Lung Cancer UPDATES
ASCO HIGHLIGHTS
30 MAYO - 03 JUNIO 2025
Chicago, USA

Iniciativa científica de:
GECP lung cancer research

Microcítico, Mesotelioma, Tumores Tímicos

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Carcinoma microcítico

Limited Stage

- Surgery / SBRT → Adjuvant Plt-Etoposide x 4 → PCI
- Concurrent CT/RT → Durvalumab → PCI

→ 65-75% Reccurrences

Extended Stage and Relapse

First-line therapy

Chemoimmunotherapy (IMpower 133, CASPIAN)
Platinum + Etoposide + ICI ⟶ ICI maintenance

↑ Initial diagnosis

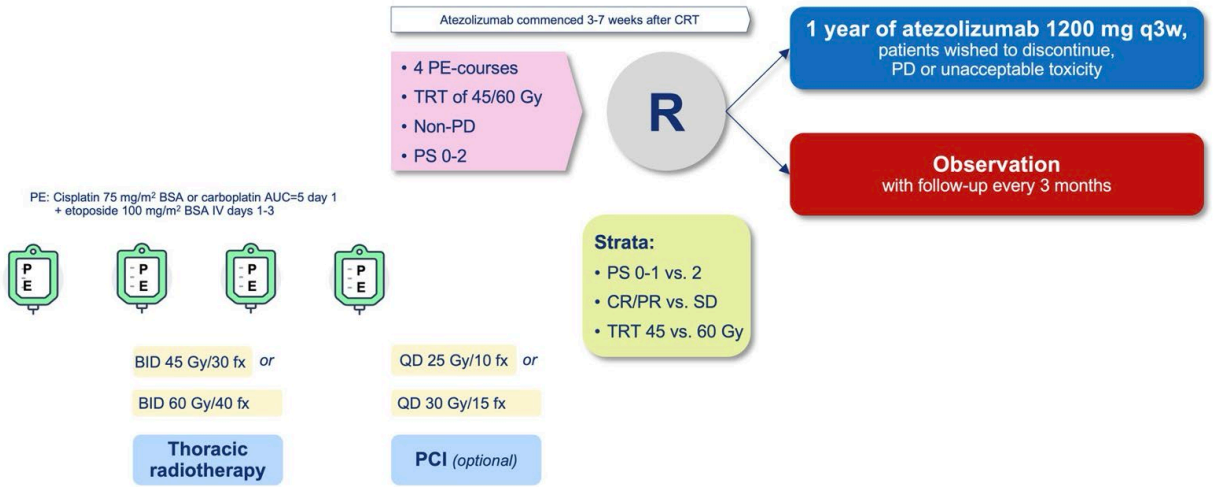
Second-line+ therapy

- Topotecan
- Lurbinectedin (2020)
- Tarlatamab (2024)

↑ Progression or toxicity

Median OS
1L: 12.5 m
2L Plt sensit: 6-8 m
2L Plt refract: 5-6 m

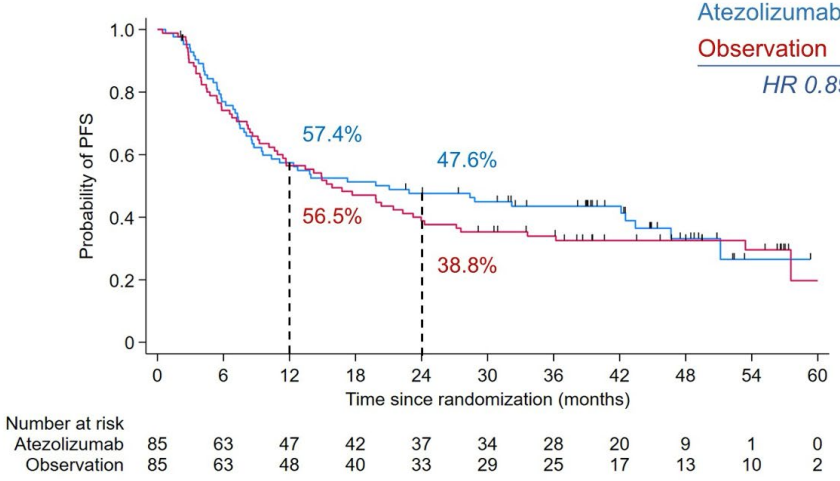
ACHILES: Atezolizumab en mantenimiento / Gronberg BH et al



		Atezolizumab (n=85)		Observation (n=85)	
		n	%	n	%
Platinum	*4 courses of cisplatin*	40	47.1%	52	61.2%
	≥1 course of carboplatin	45	52.9%	33	38.8%
TRT-dose	*45 Gy*	71	85.9%	71	83.5%
	60 Gy	12	14.1%	14	16.5%
Response to CRT	*Complete response*	12	14.1%	11	12.9%
	Partial response	69	81.2%	69	81.2%
	Stable disease	4	4.7%	5	5.9%
Received PCI		67	78.8%	67	78.8%

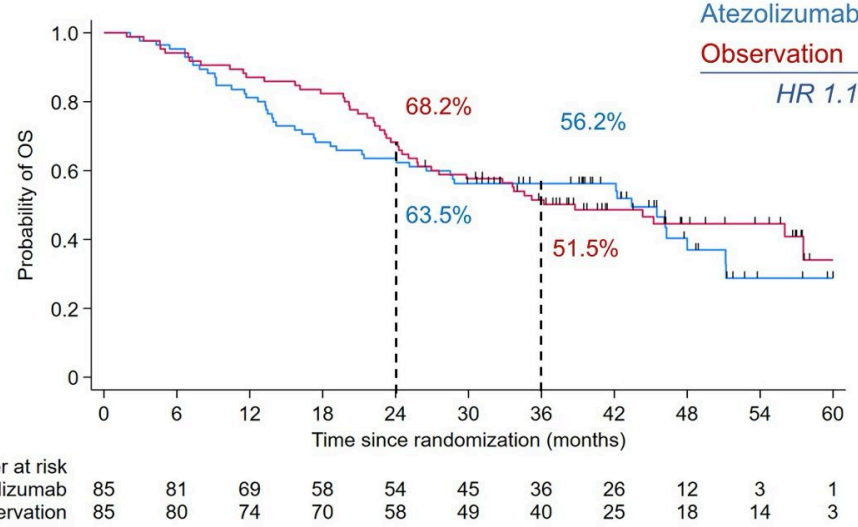
	Median	95% CI
Atezolizumab	21.1 months	9.5 – 43.4
Observation	15.9 months	10.6 – 24.0

HR 0.89, 95% CI 0.61 – 1.30, p=0.55

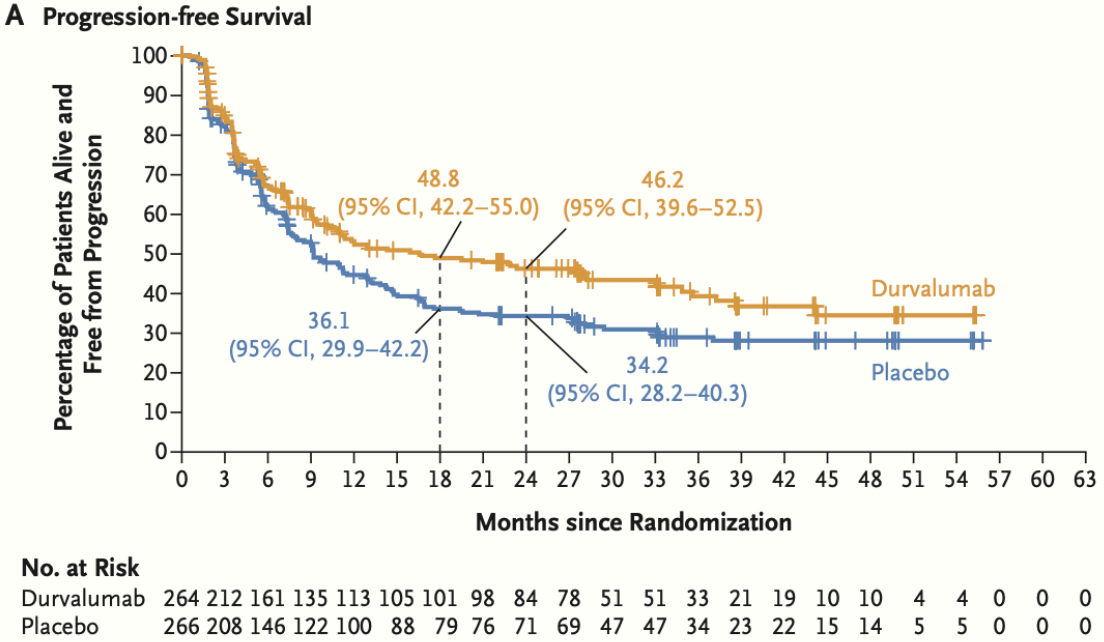


	Median	95% CI
Atezolizumab	43.4 months	25.1 – 51.2
Observation	38.8 months	25.8 – 57.6

