20th ANNUAL ATLANTA LUNG CANCER SYMPOSIUM

# Small Cell Lung Cancer: Expanding Options, More Hope

Ticiana Leal, MD

Winship Cancer Institute

Emory University

Partners for Advancing Clinical Education

Bio Ascend™

# Disclosures

Consultant, Advisor, Speaker: AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Catalyst, Genentech, Gilead, Janssen, Jazz, Lilly, Molecular Therapeutics, Novocure, Nuvation Bio, Summit Therapeutics, Synthekine, VerastemDSMB: OncoC4

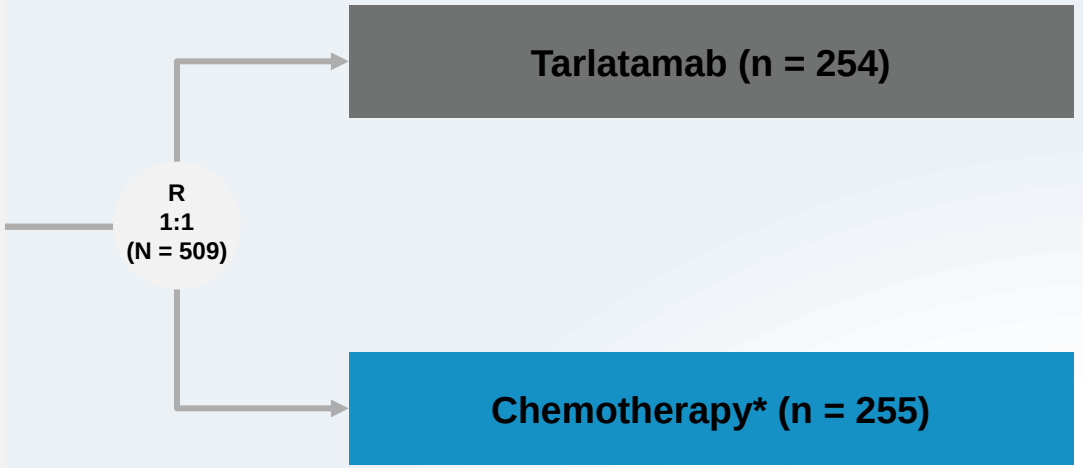
# Phase 3 DeLLphi-304 study (NCT05740566)

**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)



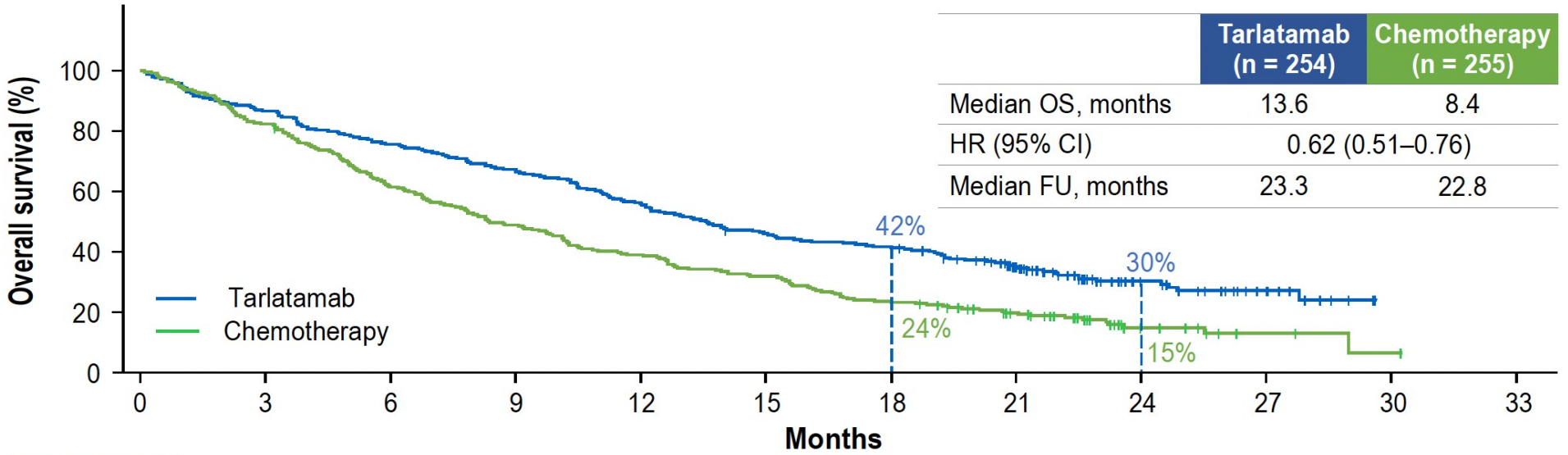

**Primary Endpoint:** Overall survival
**Key Secondary Endpoints:** Progression-free survival, patient-reported outcomes
**Other Secondary Endpoints:** Objective response, disease control, duration of response, safety

*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.

# Phase 3 DeLLphi-304 study (NCT05740566)

## Extended follow-up confirms sustained OS benefit of tarlatamab



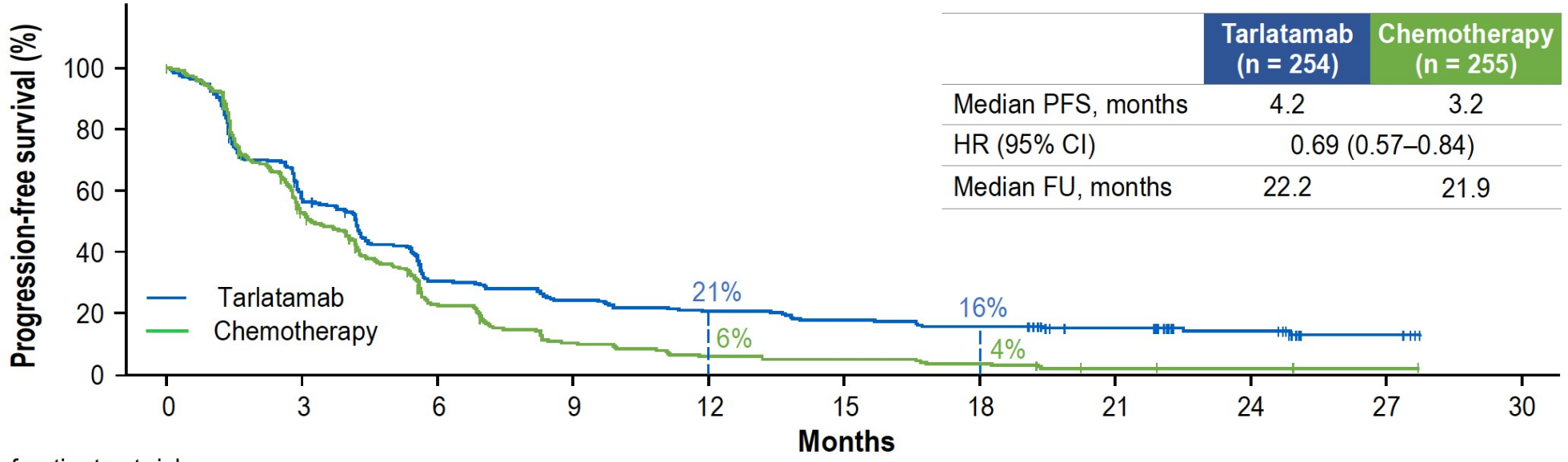

| | Tarlatamab (n = 254) | Chemotherapy (n = 255) |
|---|---|---|
| Median OS, months | 13.6 | 8.4 |
| HR (95% CI) | 0.62 (0.51–0.76) | |
| Median FU, months | 23.3 | 22.8 |

Number of patients at risk:

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tarlatamab | 254 | 220 | 192 | 171 | 142 | 116 | 105 | 73 | 33 | 14 | 0 | |
| Chemotherapy | 255 | 210 | 156 | 124 | 99 | 81 | 60 | 40 | 13 | 4 | 1 | 0 |

Data cutoff date: 18 Feb 2026.

# Tarlatamab demonstrated sustained PFS benefit during extended follow-up




| | Tarlatamab (n = 254) | Chemotherapy (n = 255) |
|---|---|---|
| Median PFS, months | 4.2 | 3.2 |
| HR (95% CI) | 0.69 (0.57–0.84) | |
| Median FU, months | 22.2 | 21.9 |

Number of patients at risk:

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Tarlatamab | 254 | 142 | 74 | 59 | 50 | 43 | 38 | 27 | 15 | 4 | 0 |
| Chemotherapy | 255 | 119 | 48 | 21 | 12 | 11 | 8 | 3 | 2 | 1 | 0 |

Data cutoff date: 18 Feb 2026.

# Real World Implementation of Tarlatamab

| 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) |

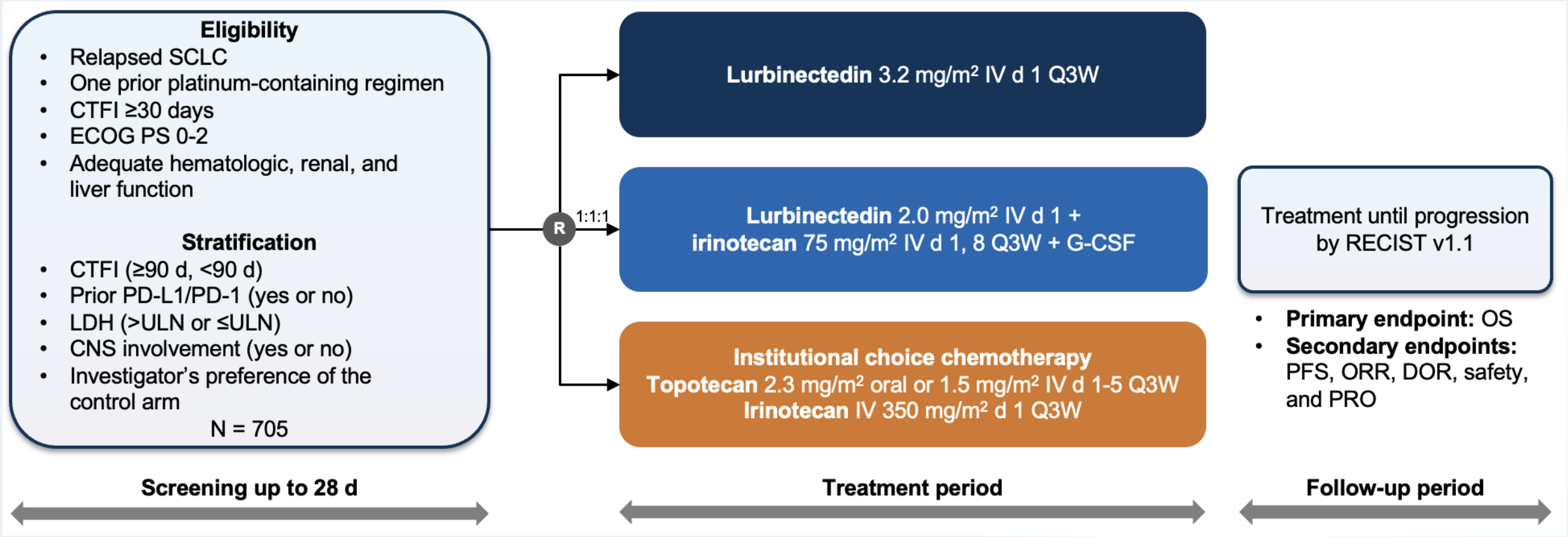
- Median PFS was 3.7 months (95% CI, 2.7 to 5.2)
- Median OS was 7.1 months (95% CI, 4.9 to 9.3)

- 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.**



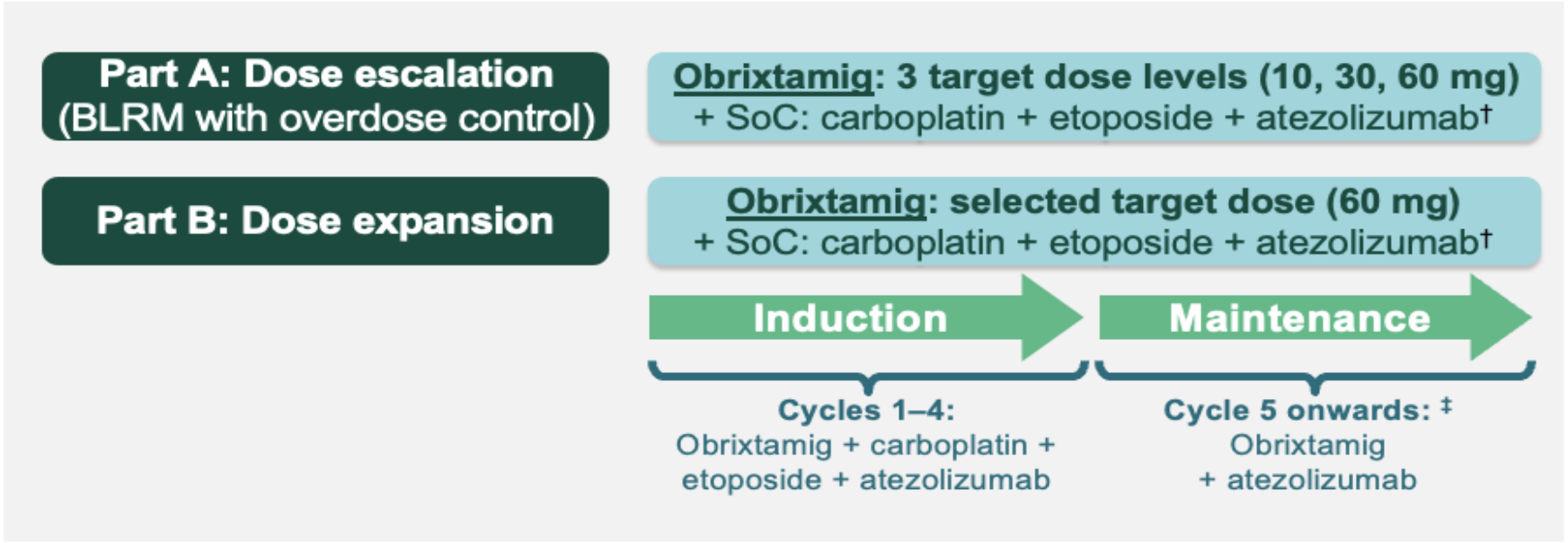

Besse B et al. ASCO 2023. Abstract TPS8613.

