15th CONGRESS on Lung CANCER

MADRID

23&24 November 2023

#15CongressGECP

Fundación GECP lung cancer research

New hopes in relapse/progression SCLC

Noemí Reguart

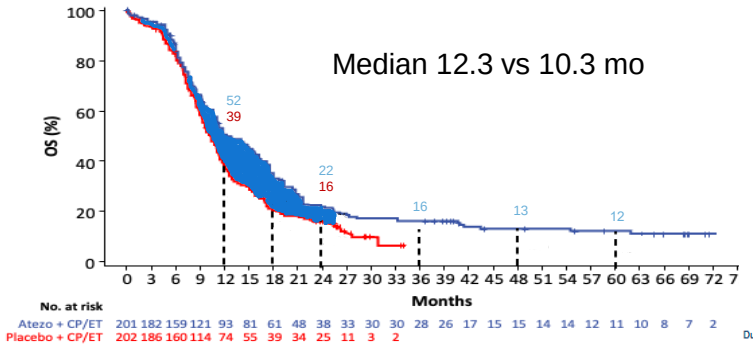
Hospital Clínic Barcelona

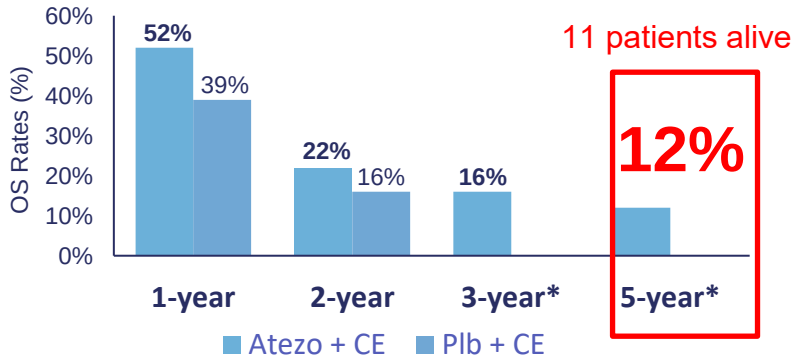
Friday, 24 November 2023

First Line anti-PD-(L)1 plus chemotherapy in ES-SCLC

IMpower133 and IMbrella A

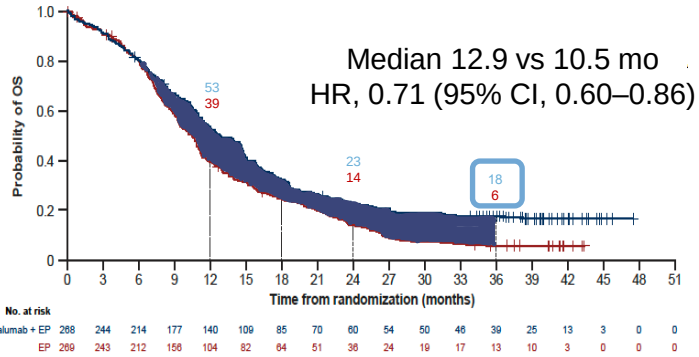
Atezolizumab + CP/ET vs CP/ET + Plb[1-2]

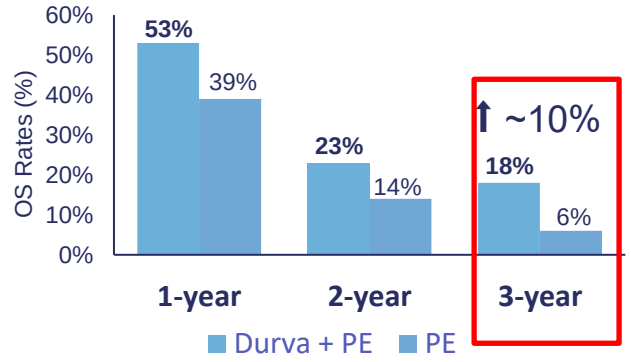




CASPIAN

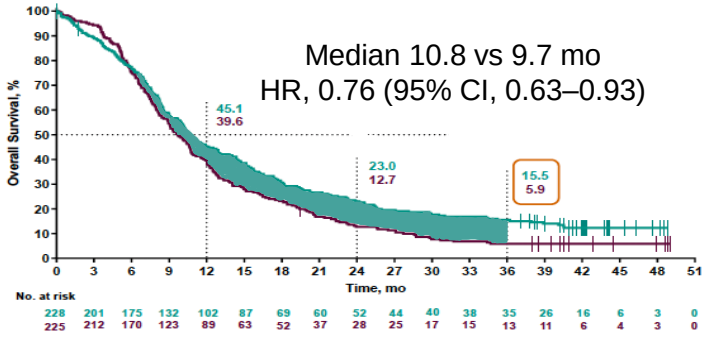
Durvalumab + P/ET vs P/ET[3-4]

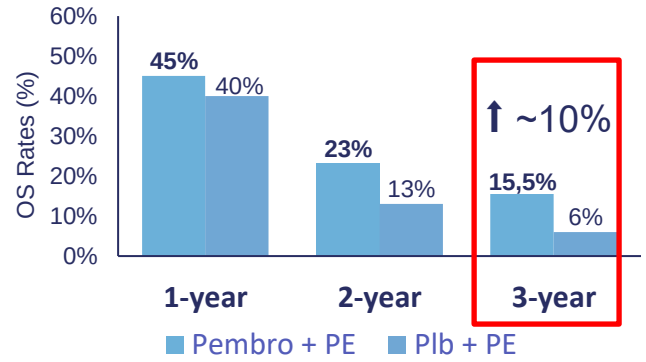




KEYNOTE-604

Pembrolizumab + P/ET vs P/ET + Plb[5-6]

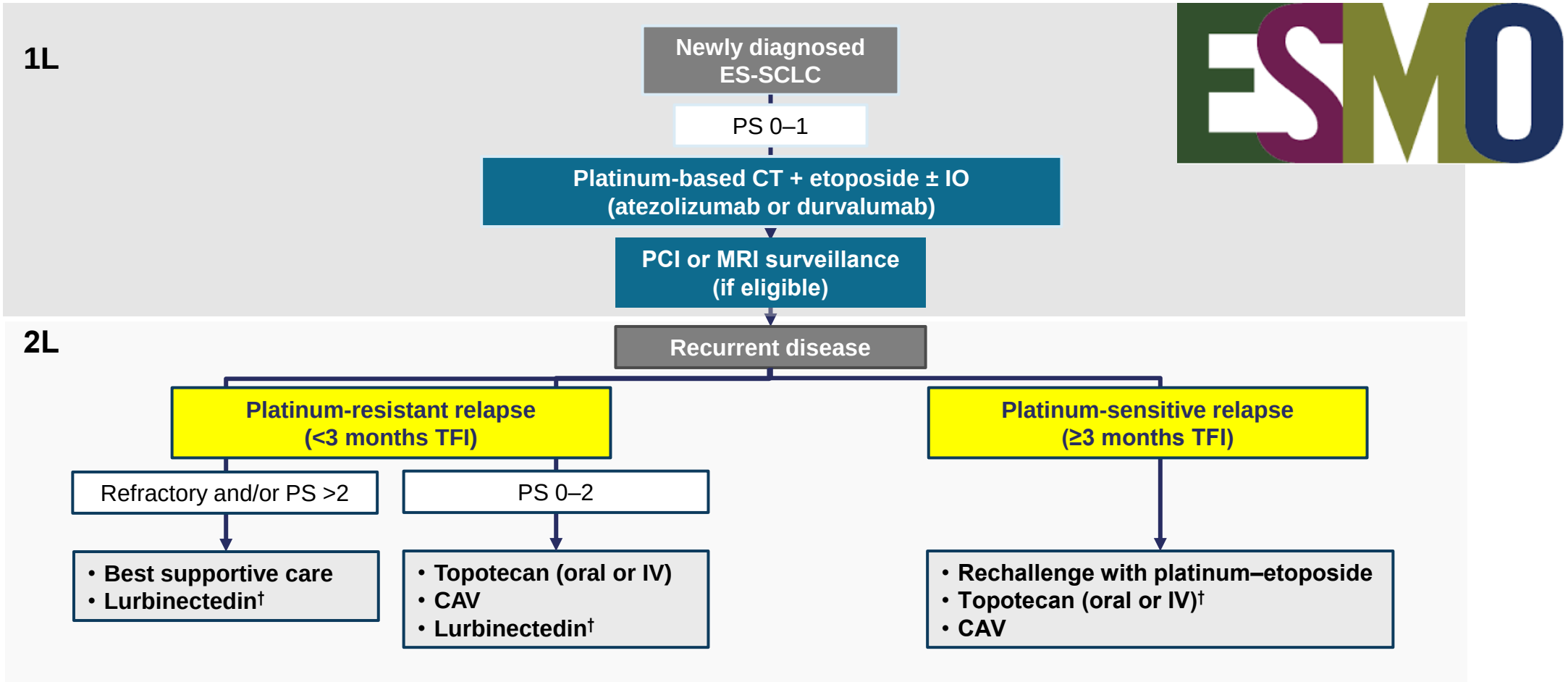




CP, carboplatin; ET, etoposide; P, platinum; Plb, placebo; NE, not estimable. * OS rates at 3-5 years were not estimable in the control arm as rollover to IMbrella A was not permitted.

1.- Horn L, et al. N Engl J Med 2018; 2.- Liu S, et al. OA01.04, WCLC 2023; 3.- Paz-Ares L, et al. Lancet 2019; 4.- Paz-Ares L, et al. ESMO Open 2022; 5.- Rudin CM, et al. J Clin Oncol 2020; 6.- Rudin CM, et al. WCLC 2022

Treatment algorithm for ES-SCLC: ESMO guidelines

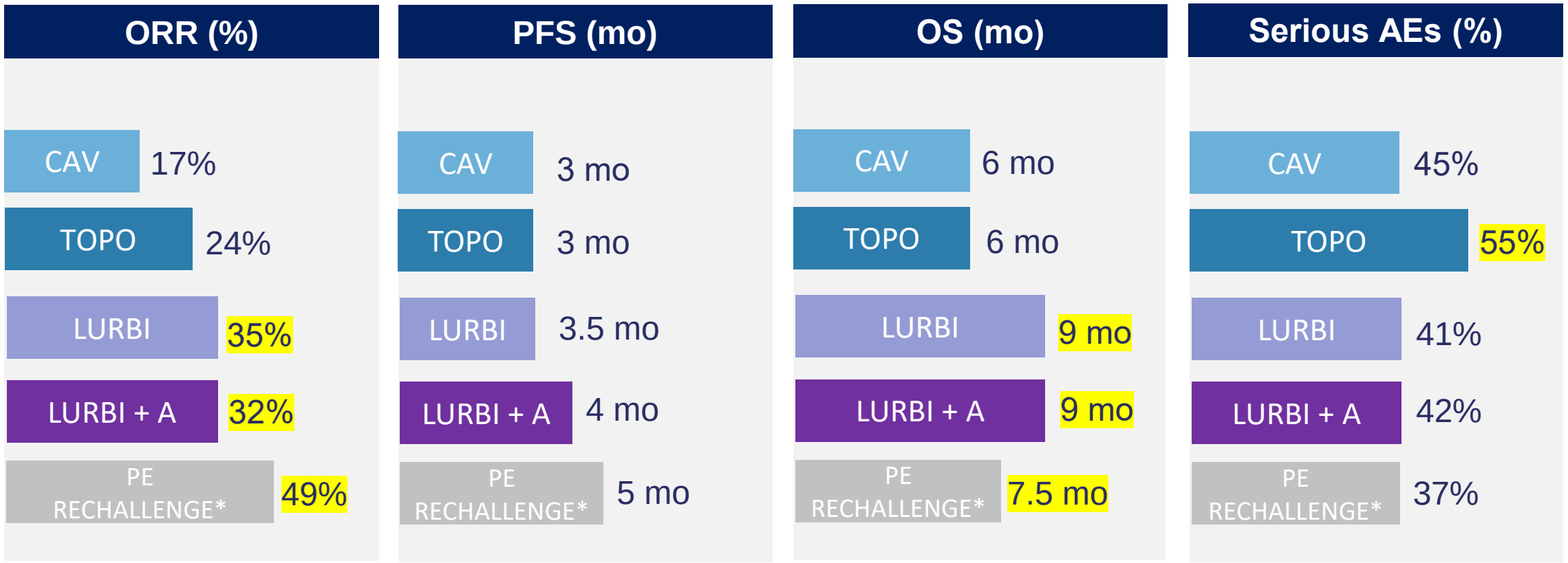


† Granted approval in the **USA** (June 2020), **Canada** (September 2021), **Australia** (September 2021), and the **UAE** (September 2021). Lurbinectedin is **not approved by the EMA** for treatment of SCLC, only given orphan designation by the EMA in Feb 2019.