HR 1.14, 95% CI 0.76 – 1.71, p=0.53



Durvalumab mantenimiento: EC Fase III ADRIATIC

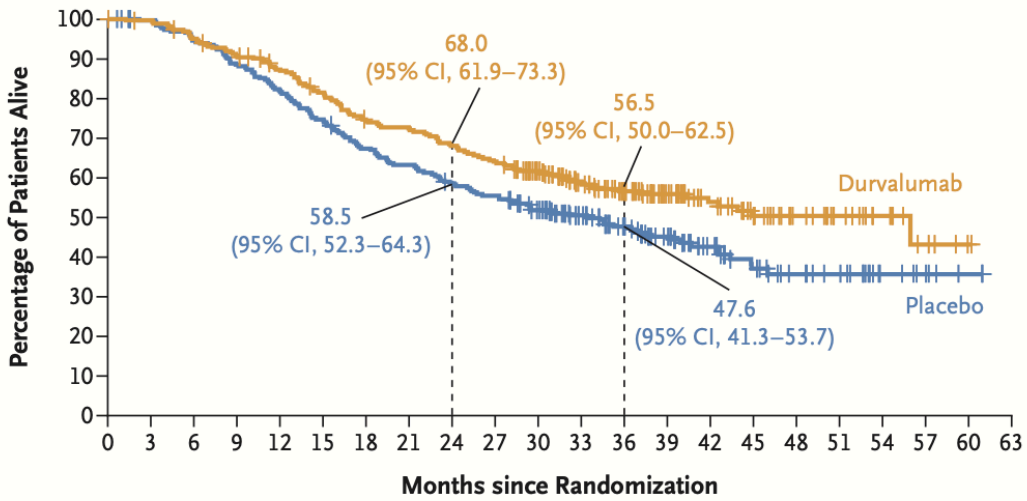


No. at Risk																					
Durvalumab	264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	0	0
Placebo	266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	0	0

	No. of Events/ Total No. (%)	Median Progression-free Survival (95% CI)
		mo
Durvalumab	139/264 (52.7)	16.6 (10.2–28.2)
Placebo	169/266 (63.5)	9.2 (7.4–12.9)

Stratified hazard ratio for disease progression or death, 0.76
(99.816% CI, 0.53–1.08)
(97.195% CI, 0.59–0.98)
P=0.02

N Engl J Med 2024;391:1313-27.
DOI: 10.1056/NEJMoa2404873



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

	No. of Deaths/ Total No. (%)	Median Overall Survival (95% CI)
		mo
Durvalumab	115/264 (43.6)	55.9 (37.3–NR)
Placebo	146/266 (54.9)	33.4 (25.5–39.9)

Stratified hazard ratio for death, 0.73 (98.321% CI, 0.54–0.98)
P=0.01

SMALL2: Lurbinectedina + Atezolizumab en 2L / Ponce S et al

Key Eligibility Criteria:
- Age ≥ 18 years
- Histologically/cytologically confirmed advanced SCLC
- Progression to 1L platinum based CT ± PD1/PDL1
- CTFI ≥30 days
- Measurable disease
- ECOG PS (0/1)
- Brain metastasis allowed if treated and asymptomatic

SCLC Progression after 1L CT±PD1/PDL1

- Cohort 1: **IO-naïve**
- Cohort 2: **IO-exposed**

RP2D

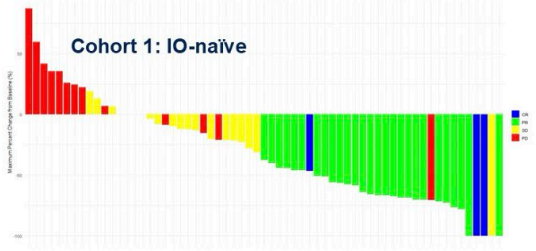
Lurbinectedin 3.2 mg/m² IV Q3W + Atezolizumab 1200 mg IV Q3W

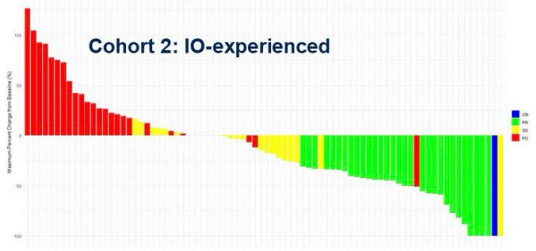
(with prophylactic G-CSF)

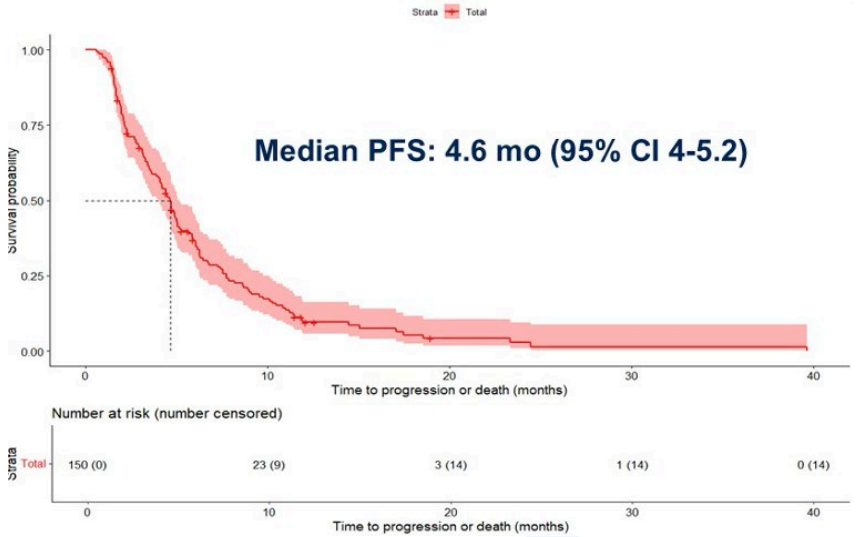
Primary endpoints
- Safety
- ORR (per RECIST v1.1)

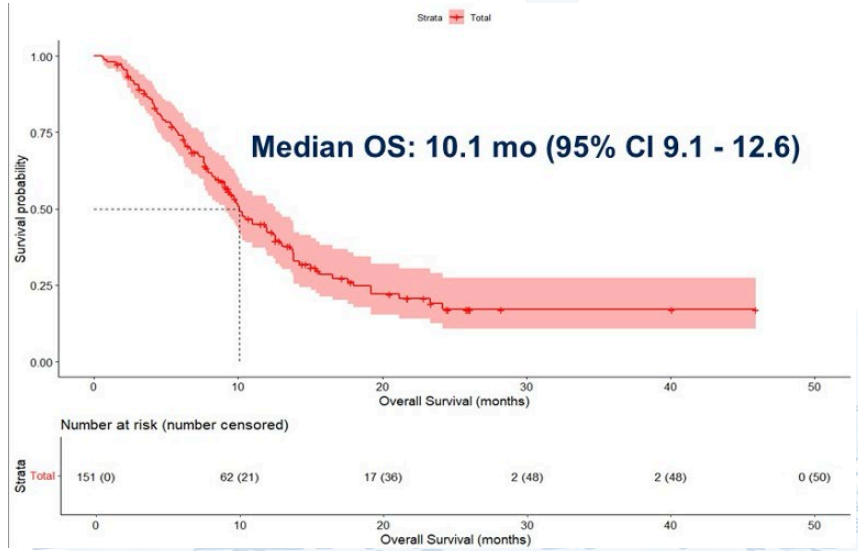
Secondary endpoints
- Duration of response (DoR)
- Clinical benefit (CB) CR, PR, SD ≥3 mo)
- PFS
- OS
- Others: PK, PGt and PGx