# 1L chemoimmunotherapy for ES-SCLC

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




## Endpoints

- **Primary endpoint:** DLTs
- **Secondary endpoints:** Safety; Part B: ORR and DoR by RECIST v1.1 (investigator-assessed)
- **Further endpoints:**
  Part A: efficacy, biomarker analyses, PK
  Part B: PFS and DCR by RECIST v1.1 (investigator-assessed), biomarker analyses, PK, PROs

## Key inclusion criteria

- Histologically/cytologically confirmed ES-SCLC
- Eligible for carboplatin + etoposide + atezolizumab
- Adequate liver, bone marrow, and renal function

## Key exclusion criteria

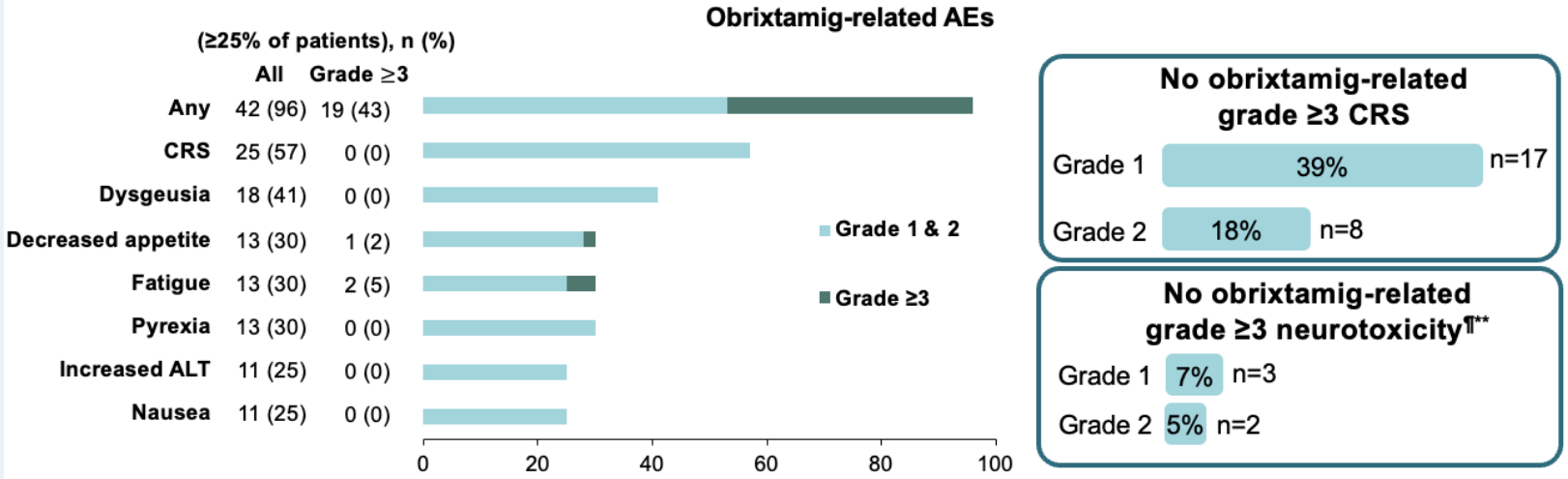
- Previous TcEs or DLL3-targeting therapies
- Active or documented history of autoimmune disease requiring systemic treatment
- Presence of LMD or symptomatic brain metastases (untreated asymptomatic brain metastases are eligible)

†SoC administered per label; ‡Until disease progression or another reason requiring termination of treatment.

Peters S, , Dziadziusko R, Kalinka E, Gazzah A, Cousin S, Garcia M, Vicente D, Johnson T,Yoshida T, Ma Y, Dorleacq N, Yang D, Leal T. ASCO 2026

# DAREON-8 Phase I obrixtamig + chemotherapy: Safety

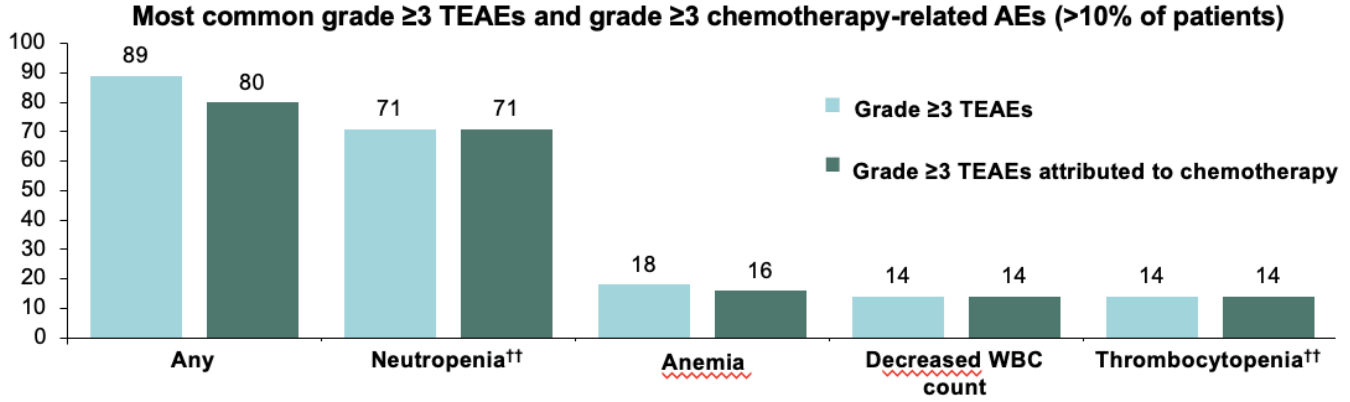
- MTD was not reached[§]
- Obrixtamig 60 mg was selected as the target dose for Part B









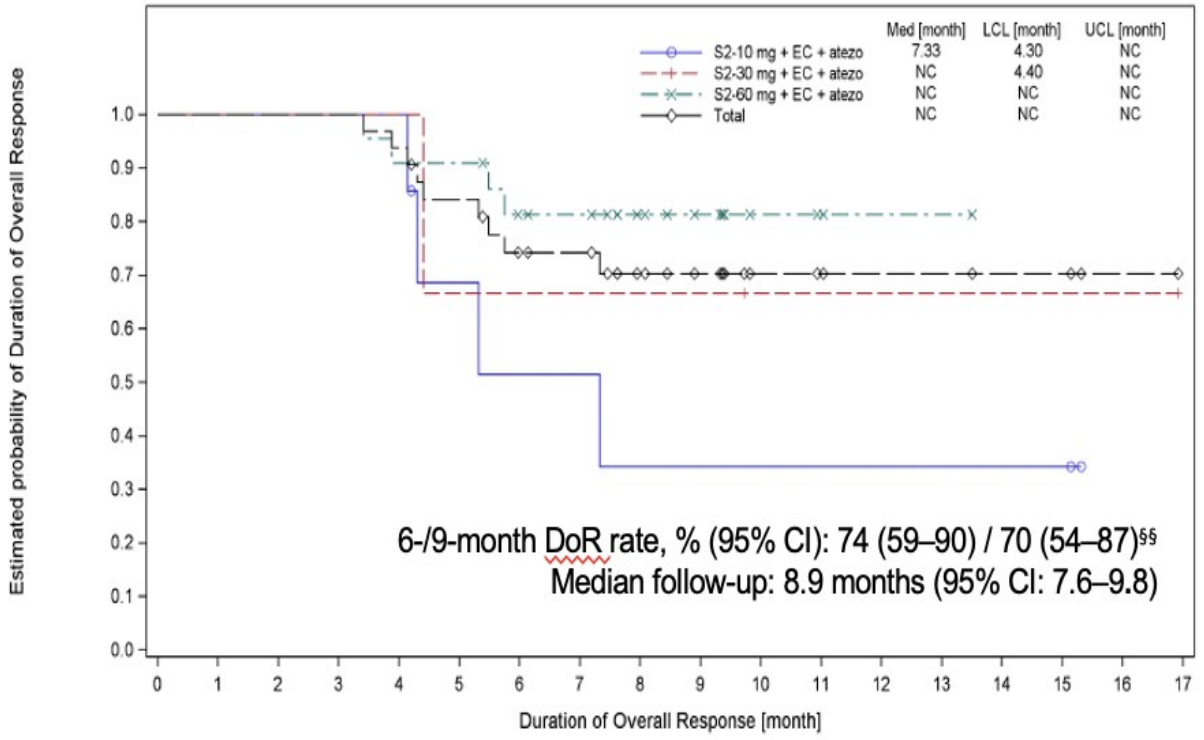



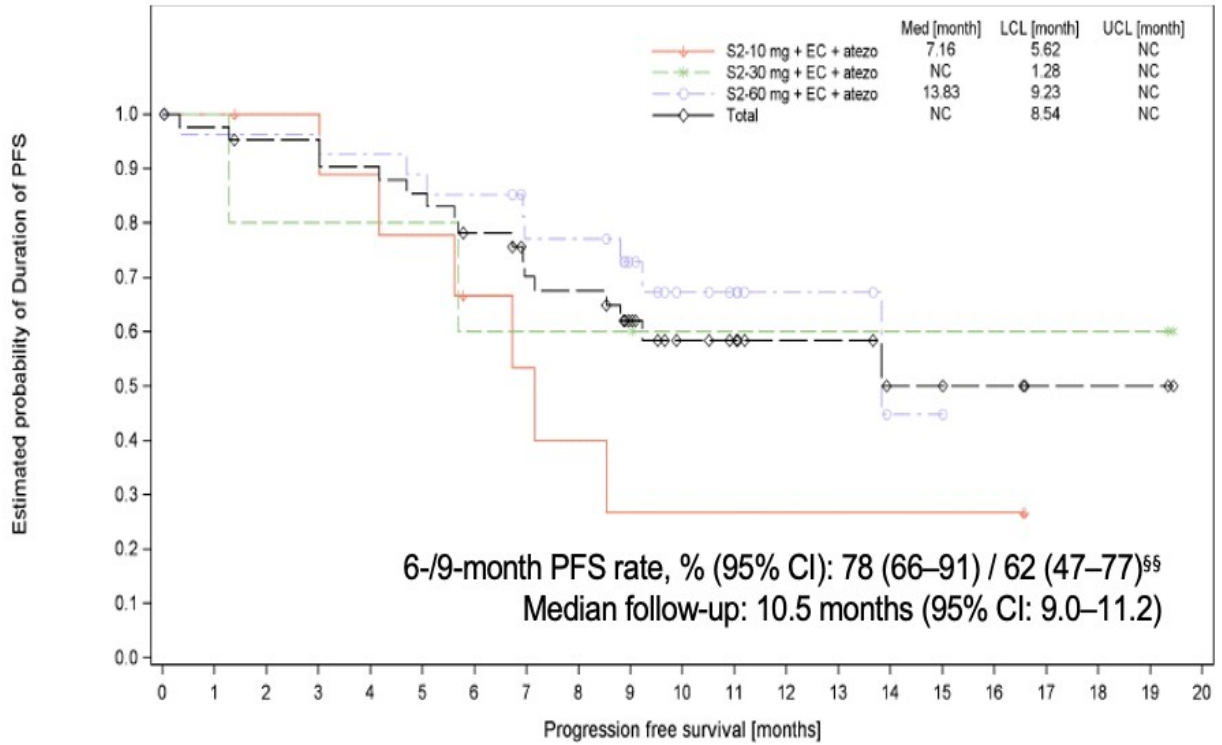

[§]Three patients experienced DLTs: tumor pain, increased blood creatine phosphokinase, and pneumonitis; ¶ICANS or potential ICANS-like neurotoxicity events; **Neurotoxicity events were ICANS (n=3), confusional state (n=1), and memory impairment (n=1); ††Combined term including neutropenia and decreased neutrophil count, and thrombocytopenia and decreased platelet count.

Peters S, , Dziadziusko R, Kalinka E, Gazzah A, Cousin S, Garcia M, Vicente D, Johnson T,Yoshida T, Ma Y, Dorleacq N, Yang D, Leal T. ASCO 2026

# DAREON-8 Phase I obrixtamig + chemotherapy: Efficacy

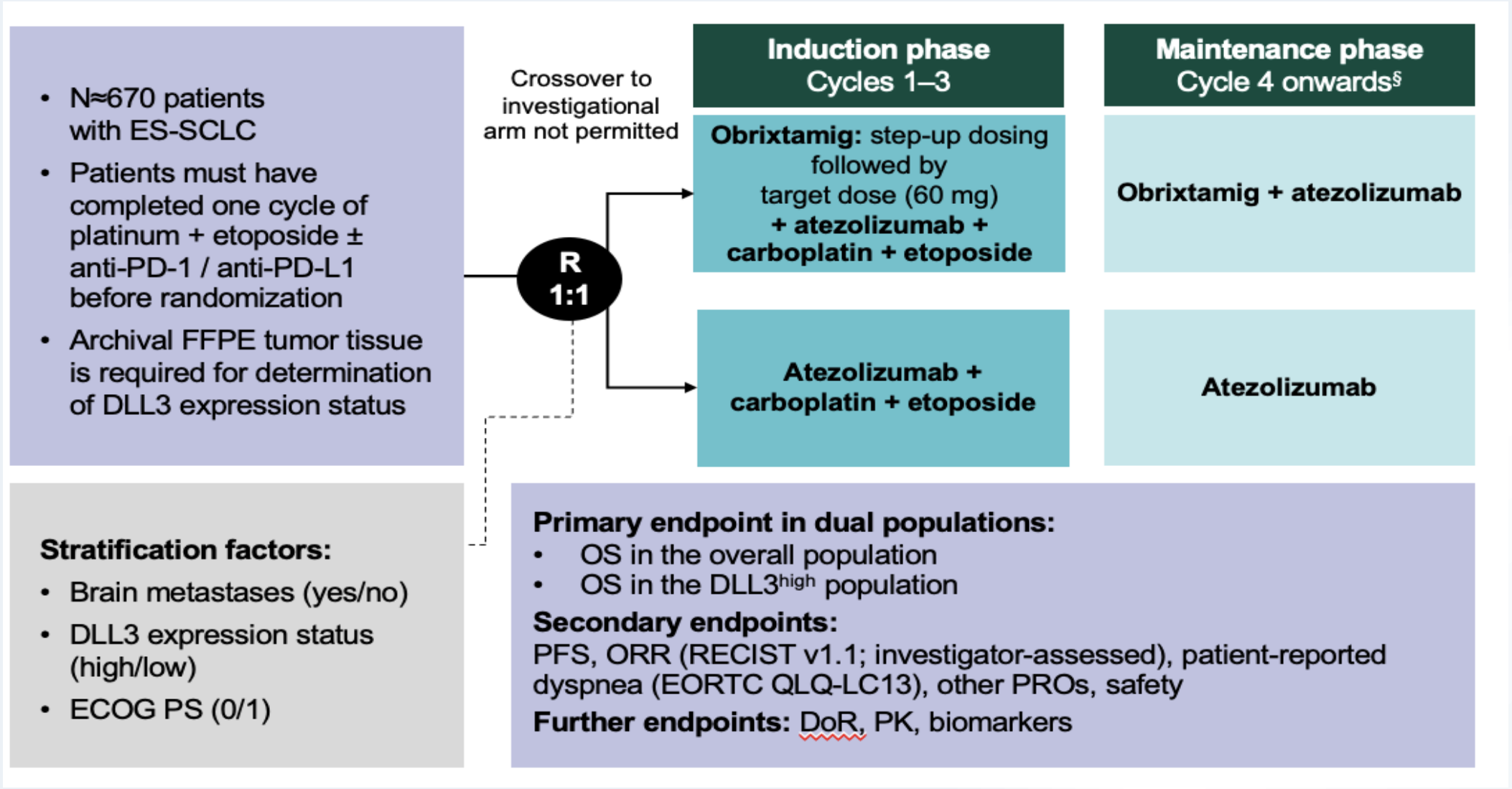
- First-line obrixtamig demonstrated encouraging efficacy and durable responses in combination with SoC, particularly in patients receiving the obrixtamig target dose (60 mg), with three patients showing CR
- At data cut-off, 22 patients remained on treatment



