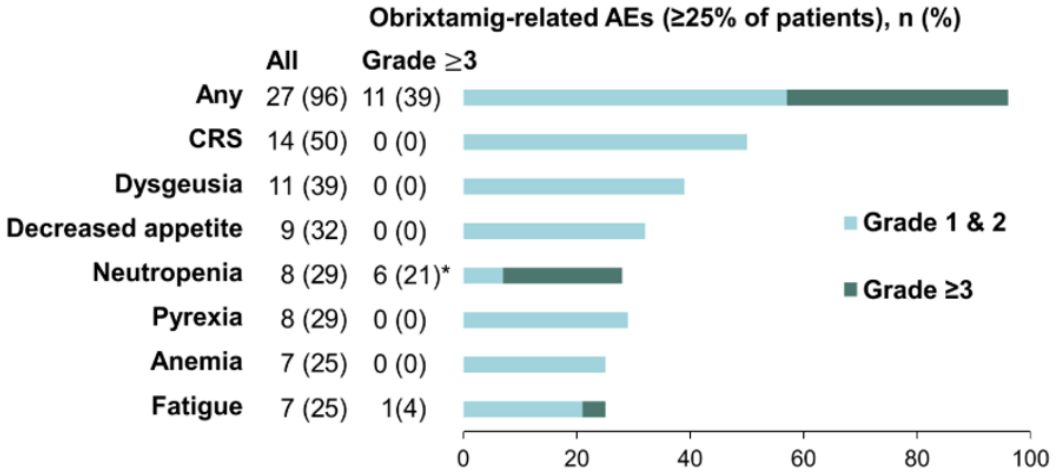
Study	Agent	Sample Size	mPFS / HR	mOS / HR	1y OS Rate
IMpower 133 *Liu, JCO 2021*	Atezolizumab	403 pts	5.2m HR 0.77	12.3m HR 0.76	52%
CASPIAN *Paz-Ares, ESMO Open 2022*	Durvalumab	805 pts	5.1m HR 0.80	12.9m HR 0.71	53%
EA5161 (phase II) *Leal, ASCO 2020*	Nivolumab	160 pts	5.5m HR 0.68	11.3m HR 0.73	50%
KEYNOTE 604 *Rudin, WCLC 2022*	Pembrolizumab	453 pts	4.8m HR 0.70	10.8m HR 0.76	45%
ASTRUM 005 *Cheng, JAMA 2022*	Serplulimab	585 pts	5.7m HR 0.48	15.4m HR 0.63	61%
CAPSTONE-1 *Wang, Lancet Oncol 2022*	Adebrelimab	462 pts	5.8m HR 0.67	15.3m HR 0.72	63%
RATIONALE-312 *Cheng, WCLC 2023*	Tislelizumab	457 pts	4.8m HR 0.63	15.5m HR 0.75	63%

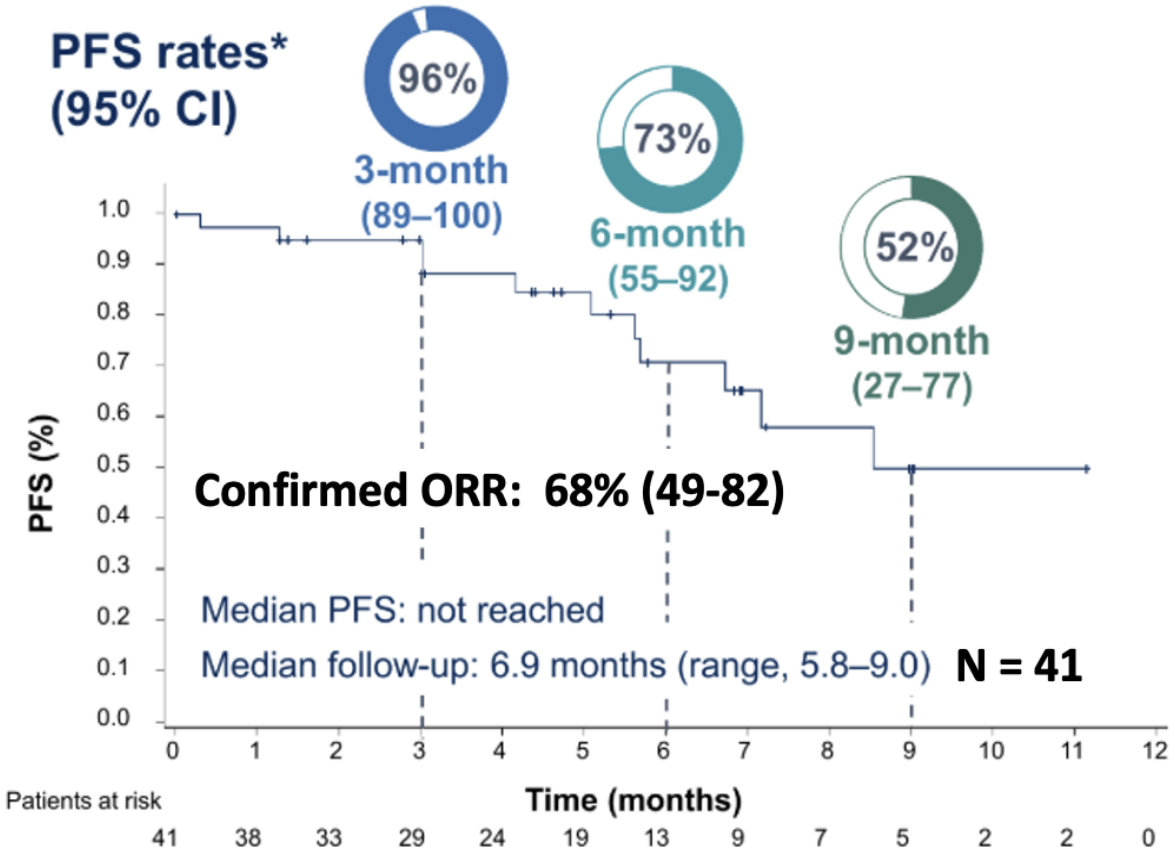
Canaslan K, Leal T. Maxing Out with Chemoimmunotherapy in ES-SCLC. Chinese Clinical Oncology, 2025.

DAREON-8: Phase I obrixtamig + chemotherapy



DAREON-8: Phase I trial of 1st line obrixtamig + chemotherapy and atezolizumab in ES-SCLC





Peters et al. ESMO 2025.

DAREON-Lung-1

- N≈670 patients with ES-SCLC
- Patients must have completed one cycle of platinum + etoposide ± anti-PD-1 / anti-PD-L1 before randomization
- Archival FFPE tumor tissue is required for determination of DLL3 expression status

Crossover to investigational arm not permitted

R 1:1

Induction phase Cycles 1–3	Maintenance phase Cycle 4 onwards§
Obrixtamig: step-up dosing followed by target dose (60 mg) **+ atezolizumab + carboplatin + etoposide**	**Obrixtamig + atezolizumab**
Atezolizumab + carboplatin + etoposide	**Atezolizumab**

Stratification factors:

- Brain metastases (yes/no)
- DLL3 expression status (high/low)
- ECOG PS (0/1)

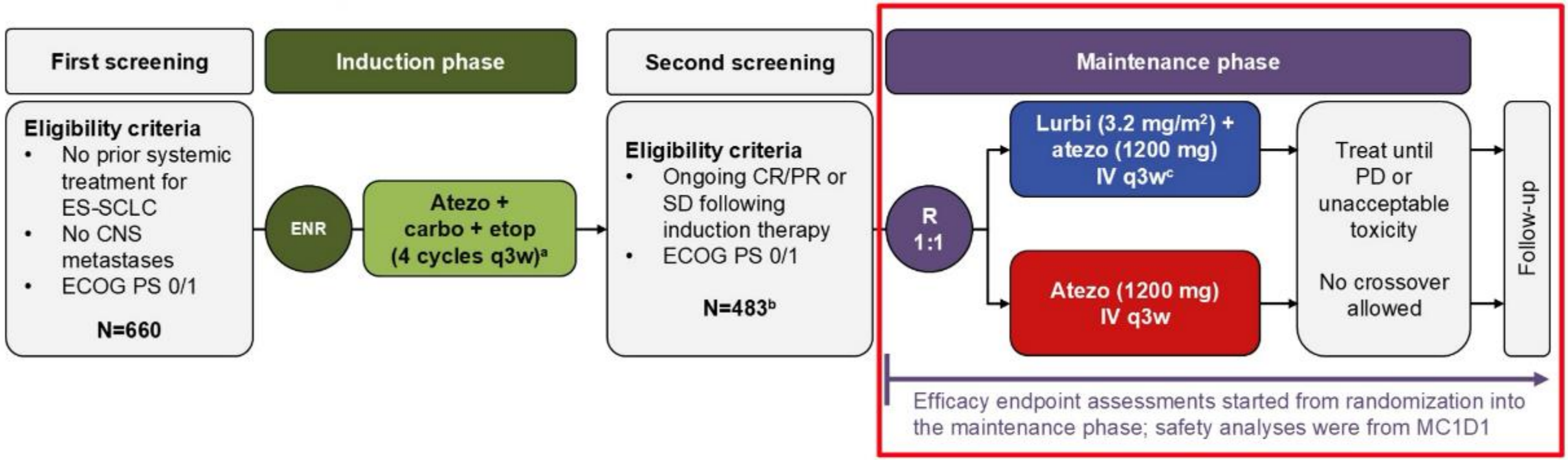
Primary endpoint in dual populations:

- OS in the overall population
- OS in the DLL3^{high} population

Secondary endpoints:
PFS, ORR (RECIST v1.1; investigator-assessed), patient-reported dyspnea (EORTC QLQ-LC13), other PROs, safety

Further endpoints: DoR, PK, biomarkers

IMforte Study Design



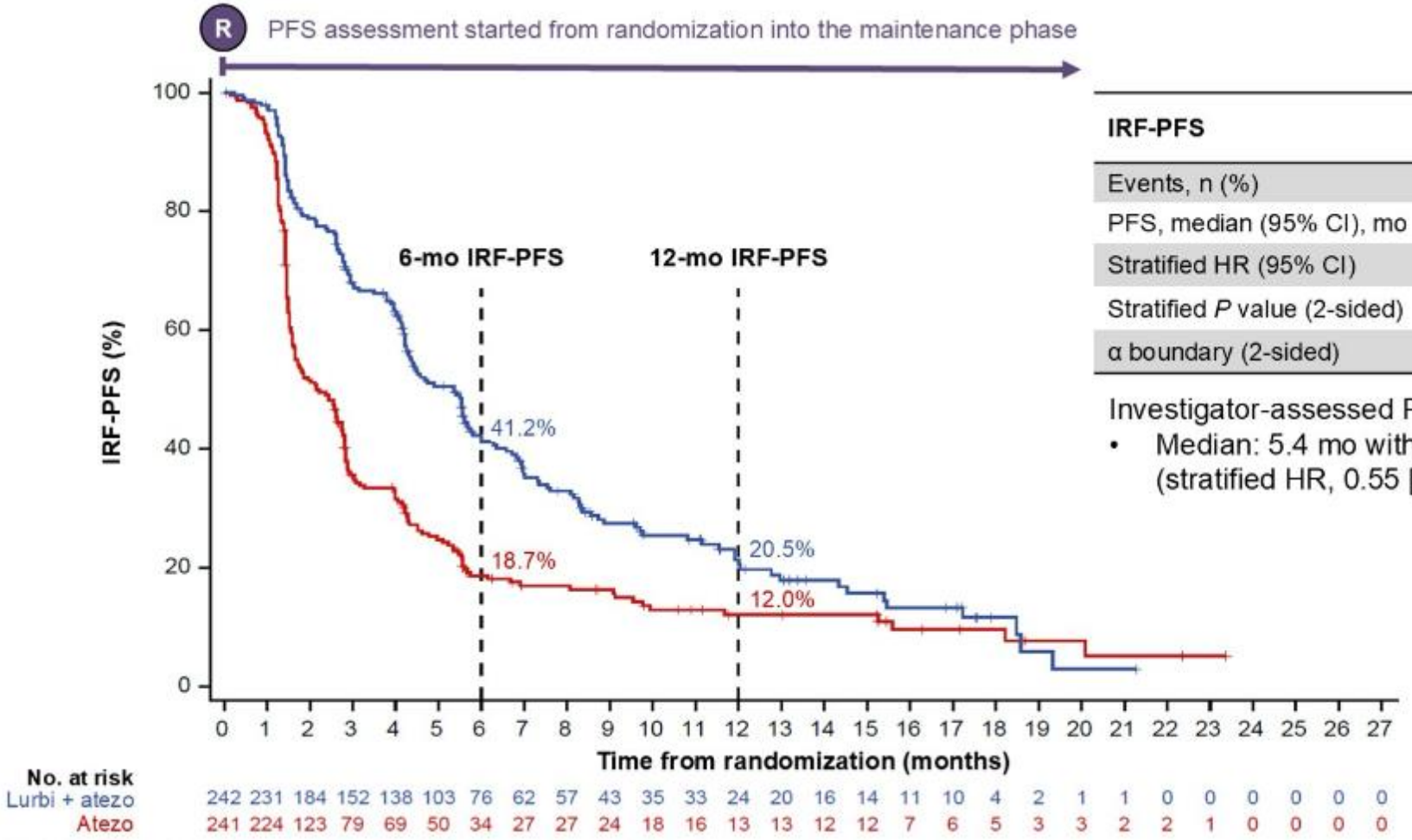
Stratification factors for randomization
- ECOG PS (0/1)
- LDH (≤ULN/>ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