	Cohort 1 IO-naïve (n=68)	Cohort 2 IO-experienced (n= 83)	TOTAL n=151	Platinum - sensitive CTFI ≥90 days (n=92)	Platinum - resistant CTFI 30 to <90 days (n=59)
ORR n, % (95% CI)	30, 44.1% (32.3 - 56.6 %)	31, 37.3% (27.2 - 48.7%)	61, 40.4% (32.6 - 48.7%)	40, 43.5% (33.3 - 54.2%)	21, 35.6% (23.9% - 49.2%)
DoR, mo, median (95% CI)	5.6 (3.9 - 7.5)	3.97 (3 - 4.4)	4.1 (3.3 - 5.6)	4.4 (3.3 - 7.0)	4.07 (2.9 - 6.0)
DCR (%)	51 (75%)	56 (67.5%)	107 (70.9%)	66 (71.7%)	41 (69.5%)

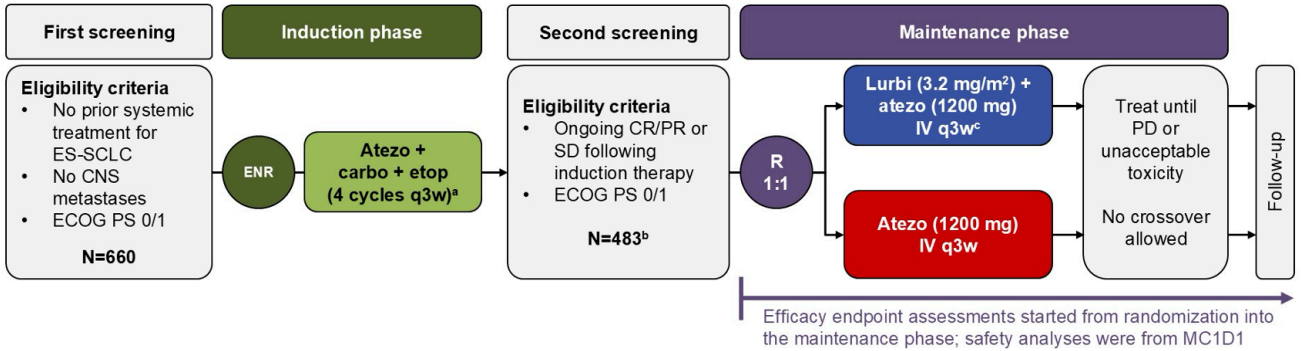








IMforte: Atezo +/- Lurbenectedina en mantenimiento / Paz-Ares et al

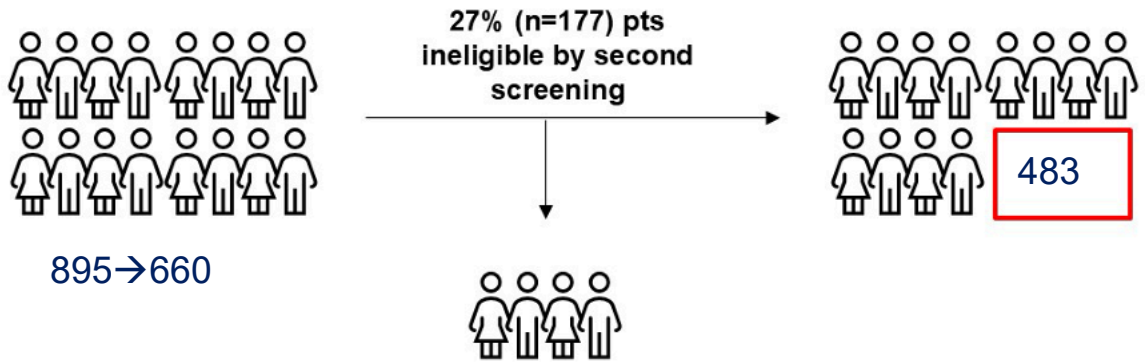


Last patient randomized: April 30, 2024
Clinical cutoff: July 29, 2024

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



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Characteristic	Lurbi + atezo (n=242)	Atezo (n=241)
Age, median (range), years	65.0 (38-85)	67.0 (35-85)
<65 years, n (%)	118 (48.8)	90 (37.3)
Sex, male, n (%)	151 (62.4)	151 (62.7)
Race, n (%)		
White	195 (80.6)	199 (82.6)
Asian	31 (12.8)	31 (12.9)
Other[a]	16 (6.6)	11 (4.6)
Current or previous tobacco use history, n (%)	235 (97.1)	236 (97.9)
Liver metastases at induction BL, n (%)[b]	100 (41.3)	94 (39.0)
Prior PCI, n (%)[b]	34 (14.0)	37 (15.4)
ECOG PS 0 at maintenance BL, n (%)[b]	105 (43.4)	102 (42.3)
LDH ≤ULN at maintenance BL, n (%)[b]	176 (72.7)	179 (74.3)
Time from induction Cycle 1 Day 1 to randomization, median (range), mo	3.2 (2.6-4.6)	3.2 (2.7-5.2)
Response to induction therapy, n (%)[c]		
CR/PR	206 (87.3)	213 (88.8)
SD	28 (11.9)	25 (10.4)
PD[d]	2 (0.8)	2 (0.8)

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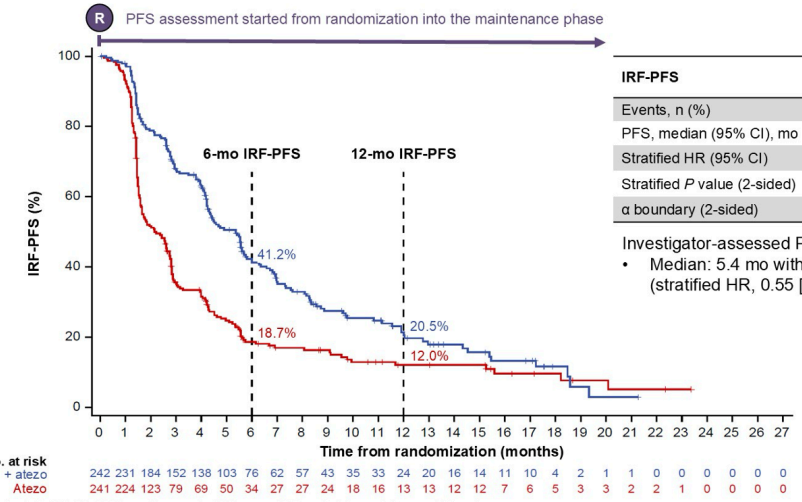
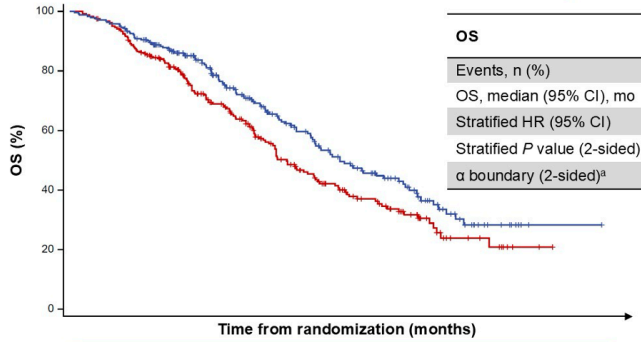
IMforte: Atezo +/- Lurbenectedina en mantenimiento / Paz-Ares et al