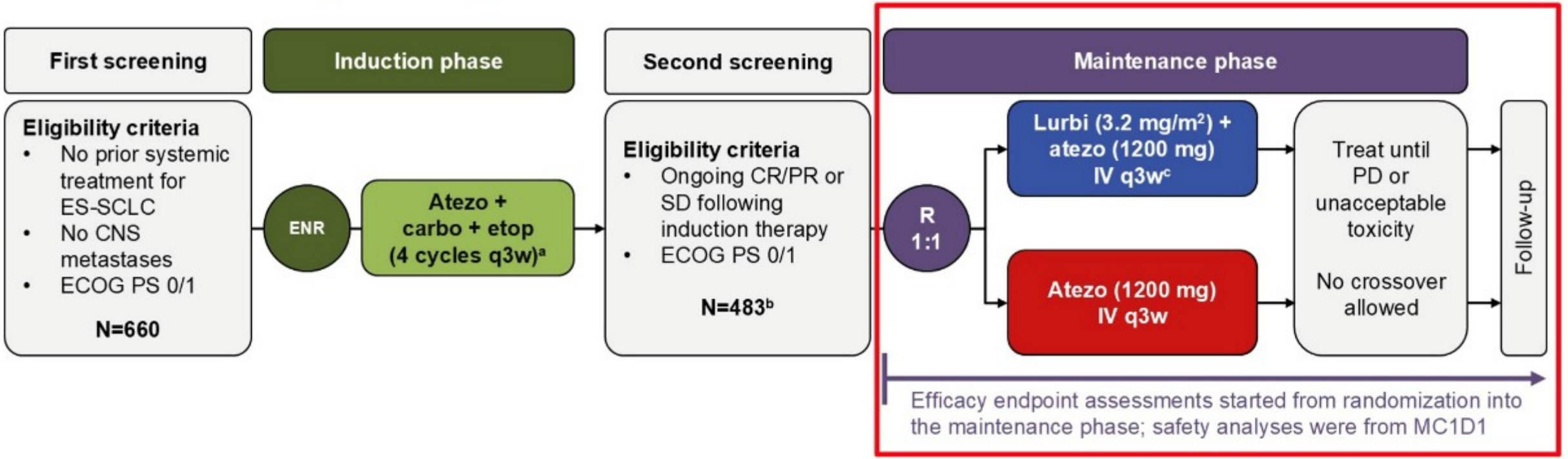

Peters S, Dziadziusko R, Kalinka E, Gazzah A, Cousin S, Garcia M, Vicente D, Johnson T,Yoshida T, Ma Y, Dorleacq N, Yang D, Leal T. ASCO 2026

# DAREON-Lung-1




Leal T, WCLC 2026

# IMforte Study Design




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

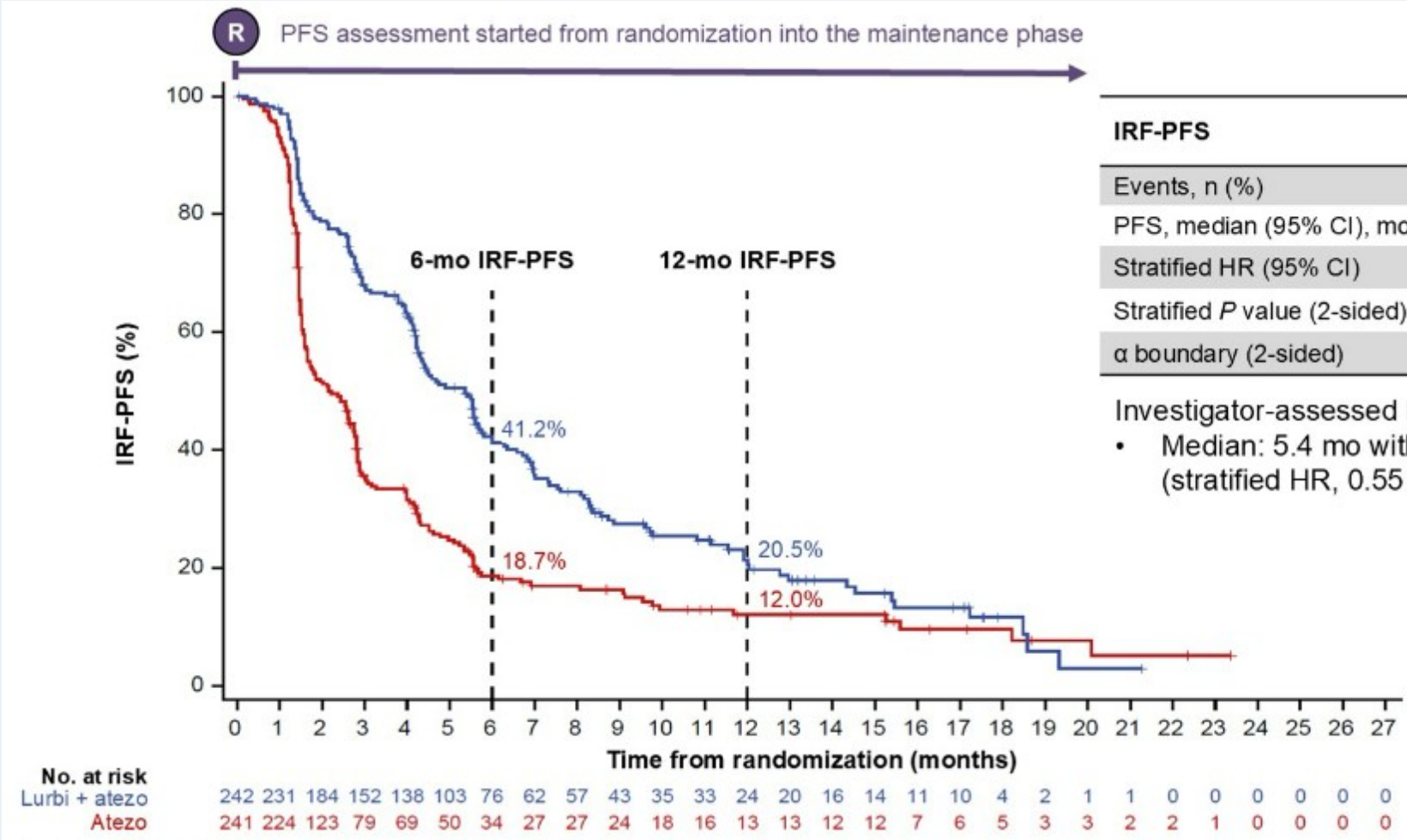
**Stratification factors for randomization**
- ECOG PS (0/1)
- LDH (≤ULN/>ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

**Primary endpoints**
IRF-PFS and OS

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

Paz-Ares et al. ASCO 2025

# IMforte: PFS

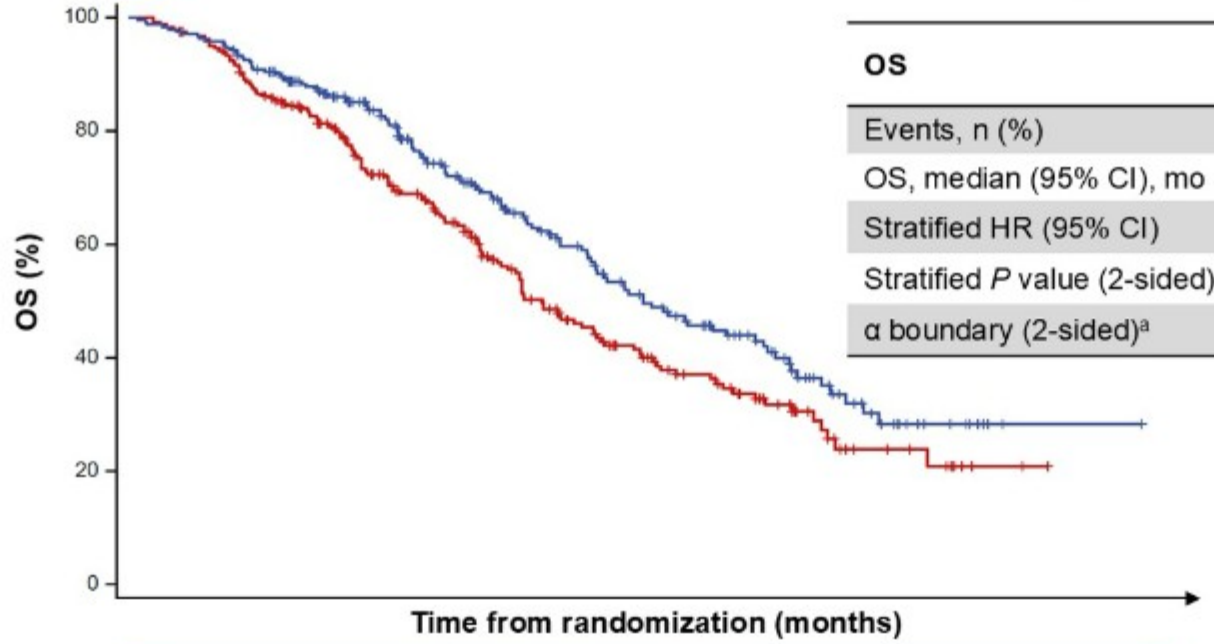



| IRF-PFS | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Events, n (%) | 174 (71.9) | 202 (83.8) |
| PFS, median (95% CI), mo | 5.4 (4.2, 5.8) | 2.1 (1.6, 2.7) |
| Stratified HR (95% CI) | **0.54 (0.43, 0.67)** | |
| Stratified *P* value (2-sided) | <0.0001 | |
| α boundary (2-sided) | 0.001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

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**

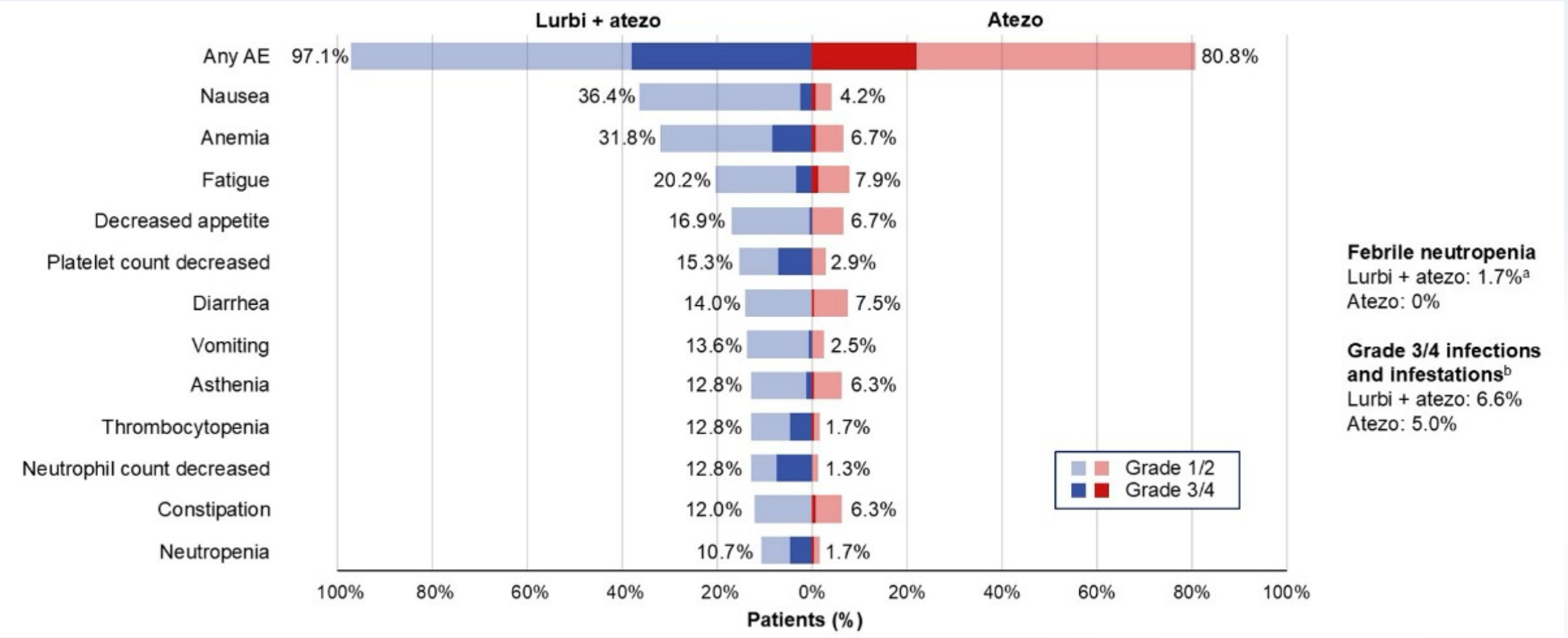
# Phase 3 IMforte: Safety Summary—Maintenance Phase