1. Dingemans AC, et al. Ann Oncol 2021

*SCLC standard treatment algorithms may show regional differences; †Not indicated by the EMA for treatment in this setting.
CAV, cyclophosphamide, doxorubicin, vincristine; CT, chemotherapy; ESMO, European Society for Medical Oncology; IO, immunotherapy; IV, intravenous; PCI, prophylactic cranial irradiation; PS, performance status; TFI, treatment-free interval.

There Remains a Need for Improved Therapies in Relapsed SCLC



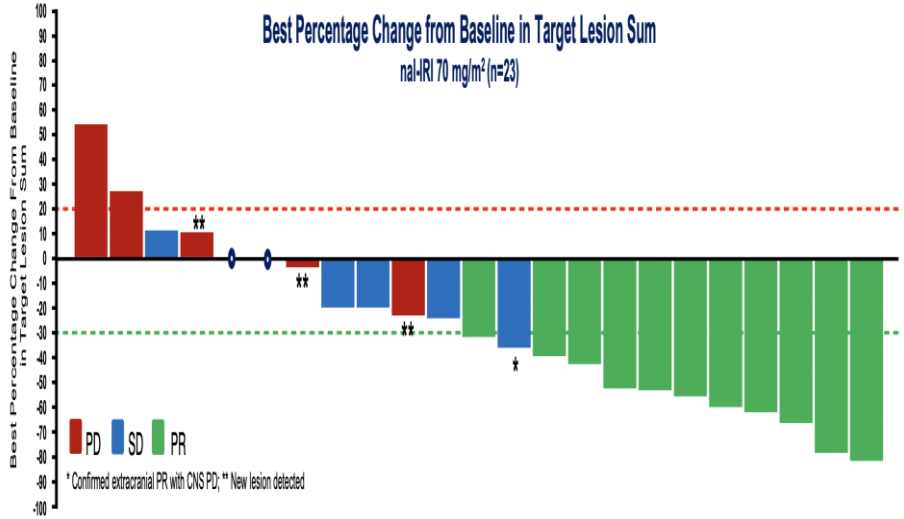
*CTFI ≥90 days

1.- von Powel J, et al. J Clin Oncol; 2.- Trigo, Lancet Oncol 2020; 3.- Ponce S et al. The Lancet 2022; 4.- Baize N, et al. Lancet Oncol 2020

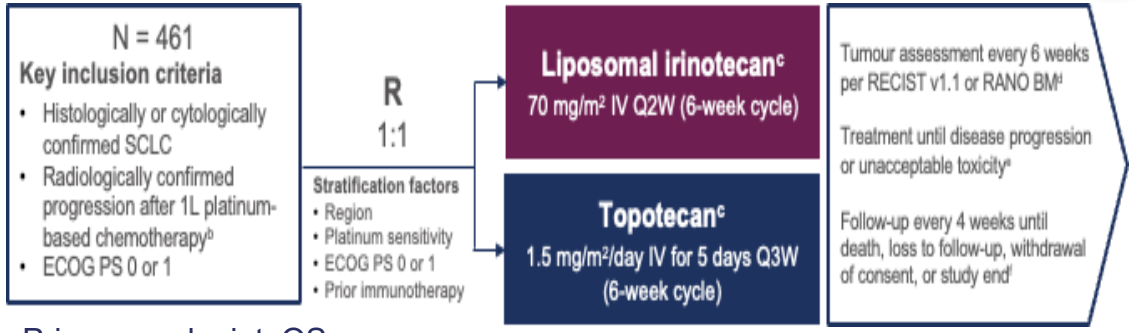
Some Failures: Liposomal Irinotecan (Nal-Iri)

RESILIENT part 1: phase 2 dose-exploration
Liposomal irinotecan 70 mg/m2 weekly1-2

- **ORR: 44%**
- Median DOR: 2.99 months
- Median PFS: 3.98 months

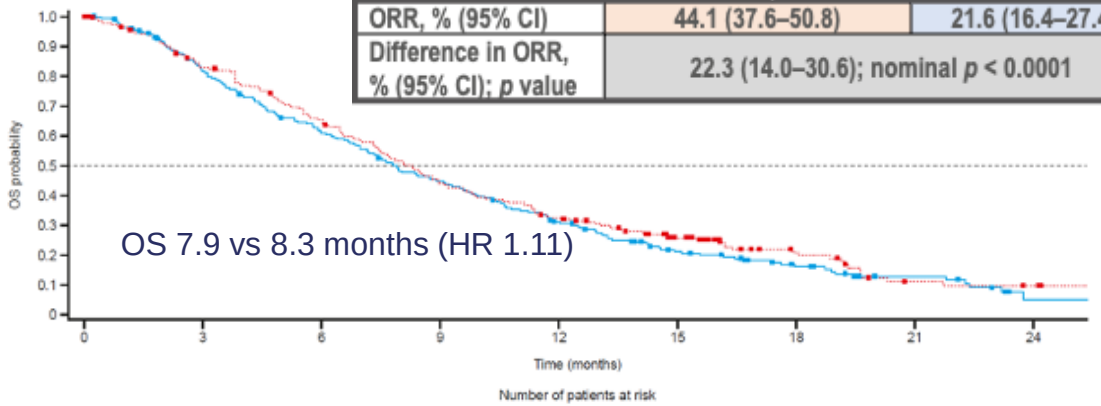


RESILIENT part 2: phase 3 (NCT03088813)
Liposomal irinotecan vs topotecan (n=480)3



Primary endpoint: OS

	Liposomal irinotecan (n = 229)	Topotecan (n = 232)
ORR, % (95% CI)	44.1 (37.6–50.8)	21.6 (16.4–27.4)
Difference in ORR, % (95% CI); *p* value	22.3 (14.0–30.6); nominal $p < 0.0001$	



OS 7.9 vs 8.3 months (HR 1.11)

1. Paz-Ares L, et al. Presented at WCLC 2019. Abstract OA03.03; 2. Paz-Ares L, et al. Cancer 2022; Rudin C, et al, ELCC 2023

Combination of Lurbinectedin-Irinotecan in relapsed SCLC

Phase 1b/2 trial

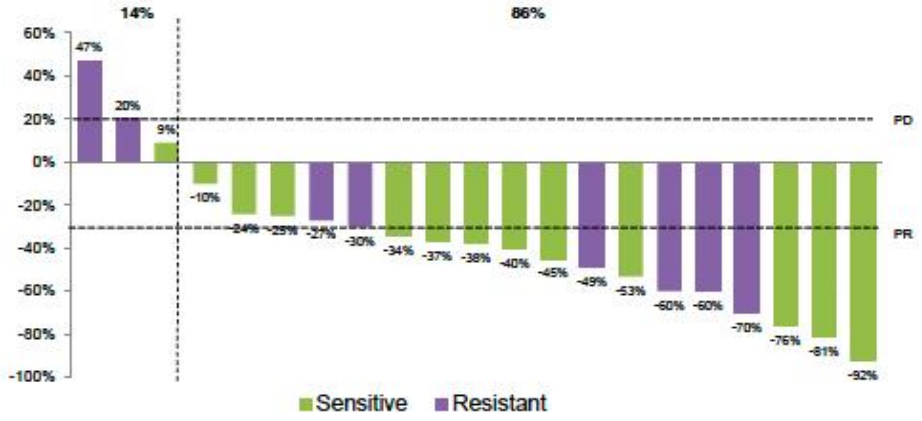
Lurbinectedin 2 mg/m2 on D1 plus Irinotecan 75 mg/m2 on D1 and D8, WITH G-CSF (n=21)

Efficacy summary

Outcome	All pts (N=21)	CTFI		Disease setting	
		≥90 days (n=13)	<90 days (n=8)	2L (n=13)	3L (n=8)
ORR, %	**62**	**69**	**50**	**77**	**38**
Clinical benefit, %*	81	92.3	62.5	92.3	62.5
Disease control, %†	90	100	75	100	75
Median DOR, m (95% CI)	6.7 (3.0, NR)	7.5 (3.0, NR)	3.7 (2.8, 3.7)	6.7 (3.0, NR)	3.0 (3.0, NR)
Median PFS, m (95% CI)	**6.2 (4.3, 8.5)**	**8.1 (4.3, NR)**	**4.8 (0.7, 5.0)**	**8.5 (4.8, NR)**	**4.2 (0.7, 7.2)**

Safety profile

- Grade ≥3 AEs in 16 patients (**76%**)
- Serious AEs in 6 patients (**28.5%**)
- Most common Grade ≥3 AEs: neutropenia (**62%**), diarrhea (**29%**), fatigue (24%), anemia (**19%**)
- No AEs leading to death or discontinuation
- Dose reductions **52%**



*Clinical benefit rate defined as PR or SD for more than 4 months; †Disease control rate defined as PR + SD.

1.-Ponce S, et al. Presentation at WCLC 2020.

Combination of Lurbinectedin-Pembrolizumab in relapsed SCLC

Phase 1/2 trial (LUPER)

Lurbinectedin 3.2 mg/m2 plus Pembro 200 mg IV on D1 Q3W , WITHOUT G-CSF (n=28) in pts who did not receive previous IO

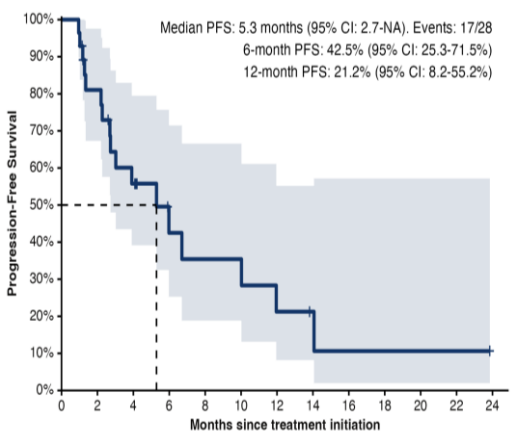
Efficacy summary

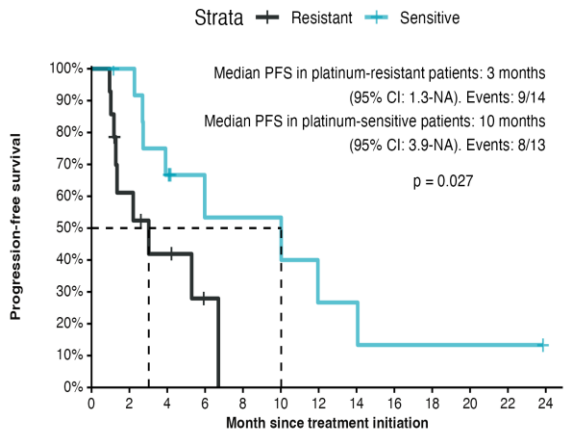
Outcome	All pts (N=28)	CTFI	
		≥90 days (n=13)	<90 days (n=14)
ORR, %	**46**	**54**	**36**
Clinical benefit, %*	61	77	43
Median DOR, m (95% CI)	3 (0.03, 21NR)	-	-
Median PFS, m (95% CI)	**5.3 (2,7, NA)**	**10 (3.9, NA)**	**3 (1.3, NA)**

NCT04358237

Safety profile

- Grade ≥3 AEs in 23 patients (**82%**)
- Serious AEs in 12 patients (**43%**)
- Most common Grade ≥3 AEs: neutropenia (**64%**), ALAT increase (**14%**), anemia (**11%**)
- Discontinuation of any study-drug (**14%**)
- Dose reductions **29%** (Lurbinectedin)





*Clinical benefit rate defined as PR or SD for more than 4 months; †Disease control rate defined as PR + SD.