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])



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]

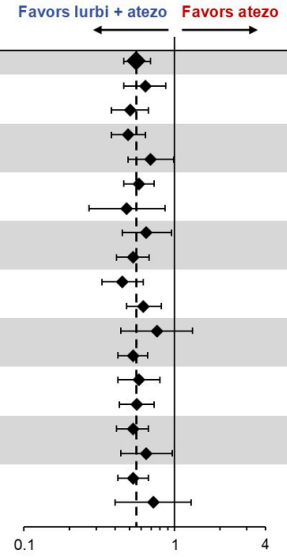
R

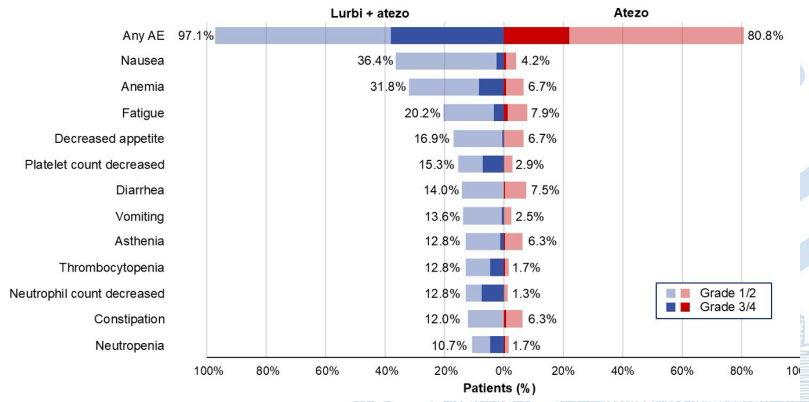
Maintenance treatment
Lurbi + atezo
Median OS from randomization: 13.2 months

Maintenance treatment
Atezo
Median OS from randomization: 10.6 months

IMforte results do not include time on induction treatment

Baseline risk factors		Events/patients, n/N Lurbi + atezo	Atezo	Unstratified IRF-PFS HR (95% CI)
All patients		174/242	202/241	0.56 (0.46, 0.69)
Age, years	<65	86/118	73/90	0.64 (0.46, 0.87)
	≥65	88/124	129/151	0.51 (0.38, 0.67)
Sex	Male	110/151	131/151	0.49 (0.38, 0.64)
	Female	64/91	71/90	0.69 (0.49, 0.98)
Race[a]	White	140/195	167/199	0.58 (0.46, 0.73)
	Asian	22/31	26/31	0.48 (0.27, 0.86)
Tobacco use history[a]	Current	61/88	57/73	0.65 (0.45, 0.95)
	Previous	107/147	141/163	0.53 (0.41, 0.68)
Liver metastases at induction BL[b]	Yes	75/100	87/94	0.45 (0.33, 0.62)
	No	99/142	115/147	0.62 (0.48, 0.82)
Prior PCI[b]	Yes	25/34	29/37	0.76 (0.44, 1.31)
	No	149/208	173/204	0.53 (0.42, 0.66)
ECOG PS[b]	0	76/105	82/102	0.58 (0.42, 0.80)
	1	98/137	120/139	0.56 (0.43, 0.73)
LDH[b]	≤ULN	123/176	150/179	0.53 (0.41, 0.67)
	>ULN	51/66	52/62	0.65 (0.44, 0.96)
Response to induction therapy[a,c]	CR/PR	143/206	176/213	0.53 (0.42, 0.67)
	SD	26/28	23/25	0.72 (0.40, 1.29)





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)