| 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%

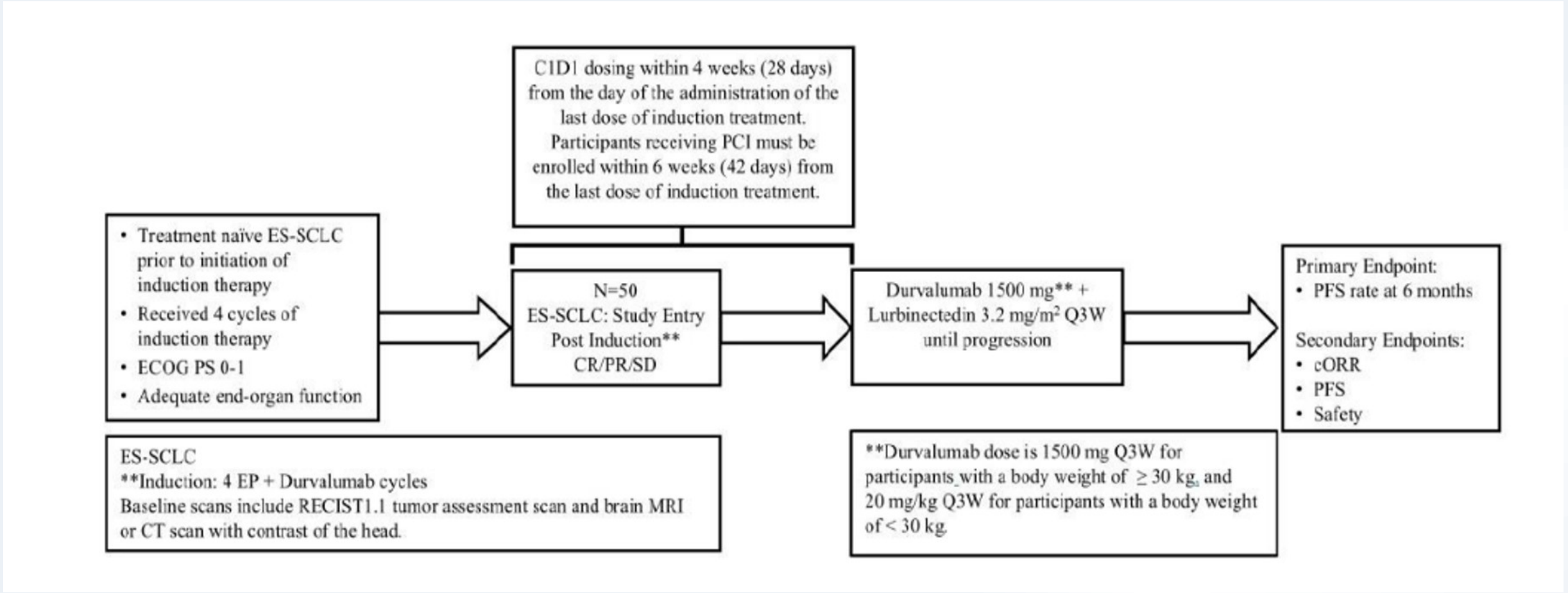



**Febrile neutropenia**
Lurbi + atezo: 1.7%[a]
Atezo: 0%

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

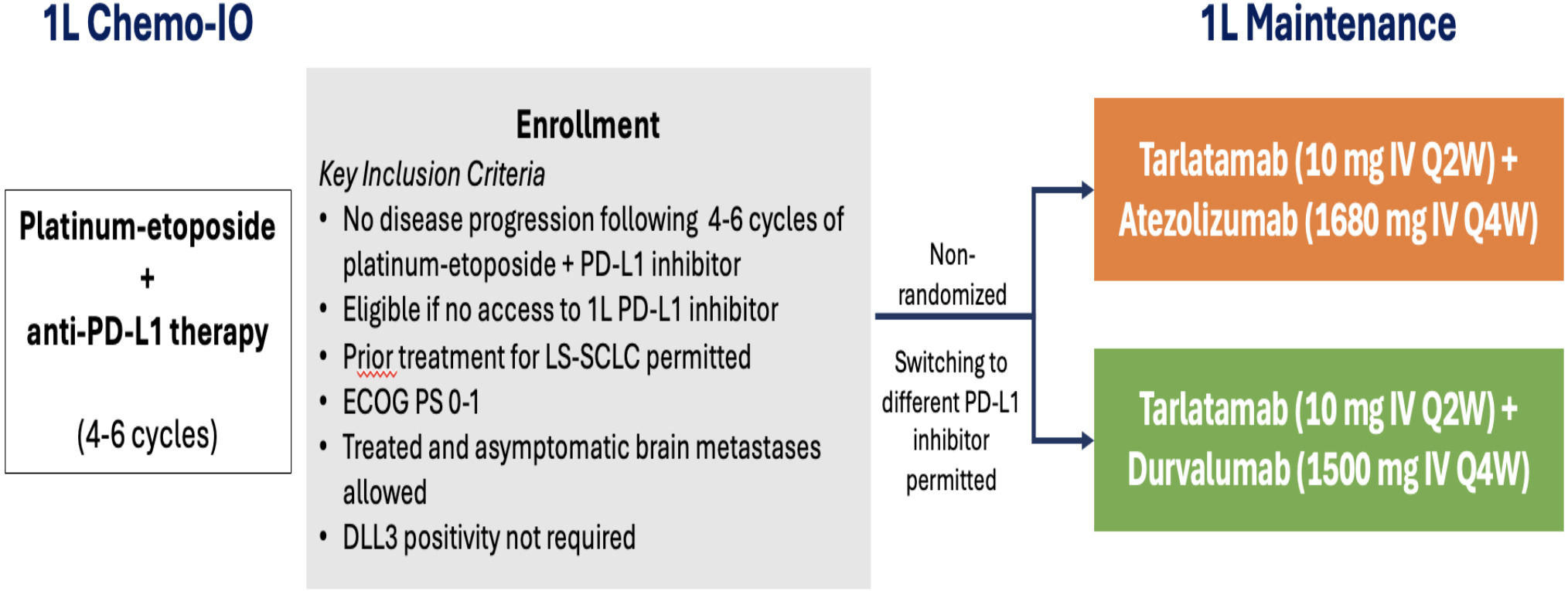
Paz-Ares et al. ASCO 2025

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



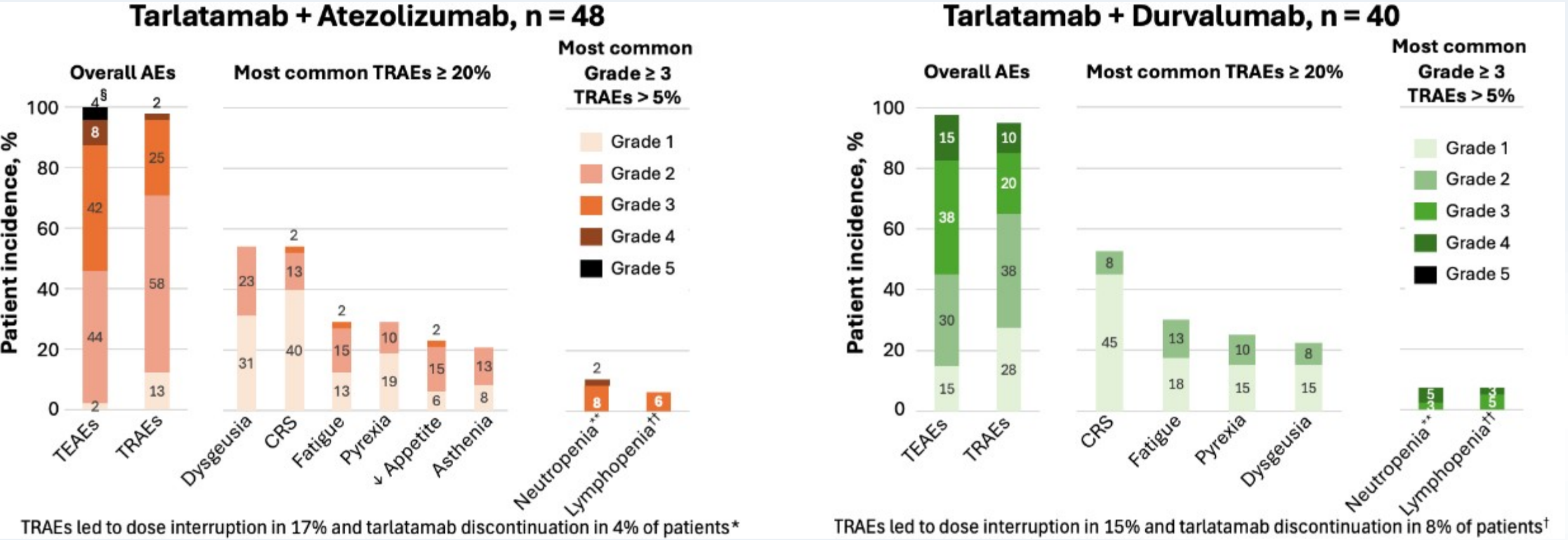

Leal T et al. WCLC 2026

# 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)

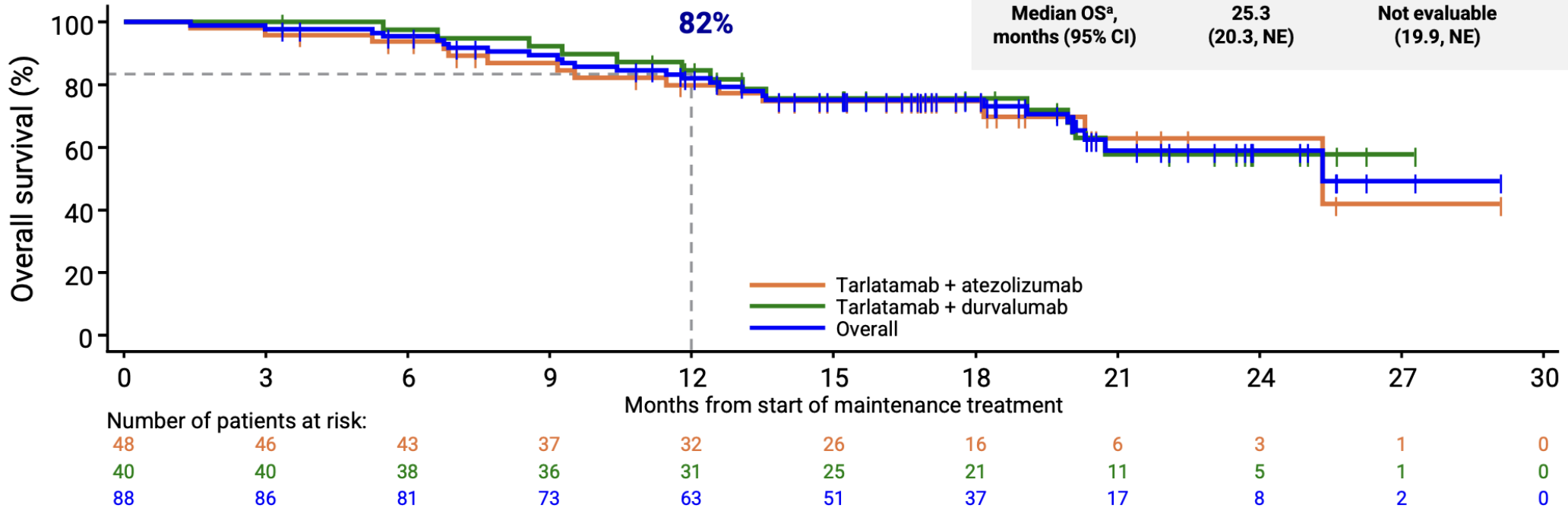
# DeLLphi-303: Safety




- 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) |

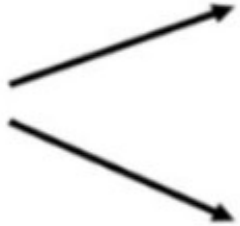



**With a median follow-up time of 18.4 months, tarlatamab with anti-PD-L1 as 1L maintenance therapy led to a median OS of 25.3 months (95% CI, 20.3, NE).**

# 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)

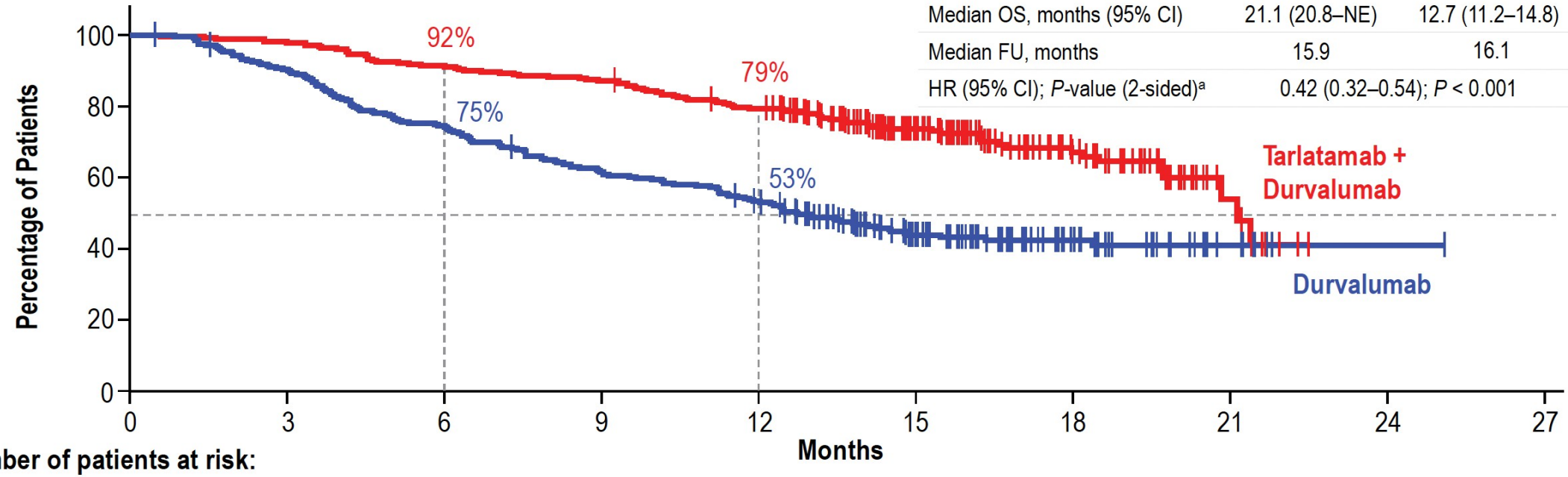
- Primary endpoint: Overall Survival
- Secondary endpoints: PFS, ORR, DCR, DoR, TTP, safety, QoL

NCT06211036

# Tarlatamab plus durvalumab significantly improved overall survival versus durvalumab alone as first-line maintenance therapy

DeLLphi 305

| | Tarlatamab + Durvalumab (n = 282) | Durvalumab (n = 281) |
|---|---|---|
| Median OS, months (95% CI) | 21.1 (20.8–NE) | 12.7 (11.2–14.8) |
| Median FU, months | 15.9 | 16.1 |
| HR (95% CI); *P*-value (2-sided)[a] | 0.42 (0.32–0.54); $P < 0.001$ | |




**Number of patients at risk:**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Tarlatamab + Durvalumab | 282 | 276 | 258 | 246 | 222 | 132 | 55 | 9 | 0 |
| Durvalumab | 281 | 252 | 208 | 171 | 146 | 81 | 33 | 8 | 1 | 0 |

Data cut-off date: 7 JUL 2026.

At the time of data cut-off, 87 events had occurred in the tarlatamab-durvalumab arm, and 156 events had occurred in the durvalumab arm.

[a]*P* value was calculated using a stratified log-rank test.

CI, confidence interval; FU, follow-up; HR, hazard ratio; NE, not estimable; OS, overall survival.

**Jacob Sands, MD | Tarlatamab plus durvalumab as 1L M therapy in ES-SCLC: primary analysis from DeLLphi-305 phase 3 study**



Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

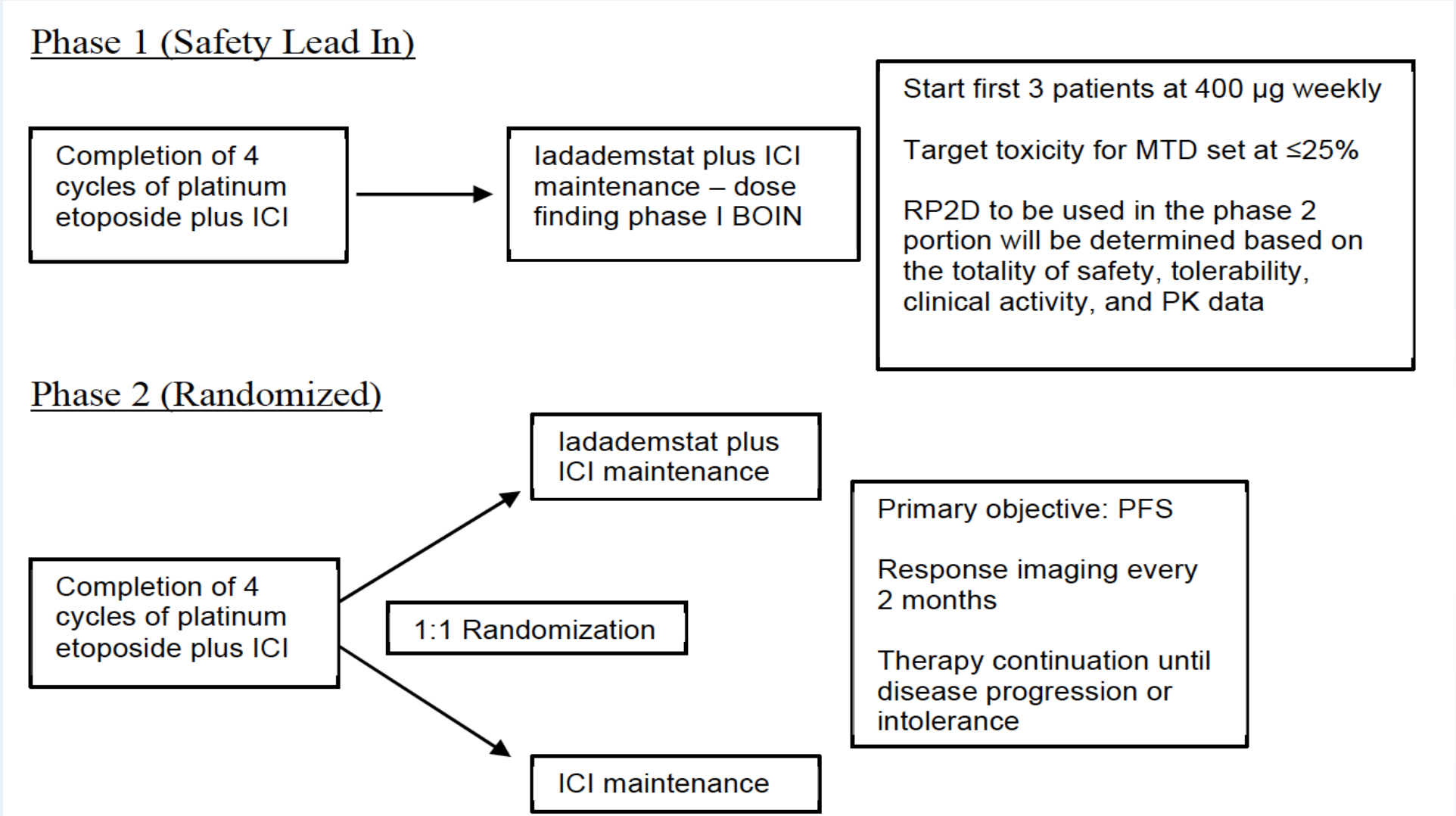
MADRID 2026 ESMO congress

20th ANNUAL ATLANTA LUNG CANCER SYMPOSIUM

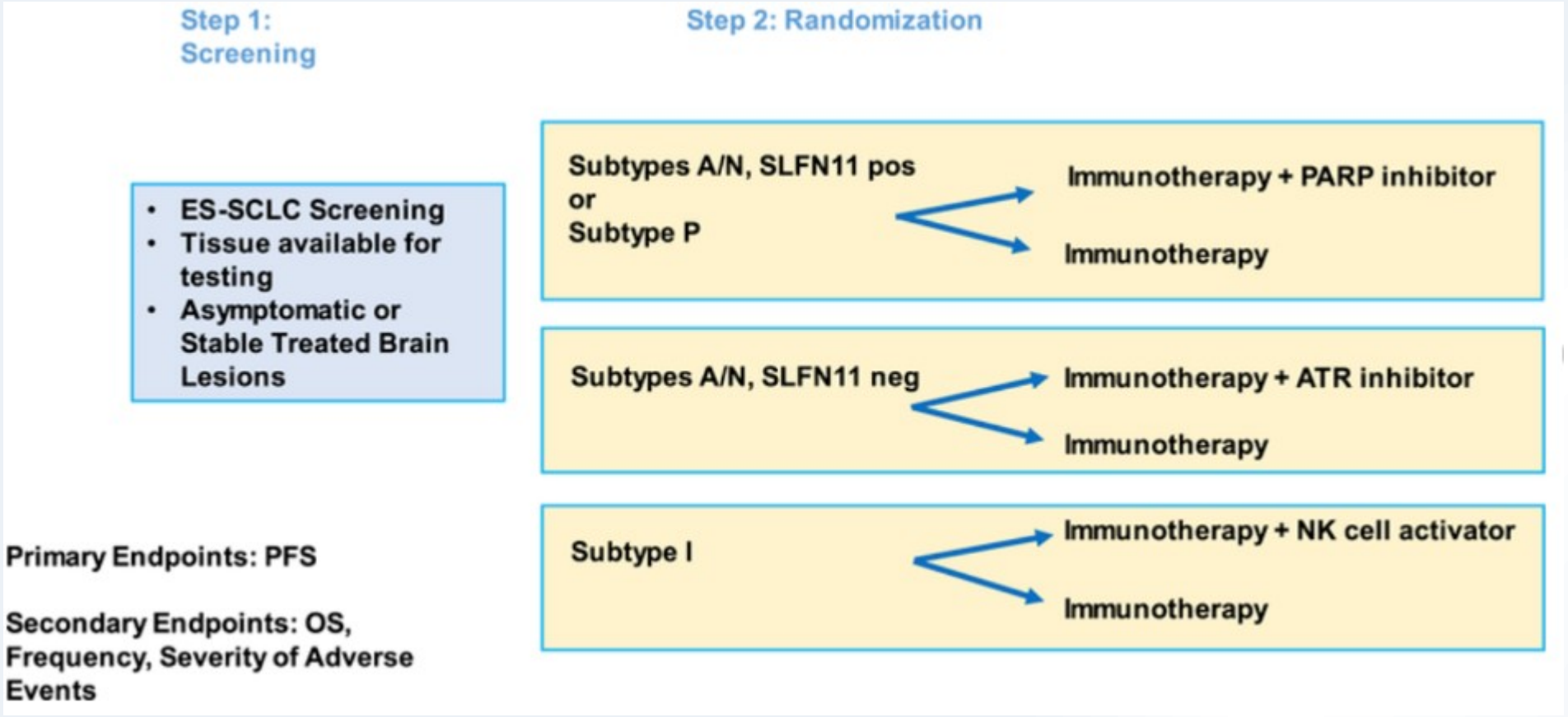
Partners for Advancing Clinical Education

Bio Ascend

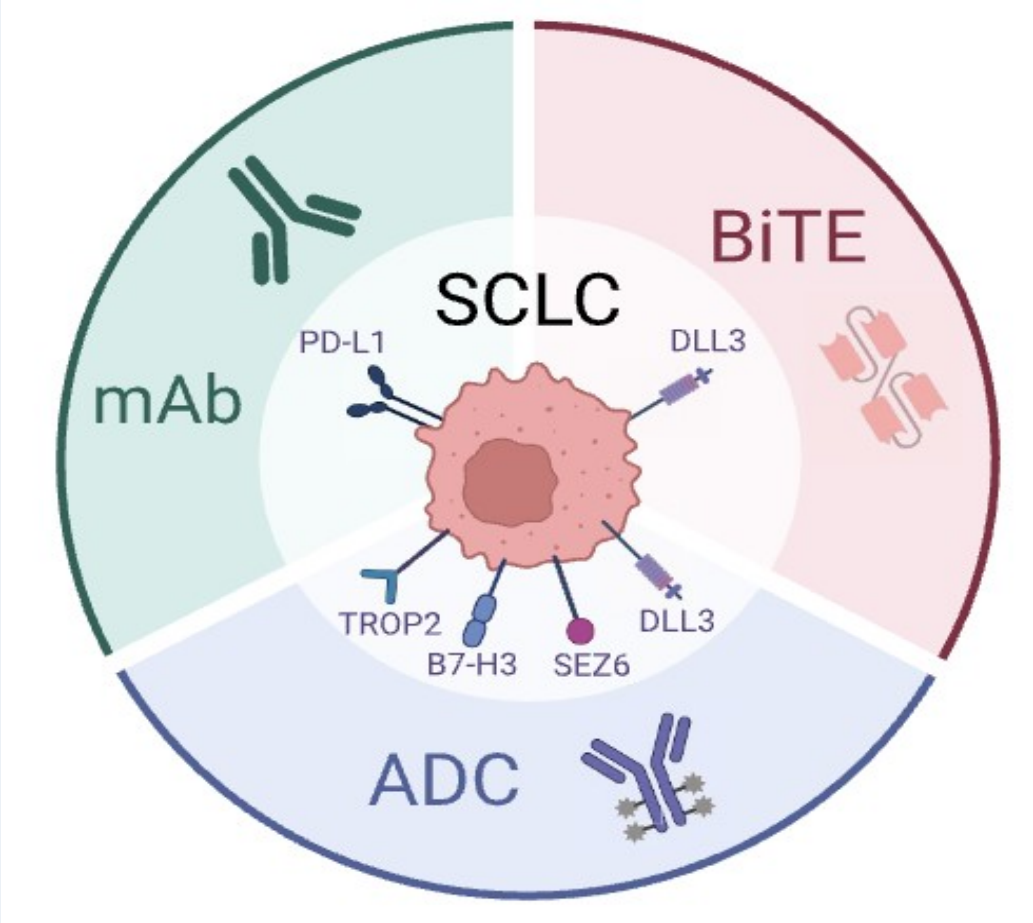
# Phase I Dose Finding and Phase II Randomized Trial of Iadademstat Combined with Immune Checkpoint Inhibition Maintenance After Initial Chemoimmunotherapy in Patients with ES-SCLC (NCT06287775)



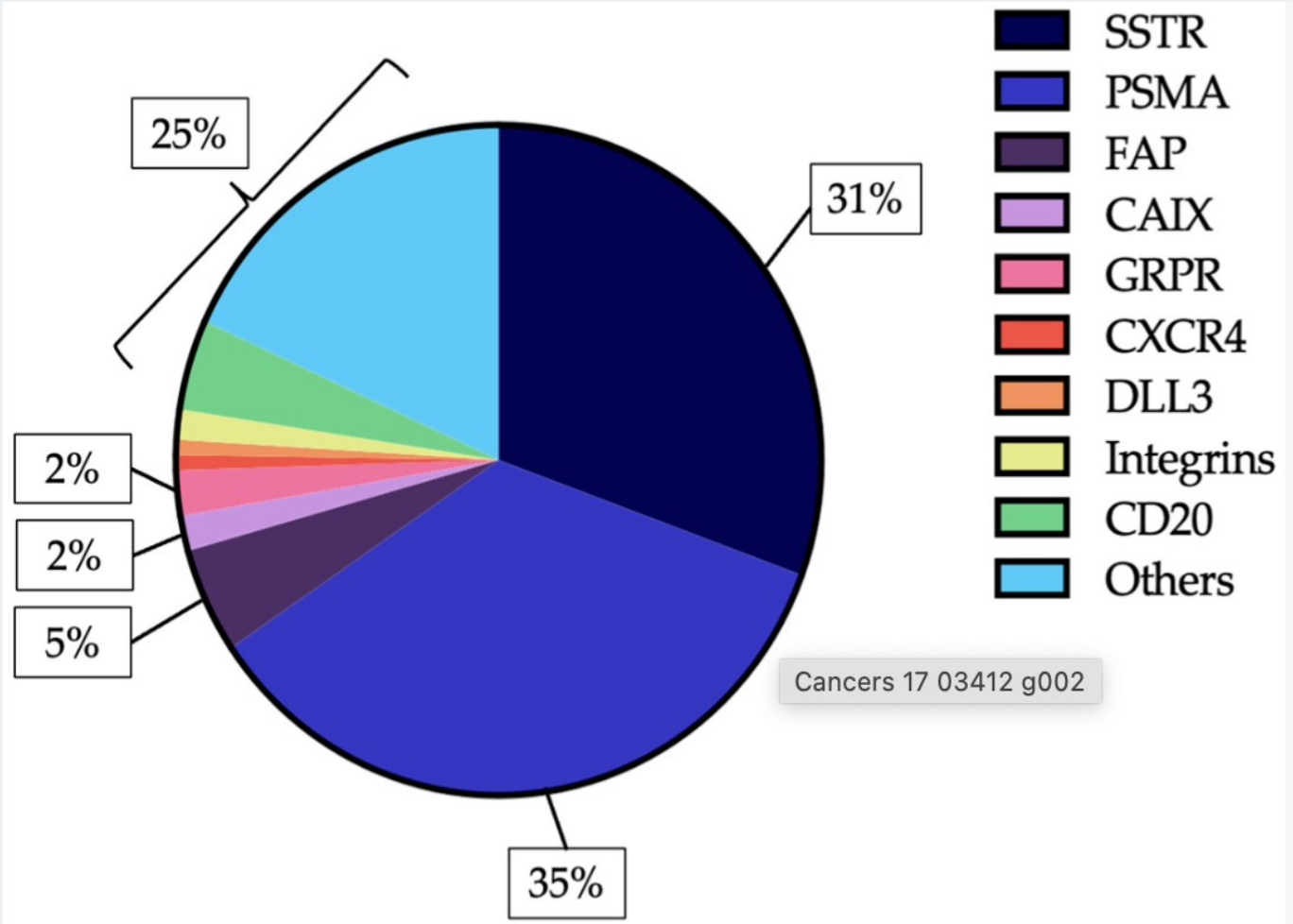
# S2409-PRISM: A Multicohort PRecIsion SCLC Subtype Maintenance Phase II Trial of Durvalumab vs Biomarker-Directed Novel Agents in Combination With Durvalumab



# Future Strategies




## Radioligand therapy in SCLC




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

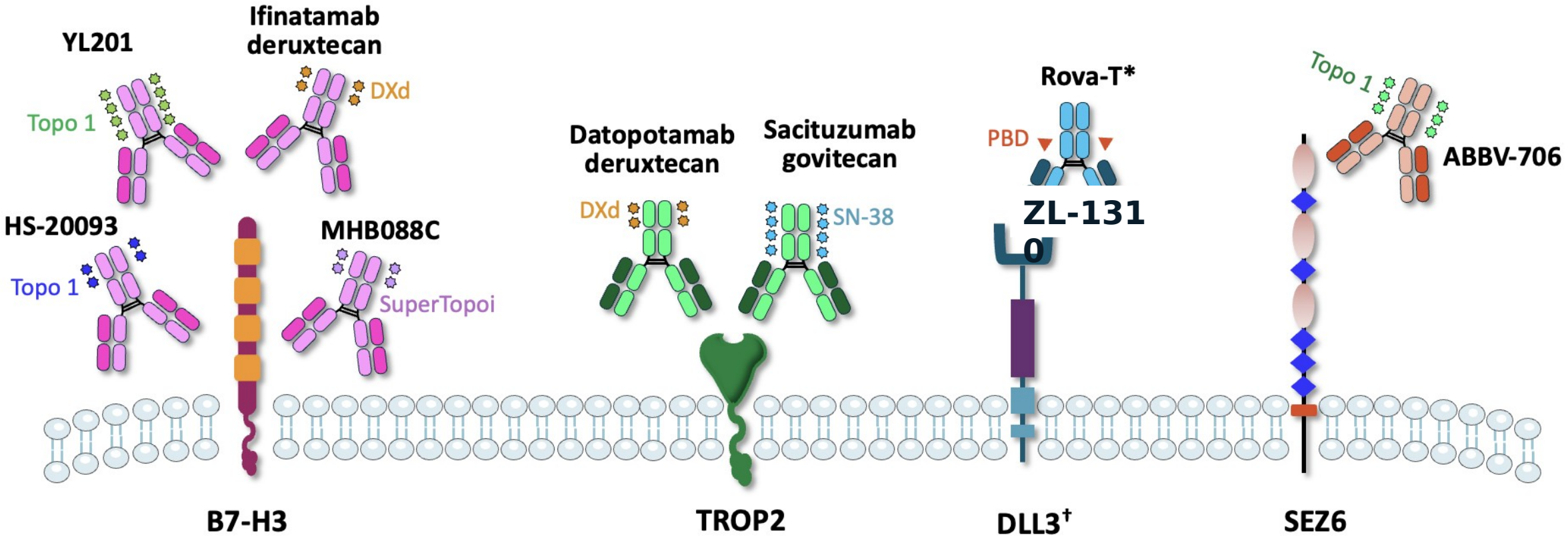
# DLL3-targeting bispecifics/trispecifics in clinical development