1.-Calles A, et al. Presentation at ESMO 2023.

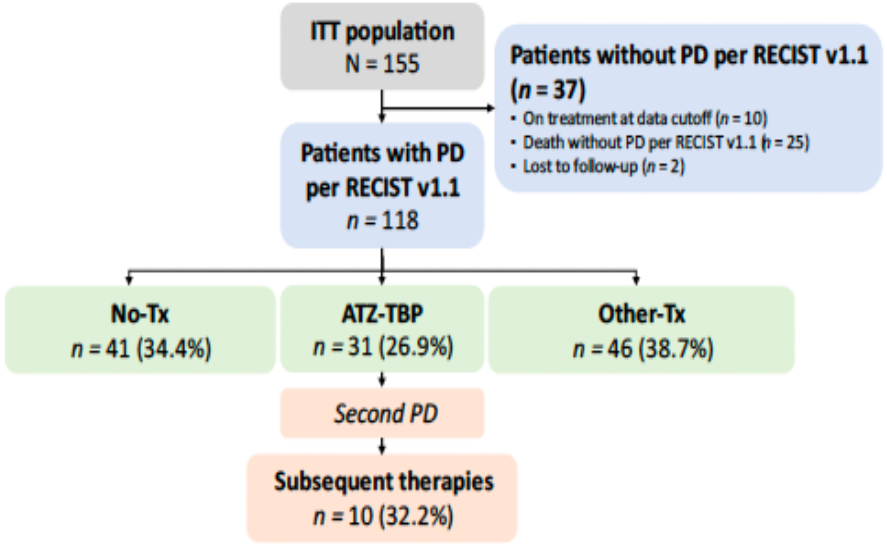
Ongoing combination trials of Lurbinectedin in Relapsed SCLC

Study identifier	Setting	Phase	Treatment arms	Estimated PCD
IMforte (Global)[1]	1L-M	3	Maintenance lurbinectedin + atezolizumab vs atezolizumab	Ongoing
LAGOON (Global)[2]	2L	3	Lurbinectedin + irinotecan vs lurbinectedin vs topotecan/irinotecan	Ongoing
LURBIMUNE (France)[3]	2L	2	Lurbinectedin + durvalumab vs carboplatin/etoposide	Ongoing
NCT04610658 (US)[4]	2L	1/2	Lurbinectedin + nivolumab–ipilimumab	Ongoing
2SMALL (Spain)[5]	2L	1/2	Lurbinectedin + atezolizumab	Ongoing

1. ClinicalTrials.gov: NCT05091567. Available at: https://clinicaltrials.gov/ct2/show/NCT05091567;
2. ClinicalTrials.gov: NCT05153239. Available at: https://clinicaltrials.gov/ct2/show/NCT05153239;
3. ClinicalTrials.gov: NCT05572476. Available at: https://clinicaltrials.gov/ct2/show/NCT05572476;
4. ClinicalTrials.gov: NCT04610658. Available at: https://clinicaltrials.gov/ct2/show/NCT04610658;
5. ClinicalTrials.gov: NCT04253145. Available at: https://clinicaltrials.gov/ct2/show/NCT04253145;

PCD, primary completion date. M, maintenance.

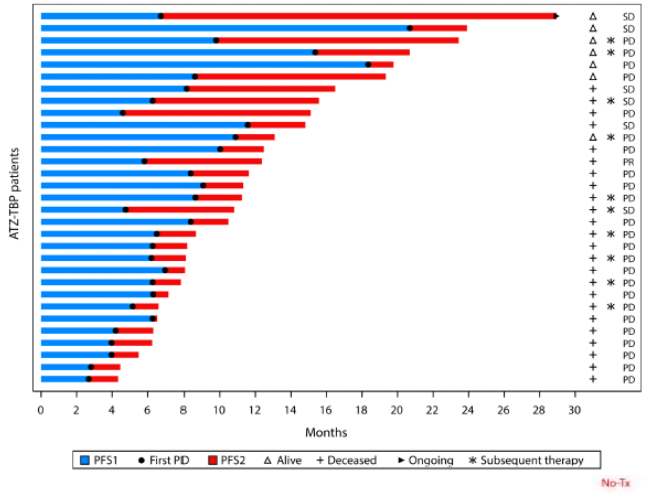
IMfirst Study: Exploratory analysis of ATZ beyond progression

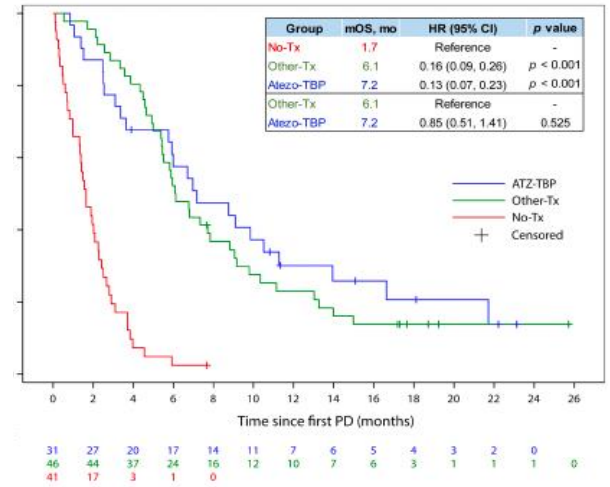


- Patients were allowed to continue ATZ after radiographic PD per RECIST v1.1, provided that the following criteria were met:
  - Evidence of clinical benefit assessed by the investigator
  - No decline in ECOG PS attributable to PD
  - Absence of tumor progression at critical anatomical sites not manageable with protocol-allowed medical interventions
  - Patients' written consent deferring other treatments at the time of initial progression

Months (95% CI)	Patients with PD per RECIST v1.1 (*n* =118)		
	ATZ-TBP (*n* = 31)	Other-Tx (*n* = 46)	No-Tx (*n* = 41)
Progression-free survival (PFS) ¥			
mPFS1	6.5 (6.2, 8.4)	6.2 (5.0, 6.7)	5.1 (4.6, 6.4)
mPFS2 (since TBP)	2.2 (1.9, 3.24)	n.a.	n.a.
Overall survival (OS)			
mOS since treatment initiation	14.3 (9.9, 21.4)	12.6 (10.2, 15.2)	7.3 (5.7, 8.6)
mOS Post-PD	7.2 (3.6, 11.3)	6.1 (5.4, 8.8)	1.7 (0.9, 2.3)

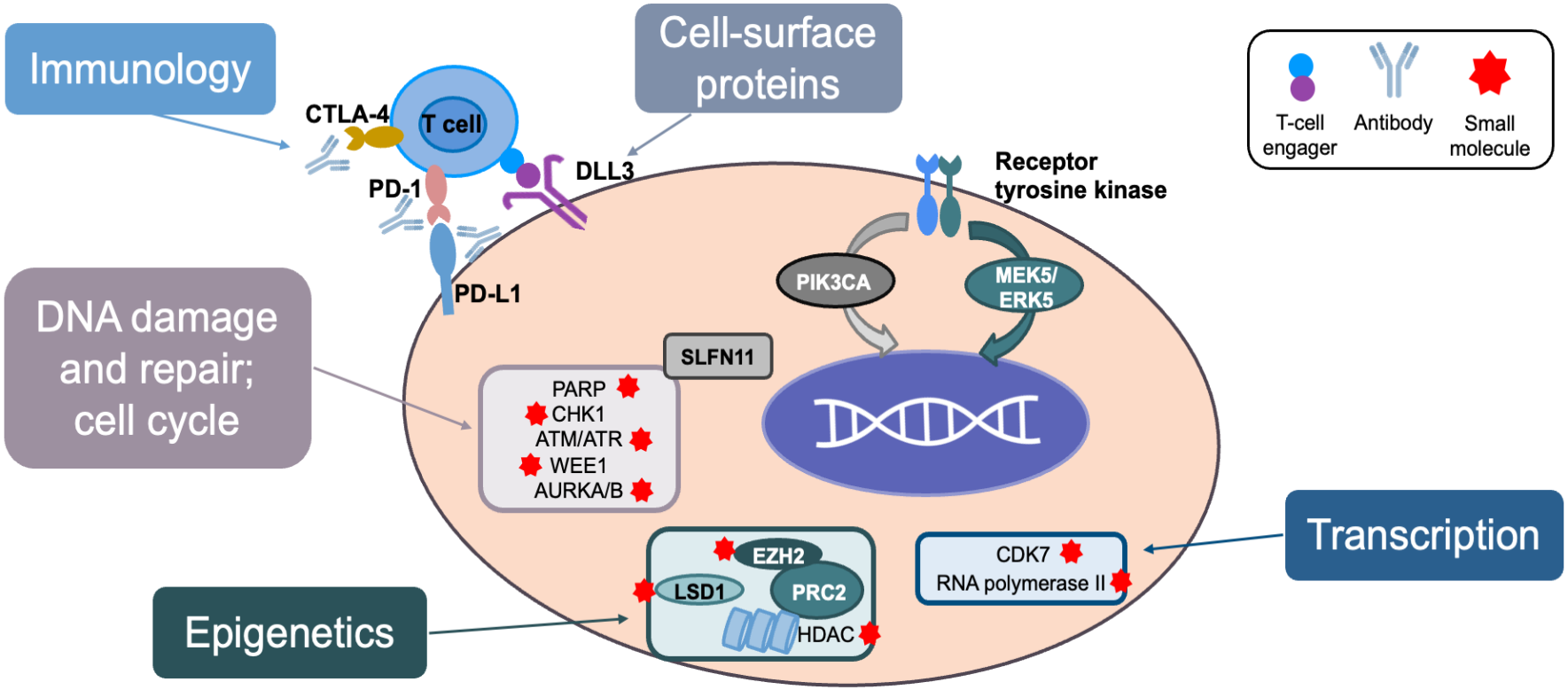
CI, confidence interval; n.a., not available; ¥ Tumor assessments were performed every 6 weeks during the induction phase and every 9 weeks after completion of the induction phase.