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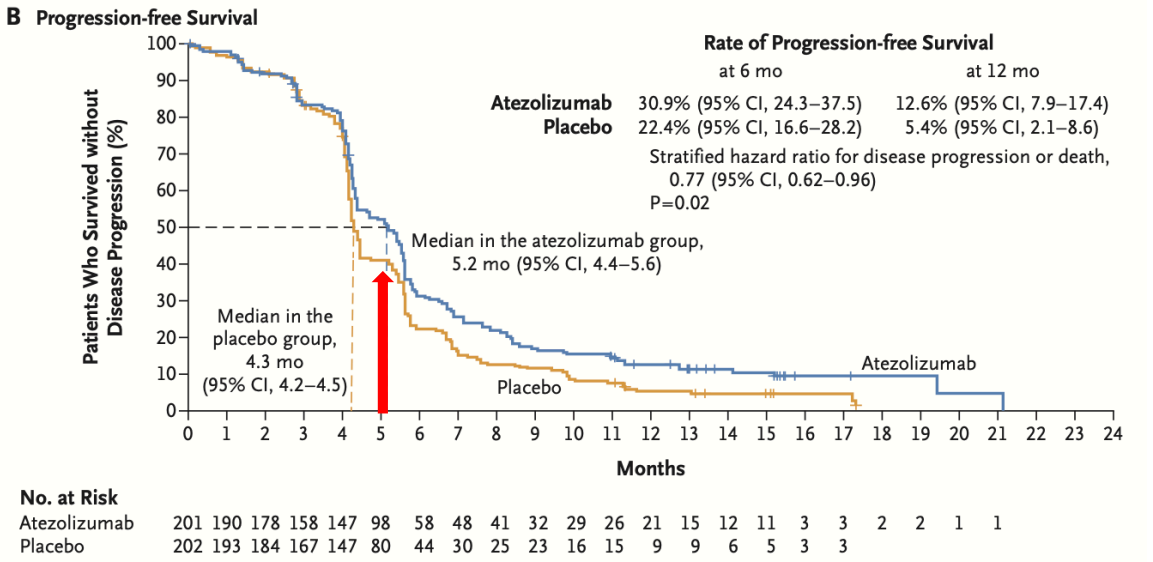
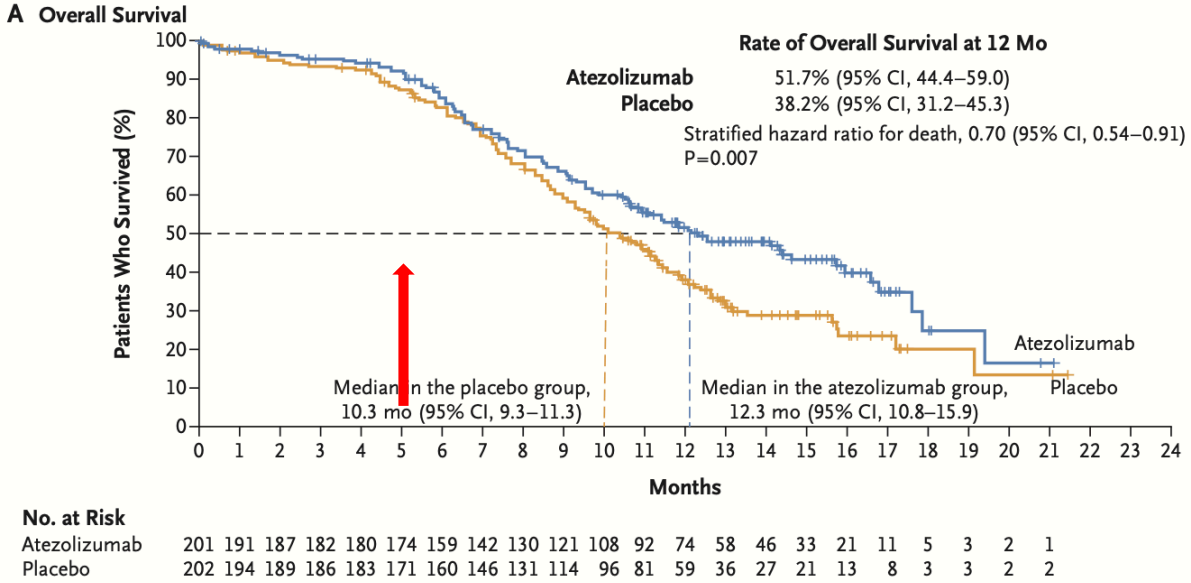
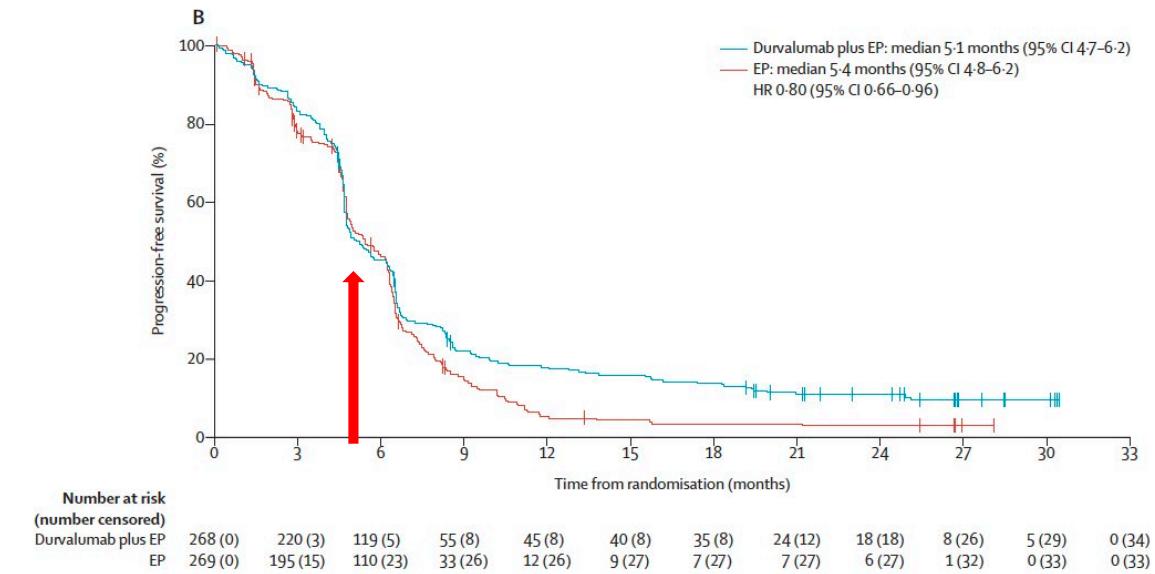
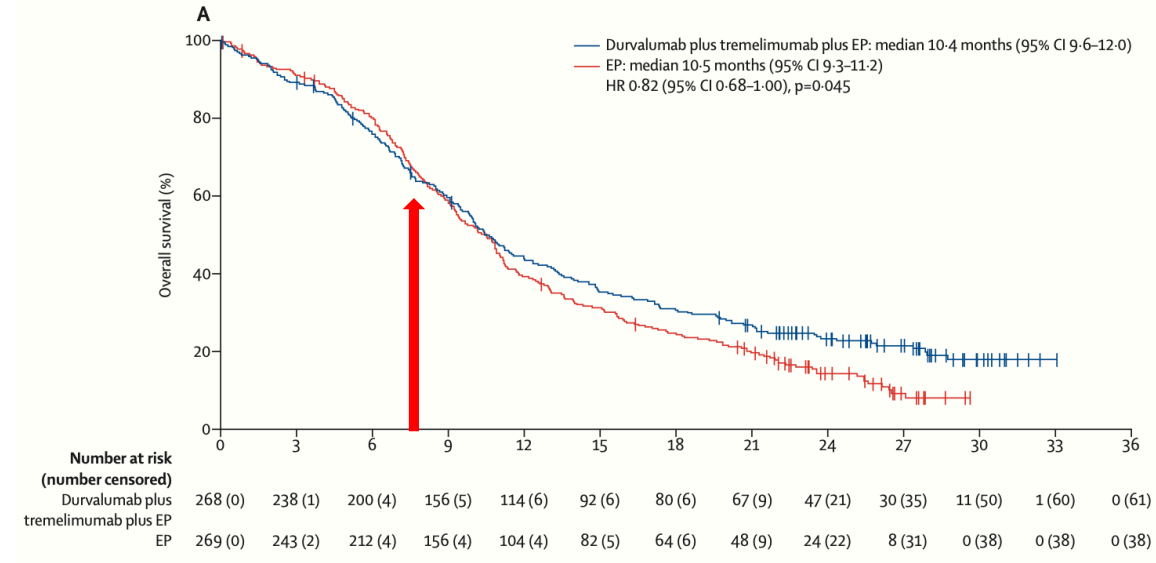
Atezolizumab (IMPower 132); Durvalumab (CASPIAN)