| 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

*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

**Part 1: Dose optimization Extension**

R 1:1

**Arm 1: I-DXd 8 mg/kg Q3W** n=46

**Arm 2: I-DXd 12 mg/kg Q3W** n=42

**Part 2:**

**I-DXd 12 mg/kg Q3W** n=95

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

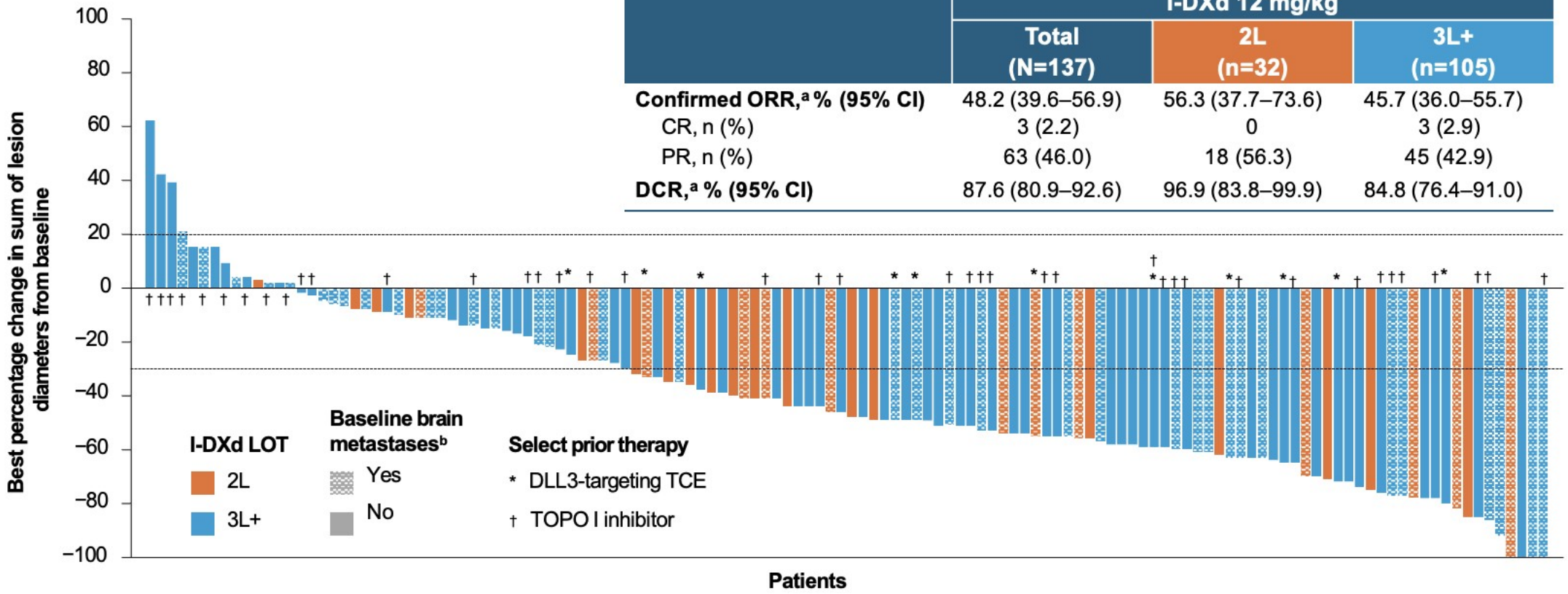
**Exploratory analysis**

- Intracranial ORR by BICR[d]

Ahn MJ, et al. WCLC 2025. Abstract OA06.03.

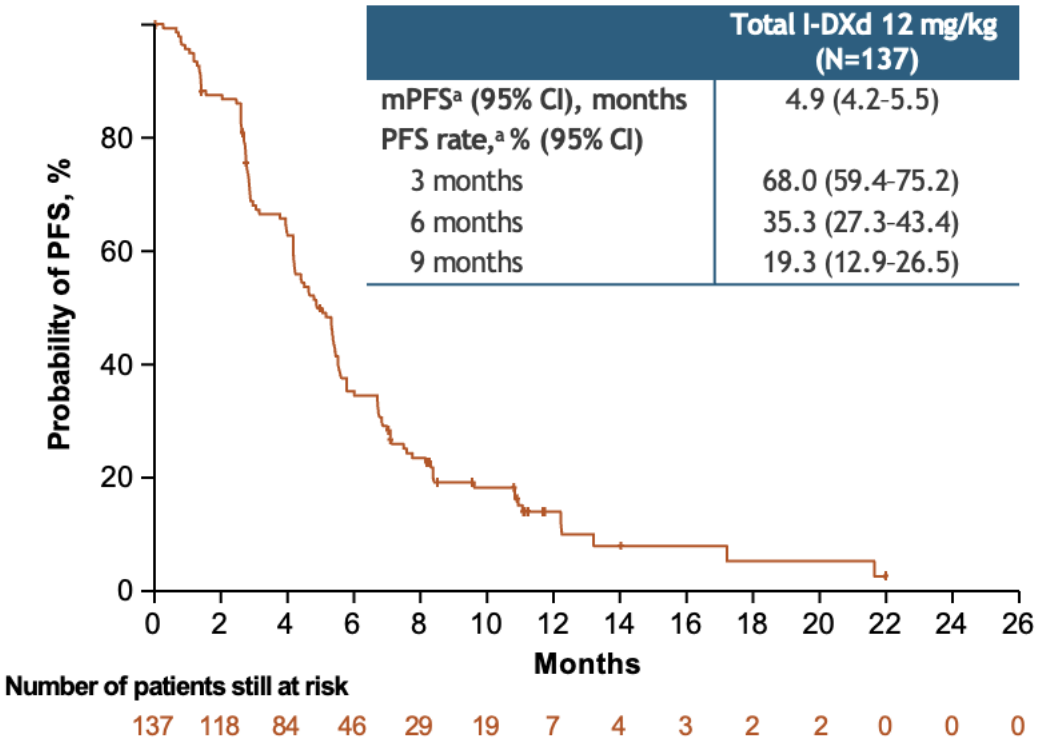
# IDEATE-Lung-1: ORR

| | 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) |

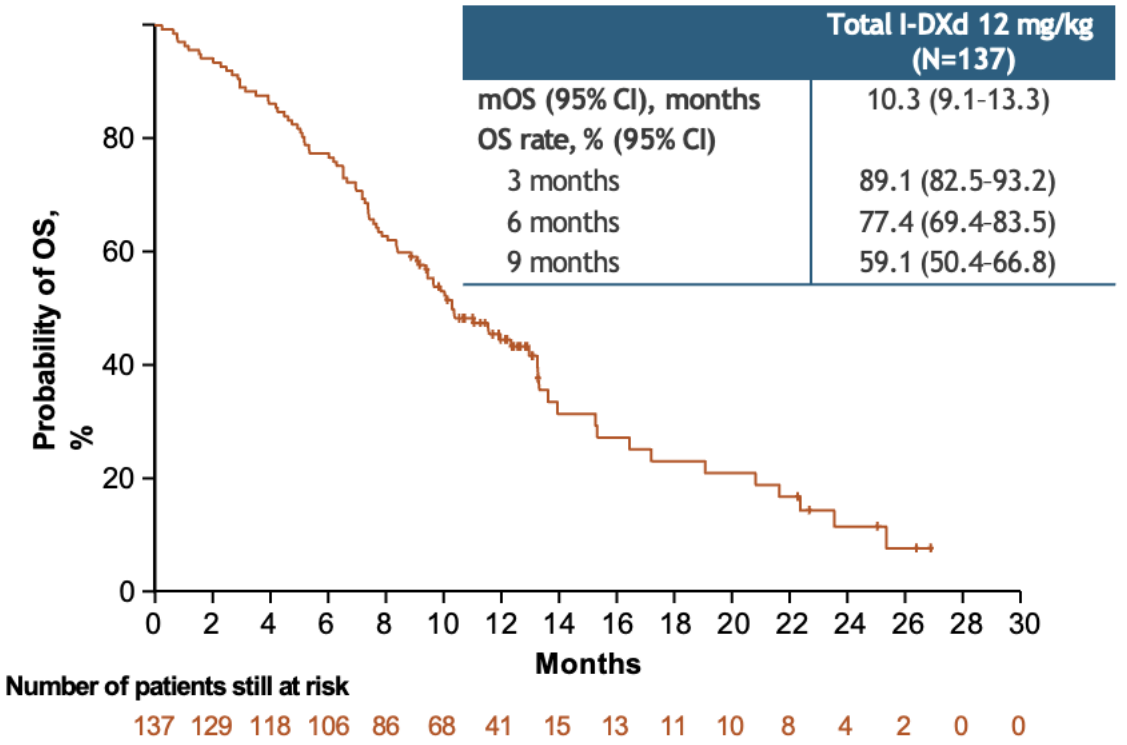



Ahn MJ, et al. WCLC 2025. Abstract OA06.03. Rudin CM, et al. *J Clin Oncol*. Published online October 14, 2025. doi:10.1200/JCO-25-02142.

# 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)

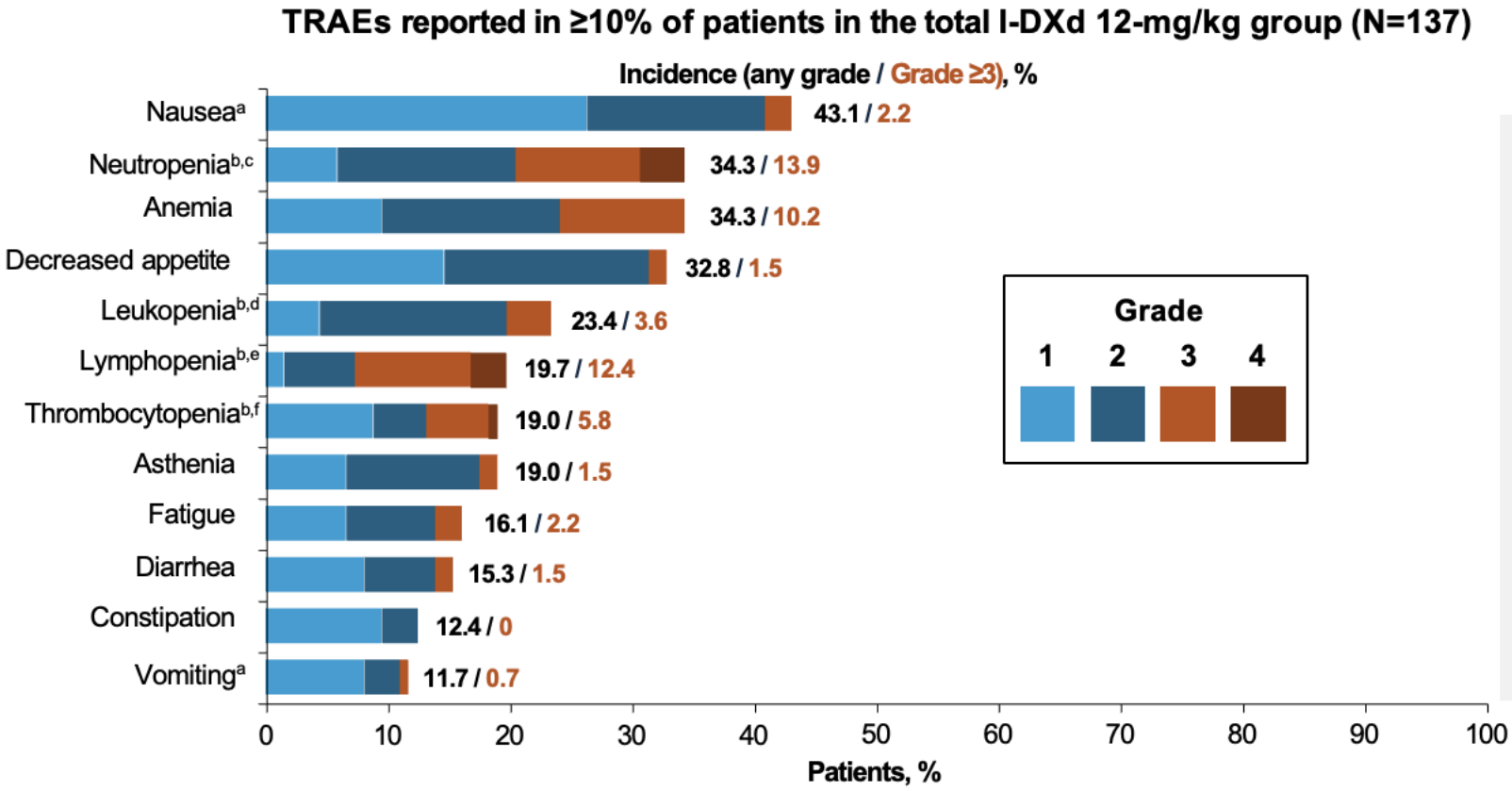
Ahn MJ, et al. WCLC 2025. Abstract OA06.03. Rudin CM, et al. *J Clin Oncol*. Published online October 14, 2025. doi:10.1200/JCO-25-02142.

# 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



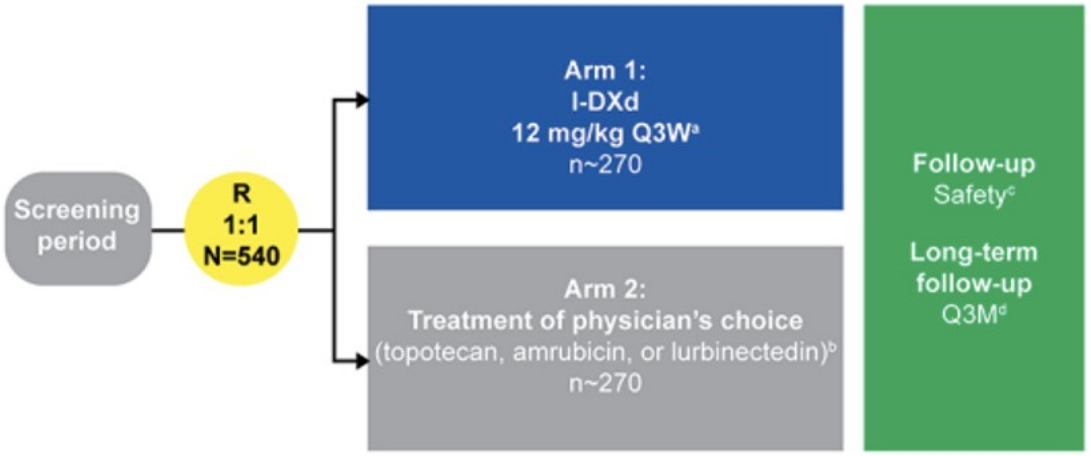

- Among the most common TRAEs, the majority were Grade 1 or 2
- Adjudicated treatment-related ILD/pneumonitis was reported in 17 (12.4%) patients:
  - Grade 1 or 2, n=11 (8.0%)
  - Grade 3, n=4 (2.9%)
  - Grade 5, n=2 (1.5%)[g]
- No ILD events were pending adjudication at data cutoff

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



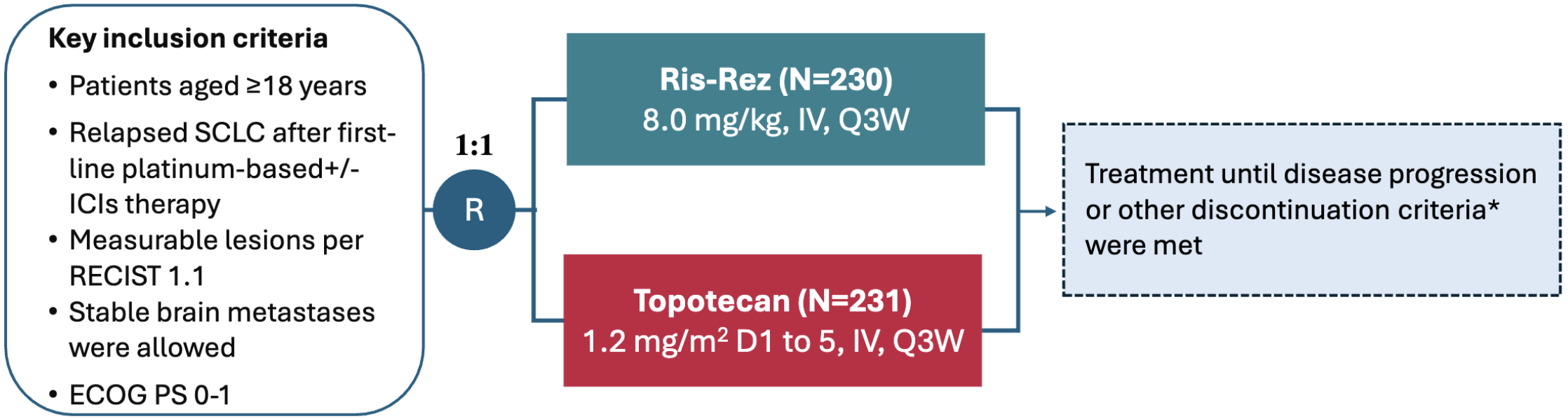

**Stratification**

- 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.