1. Garcia-Campelo C, et al. Presented at WCLC 2023. Poster: P2.14-04

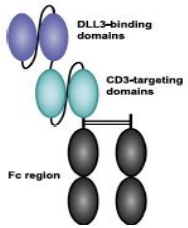
Targeting SCLC Surfaceome



1. Sabari JK, et al. Nat Rev Clin Oncol 2017; 2. Taniguchi H, et al. Front Oncol 2020.

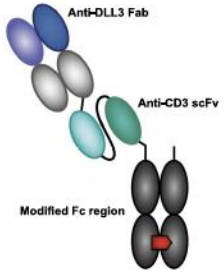
DLL3/CD3 Targeted Therapies: T-Cell Engagers

Tarlatamab
Bispecific mAb (BiTE®)
Amgen
(Phase 2-3)

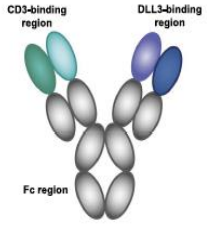


Fc domain
(to extend half-life)

QLS31904
Bispecific mAb
Qilu Pharmaceuticals
(Phase 1)

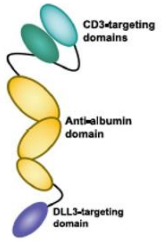


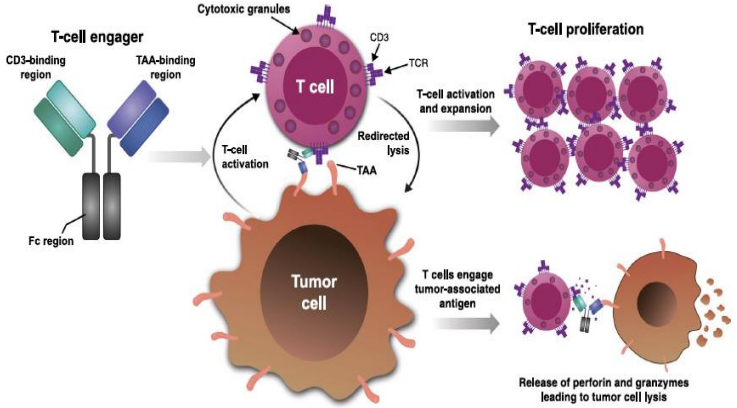
BI 764532[2]
Bispecific mAb
Boehringer Ingelheim
(FIH)



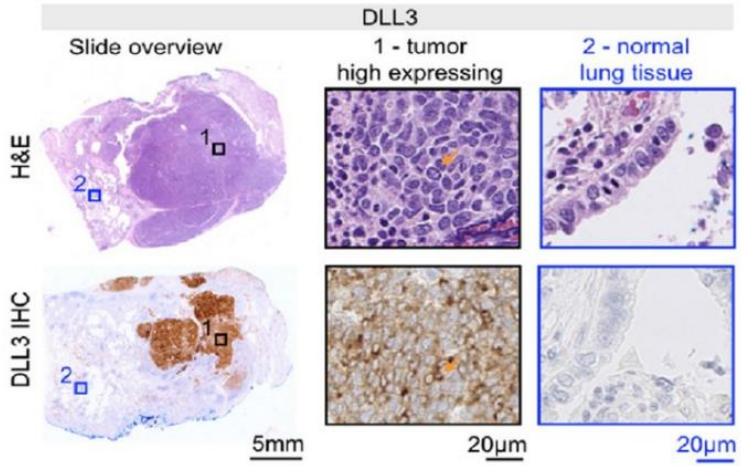
IgG-like
structure

HPN328
Trispecific mAb (TriTAC®)
Harpoon Therapeutics
(Phase 1/2)





DLL3 is highly upregulated and expressed on the surface of SCLC tumour cells (80% RNA and protein) and other neuroendocrine tumours[3,4]



1.-Rudin C, et al. J Hematol Oncol 2023; 2.- Wermke M et al. ASCO 2023; 3.- Sabari JK, et al. Nat Rev Clin Oncol 2017; 4.-Owen DH, et al. J Hematol Oncol 2019

Tarlatamab (AMG 757): DeLLphi-300 Trial

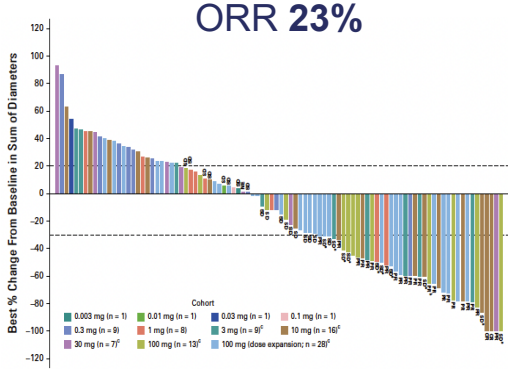
Preliminary Safety and Efficacy of Tarlatamab in Relapsed/Refractory SCLC

Dose Exploration (0.003–100 mg) → **Dose Expansion (10 mg and 100 mg)**

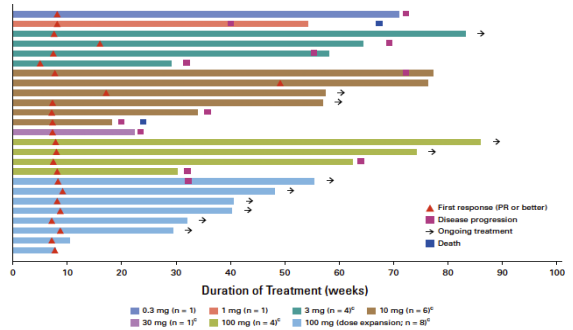
SAFETY	TARLATAMAB[2-3]
N	107 SCLC
Grade ≥ 3 AEs	**31%**
CRS (all/Grade ≥ 3)	**52%/1%**
ICANs (all/Grade ≥ 3)	**50%/7%**
Neutropenia (all/Grade ≥ 3)	16%/10%
Grade 5 AEs	1 pneumonitis
Discontinuation rate	**4%**

ICANS, Immune effector cell-associated neurotoxicity syndrome
CRS, Cytokine release syndrome

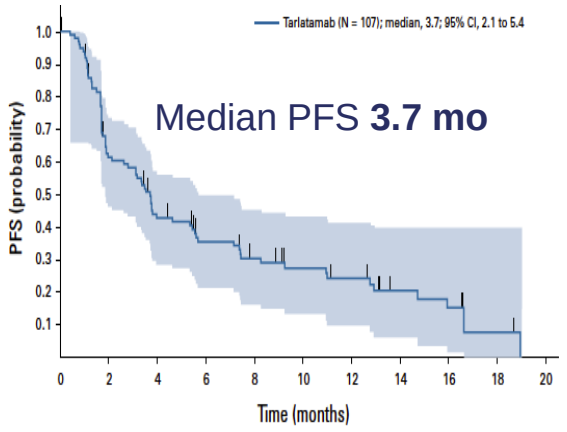
ORR **23%**



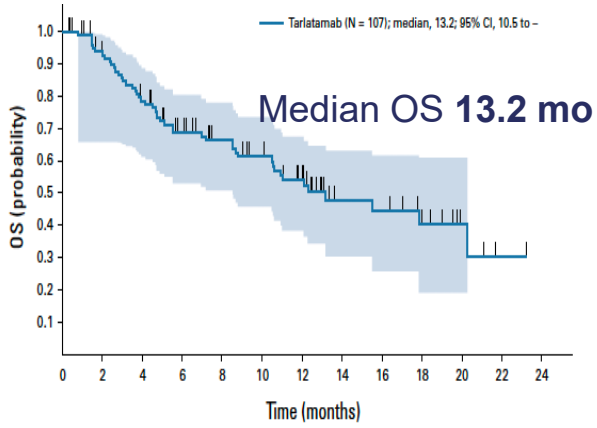
Median DoR **12 mo**



Median PFS **3.7 mo**



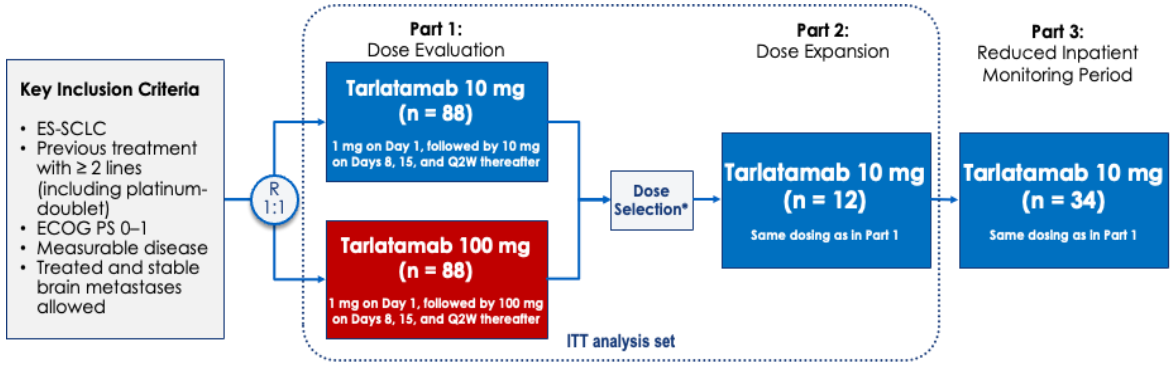
Median OS **13.2 mo**



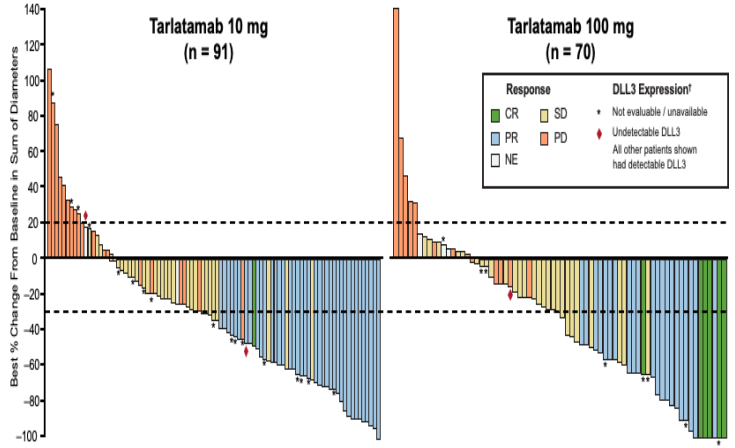
1.- Borghaei H, et al, WCLC 2022; 2.- Paz-Ares, et al JCO 2023

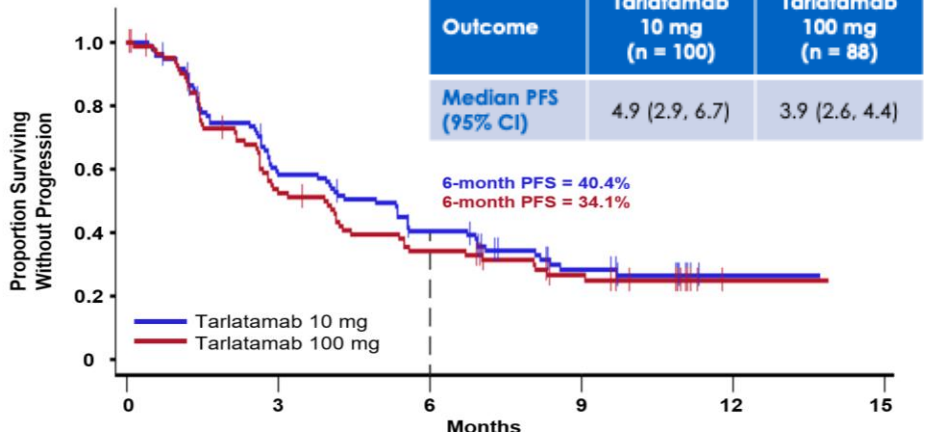
Tarlatamab (AMG 757): DeLLphi-301 Trial

Phase 2 Study of Tarlatamab in 3L or Later SCLC

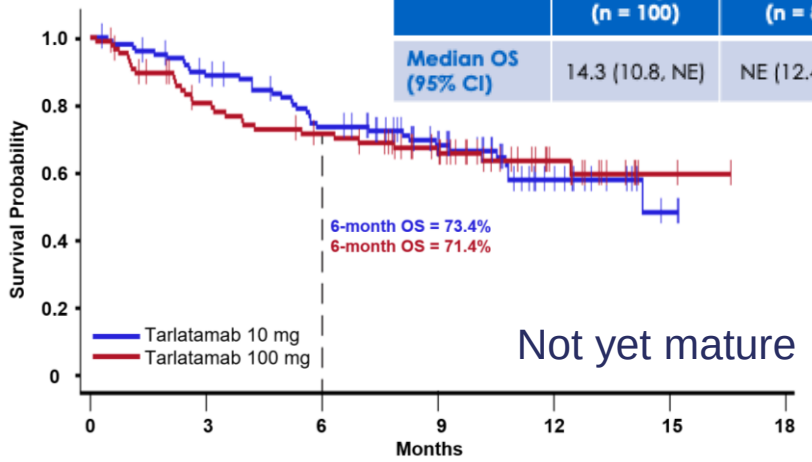


EFFICACY	T 10 mg (n = 100)	T 100 mg (n = 88)
ORR	40%	32%
CR	1%	8%
DoR 6 mo	59%	





Outcome	Tarlatamab 10 mg (n = 100)	Tarlatamab 100 mg (n = 88)
Median PFS (95% CI)	4.9 (2.9, 6.7)	3.9 (2.6, 4.4)