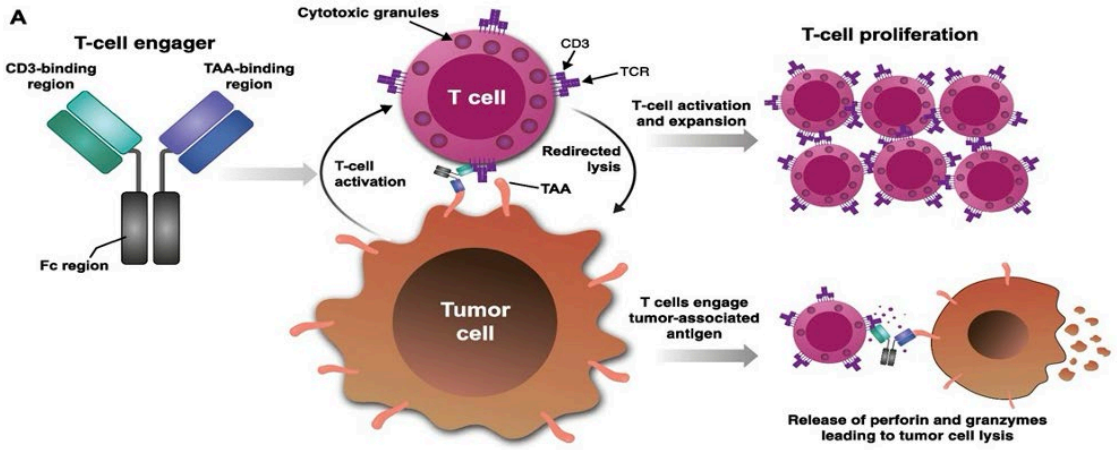


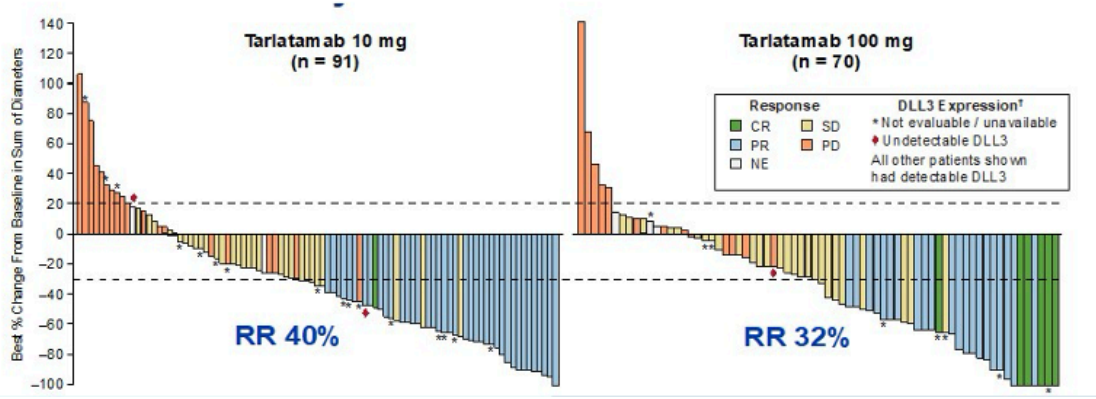


N Engl J Med 2018;379:2220-9. DOI: 10.1056/NEJMoa1809064

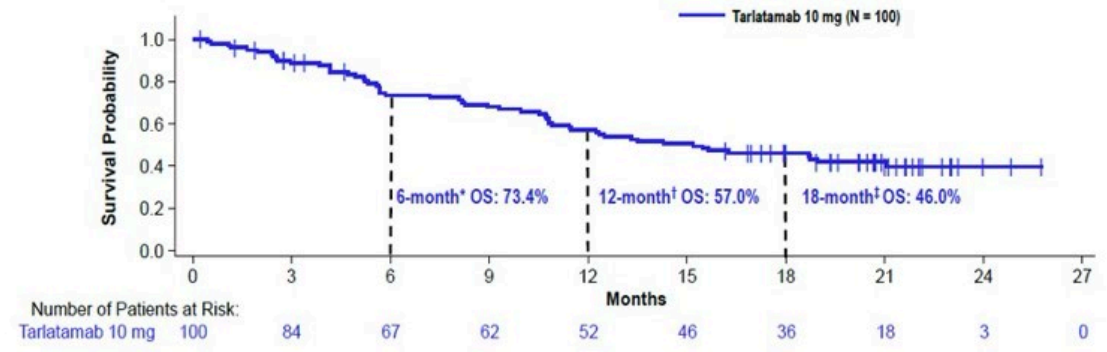
Lancet Oncol 2021; 22: 51–65

DeLLphi 304 Tarlatamab vs CT en 2L / Rudin Ch et al





Overall Survival



Median OS was 15.2 months (95% CI, 10.8–NE)

Randomized, controlled, 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)

R 1:1 (N = 509)

- Tarlatamab (n = 254)
- Chemotherapy* (n = 255)

Topotecan (n = 185); Lurbinectedin (n = 47); Amrubicin (n = 23)

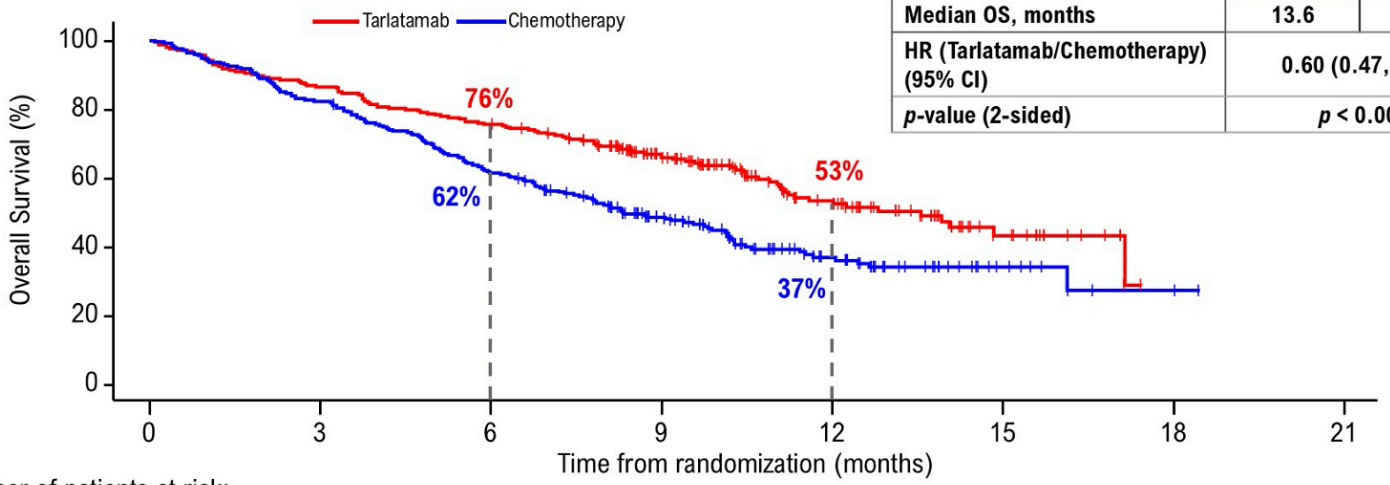
Primary Endpoint: Overall survival
Key Secondary Endpoints: Progression-free survival, patient-reported outcomes
Other Secondary Endpoints: Objective response, disease control, duration of response, safety

*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.

published on June 2, 2025, at NEJM.org. DOI: 10.1056/NEJMoa2502099

DeLLphi 304 Tarlatamab vs CT en 2L / Rudin Ch et al

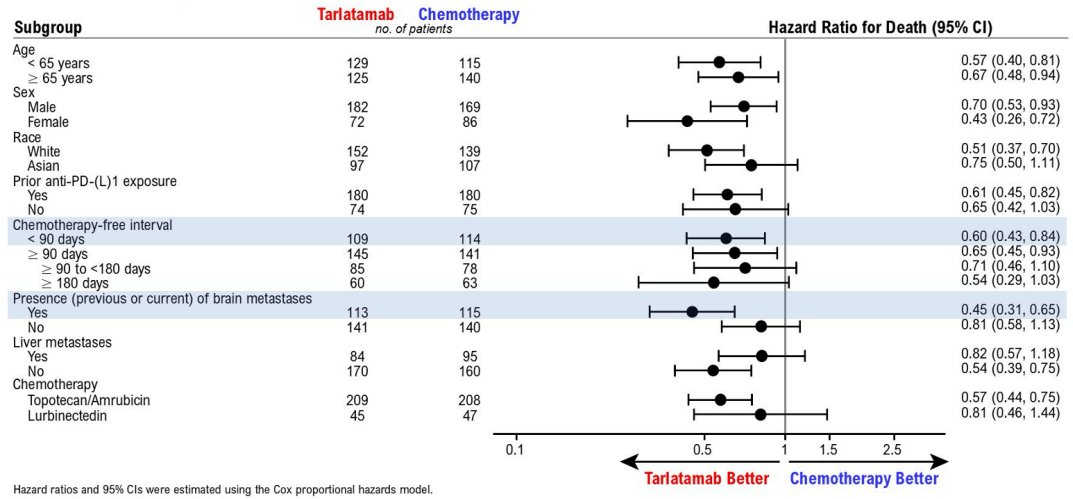
	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median age, years (range)	64 (20 – 86)	66 (26 – 84)
Male / Female, %	72 / 28	66 / 34
Race		
Asian / Black / White, %	38 / 1 / 60	42 / 1 / 55
Smoking history		
Current or former smokers / Never smokers, %	91 / 9	88 / 12
ECOG performance status, 0 / 1, %	33 / 67	31 / 68
Prior anti-PD-(L)1 therapy, %	71	71
Prior radiotherapy for current malignancy*, %	63	63
Chemotherapy-free interval,%		
< 90 days	43	45
≥ 90 to < 180 days	33	31
≥ 180 days	24	25
Presence of brain / liver metastases, %	44 / 33	45 / 37
DLL3 expression, %, (n/N†)	95 (207/217)	93 (198/214)



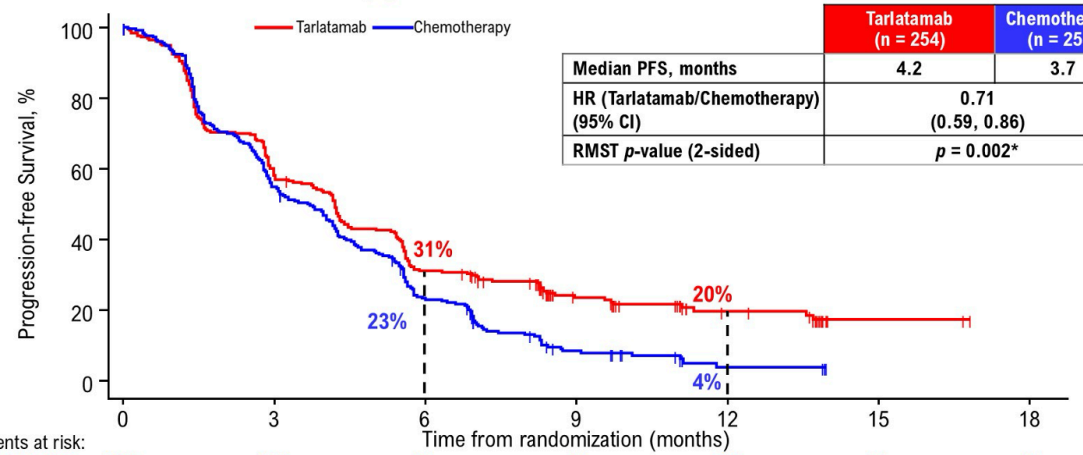
	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median OS, months	13.6	8.3
HR (Tarlatamab/Chemotherapy) (95% CI)	0.60 (0.47, 0.77)	
***p*-value (2-sided)**	*p* < 0.001	

Number of patients at risk:

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



Hazard ratios and 95% CIs were estimated using the Cox proportional hazards model.
PD-(L)1, programmed cell death (ligand)-1.