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

IMforte: PFS

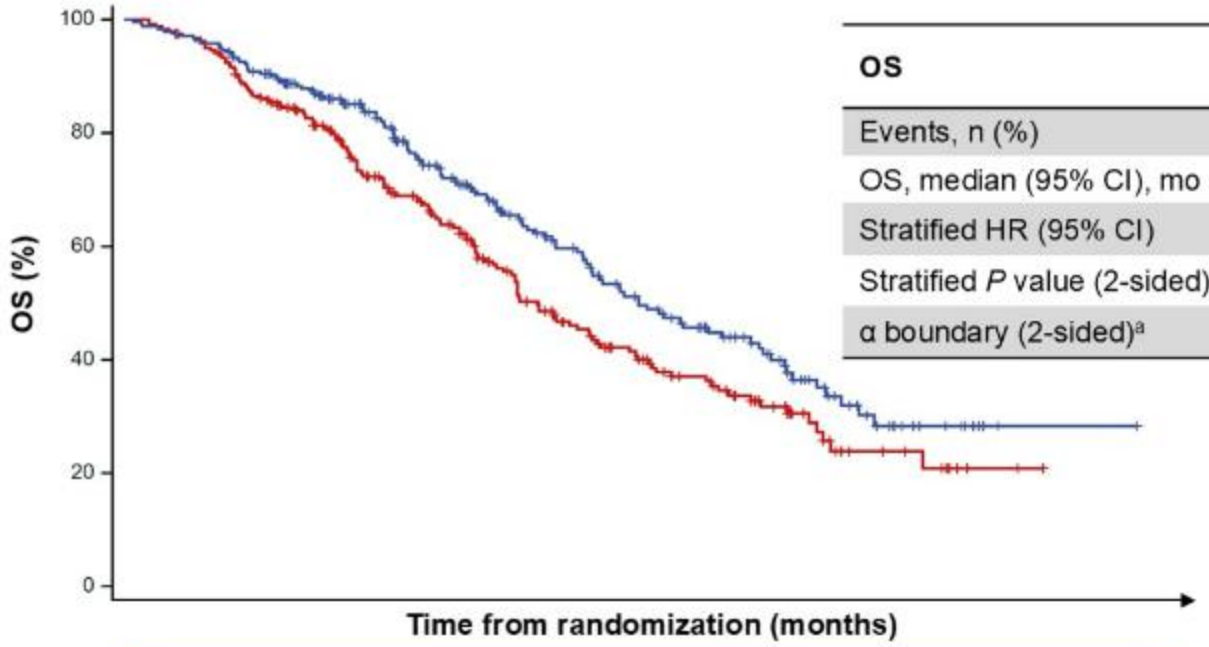


IRF-PFS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	174 (71.9)	202 (83.8)
PFS, median (95% CI), mo	5.4 (4.2, 5.8)	2.1 (1.6, 2.7)
Stratified HR (95% CI)	**0.54 (0.43, 0.67)**	
Stratified *P* value (2-sided)	<0.0001	
α boundary (2-sided)	0.001	

Investigator-assessed PFS was consistent with IRF-PFS

- Median: 5.4 mo with lurbi + atezo and 2.7 mo with atezo (stratified HR, 0.55 [95% CI: 0.45, 0.68])

IMforte: OS



OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

Induction treatment
Atezo + carbo + etop

3.2 months[a]

R

Maintenance treatment
Lurbi + atezo
Median OS from randomization: 13.2 months

Maintenance treatment
Atezo
Median OS from randomization: 10.6 months

IMforte results do not include time on induction treatment

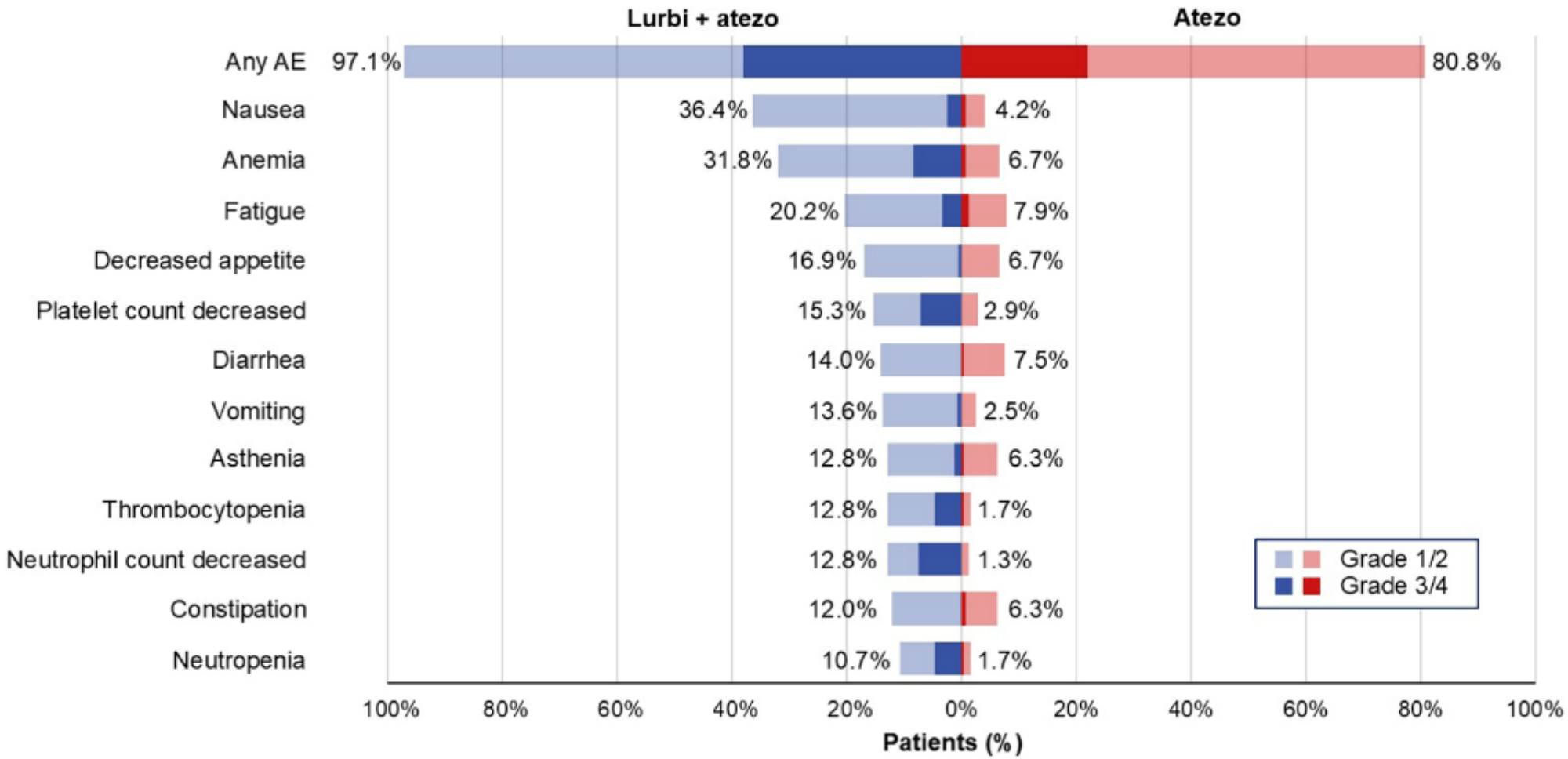
Phase 3 IMforte: Safety Summary—Maintenance Phase

Patients with ≥1 AE, n (%)	Lurbi + atezo (n=242)	Atezo (n=240)
All-cause AEs	235 (97.1)	194 (80.8)
Grade 3/4 AEs	92 (38.0)	53 (22.1)
Treatment-related Grade 3/4 AEs	62 (25.6)	14.0 (5.8)
Grade 5 AEs	12 (5.0)	6 (2.5)
Treatment-related Grade 5 AEs	2 (0.8)[a]	1 (0.4)[b]
Serious AEs	75 (31.0)	41 (17.1)
AEs leading to discontinuation of any study drug	15 (6.2)	8 (3.3)
AEs leading to dose interruption/ modification of any study drug[c]	92 (38.0)	33 (13.8)

Patients with ≥1 AE, n (%)	Lurbi + atezo (n=242)	Atezo (n=240)
Lurbinectedin AESI[d]	93 (38.4)	62 (25.8)
Grade 5 AESI	7 (2.9)	4 (1.7)
Atezolizumab AESI[d]	76 (31.4)	54 (22.5)
Grade 5 AESI	0	0
Atezolizumab AESI requiring corticosteroids	40 (16.5)	18 (7.5)
Median treatment duration, mo	4.1 (lurbi)/ 4.2 (atezo)	2.1
Median number of doses received	6.5 (lurbi)/ 7.0 (atezo)	4.0

Clinical cutoff: July 29, 2024.
Median follow up: 15.0 mo.
Paz-Ares L, et al. *Lancet*. 2025;405:2129-2143.
Paz-Ares L, et al. ASCO 2025. Abstract 8006.

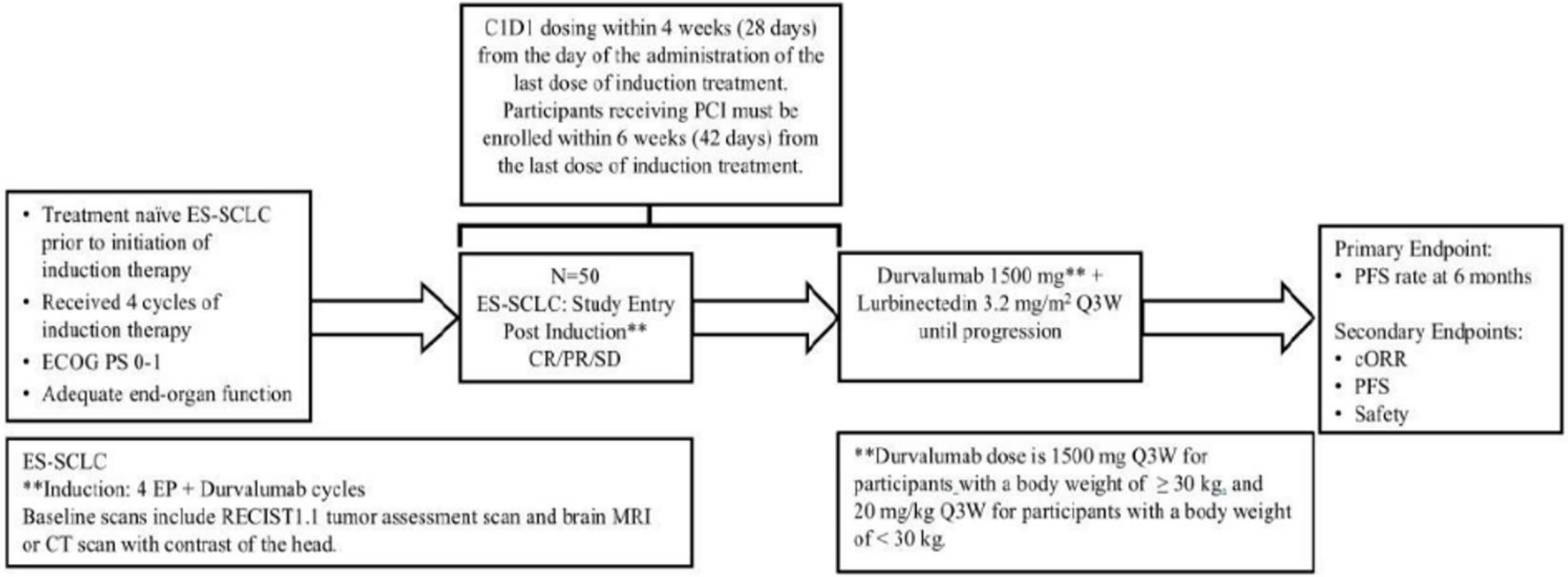
Safety: All-Cause AEs With Incidence ≥10%