Outcome	Tarlatamab 10 mg (n = 100)	Tarlatamab 100 mg (n = 88)
Median OS (95% CI)	14.3 (10.8, NE)	NE (12.4, NE)

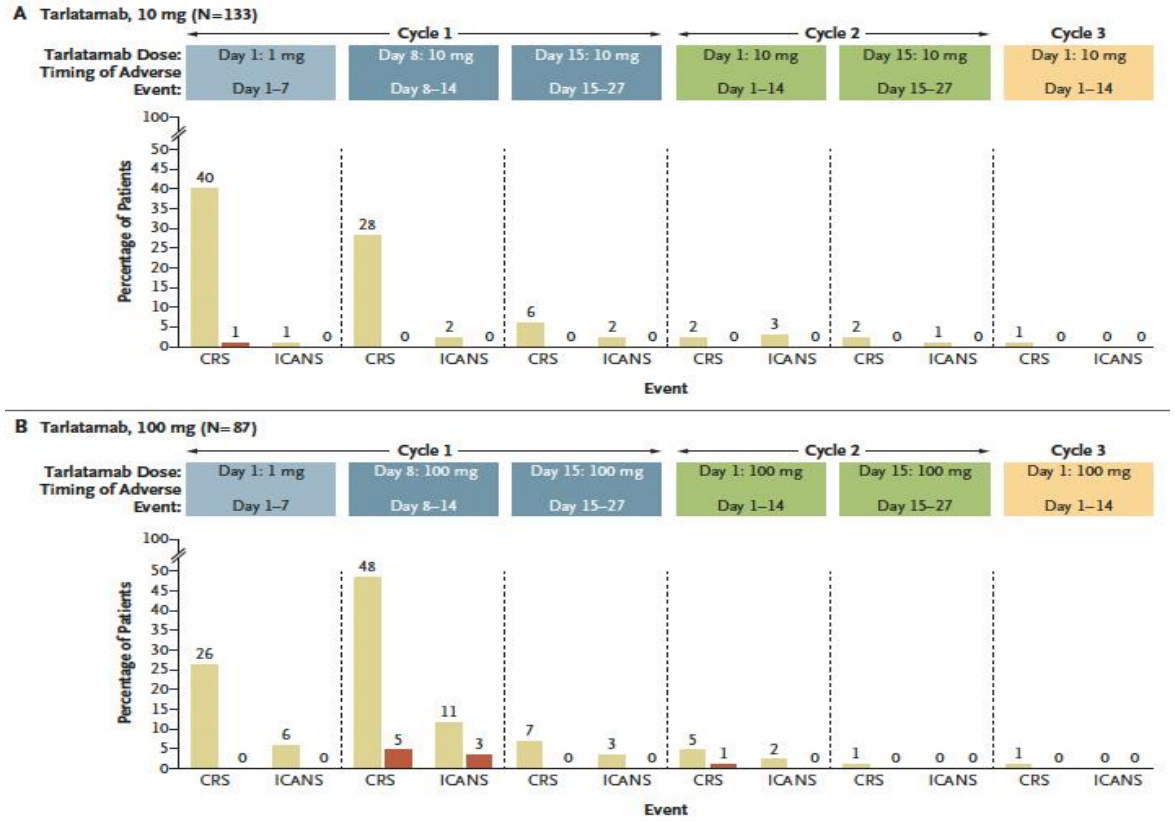
1.- Paz-Ares L. et al ESMO 2023; 2.- Ahn MJ, et al. NEJM 2023

DeLLphi-301 Trial: Safety

TEAEs, n (%)	Part 1 + 2 T 10 mg (n = 99)	Part 3 T 10 mg (n = 34)	Part 1 T 100 mg (n = 87)
Any grade	96 (97)	34 (100)	87 (100)
≥ Grade 3	57 (58)	22 (65)	56 (64)
Related to tarlatamab, any	89 (90)	29 (85)	81 (93)
≥ Grade 3	**20 (29)**	5 (15)	**29 (33)**
Fatal	0	1 (3)†	0
CRS, any	**49 (49)**	19 (56)	**53 (61)**
≥ Grade 3	0	1 (3)	**5 (6)**
ICANs, any	**7 (7)**	4 (12)	**24 (28)**
≥ Grade 3	0	0	**4 (5)**
Leading to dose interruption/reduction	14(14)	3 (9)	**25 (29)**
Leading to discontinuation	**4 (4)**	0	3 (3)

1.- Paz-Ares L. et al ESMO 2023; 2.- Ahn MJ, et al. NEJM 2023

CRS and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)*

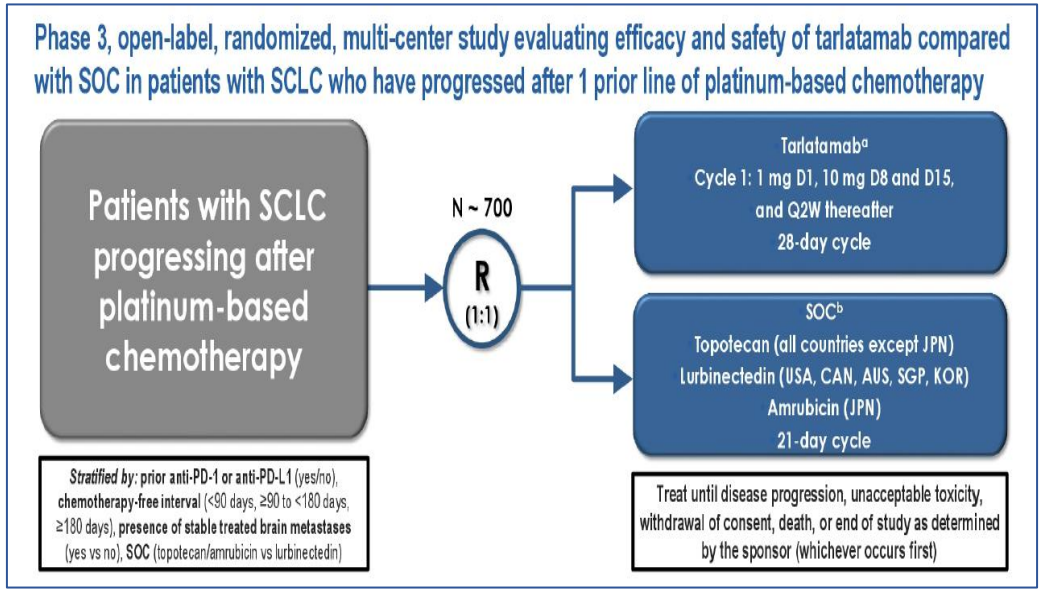


Tarlatamab **10 mg Q2w** selected dose for further development

Tarlatamab Clinical Development in ES-SCLC

DeLLphi-304

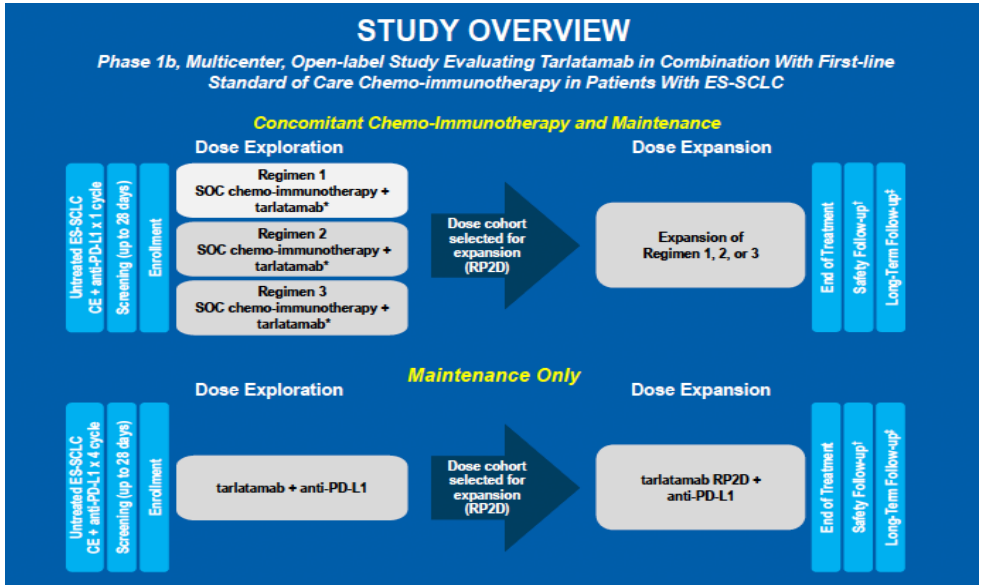
Phase 3 AMG 757 in 2L[1]
Tarlatamab vs SoC



NCT05740566, ongoing

DeLLphi-303

Phase 1b AMG 757 in 1L[2]
Chemo+IO+T-> maintenance IO+T
Maintenance IO+T



NCT05361395, ongoing

1.- Paz-Ares L et al, ASCO 2023, TiP; 2.- Gadgeel SM et al, ESMO 2022, TiP

FIH dose escalation trial of BI 764532

ECOG 0-1 and DLL3-positive required for inclusion

SCLC N=57

epNEC N=41

LCNEC N=9

PRIMARY ENDPOINT SAFETY (MTD/DLT)	BI 764532 (SCLC/LCNEC)
N	66 (57 SCLC/ 9 LCNEC)
CRS (all/G3)	48%/2%
ICANs	2 cases (all G3)
Grade ≥ 3 AEs	53%
Most common Grade ≥ 3	Lymphopenia (18%)
Grade 5 AEs	1 pneumonitis
Discontinuation rate	6%

ICANS, Immune effector cell-associated neurotoxicity syndrome
CRS, Cytokine release syndrome
epNEC: extrapulmonary neuroendocrine

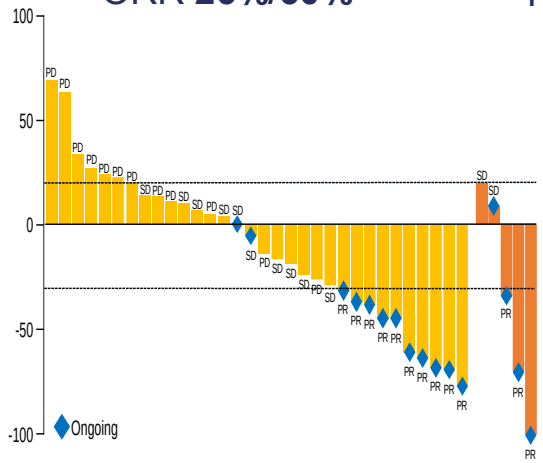
Secondary endpoint: EFICACY (ORR in SCLC/LCNEC, N=44)