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

Number of patients at risk:

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

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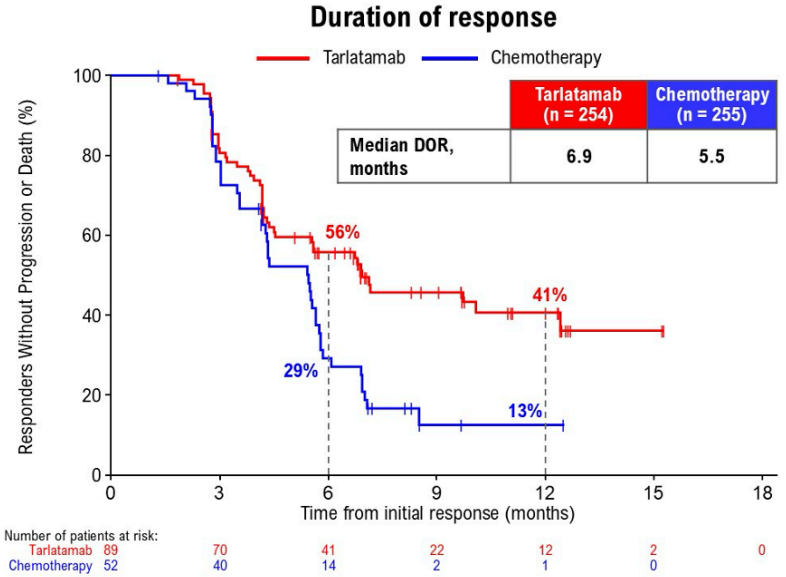
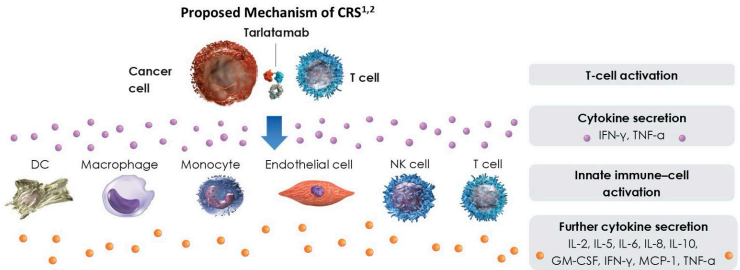
DeLLphi 304 Tarlatamab vs CT en 2L / Rudin Ch et al

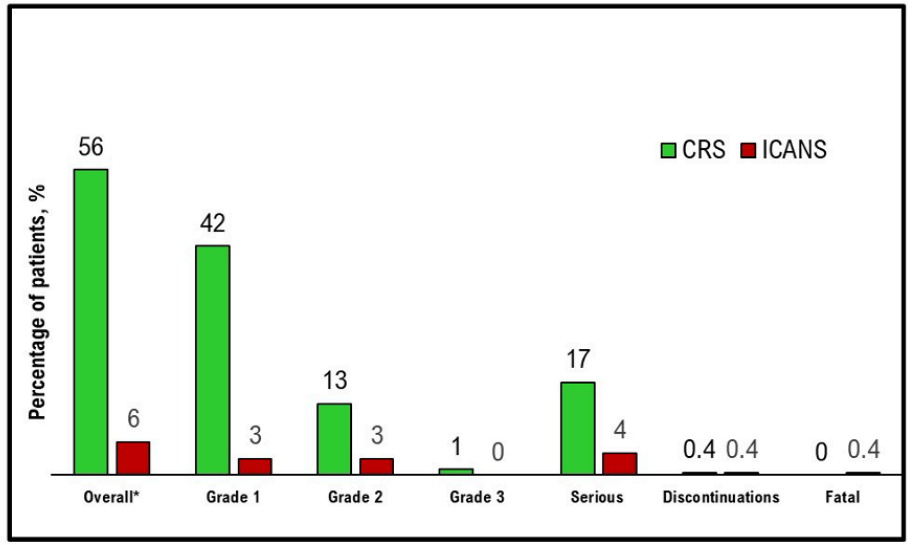
	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Best overall response*†, n (%)		
Complete response	3 (1)	0 (0)
Partial response	86 (34)	52 (20)
Stable disease	84 (33)	112 (44)
Progressive disease	56 (22)	50 (20)
Not evaluable/no post-baseline scan	25 (10)	41 (16)
Objective response rate‡, % (95% CI)	35 (29–41)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

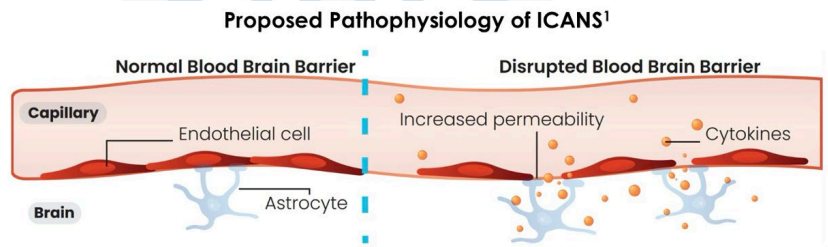




CRS with first two infusions

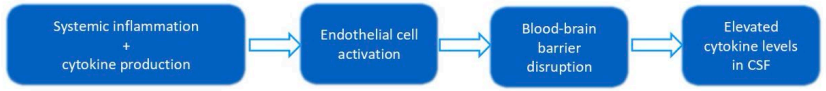
Tarlatamab (N = 252)	Minimum required monitoring duration: 6 - 8 Hours (n = 43)	48 Hours (n = 209)
Treatment emergent CRS, n (%)*	16 (37)	125 (60)
Grade 1	12 (28)	94 (45)
Grade 2	4 (9)	28 (13)
Grade 3	0 (0)	3 (1)
Serious adverse events	3 (7)	39 (19)
Leading to discontinuation of IP	0 (0)	1 (0.5)
Median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





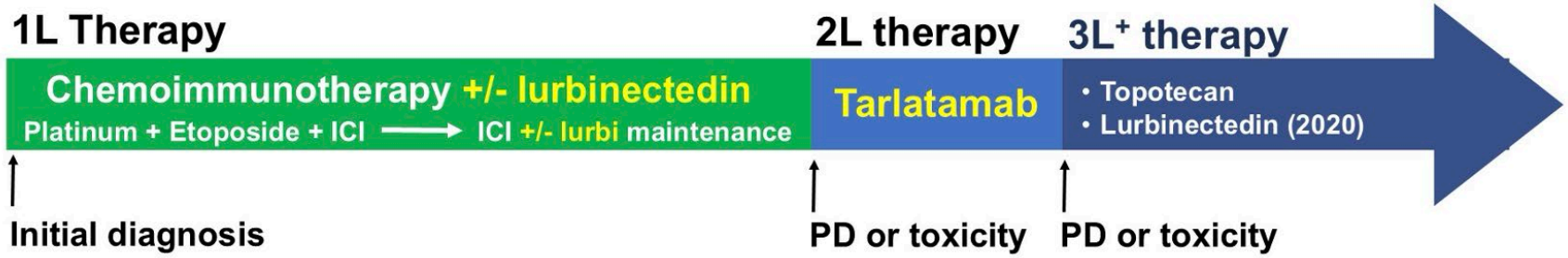
The pathophysiology of ICANS is poorly understood[2]

Proposed mechanism:[3]



published on June 2, 2025, at NEJM.org. DOI: 10.1056/NEJMoa2502099

Evolución de la diana terapéutica DLL-3 en SCLC



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

Is tarlatamab more effective in combination?