# **ARTEMIS-008:** A multi-center, open-label, randomized, controlled phase 3 (NCT06498479)




**Stratification:**

- Chemo-free interval (<90 days or ≥90 days)
- Baseline brain metastases (yes or no)
- Disease stage at study entry (LS or ES)

- **Primary endpoint**: OS
- **Secondary endpoints:** PFS, ORR, DCR, DoR by BICR and investigator; safety

**OS IA was pre-planned at 192 events (75% information fraction of the 256 OS events at the final analysis)**

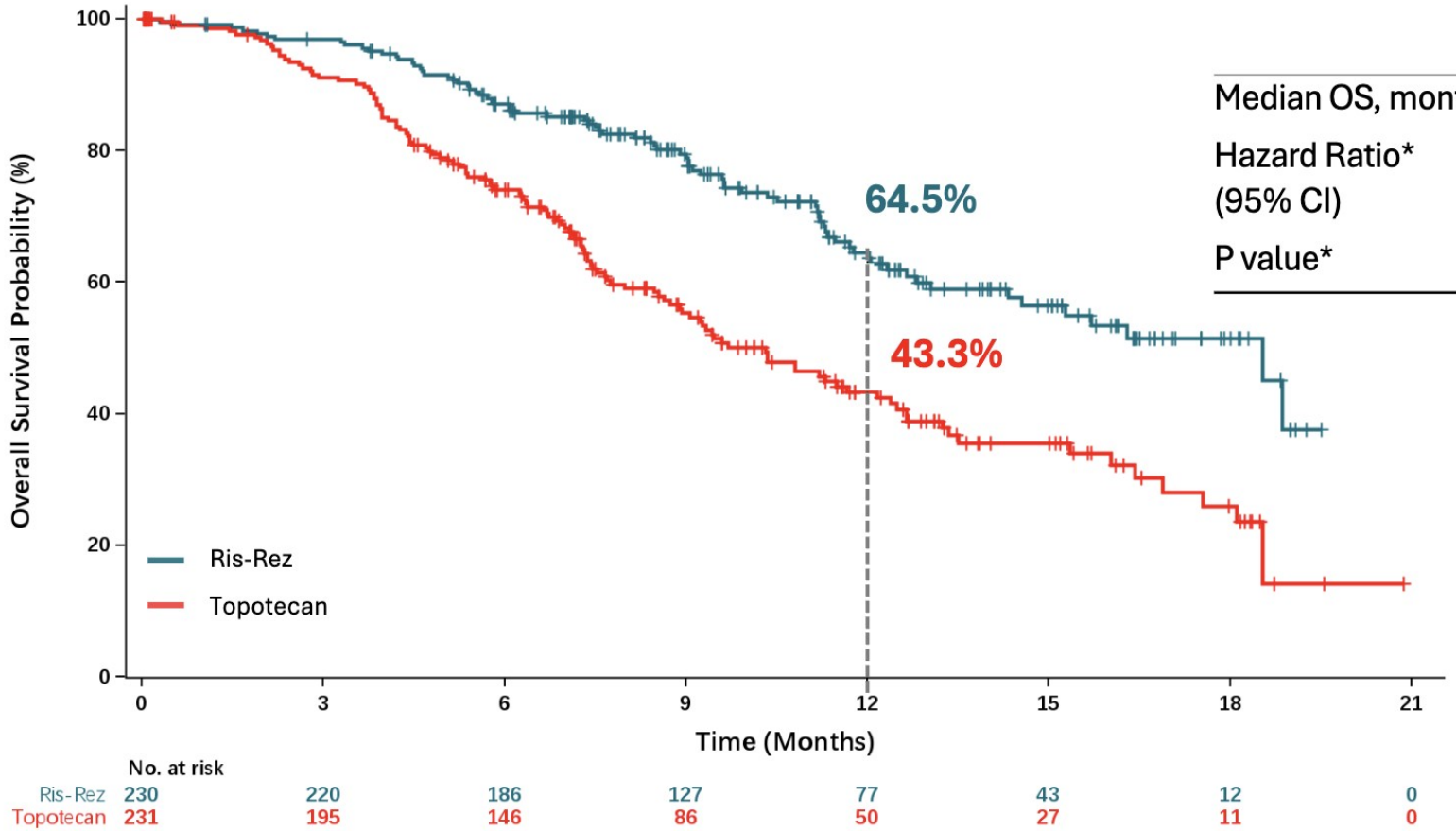
Data cut-off (DCO) date: June 6, 2026

*Including adverse events, the decision of the investigator or sponsor, participant withdrawal of consent, death, loss to follow up, pregnancy, among others.

Wang et al. WCLC 2026

# Primary Endpoint: OS

- At this IA (DCO June 6, 2026), there're 77 (33.5%) OS events in Ris-Rez arm and 121(52.4%) in Topotecan arm.
- With a median follow-up of 12.2 months, Ris-Rez demonstrated statistically significant and clinical meaningful improvement in OS.




| | Ris-Rez N=230 | Topotecan N=231 |
|---|---|---|
| Median OS, months | **18.5** | **10.3** |
| Hazard Ratio* (95% CI) | **0.46** (0.35, 0.62) | |
| P value* | **<0.0001** | |

*Hazard ratio and P value were estimated using a Cox proportional hazards model and Log-rank test, stratified by baseline brain metastasis status, CTFI, and VALG stage at study entry.

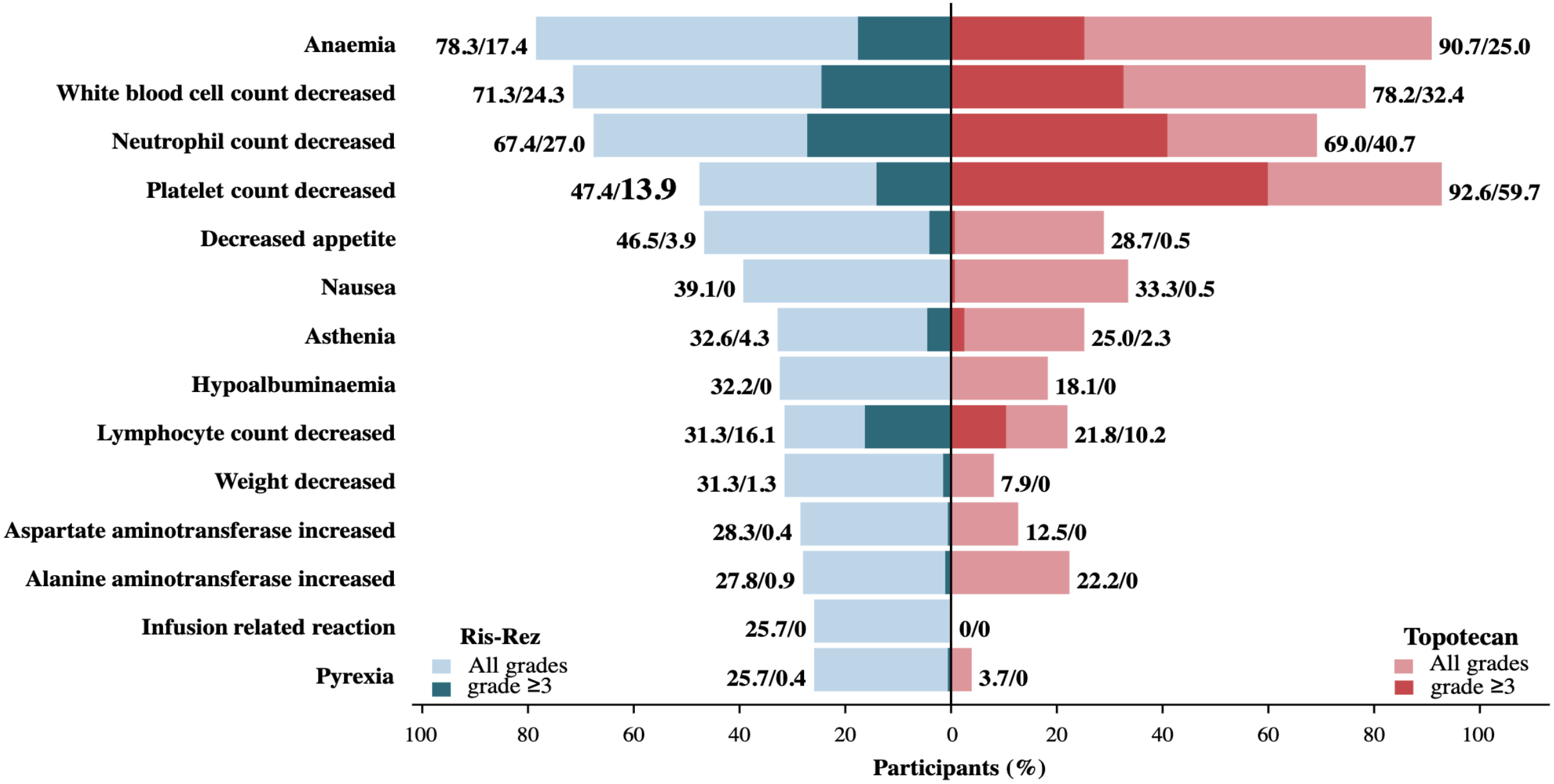
# Safety Summary

- Median exposure duration was 6.9 months for Ris-Rez and 2.8 months for topotecan.
- Ris-Rez demonstrated a favorable safety profile with no new safety signals and no Grade 4/5 ILD events.

| | Ris-Rez (n= 230) | Topotecan (n= 216) |
|---|---|---|
| TRAEs, n (%) | 230 (100.0) | 216 (100.0) |
| Leading to dose delay | 88 (38.3) | 86 (39.8) |
| Leading to dose interruption | 26 (11.3) | 1 (0.5) |
| Leading to dose reduction | 47 (20.4) | 82 (38.0) |
| Leading to treatment discontinuation | 21 (9.1) | 9 (4.2) |
| Grade ≥3 | **140 (60.9)** | **169 (78.2)** |
| Serious TRAEs | 79 (34.3) | 81 (37.5) |
| Leading to death# | 3 (1.3) | 2 (0.9) |
| ILD events*, n (%) | 27 (11.7) | 4 (1.9) |
| Grade ≥3 | 9 (3.9) | 2 (0.9) |

#In Ris-Rez arm: pneumonia (n=1), septic shock (n=1), pneumocystis jirovecii pneumonia (n=1). In topotecan arm: septic shock and respiratory failure (n=1), myelosuppression (n=1)

# Most Common TRAEs (≥20% of patients) and Grade ≥3 TRAEs



# TAISHAN-302 Study Design

A multicenter, randomized, open-label, phase 3 study (NCT06612151)

**Key eligibility criteria:**

- Histologically or cytologically confirmed SCLC
- Progressed after 1 prior line of platinum-based therapy
- At least one measurable lesion per RECIST v1.1
- ECOG PS 0-1

Treatment until disease progression per RECIST v1.1 or intolerable toxicity. Crossover between arms is not permitted.

R 1:1

N=451

**Tam-Peli**
2.0 mg/kg, D1 Q3W, maximum dose of 200 mg

**Topotecan**
1.2 mg/m$^2$ , D1-5 Q3W*

**Primary endpoint:**
- OS

**Key secondary endpoints:**
- PFS by investigators
- ORR by investigators

**Other secondary endpoints:**
- DCR, DoR, TTR by investigators
- Safety, PK, and immunogenicity

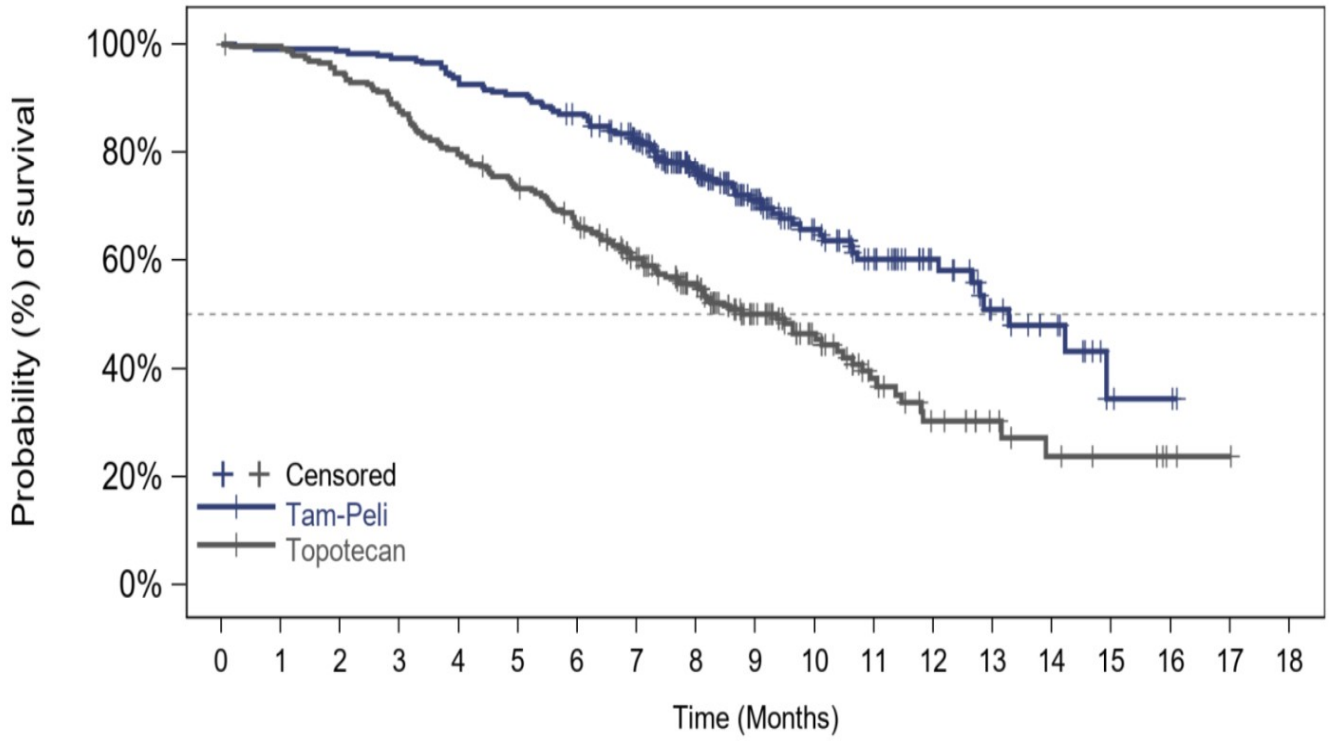
**Exploratory endpoints:**
- Intracranial efficacy