Efficacy observed at doses **≥ 90 µg/kg**

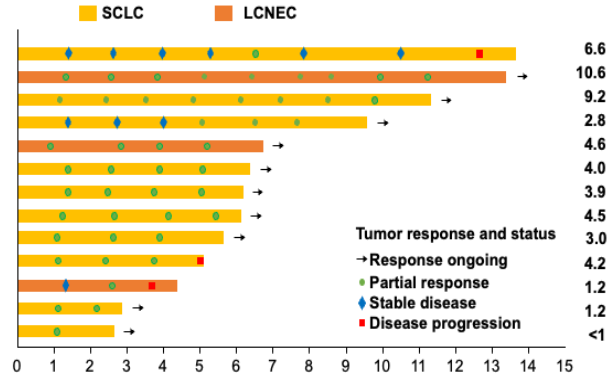
ORR (at doses ≥ 90 µg/kg): **SCLC 26%, LCNEC 60%**

Durable responses the majority ongoing (10/13)

ORR **26%/60%**



Responses ongoing in **10/13** responders



1.- Presented by Wermke M, et al. OA01.05. WCLC 2023

FIH dose escalation trial of HPN328 Trial

ECOG 0-1 and DLL3-positive required for inclusion

65% **SCLC N=46**

15% **NEPC N=11**

20% **NENs N=14**

SAFETY (MTD/DLT)	HPN328 (Minimal Effective Dose)
N	71
CRS (all/G3)	59%/3%
ICANs	5 cases (all grade 1-2)
Grade ≥ 3 AEs	46.5%
Most common Grade ≥ 3	Neutropenia (6%)
Grade 5 AEs	-
Discontinuation rate	6%

ICANS, Immune effector cell-associated neurotoxicity syndrome
CRS, Cytokine release syndrome
NEPC, relapsed/refractory neuroendocrine prostate cancer
NENs, high grade relapsed/refractory neuroendocrine neoplasms

1.- Presented at ESMO 2023, POSTER

EFICACY (ORR in SCLC, N=23)

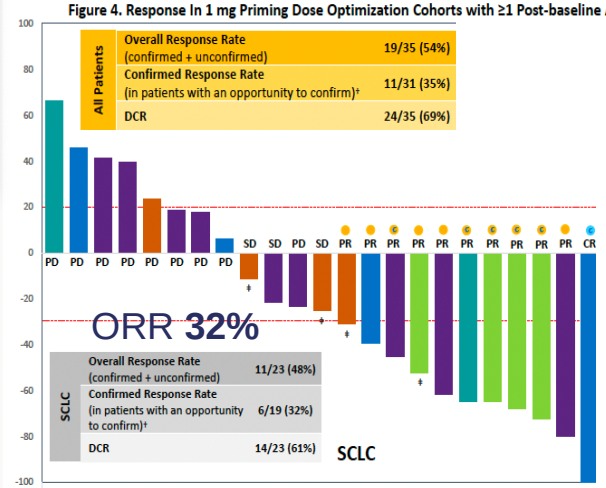
Responses in the **1 mg priming dose optimization cohorts**

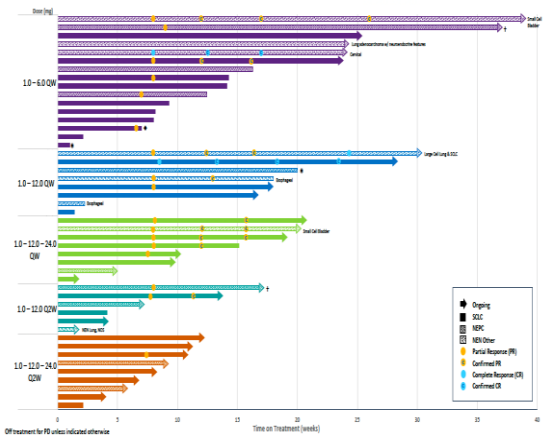
ORR (at dose optimization cohorts): **SCLC 32%**

Some durable responses

Still maturing data in 12 and 24 mg cohorts to inform RP2D

Figure 4. Response In 1 mg Priming Dose Optimization Cohorts with ≥1 Post-baseline Assessment (N=35)





Antibody-Drug Conjugates (ADCs) in SCLC

Target	Agent	Payload	Payload MoA	Clinical Development
DLL-3	ROVA-T (Rovalpituzumab Tesirine)	Pyrrolobenzodiazepine	DNA-crosslinking	Phase 3 Discontinued
TROP-2	IMMU-132 (Sacituzumab Govitecan) SKB264	SN-38 (irinotecan metab) KL610023 (Belotecan metab)	TOPO I inhibitor TOPO I inhibitor	Phase 2 (TROPiCS-03) Phase 1 (NCT04152499)
SEZ6	ABBV-011 ABBV-706	Calicheamicin Undisclosed cytotoxic	DNA-cleaver TOPO I inhibitor	FIH/Phase 1 (NCT03639194) FIH/Phase 1 (NCT05599984)
B7-H3	DS-7300a (Ifinatamab Deruxtecan, I-DXd) ABBV-155 (Mirzotamab Clezutoclax)	Deruxtecan (DXd) Clezutoclax	TOPO I inhibitor BCL2/XL inhibitor	Phase 2/3 (IDeate-1, IDeate-2) Phase 1 (NCT03595059)
CEACAM5	SARA08701 (Tusamitamab ravtansine)	Maytansine (DM4)	Microtubule inhibitor	Phase 1 (NCT02187848)

Learnings from the ROVA-T (DLL3-targeted ADC):

Bad Target or a Bad Payload?

TRINITY Phase 2 (NCT02674568)[1]
- → Rova-T monotherapy in 3L or beyond
- → ORR 12.4%, OS 5.6 months
- → Serious TRAEs 30% (3 patient fatalities)

TAHOE Phase 3 (NCT03061812)[2]
- → Rova-T vs topotecan in 2L
- → Shorter OS in the Rova-T arm vs control arm

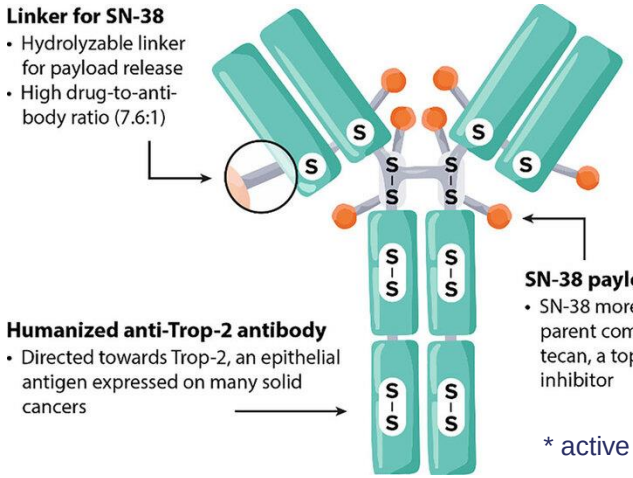
MERU Phase 3 (NCT03033511)[3]
- → Rova-T as 1L as maintenance
- → Stopped: lack of OS benefit at the interim analysis

- **Rova-T (rovalpituzumab teserine)** is a DLL3-targeted **antibody drug conjugate** that delivers cytotoxic PBD when internalised[4]
- Research and development of Rova-T discontinued in 2019[3]
- **DLL3 remains an intriguing target** for multiple alternative therapeutic strategies[5]

1. Morgensztern D, et al. Clin Cancer Res 2019; 2. Blackhall F, et al. J Thorac Oncol 2021; 3. AbbVie Press release 2019. Available at: https://news.abbvie.com/news/press-releases/abbvie-discontinues-rovalpituzumab-tesirine-rova-t-research-and-development-program.htm; 4. Lashari B, et al. Drugs R D 2018; 5. Serzan MT, et al. J Thorac Dis 2020.

Targeting TROP2

Sacituzumab Govitecan (IMMU-132-01, Gilead)

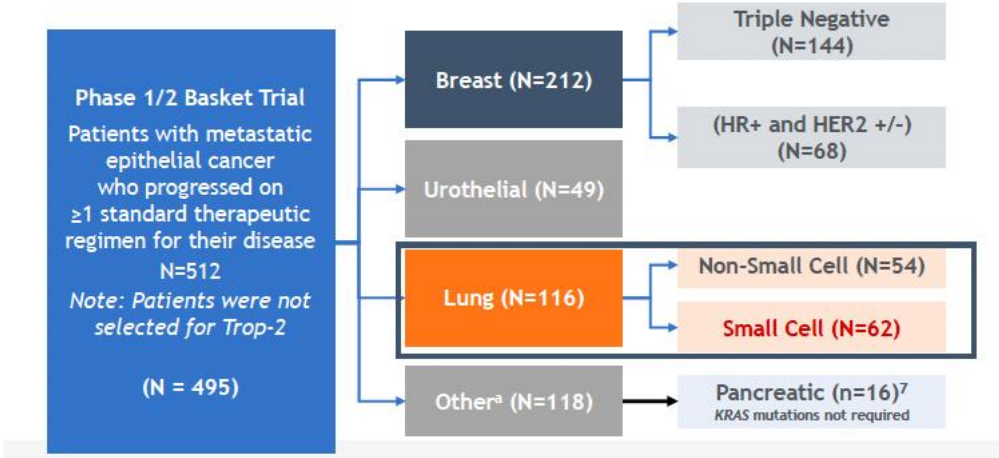


IMMU-132-01
SN-38 payload (Topo1i)*

* active metabolite of irinotecan

- TROP-2 overexpression in high-grade neuroendocrine tumors (**SCLC ~10%)**
- Phase I/II SCLC cohort preliminary ORR **18% patients with SCLC**
- Responses despite prior exposure to etoposide (100%) or irinotecan (34%)

Phase I Basket trial (Pretreated SCLC n=62)



Cohort[a]	N	ORR (%)	Median DOR, Months	Median PFS, Months (95% CI)	Median OS, Months (95% CI)
mTNBC[b,1]	108[c]	33	7.7	5.5 (4.1-6.3)	13.0 (11.2-13.7)
HR+/HER2- mBC[2]	54[c]	31	8.7	5.5 (3.6-7.6)	12.0 (9.0-18.2)
mUC[b,3]	45	31	12.9	6.8 (3.6-9.7)	16.8 (9.0-21.9)
NSCLC[4]	54	17	6.0	5.2 (3.2-7.1)	9.5 (5.9-16.7)
SCLC[3]	62	18	5.7	**3.7 (2.1-4.8)**	**7.1 (5.6-8.1)**

1.-Bardia A et al. Ann Oncol. 2021; 2.-Inamura K et al. *Oncotarget*. 2017; 3.-Gray JE et al. Clin Cancer Res. 2017

TROPiCS-03:

Phase 2 Basket Trial Study Of Sacituzumab Govitecan In Subjects With SCLC

- The ongoing, open-label, multicohort, phase 2 TROPiCS-03 study (NCT03964727) is evaluating SG in patients with metastatic or locally advanced solid tumors

Key eligibility criteria
- Histologically confirmed ES-SCLC
- Disease progression after no more than 1 prior line of platinum-based chemo and anti–PD-(L)1 therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0-1
- No known active CNS metastases and/or carcinomatous meningitis[a]

N=40

ES-SCLC Cohort N ≈ 40 → **21-day cycles:** SG 10 mg/kg IV on D1 and D8 (until PD or unacceptable toxicity) → Survival follow-up