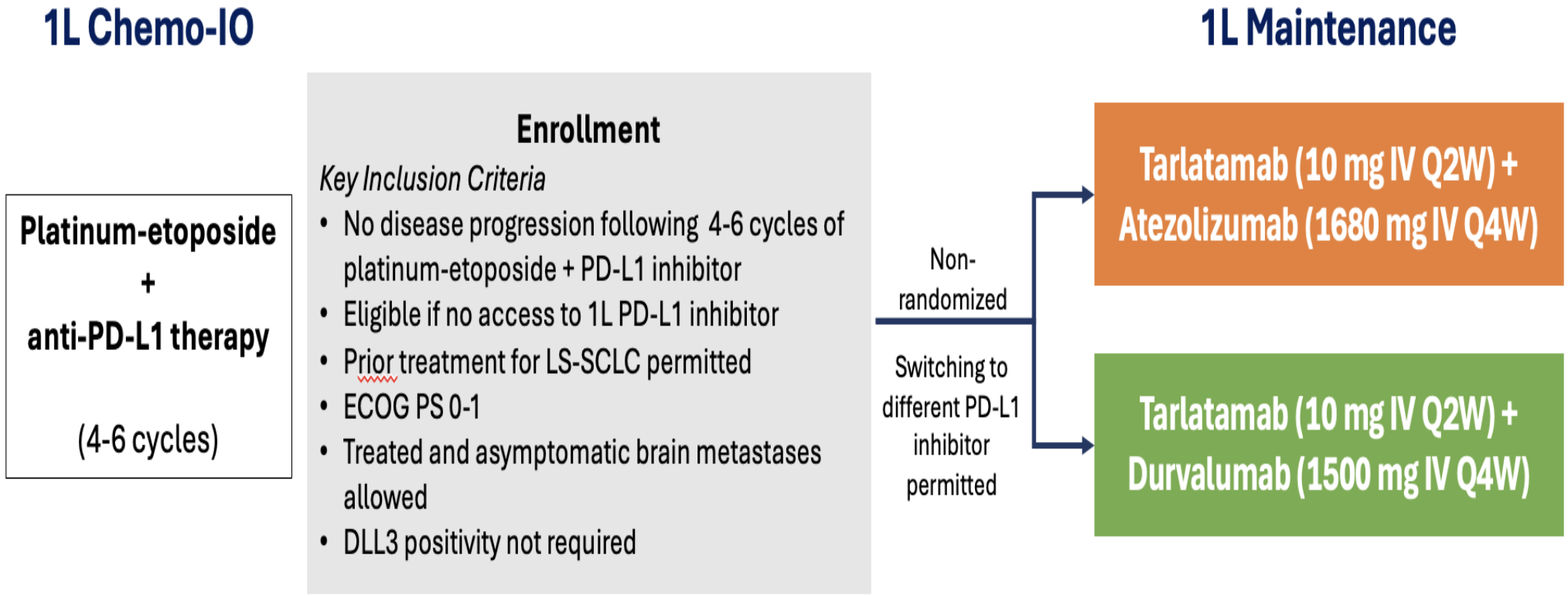
Febrile neutropenia
Lurbi + atezo: 1.7%[a]
Atezo: 0%

Grade 3/4 infections and infestations[b]
Lurbi + atezo: 6.6%
Atezo: 5.0%

JZP7-702-213: Phase 2 Study of Lurbinectedin + Durvalumab in 1L Maintenance



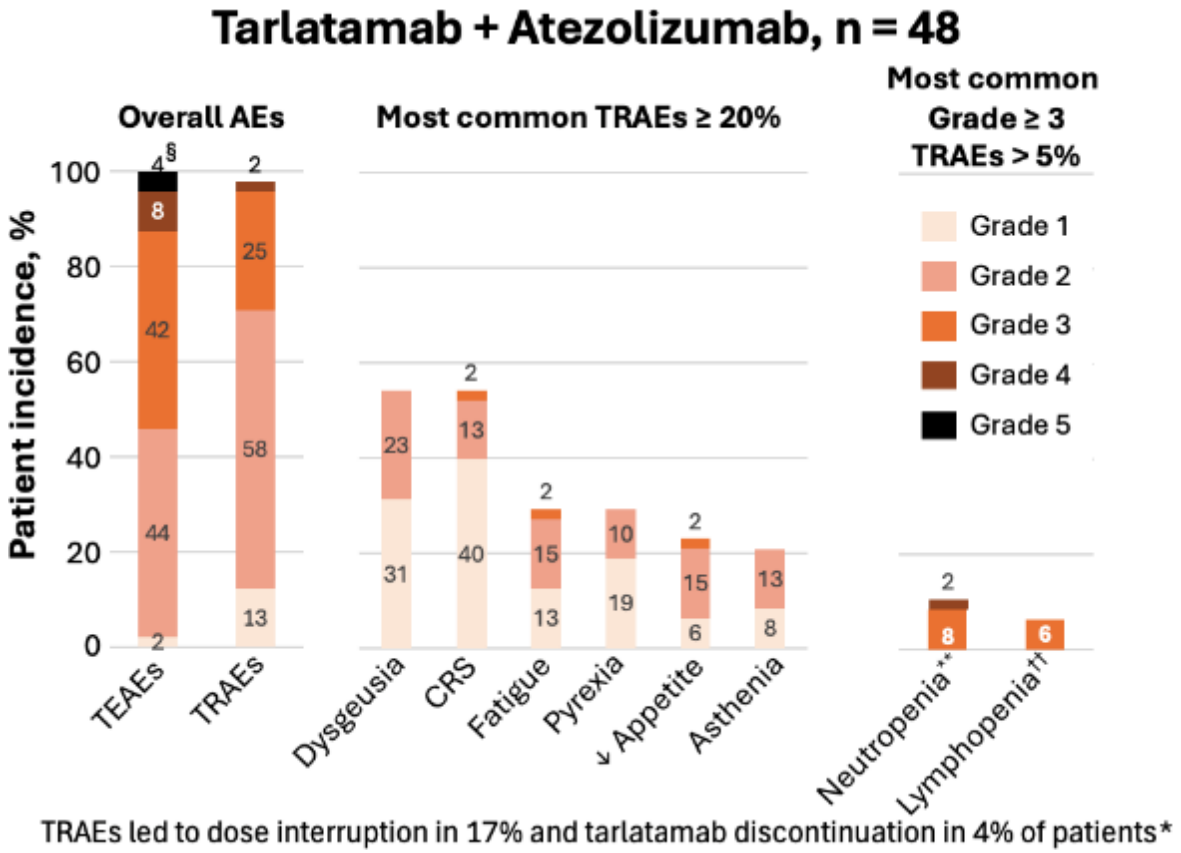
Tarlatamab with a PD-L1 Inhibitor as First-Line Maintenance after Chemo-immunotherapy for ES-SCLC: DeLLphi-303 Phase 1b Study



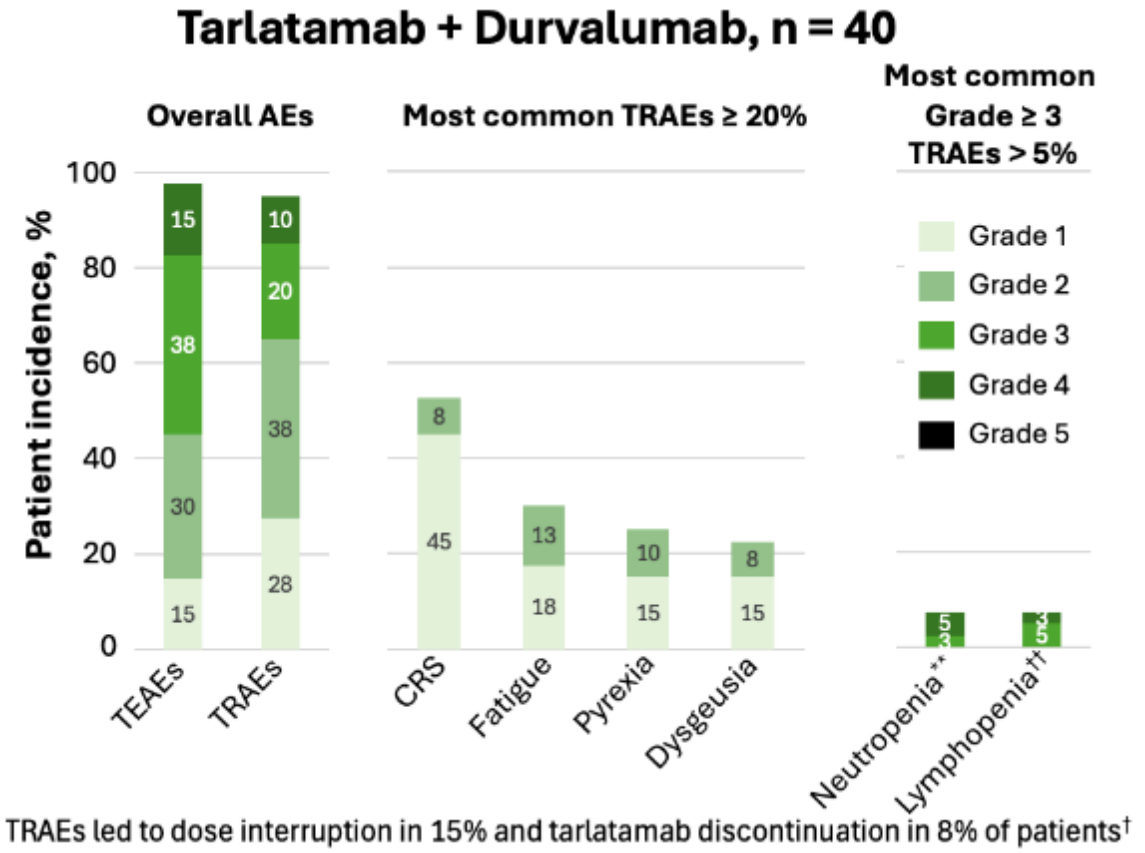
- Must initiate C1D1 of maintenance phase within 8 weeks of the start of the last cycle of 1L chemo-immunotherapy
- Median follow-up time (N = 88): 10.0 months (range: 1.4–20.4)

Lau S et al. WCLC 2024

DeLLphi-303: Safety



TRAEs led to dose interruption in 17% and tarlatamab discontinuation in 4% of patients*

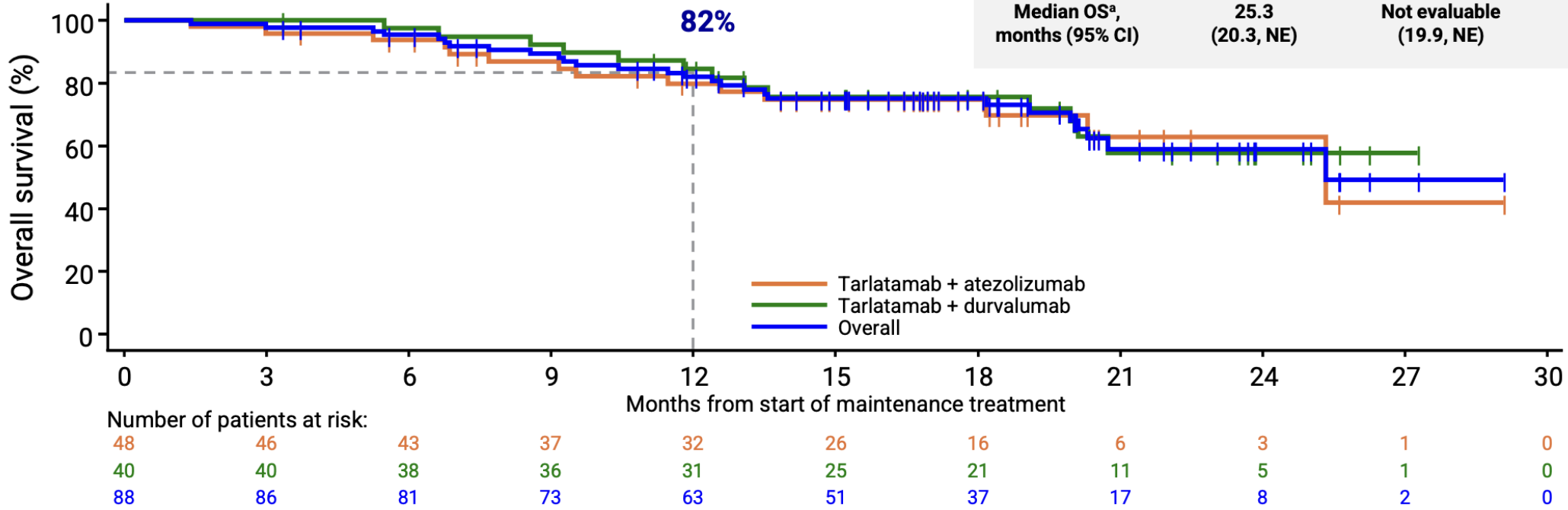


TRAEs led to dose interruption in 15% and tarlatamab discontinuation in 8% of patients†