**Stratification factors**
- Disease status (local** or systemic disease)
- Brain metastasis (yes or no)
- Chemotherapy-free interval (<90 or ≥90 days)

Zhang et al. WCLC 2026

# TAISHAN-302: Efficacy

**Tam-Peli demonstrated statistically significant and clinically meaningful improvement in OS *vs.* topotecan, with a 54% reduction in rate of death**




| | Tam-Peli (N = 225) | Topotecan (N = 226) |
|---|---|---|
| OS events, n (%) | 76 (33.8) | 124 (54.9) |
| Median OS, months (95% CI) | **13.3** (12.1, NE) | **9.4** (7.7, 10.5) |

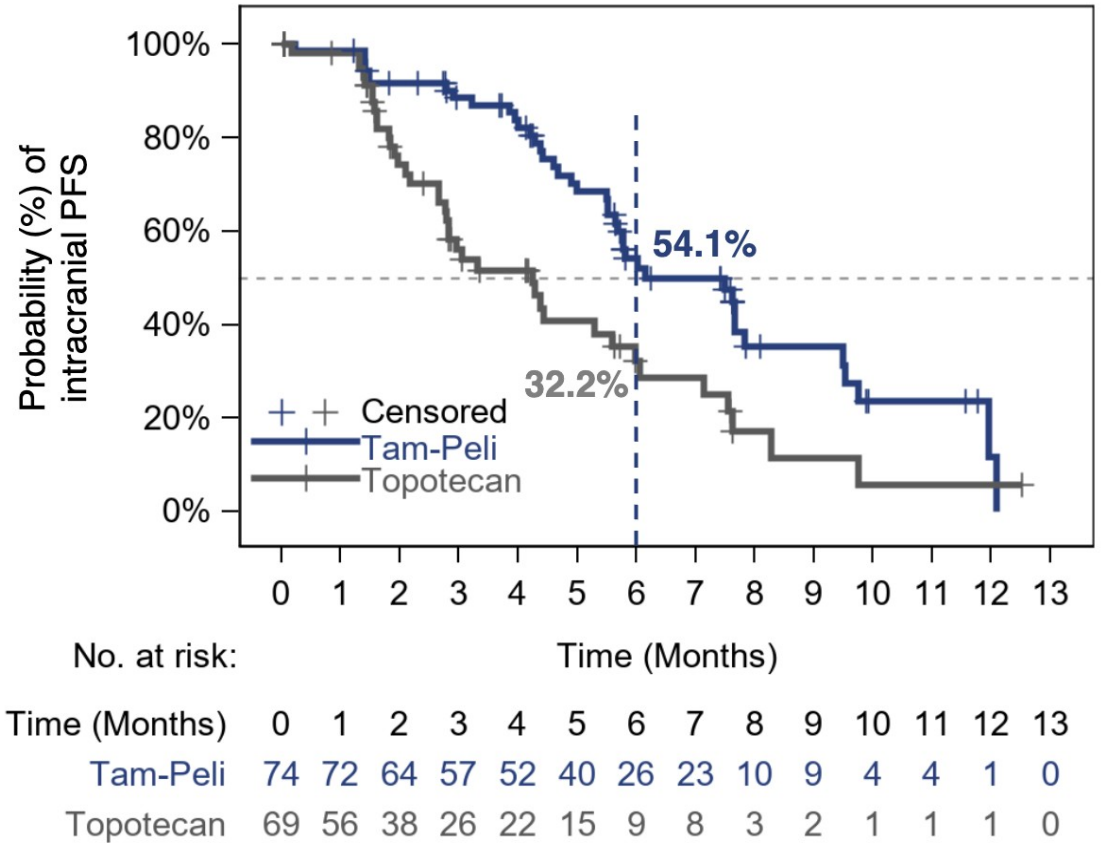
**HR 0.46 (95% CI: 0.35, 0.62)**

**P <0.0001***

Zhang et al. WCLC 2026

# TAISHAN-302: Efficacy

## Tam-Peli improved intracranial PFS, ORR and DCR *vs.* topotecan




| | | Tam-Peli (N = 74) | Topotecan (N = 69) |
|---|---|---|---|
| Intracranial PFS | Median, months (95% CI) | **6.1** (5.7, 7.8) | **4.2** (2.8, 5.6) |
| | HR (95% CI) P-value* | 0.43 (0.27, 0.68) 0.0002 | |
| Intracranial cORR | Percentage (95% CI) | **32.4** (22.0, 44.3) | **2.9** (0.4, 10.1) |
| | P-value* | <0.0001 | |
| Intracranial DCR | Percentage (95% CI) | **90.5** (81.5, 96.1) | **59.4** (46.9, 71.1) |
| | P-value* | <0.0001 | |

Intracranial efficacy was assessed by investigators as per modified RECIST version 1.1.
Data cut-off: May 20, 2026. * nominal P-value.
CI, confidence interval; cORR, confirmed objective response rate; DCR, disease control rate; HR, hazard ratio; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

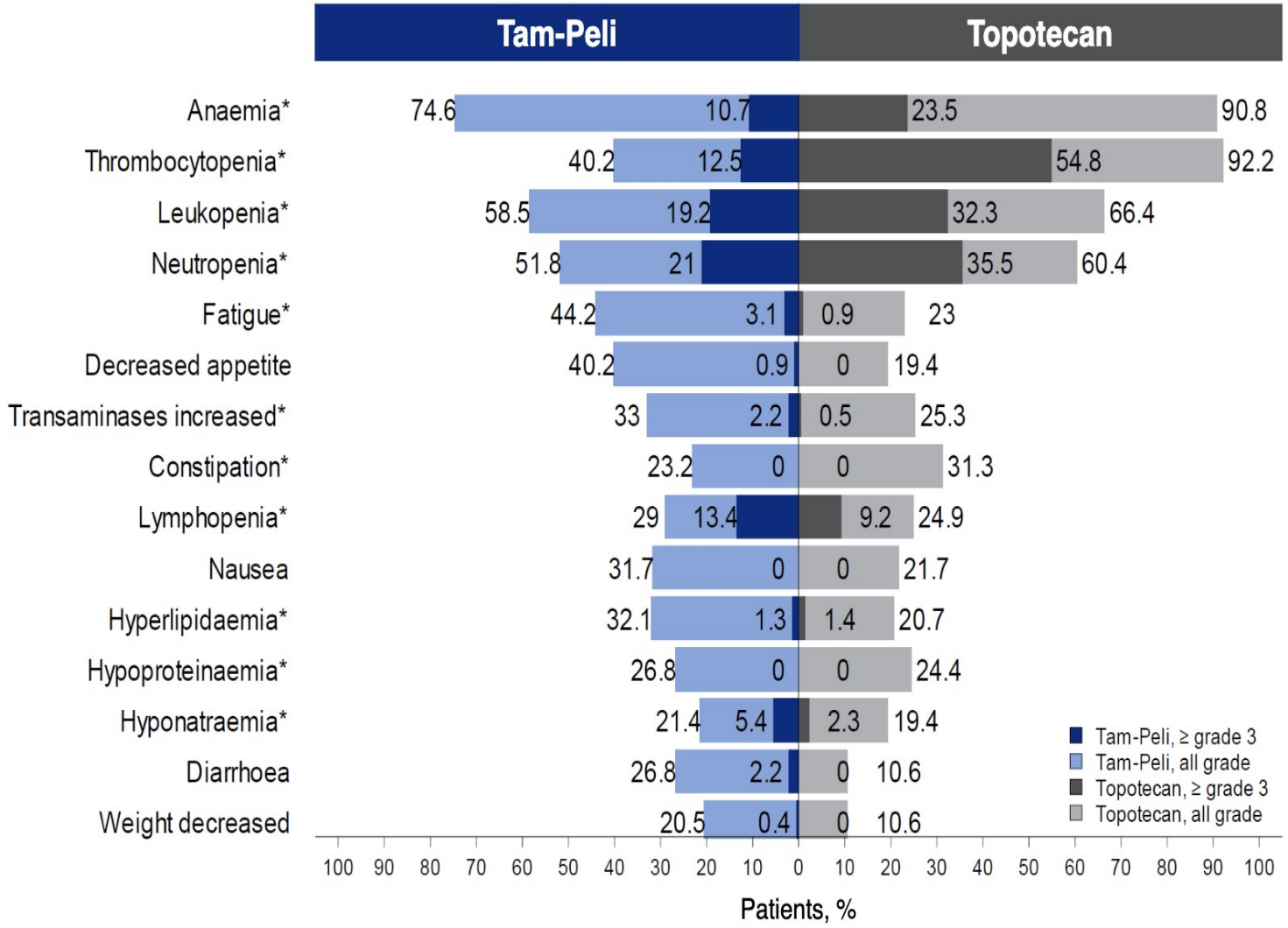
Zhang et al. WCLC 2026

# Safety Summary

| | Tam-Peli (N = 224) | Topotecan (N = 217) |
|---|---|---|
| Median duration of exposure, weeks (range) | 31.1 (3, 72.9) | 10.1 (3, 70.4) |
| TRAEs, n (%) | | |
| All grades | 221 (98.7) | 216 (99.5) |
| Grade ≥3 | **104 (46.4)** | **162 (74.7)** |
| Serious TRAEs | **58 (25.9)** | **79 (36.4)** |
| Leading to dose interruption | 78 (34.8) | 80 (36.9) |
| Leading to dose reduction | **58 (25.9)** | **80 (36.9)** |
| Leading to discontinuation | 13 (5.8) | 6 (2.8) |
| Leading to death | **0** | **1 (0.5)** |

- Fewer grade ≥3 TRAEs, serious TRAEs and TRAEs leading to dose reduction were observed with Tam-Peli compared with topotecan (46% vs 74% and 25% vs 36%).
- No treatment-related deaths were reported in the Tam-Peli arm.
- The incidences of all-grade TRAEs and dose interruptions were similar between arms.

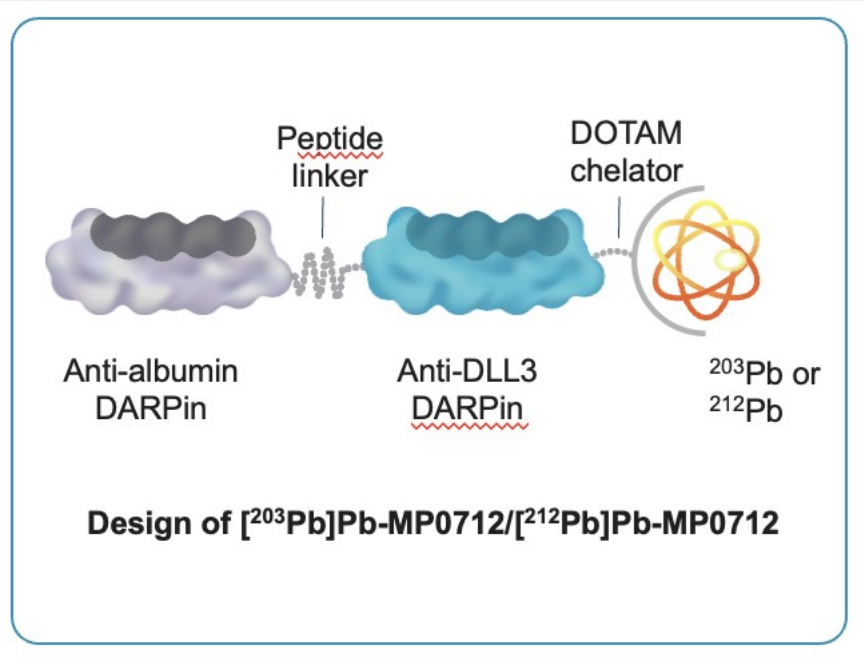
# TRAEs in ≥20% of Patients




- The most common grade ≥3 TRAEs were hematologic toxicities, with lower incidence observed in the Tam-Peli arm.
- Treatment-emergent ILD/pneumonitis events were observed at 4.9% in the Tam-Peli arm *vs.* 1.4% with topotecan; grade 3 events occurred at 0.9% in each arm, and no grade 4 or 5 events were reported.

# 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]

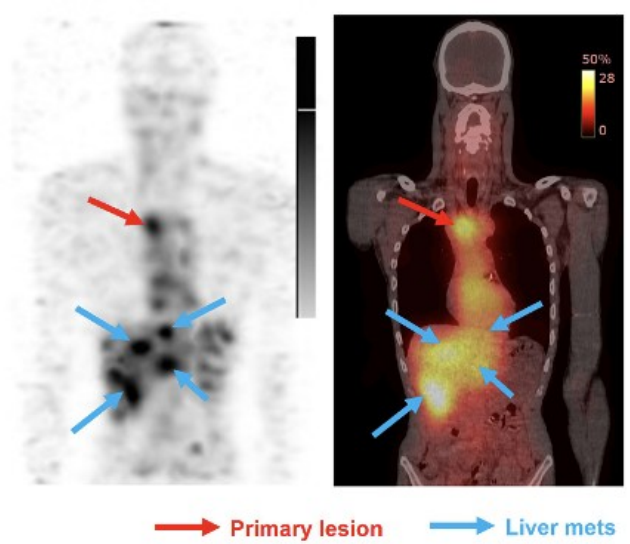


**Design of [$^{203}$Pb]Pb-MP0712/[$^{212}$Pb]Pb-MP0712**

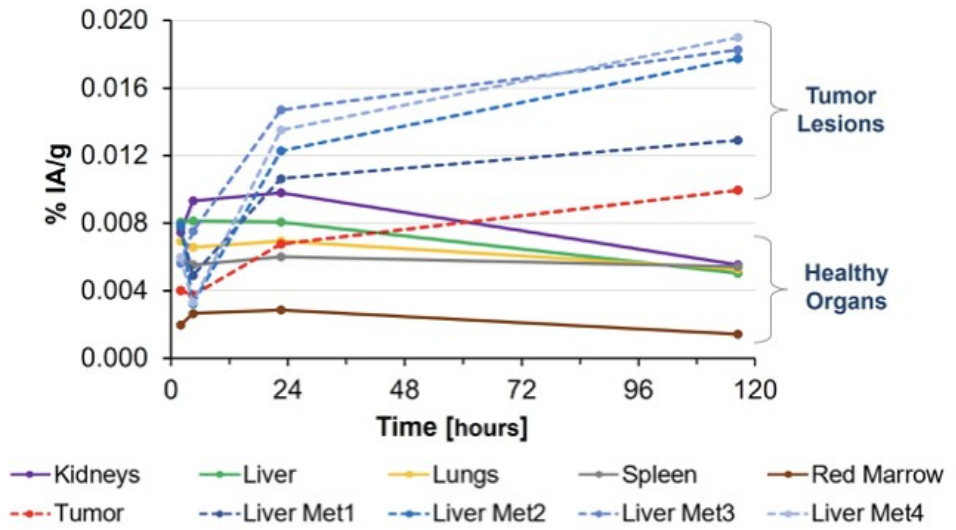
# MP0712 First-in-Human Imaging

- 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**



# 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)

# Take-Home Messages

- 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 will move into earlier lines of therapy.
- B7H3 ADCs are superior to chemotherapy in previously treated SCLC.



20th ANNUAL

ATLANTA

LUNG CANCER SYMPOSIUM

# Small Cell Lung Cancer: Expanding Options, More Hope

Ticiana Leal, MD

Partners for Advancing Clinical Education

Bio Ascend™