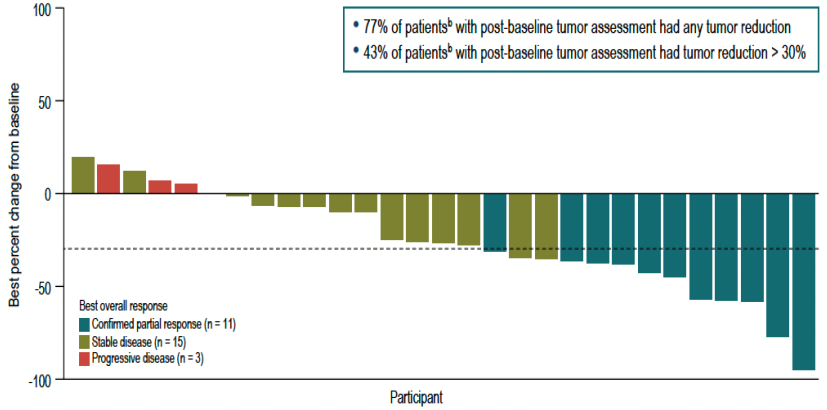
10 mg/kg d1-8

End points

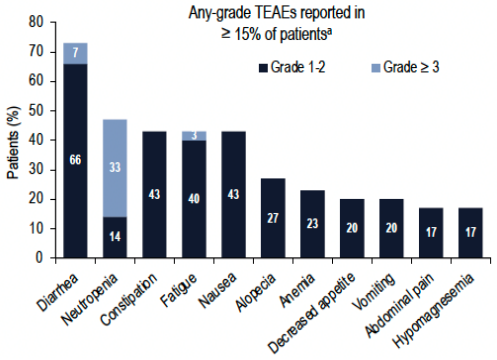
Primary
- ORR by INV[b]

Secondary
- DOR, CBR, PFS (all by INV[b])
- ORR, DOR, CBR, PFS (all by BICR[b])
- OS
- Safety

- At data cutoff (27 July 2023), median follow-up was 5.1 months (range, 1.9-12.2)



Safety-evaluable patients, n (%)	ES-SCLC N = 30[a]
Any-grade TEAEs	30 (100)
Related to study treatment	28 (93)
Grade ≥ 3 TEAEs	18 (60)
Related to study treatment	15 (50)
Serious TEAEs	9 (30)
Related to study treatment	4 (13)
TEAEs leading to dose reduction	8 (27)
TEAEs leading to discontinuation	0
Related to study treatment	0
TEAEs leading to death	0
Related to study treatment	0



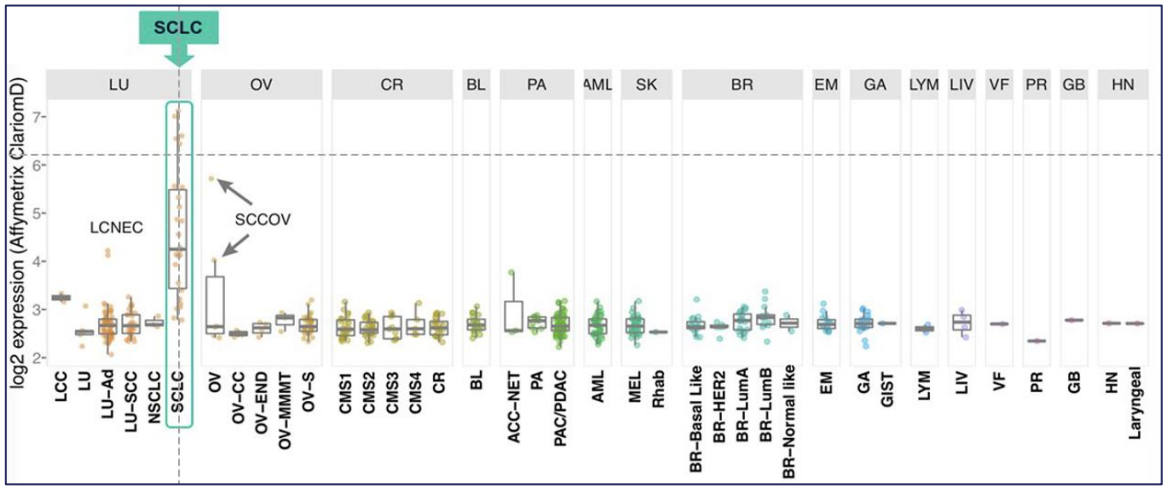
Most common AEs: diarrhea, neutropenia

Efficacy by INV[a]	ES-SCLC N = 30[b]
ORR [Confirmed CR + PR] **(95% CI), %**	37 (20-56)
BOR, n (%)	
Confirmed PR	11 (37)
SD	15 (50)
PD	3 (10)
DCR [Confirmed CR + PR + SD] **(95% CI), %**	87 (69-96)
CBR [Confirmed CR + PR + SD ≥ 6 months] **(95% CI), %**	40 (23-59)
Median DOR (95% CI),[c,d] months	6.3 (2.7-NR)
DOR rate at 6 months (95% CI),[c,d] %	63 (14-89)

1.- Dowlati A et al, ESMO 2023

SEZ6-targeted ADCs (ABBV-011; ABBV-706)

- **Seizure-related homolog 6** (SEZ6) is a transmembrane protein on select neuronal lineage cells[1]
- SEZ6 is **highly expressed in SCLC** and in other NE tumors with minimal expression in normal tissues[1]



ABBV-011, Calicheamicin-Based

FIH in relapsed or refractory SCLC[2]

ABBV-011 Monotherapy	Combination Therapy
Part A: Monotherapy ABBV-011 Dose Escalation	Part C: ABBV-011 + Budigalimab Combination Escalation and Expansion
Part B: Monotherapy ABBV-011 Dose Expansion	NCT03639194
Part D: Monotherapy ABBV-011 Dose Evaluation in Japan	

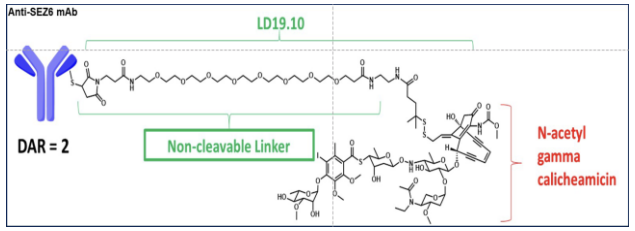
ABBV-706, TOPO-1i- Based

FIH in advanced solid tumors

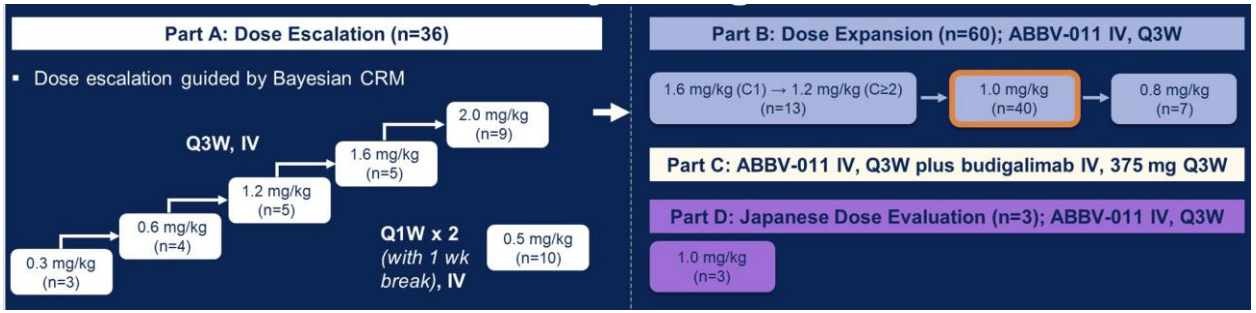
ABBV-706 Monotherapy	Combination Therapy
Part 1: Monotherapy ABBV-706 Dose Escalation	Part 3a: ABBV-706 + Budigalimab Combination Escalation and Expansion in SCLC + Neuroendocrine Carcinomas
Part 2: Monotherapy ABBV-706 Dose Optimization and Expansion in SCLC	Part 3b: ABBV-706 + Platinum Combination Escalation and Expansion in SCLC + Neuroendocrine Carcinomas
Part 4a: Monotherapy ABBV-706 Expansion in CNS Tumors	NCT05599984 (ongoing)
Part 4b: Monotherapy ABBV-706 Expansion in Neuroendocrine Carcinomas	

1. Wiedemeyer WR, et al. Mol Cancer Ther 2022; 2.- Morgensztem D, et al. ASCO 2023

FIH SEZ6-targeted ADCs (ABBV-011) in relapsed SCLC



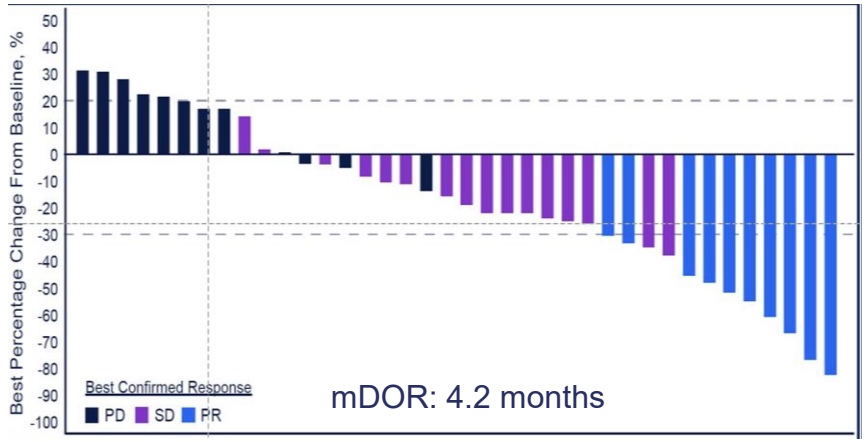
ABBV-011
Calicheamicin payload



	1 mg/kg n=40	Total N=99
Any TEAE, n (%)	39 (98%)	96 (97%)
Grade ≥3 TEAE, n (%)	26 (65%)	63 (64%)
Serious TEAEs, n (%)	18 (45%)	41 (41%)
Treatment-related AEs, n (%)	31 (78%)	76 (77%)
Associated with discontinuation	3 (8%)	13 (13%)
Associated with dose reduction	6 (15%)	8 (8%)
Associated with dose interruption	12 (30%)	29 (29%)

- AEs Gr ≥3, **64%**
- TEAE of interest: **Hepatotoxicity**
- Discontinuation **29%**
- Delayed onset of hepatotoxicity limited long-term dosing at doses higher than 1.2 mg/kg

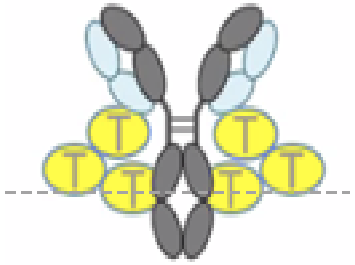
Antitumor Activity 1 mg/kg cohort (n=38)



Efficacy Outcome	1 mg/kg n=40
Confirmed ORR, n (%)	10 (25%)
[95% CI]	[13, 41]
CBR, n (%)	26 (65%)
[95% CI]	[48, 79]
CBR lasting >12 weeks, n (%)	17 (43%)
[95% CI]	[27, 59]