- CRS was mostly grade 1–2, primarily occurred in cycle 1, and was manageable with supportive care
- ICANS occurred infrequently overall, with a lower incidence and a lower grade observed with tarlatamab + durvalumab compared with tarlatamab + atezolizumab

DeLLphi-303: OS

	Tarlatamab+ Atezolizumab	Tarlatamab+ Durvalumab	Overall Tarlatamab + Anti-PD-L1
Median OS[a], months (95% CI)	25.3 (20.3, NE)	Not evaluable (19.9, NE)	25.3 (20.3, NE)

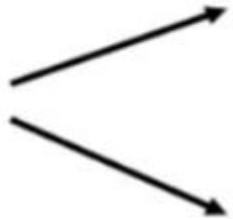


With a median follow-up time of 18.4 months, tarlatamab with anti-PD-L1 as 1L maintenance therapy led to a median OS of 25.3 months (95% CI, 20.3, NE).

DeLLphi-305: Durvalumab ± Tarlatamab in 1L Maintenance

- International, open-label, randomized phase III study

- Adults with ES-SCLC who completed 3-4 cycles of platinum/etoposide with concurrent durvalumab as first-line tx without disease progression
- no symptomatic CNS mets
- ECOG PS 0-1



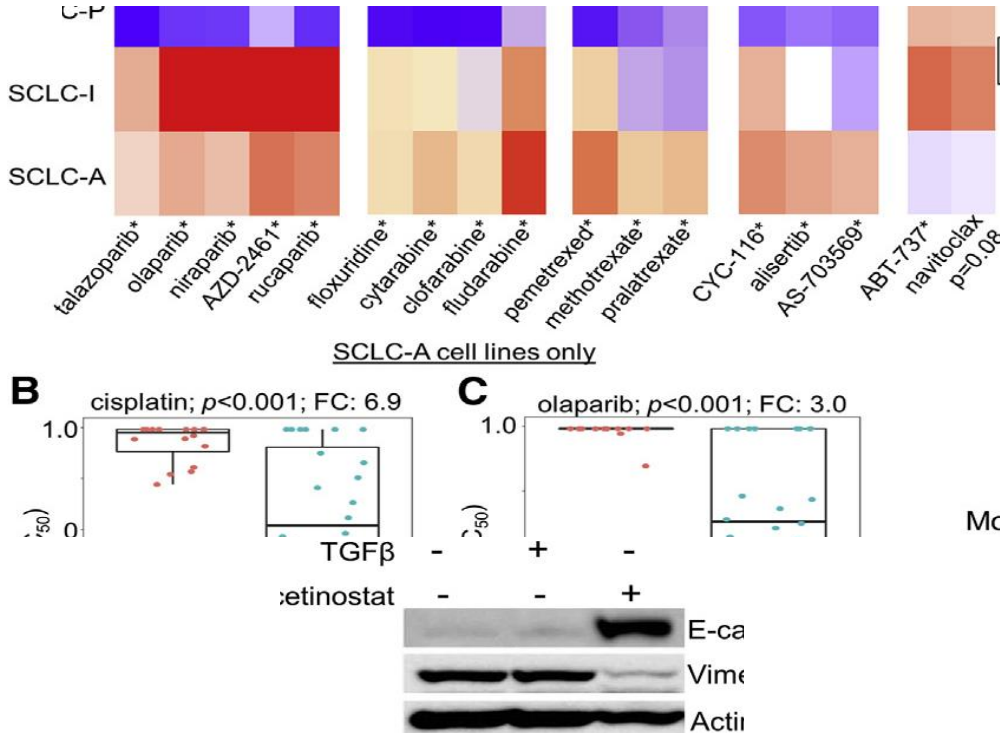
Tarlatamab IV Q2W + **Durvalumab** IV Q4W (n = 275)

Durvalumab IV Q4W (n = 275)

- Primary endpoint: Overall Survival
- Secondary endpoints: PFS, ORR, DCR, DoR, TTP, safety, QoL

SCLC subtypes defined by a dominant transcriptional regulator

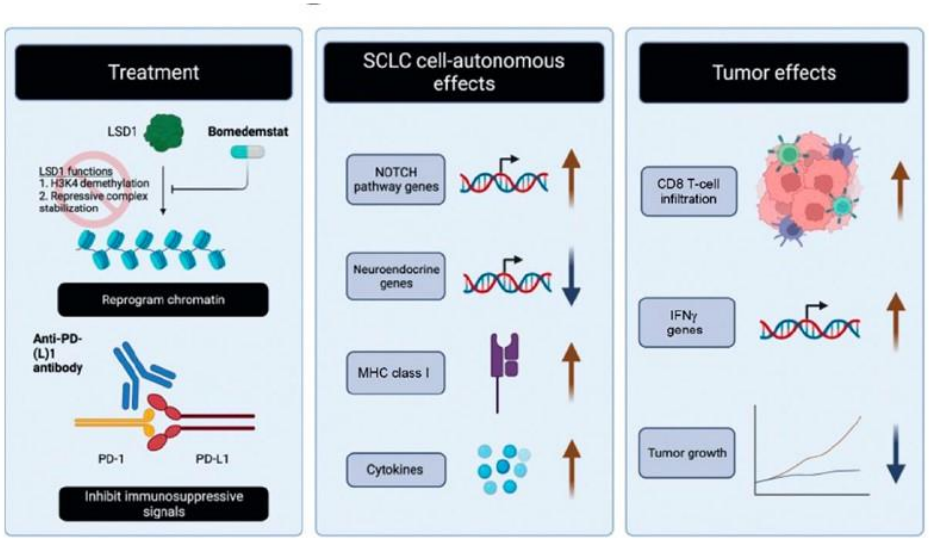
	Neuroendocrine		Non-Neuroendocrine	
Subtype	SCLC-A (36-51%)	SCLC-N (23-31%)	SCLC-P (7-17%)	SCLC-Inflamed (16-18%)
Targets	DLL3 BCL2 CD56 EZH1 LSD1	AURKA DLL3 MYC GD2	PARP1	AXL CD274 CD38 CTLA4 PD1/PDL1 BTKi



Poirier et al. JTO 2020

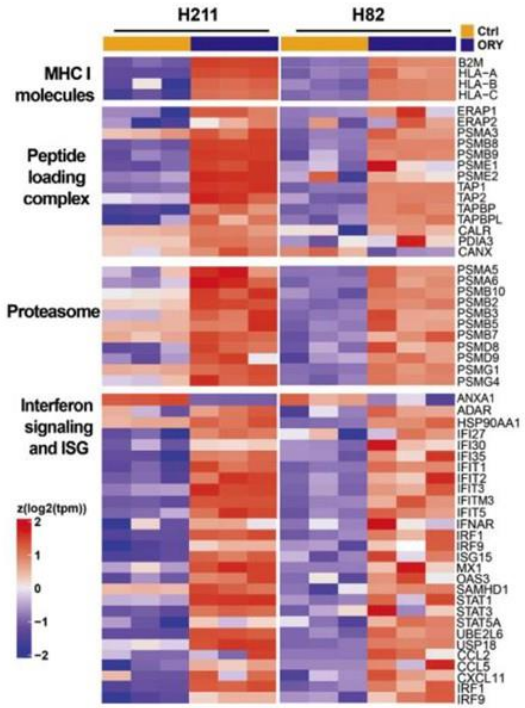
Gay et al. Cancer Cell 2021

Preclinical evidence that LSD1 inhibition increases MHC-I expression in vivo



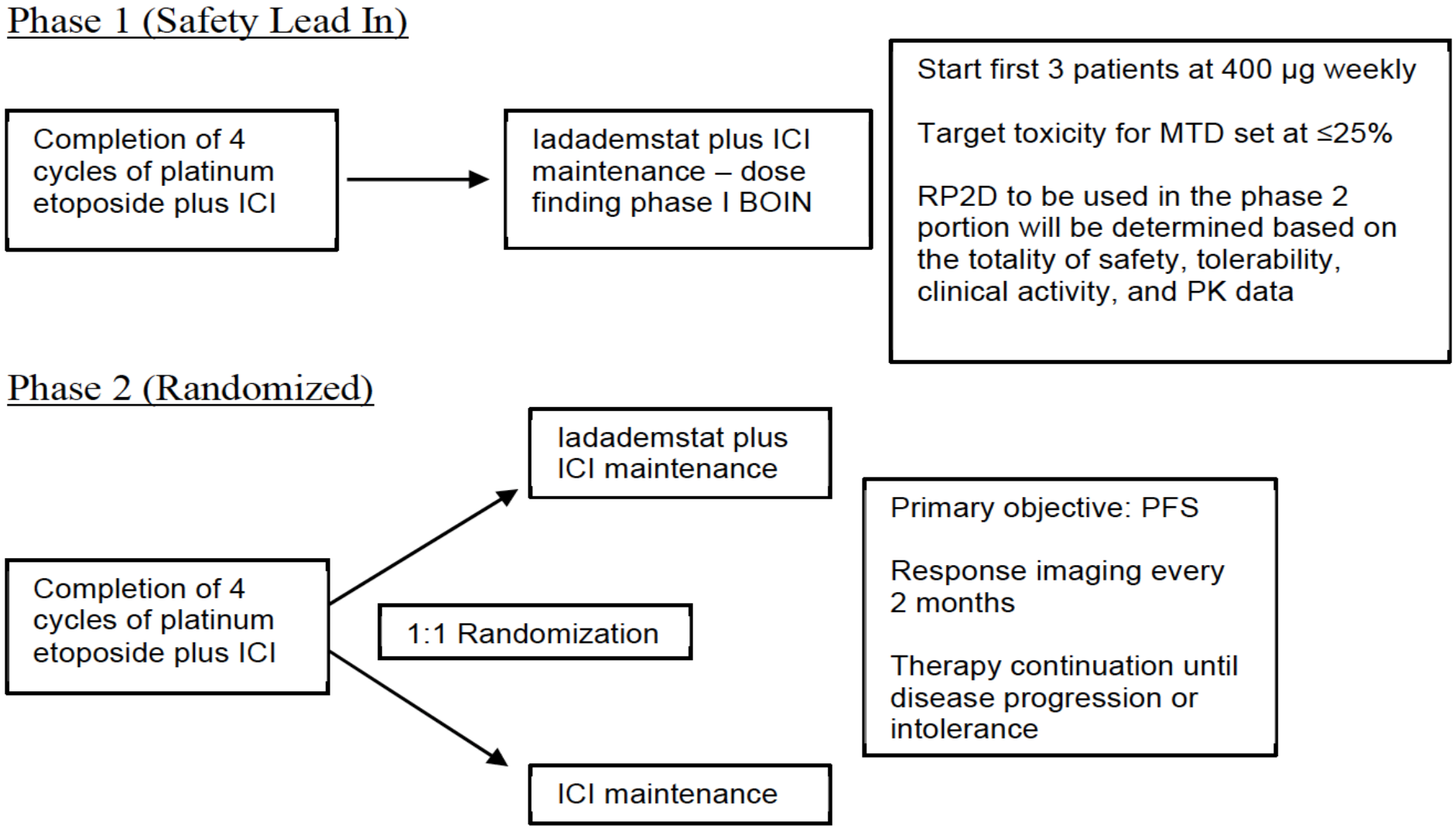
Hiatt et al. *Clinc Cancer Res*, 2022

LSD1 inhibition induces SCLC-I-like phenotype in otherwise uninflamed models.

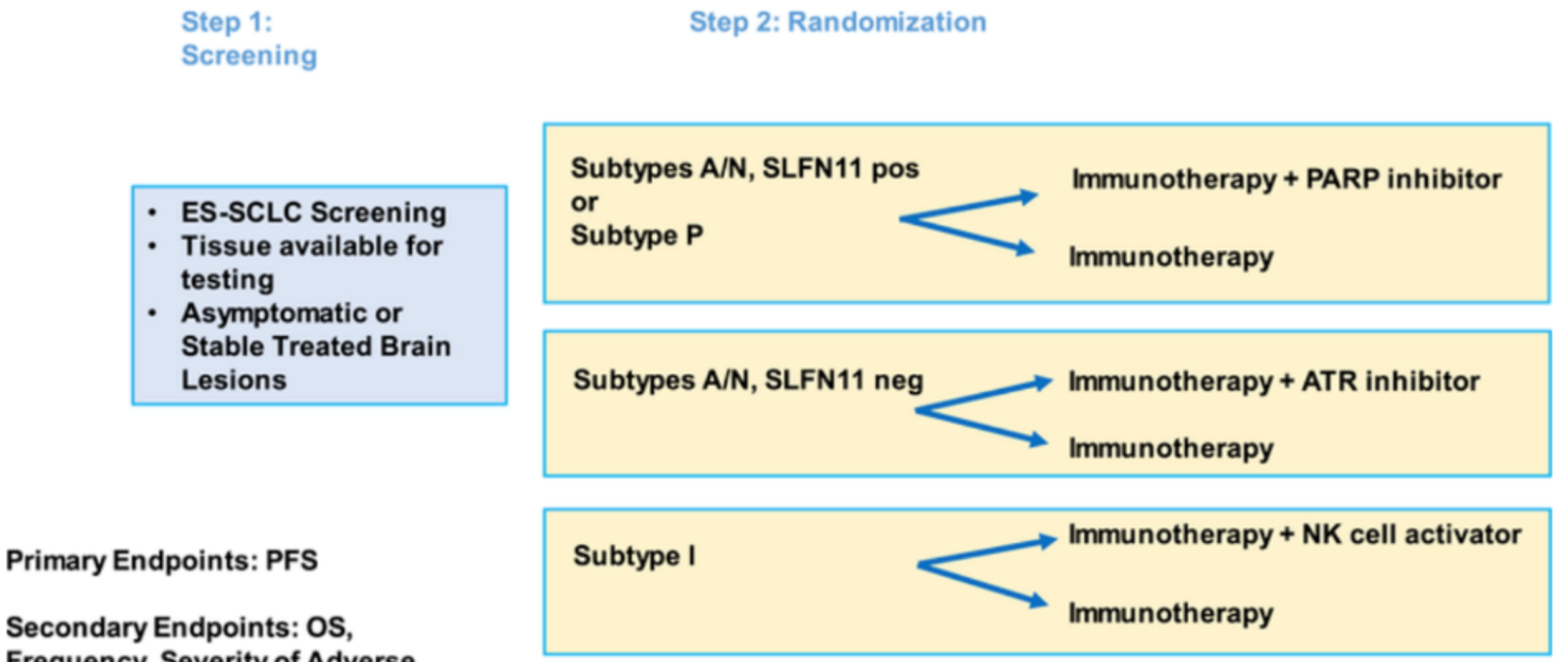


Nguyen et al. J Thorac Oncol, 2022

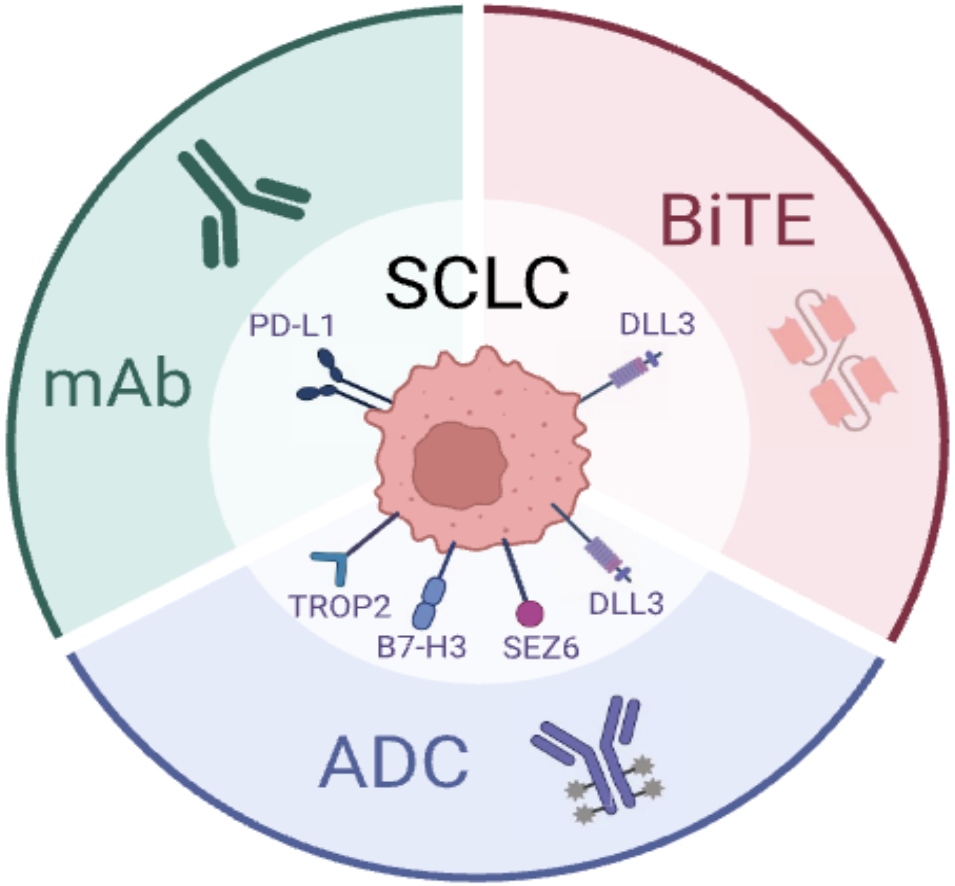
A Phase I Dose Finding and Phase II Randomized Trial of Iadademstat Combined with Immune Checkpoint Inhibition Maintenance After Initial Chemoimmunotherapy in Patients with ES-SCLC (NCT06287775)



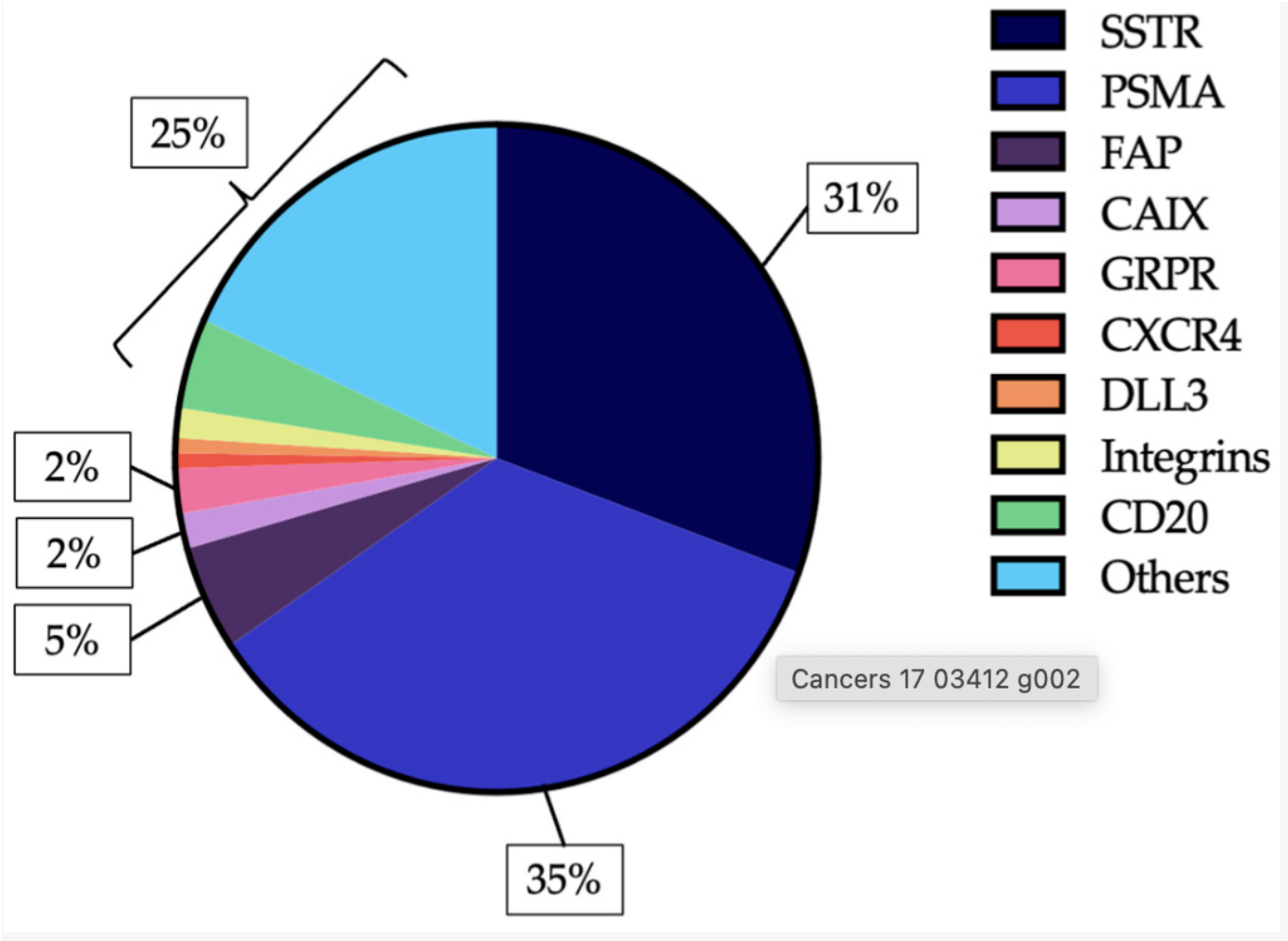
S2409-PRISM: A Multicohort PRecIsion SCLC Subtype Maintenance Phase II Trial of Durvalumab vs Biomarker-Directed Novel Agents in Combination With Durvalumab



Future Strategies



Radioligand therapy in SCLC



Shields, Chiang, Byers. Cancer. 2025.; Ninatti et al. Cancers 2025.