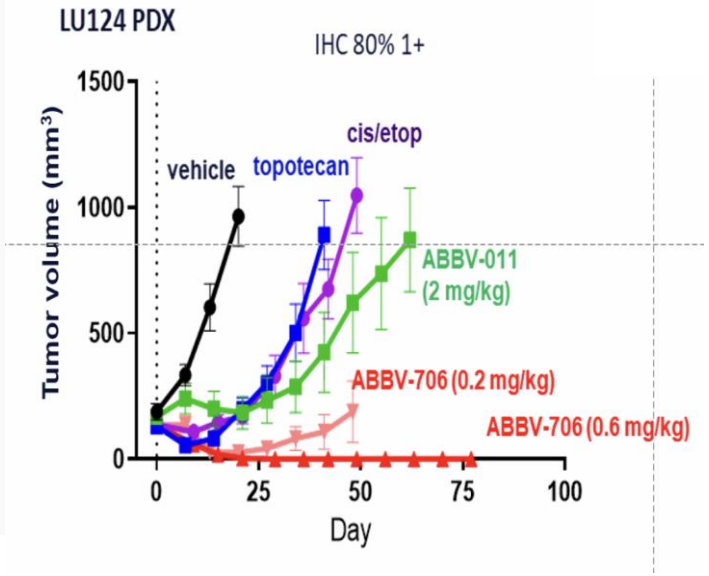
1. Morgensztem D, et al. ASCO 2023

SEZ6-targeted ADCs (ABBV-706) in SCLC and NE tumors

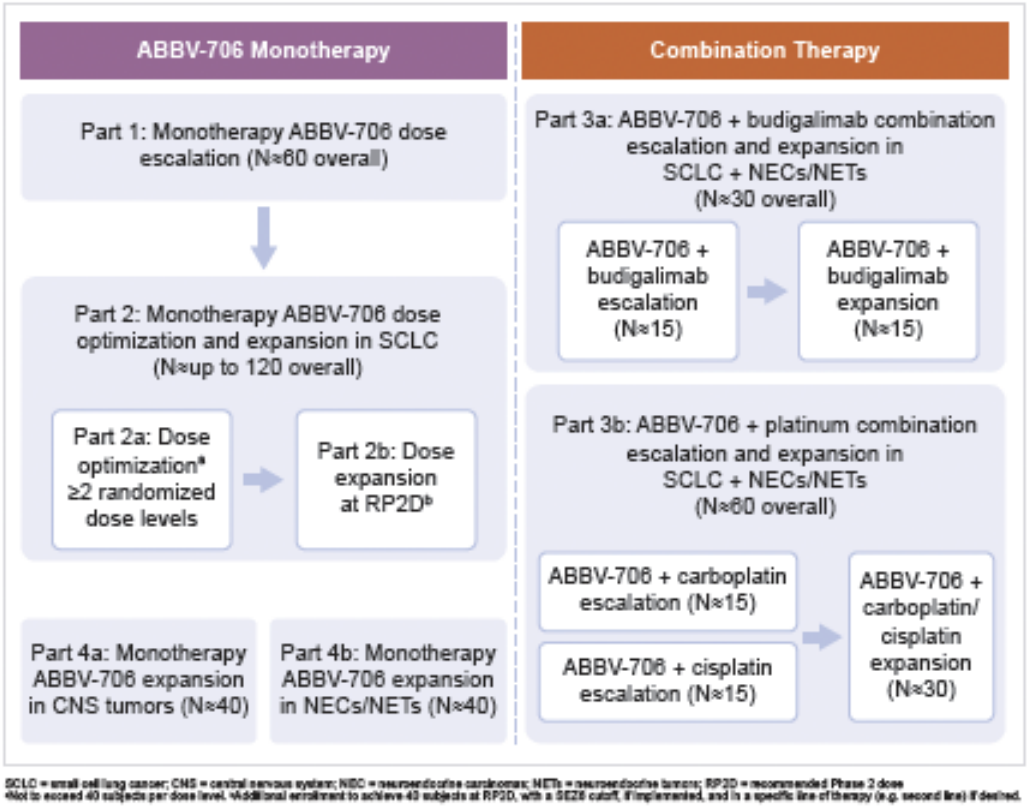


ABBV-706
TOP-1i payload

- Same payload as ABBV-400 (c-MET ADC)
- Predicted improved tolerability and therapeutic index than predecessor (ABBV-011).
- Phase 1 as monotherapy or in combination in SCLC and NE tumors ongoing



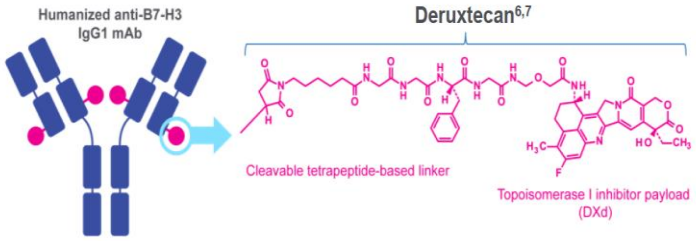
PHASE 1



NCT05599984

1. Sreenivasa Chandana et al, ESMO 2023, 2029TiP

FIH B7-H3-targeted ADC (Ifinatamab Deruxtecan, I-DXd, DS-7300)



DS-7300
TOPO-1 payload

- **B7-H3** is an **inmune checkpoint** overexpressed in several tumors[1]

Phase 1/2 antitumour activity in SCLC cohort (n=21, dosed at ≥6.4 mg/kg)2

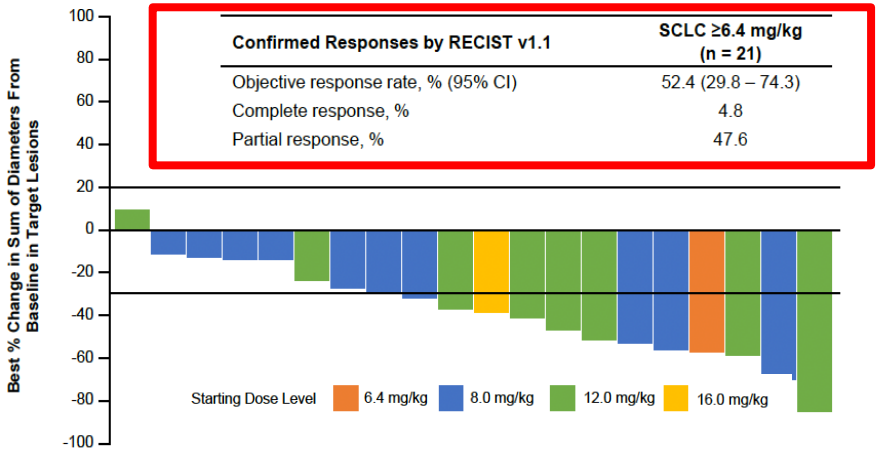
- AEs Gr ≥ 3, 36% (most common nausea)
- TEAE of interest: ILD/pneumonitis 13.6% (mostly Gr 1-2)

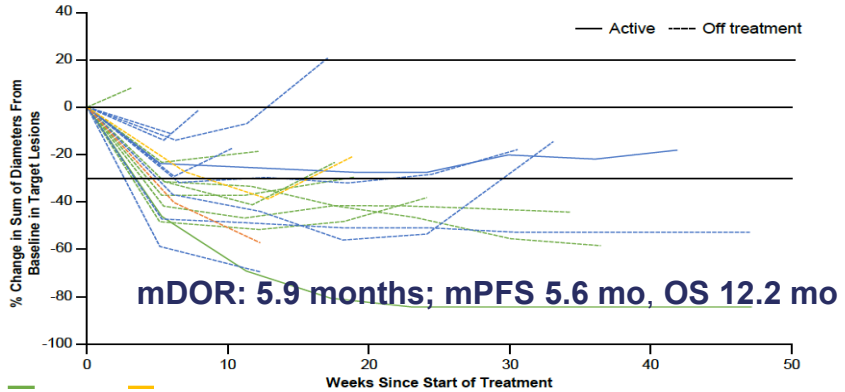
Ongoing trials:

- Phase 2, relapsed ES-SCLC (**IDeate-1**)[3]
- Phase 3, relapsed ES-SCLC (**IDeate-2**)
- Phase 1b/2, First-line or maintenance in combo with atezo

Phase 1/2 antitumour activity in SCLC cohort (n=21, dosed at **≥6.4 mg/kg**)[2]

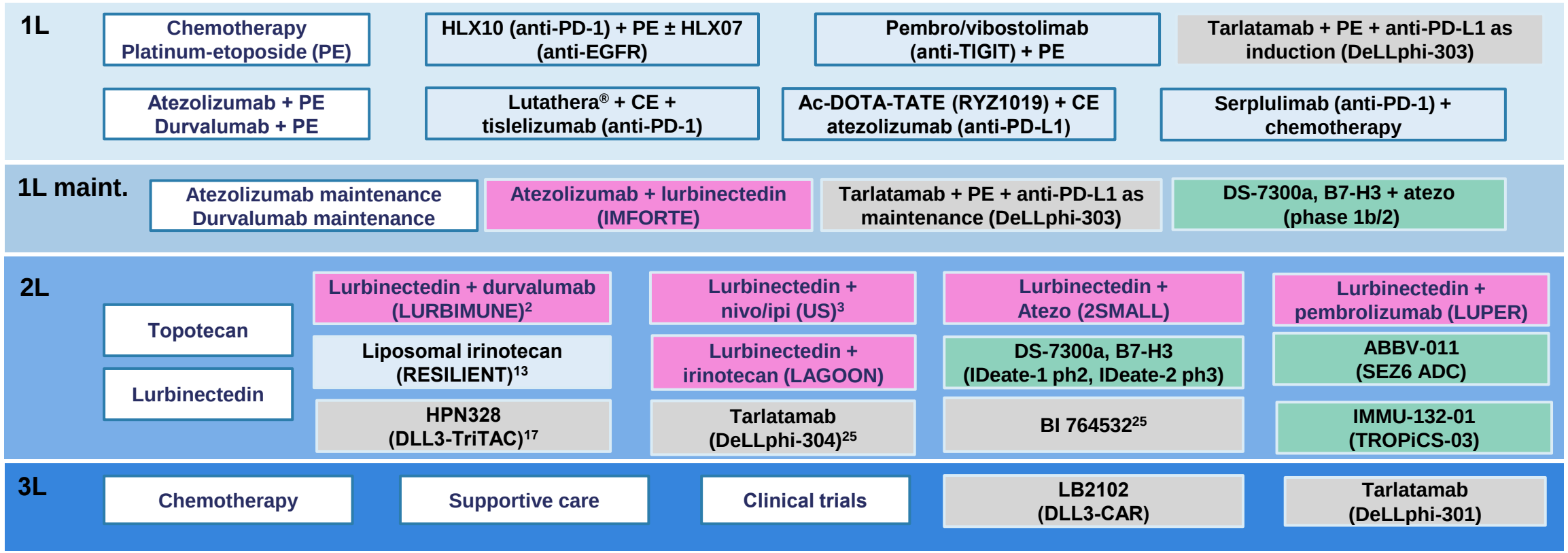
Confirmed Responses by RECIST v1.1	SCLC ≥6.4 mg/kg (n = 21)
Objective response rate, % (95% CI)	52.4 (29.8 – 74.3)
Complete response, %	4.8
Partial response, %	47.6





1. Doi T, et al. ESMO 2022; 2.- Johnson M et al, WCLC 2023.; 3.- Rudin CM et al, WCLC 2023, TIP #1561

Emerging ES-SCLC treatment landscape



Summary

- **Outcomes for patients with relapsed SCLC remain poor.**
- Second line options limited.
- New therapies under investigation with initial promising results
- Potential for novel new drugs and combinations with **lurbinectedin, DLL3 targeting-cellular therapy (BITEs) and ADCs.**


15th
MADRID
CONGRESS
on Lung CANCER
23&24
November 2023
#15CongressGECP
Fundación
GECP
lung cancer
research
Muchas Gracias