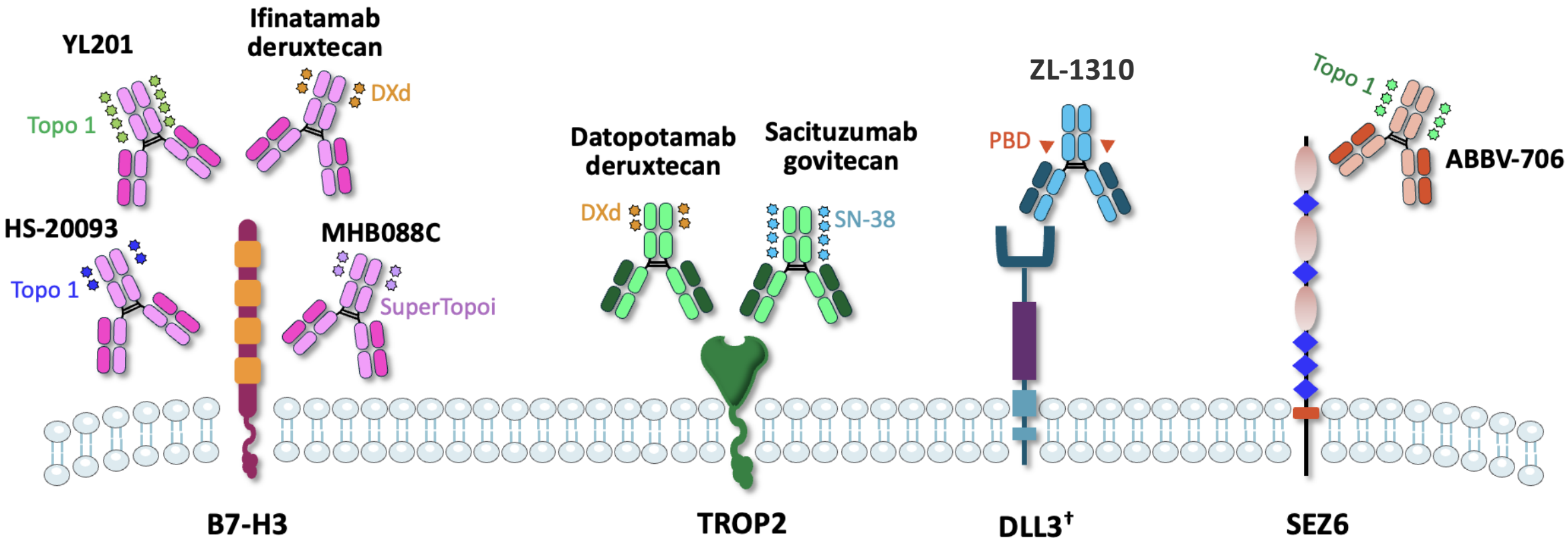
DLL3-targeting bispecifics/trispecifics in clinical development

Agent	Mechanism of action
Tarlatamab	DLL3 TCE
Obrixtamig (BI 764532)	DLL3 TCE
Alvetamig (ZG006)	DLL3 x DLL3 TCE
Gocatamig (MK-6070)**	DLL3 TCE
Peluntamig (PT217)	DLL3 x CD47 Mab
RO7616789	DLL3 x 4-1BB TCE
QLS31904	DLL3 TCE

- Delta-like ligand 3 T-cell engager

** Includes human albumin binding domain to extend half-life

Select ADC Targets Under Investigation in SCLC



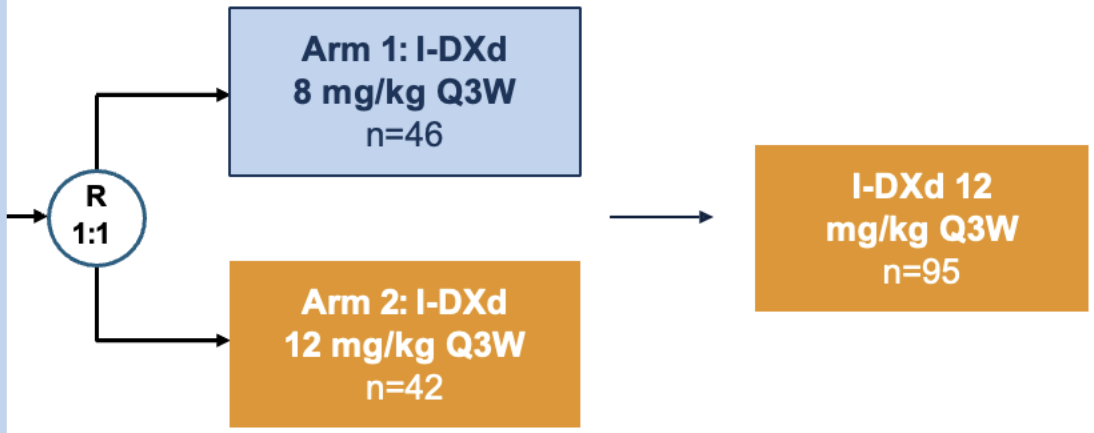
IDEATE-Lung-1: Study Design

Ifinatamab Deruxtecan Granted Priority Review in the U.S. for Adult Patients with Previously Treated ES-SCLC who Experienced Disease Progression on or After Platinum-Based Chemotherapy

Phase 2, multicenter, randomized, open-label study (NCT05280470)

Patient eligibility

- Histologically or cytologically documented ES-SCLC
- Age ≥18 years[a]
- ≥1 prior line of PBC and ≤3 prior lines of systemic therapy
- Radiologically documented PD on or after most recent prior systemic therapy
- ECOG PS 0–1
- ≥1 measurable lesion per RECIST 1.1[b]
- Patients with asymptomatic brain metastases (untreated or previously treated) were eligible



Stratification factors:

- 2L CTFI <90 days; 2L CTFI ≥90 days; 3L or 4L
- Prior anti–PD-(L)1 treatment (yes or no)

Primary endpoint

- ORR by BICR[c]

Secondary endpoints

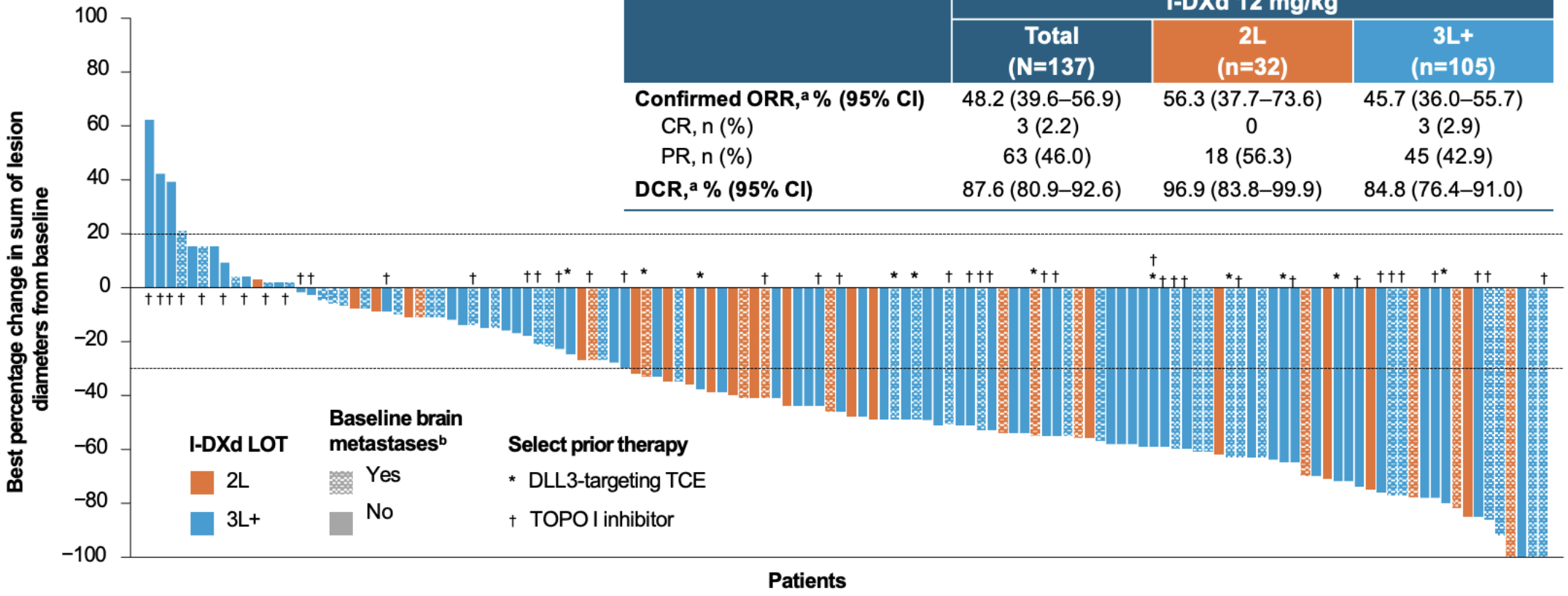
- DOR by BICR and inv[c]
- PFS by BICR and inv[c]
- OS
- DCR by BICR and inv[c]
- TTR by BICR and inv[c]
- ORR by inv[c]
- Safety
- Pharmacokinetics
- Immunogenicity

Exploratory analysis

- Intracranial ORR by BICR[d]

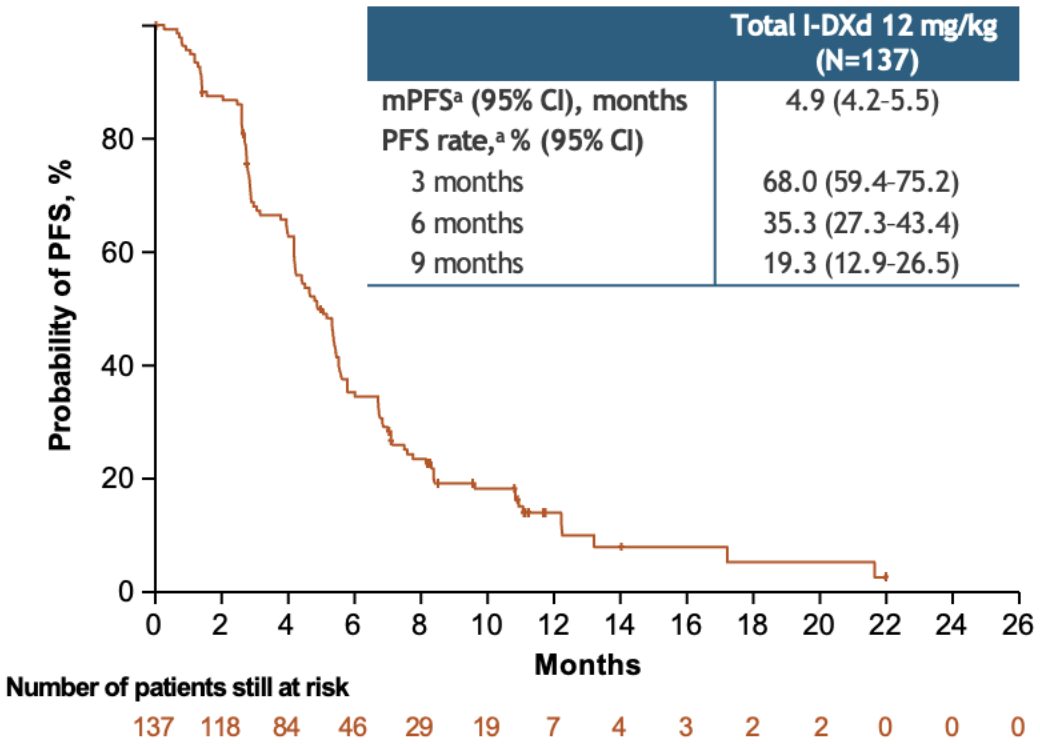
IDEATE-Lung-1: ORR

	I-DXd 12 mg/kg		
	Total (N=137)	2L (n=32)	3L+ (n=105)
Confirmed ORR,[a] % (95% CI)	48.2 (39.6–56.9)	56.3 (37.7–73.6)	45.7 (36.0–55.7)
CR, n (%)	3 (2.2)	0	3 (2.9)
PR, n (%)	63 (46.0)	18 (56.3)	45 (42.9)
DCR,[a] % (95% CI)	87.6 (80.9–92.6)	96.9 (83.8–99.9)	84.8 (76.4–91.0)

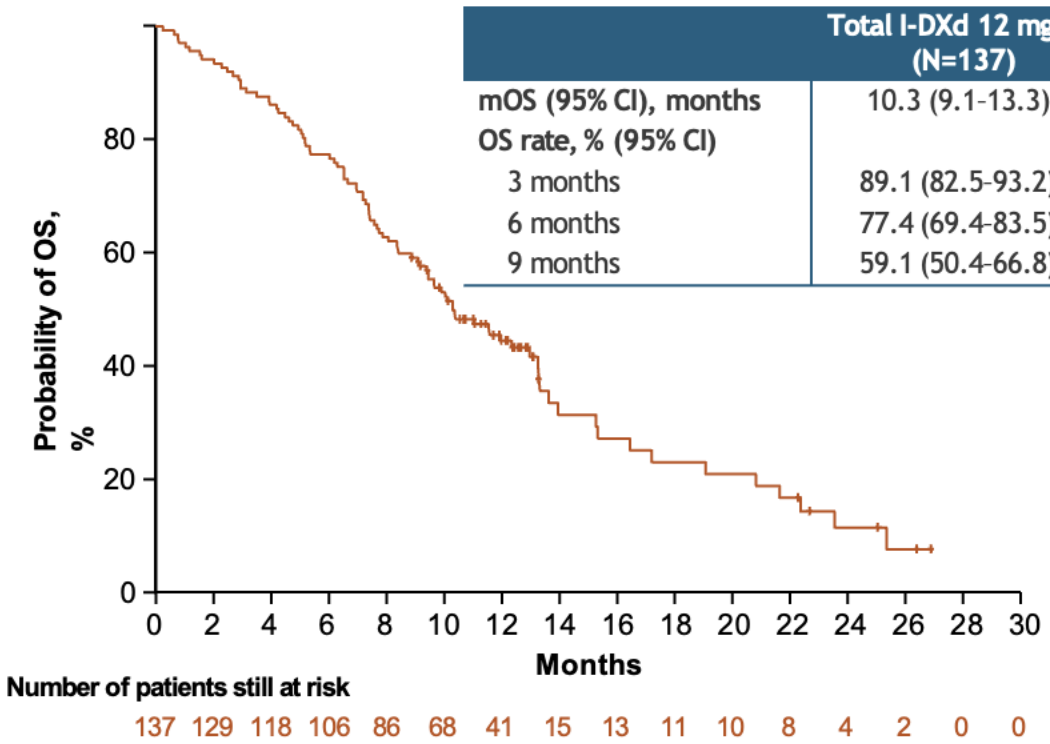


Ahn MJ, et al. WCLC 2025. Abstract OA06.03. Rudin CM, et al. *J Clin Oncol*. Published online October 14, 2025. doi:10.1200/JCO-25-02142.

IDEATE-Lung-1: PFS and OS



	Total I-DXd 12 mg/kg (N=137)
mPFS[a] (95% CI), months	4.9 (4.2-5.5)
PFS rate,[a] % (95% CI)	
3 months	68.0 (59.4-75.2)
6 months	35.3 (27.3-43.4)
9 months	19.3 (12.9-26.5)



	Total I-DXd 12 mg/kg (N=137)
mOS (95% CI), months	10.3 (9.1-13.3)
OS rate, % (95% CI)	
3 months	89.1 (82.5-93.2)
6 months	77.4 (69.4-83.5)
9 months	59.1 (50.4-66.8)

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)

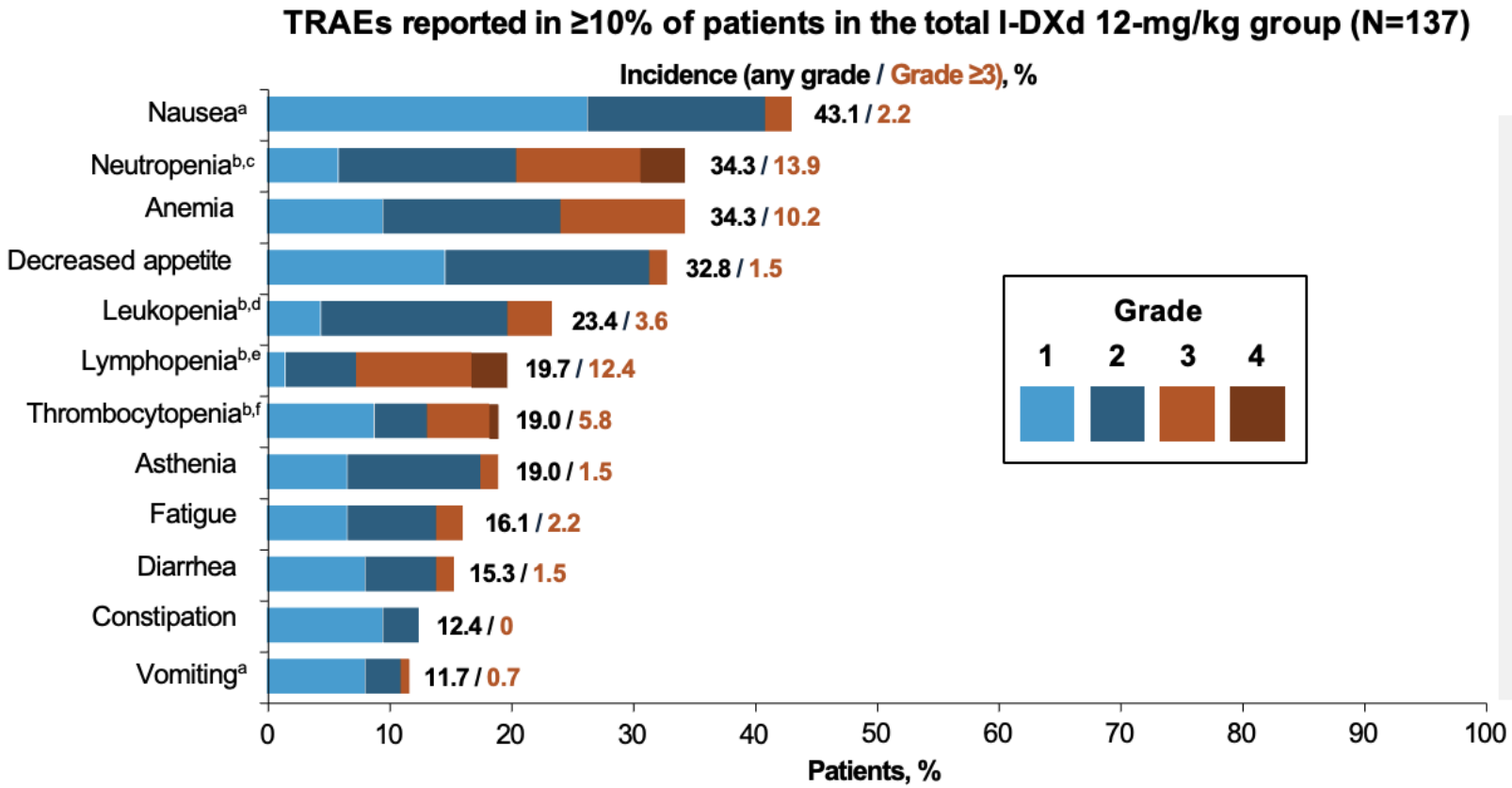
Ahn MJ, et al. WCLC 2025. Abstract OA06.03. Rudin CM, et al. *J Clin Oncol*. Published online October 14, 2025. doi:10.1200/JCO-25-02142.

IDeate-Lung01: Intracranial and Systemic Efficacy

	With Baseline BM (n=65)		Without Baseline BM (n=72)
	Intracranial	Systemic	Systemic
cORR,[a] % (95% CI)	46.2% (33.7–59.0)	46.2% (33.7–59.0)	50.0% (38.0–62.0)
cBOR,[a] n (%)			
CR	20 (30.8%)	1 (1.5%)	2 (2.8%)
PR	10 (15.4%)	29 (44.6%)	34 (47.2%)
SD	29 (44.6%)	28 (43.1%)	26 (36.1%)
PD	1 (1.5%)	5 (7.7%)	5 (6.9%)
NE	5 (7.7%)[b]	2 (3.1%)[c]	5 (6.9%)[d]
cDCR,[a] % (95% CI)	90.8% (81.0–96.5)	89.2% (79.1–95.6)	86.1% (75.9–93.1)
DOR,[a] median (95% CI), months	6.2 (4.0–7.9)	4.3 (3.0–5.8)	5.9 (4.0–8.3)
TTR,[a] median (range), months	1.4 (0.9–8.5)	1.4 (1.0–8.1)	1.4 (1.2–4.0)
PFS,[a] median (95% CI), months	—	4.5 (4.0–5.4)	5.4 (4.2–6.7)
OS, median (95% CI), months	—	10.4 (7.9–15.3)	10.1 (8.4–13.3)

Ahn MJ, et al. WCLC 2025. Abstract OA06.03. Rudin CM, et al. *J Clin Oncol*. Published online October 14, 2025. doi:10.1200/JCO-25-02142.

IDeate-Lung01: TRAEs



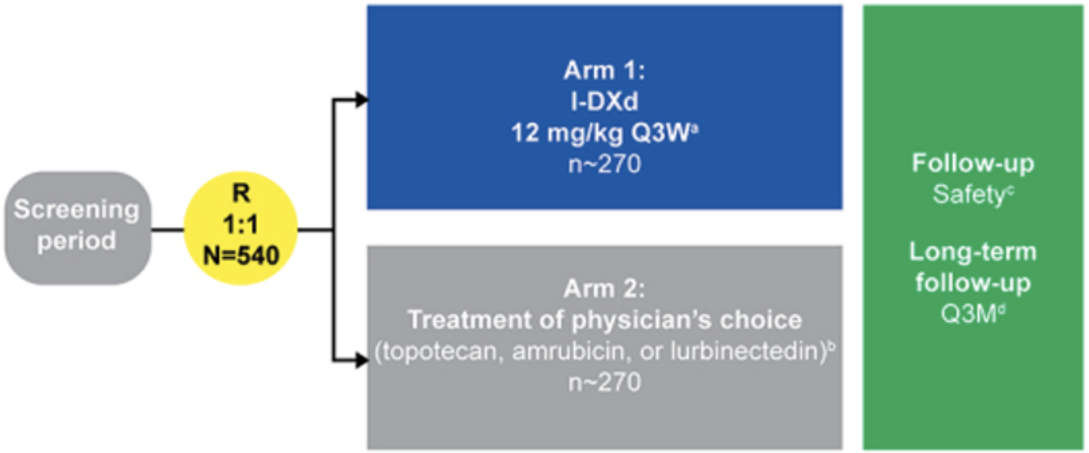
- Among the most common TRAEs, the majority were Grade 1 or 2
- Adjudicated treatment-related ILD/pneumonitis was reported in 17 (12.4%) patients:
  - Grade 1 or 2, n=11 (8.0%)
  - Grade 3, n=4 (2.9%)
  - Grade 5, n=2 (1.5%)[g]
- No ILD events were pending adjudication at data cutoff

Ahn MJ, et al. WCLC 2025. Abstract OA06.03. Rudin CM, et al. *J Clin Oncol*. Published online October 14, 2025. doi:10.1200/JCO-25-02142.

IDeate-Lung02: Phase 3 Trial of Second-Line Ifinatamab Deruxtecan in Relapsed SCLC

Key inclusion criteria

- Relapsed SCLC
- ≥18 years of age or minimum legal adult age (whichever is greater)
- Received only 1 prior line of systemic treatment, which must have included PBC ± anti–PD-(L)1 therapy
- Radiologically documented PD on or after PBC
- Eastern Cooperative Oncology Group performance status 0–1



Stratification

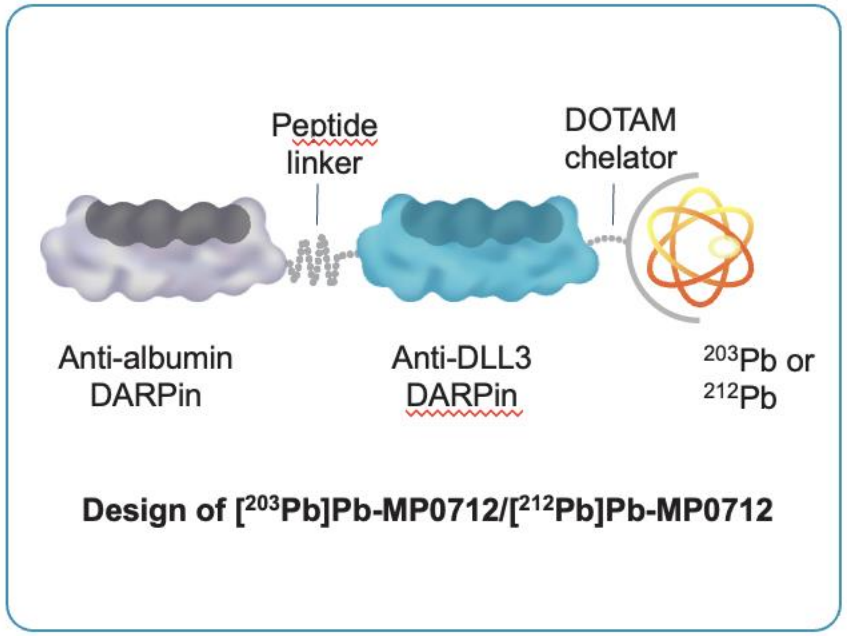
- Chemotherapy-free interval following 1L therapy (<90 vs ≥90 days)
- Treatment of physician's choice (topotecan vs amrubicin vs lurbinectedin)
- Treatment with prior anti-PD-(L)1 therapy (yes vs no)
- Presence or history of brain metastases (yes vs no)

Primary endpoints
ORR assessed by BICR[a]
OS

Ahn MJ, et al. WCLC 2025. Abstract OA06.03. Rudin CM, et al. *J Clin Oncol*. Published online October 14, 2025. doi:10.1200/JCO-25-02142.

Background: MP0712 MoA & Preclinical Profile

- DARPins are small engineered binding proteins (~18 kDa)
- [^{212}Pb]Pb-MP0712 is a clinical-stage DLL3-targeting alpha therapy combining a high-affinity DARPin with the therapeutic isotope ^{212}Pb
- It showed a favorable safety profile, biodistribution and antitumor efficacy in mice[1] and may offer a target-specific advantage:
  - Despite low surface density, repeated internalization and replenishment cycles of DLL3 could allow efficient tumor loading of [^{212}Pb]Pb-MP0712 without saturating binding sites[2]

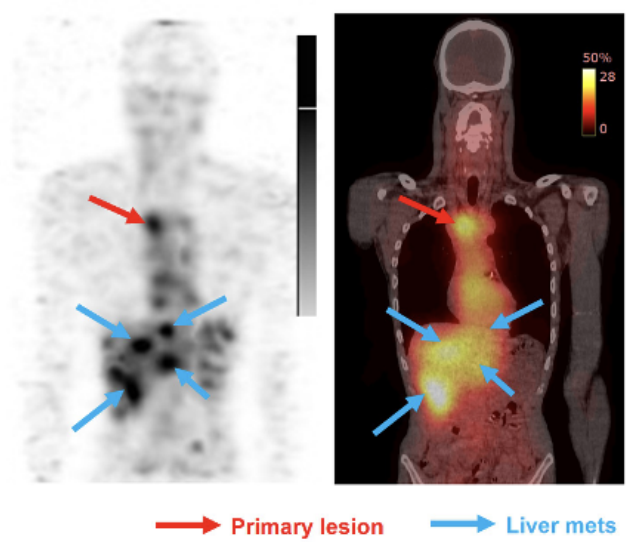


Design of [^{203}Pb]Pb-MP0712/[^{212}Pb]Pb-MP0712

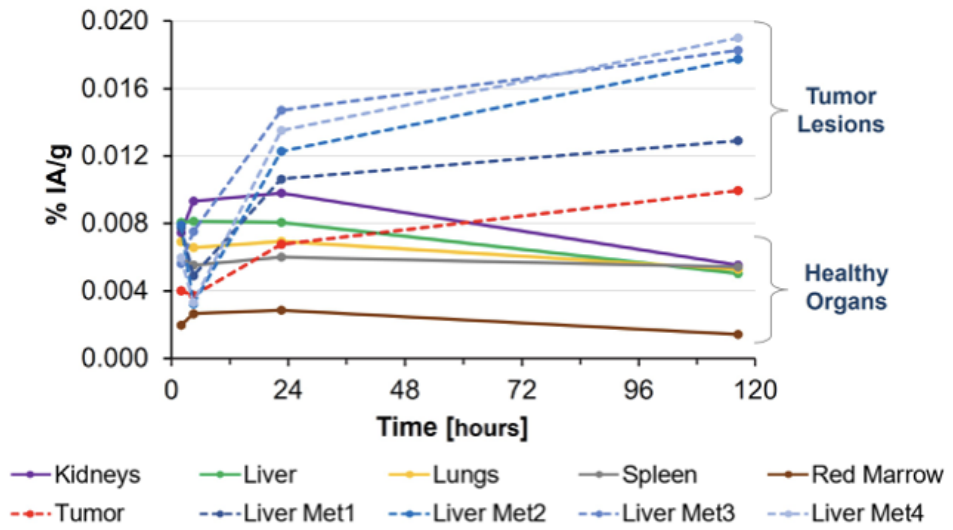
MP0712 First-in-Human Imaging

- First patient imaging and dosimetry data with [^{203}Pb]Pb-MP0712 from a compassionate care program:*
  - Robust tumor uptake that increased throughout the imaging period
  - Washout from healthy organs, including kidney, visible from 24 h onwards

SPECT/CT imaging 116 h post ^{203}Pb-MP0712 injection



Biodistribution profile of ^{203}Pb-MP0712 in a patient with metastatic SCLC



Leal T et al. ASCO 2026

MP0712 Phase 1/2a Study: Design

Key Eligibility Criteria

- Aged ≥18 years
- SCLC after ≥2 prior systemic therapies or not eligible for standard 2nd-line therapy, or
- LC NEC of the lung after ≥1 prior systemic therapy, or
- epNECs including GEP, cervical, bladder, or other DLL3-expressing epNECs (excluding Merkel cell carcinoma and neuroendocrine prostate cancer) after ≥1 prior systemic therapy
- DLL3-positive disease by [203Pb]Pb-MP0712 SPECT/CT (epNECs in Parts 1 and 2; SCLC or LC-NEC of the lung in Part 2)

Part 1 Dose Escalation* SCLC/LC NEC of the lung and epNEC
n=up to 78

[203Pb]Pb-MP0712 Imaging period

Single dose of [203Pb]Pb-MP0712 (185 MBq) and SPECT/CT

[212Pb]Pb-MP0712 Treatment period

Dose Level 1 n=3

Dose Level 2 n=3–12

Dose Level 3 n=6–12

Dose Level X n=3–12

Dose Level 4 n=6–12

Dose Level 4 n=6–12

RP2D

Part 2 Dose Expansion SCLC / LC NEC of the lung
n=up to 30

Part 2 Dose Expansion epNEC
n=up to 30

[203Pb]Pb-MP0712 Imaging period

Single dose of [203Pb]Pb-MP0712 (185 MBq) and SPECT/CT

[212Pb]Pb-MP0712 Treatment period

[212Pb]Pb-MP0712 treatment at RP2D

Main Study Endpoints

Primary
- Part 1: MTD/RP2D and safety
- Part 2: Preliminary antitumor activity (ORR)

Secondary:
- Dosimetry/PK, safety, antitumor activity (DOR, PFS, OS)

ADRIATIC Clinical Trial (NCT03703297)

Phase 3, randomized, double-blind, placebo-controlled, multicenter, international study (NCT03703297)

- Stage I–III LS-SCLC (stage I/II inoperable)
- WHO PS 0 or 1
- Had not progressed following cCRT*
- PCI* permitted before randomization

N=730

R‡

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

Durvalumab + tremelimumab
D 1500 mg Q4W + T 75 mg Q4W for 4 doses, followed by D 1500 mg Q4W
N=200

Stratified by:
Disease stage (I/II vs III)
PCI (yes vs no)

cCRT components
- Four cycles of platinum and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks
- RT must commence no later than end of cycle 2 of CT

Treatment until investigator-determined progression or intolerable toxicity, or for a **maximum of 24 months**

Dual primary endpoints:
- Durvalumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

Key secondary endpoints:
- Durvalumab + tremelimumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

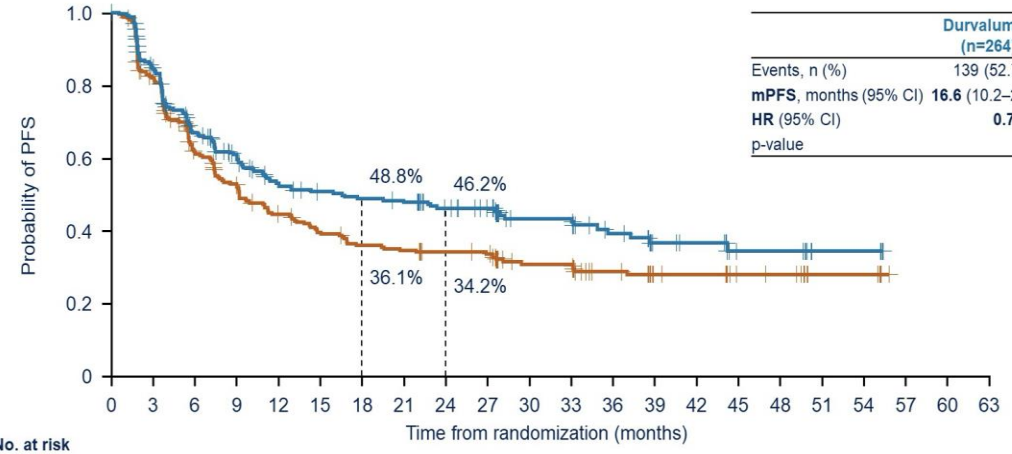
Other secondary endpoints:
- OS/PFS landmarks
- Safety

Cheng Y, DR, Cho BC, et al. Durvalumab after Chemoradiotherapy in Limited-Stage Small-Cell Lung Cancer. *N Engl J Med*. 2024;391(14):1313-1327.

ADRIATIC Clinical Trial (NCT03703297)

PFS

- Median duration of follow up in censored patients: 27.6 months (range 0.0–55.8)

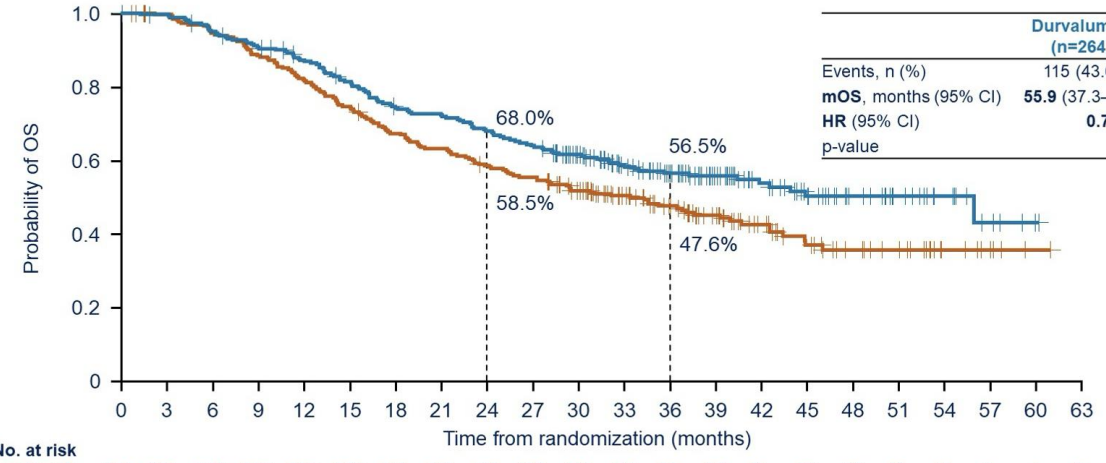


	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

No. at risk																						
Durvalumab	264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	0	0
Placebo	266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	0	0

OS

- Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

No. at risk																						
Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

Cheng Y, DR, Cho BC, et al. Durvalumab after Chemoradiotherapy in Limited-Stage Small-Cell Lung Cancer. *N Engl J Med*. 2024;391(14):1313-1327.

Clinical trials in LS-SCLC

Stage	Intervention	Phase	NCT
Limited	Consolidative sugemalimab (PDL1) after CRT	II/III	NCT04170946
Limited	Consolidative Tifcemalimab (mAB against B and T lymphocyte attenuator) +/- toripalimab (PD1)	III	NCT06095583
Limited	Pembrolizumab with concurrent chemoRT followed by consolidative pembro+/- olaparib	III	NCT04624204
Limited	Surlidumab (IL6) with concurrent CRT	II	NCT06295926
Limited	Consolidative Tarlatamab (DLL3) after CRT (DeLLphi-306)	III	NCT06117774
Limited	Serplulimab (PD1) + concurrent CRT	III	NCT05353257

TIGOS-LS

250 participants

80 sites in the US

TIGOS-LS is an open-label, randomized study to evaluate the safety and efficacy of BMS-986489 as consolidation therapy vs the new standard durvalumab following chemoradiotherapy (CRT) in LS-SCLC.

Primary endpoint	
Overall survival	
Key secondary endpoints	
Progression-free survival	Disease control rate
Duration of response	Safety parameters
Objective response rate	Clinical benefit rate

Eligible Participants

- ≥18 years old
- Histologically or cytologically confirmed LS-SCLC
- 0 or 1 ECOG performance score
- Completed concurrent CRT for LS-SCLC without progression
- Confirmation of fuc-GM1 expression not required
- PCI permitted before initiation of study treatment

Take Home Messages

- Durvalumab consolidation post-chemoRT is SOC.
- 1L maintenance Lurbinectedin in Combination With Atezolizumab improves PFS and OS.
- With extended follow-up, the efficacy and safety of tarlatamab are maintained and is the preferred second-line therapy in relapsed ES-SCLC.
- T cell engagers combination studies are being investigated and have the potential to move into earlier lines of therapy.

Thank you!

EMORY
WINSHIP
CANCER
INSTITUTE
National Cancer Institute-Designated
Comprehensive Cancer Center

Where Science Becomes Hope