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

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

Alveltamig (TriTE; Biparatópico) Fase II / Ai X et al

- This is a randomized, multicenter, open-label phase 2 study of ZG006 as monotherapy in SCLC patients who failed at least 2 prior lines of standard systemic treatments

Key Eligibility Criteria

- 18-75 years of age
- ECOG 0 or 1
- Histologically or cytologically confirmed diagnosis of primary SCLC, who have relapsed or progressed after prior treatment with platinum-based doublet therapy and at least one other systemic therapy
- At least 1 measurable lesion as defined by RECIST 1.1
- Adequate organ function
- DLL3 expression was not required for study entry but were retrospectively evaluated by the Ventana SP347 assay

R 1:1

ZG006
10 mg IV Q2W (N=30)

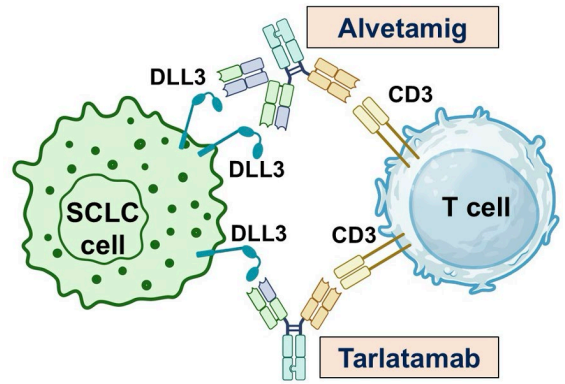
Stratification factor:
Presence or absence of brain metastases

ZG006
30 mg IV Q2W (N=30)

Dose Selection

Endpoint
- Primary: ORR
- Secondary: PFS, DoR, OS, and safety

- Priming dose of 1 mg given at C1D1, followed by the target dose (10 or 30 mg) from C2D1
- Each treatment cycle is 2 weeks



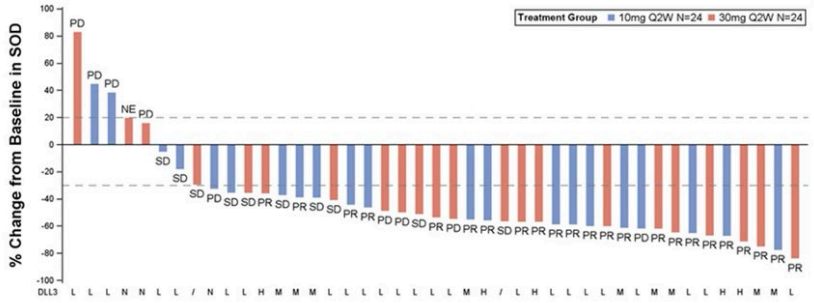
Is TriTE > BiTE?

Characteristics		10 mg Q2W (N=24)	30 mg Q2W (N=24)
Median Age (Min, Max) (years)		57 (48, 72)	57.5 (48, 73)
Gender, n (%)	Male	18 (75.0)	19 (79.2)
	Female	6 (25.0)	5 (20.8)
Baseline ECOG Performance Status, n (%)	0	2 (8.3)	2 (8.3)
	1	22 (91.7)	22 (91.7)
Metastatic Sites, n (%)	Brain	7 (29.2)	7 (29.2)
	Liver	10 (41.7)	13 (54.2)
Prior Lines of Systemic Therapy, n (%)	2	13 (54.2)	15 (62.5)
	3	9 (37.5)	4 (16.7)
	≥4	2 (8.3)	5 (20.8)
Prior PD-(L)1 Therapy, n (%)	Yes	21 (87.5)	21 (87.5)
	No	3 (12.5)	3 (12.5)
Duration of Platinum Sensitivity, n (%)	< 90 days	6 (25.0)	10 (41.7)
	≥ 90 days	17 (70.8)	11 (45.8)
Baseline DLL3 Expression, n (%)	Assessable cases	24 (100.0)	21 (87.5)
	Low expression	15 (62.5)	12 (50.0)
	Medium expression	6 (25.0)	4 (16.7)
	High expression	2 (8.3)	3 (12.5)
	Negative	1 (4.2)	2 (8.3)

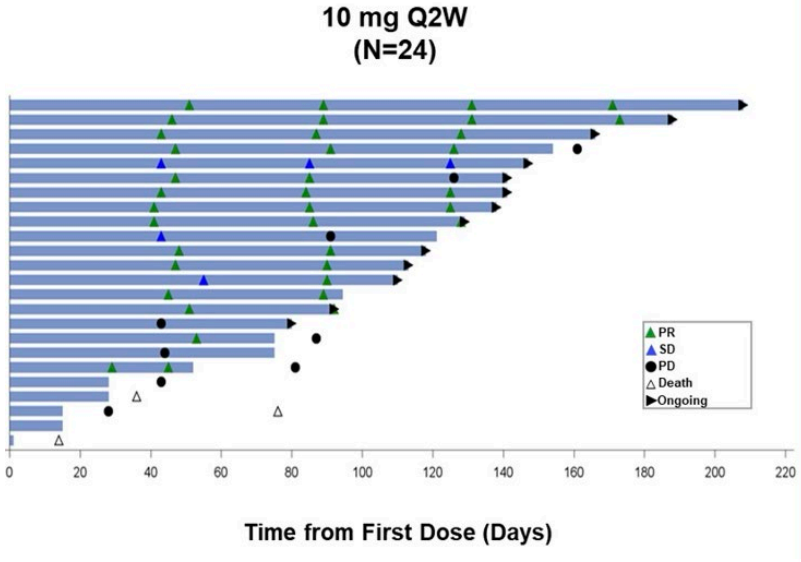
Alveltamig (TriTE; Biparatópico) Fase II / Ai X et al

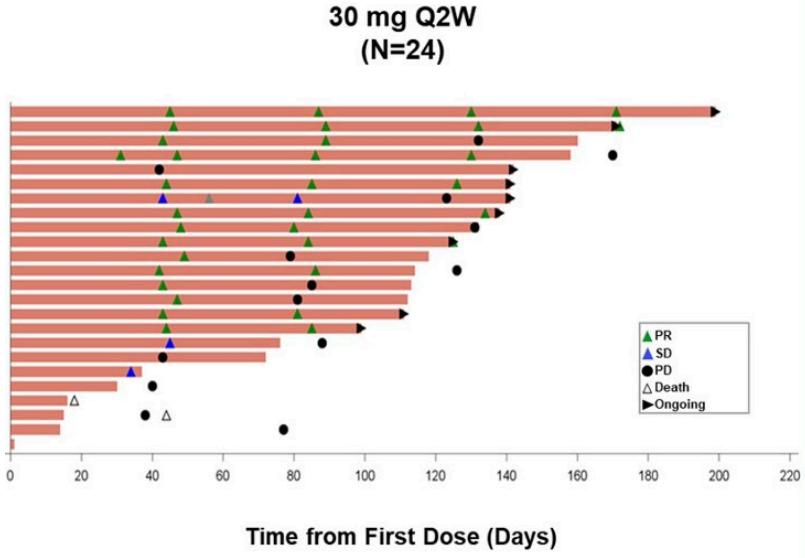
	10 mg Q2W (N=24)	30 mg Q2W (N=24)
BOR		
CR, n (%)	0	0
PR, n (%)	15 (62.5)	14 (58.3)
SD, n (%)	2 (8.3)	2 (8.3)
PD, n (%)	6 (25.0)	6 (25.0)
NE, n (%)	1 (4.2)	2 (8.3)
ORR*, n (%) **95% CI**	15 (62.5) (40.6, 81.2)	14 (58.3) (36.6, 77.9)
DCR*, n (%) **95% CI**	17 (70.8) (48.9, 87.4)	16 (66.7) (44.7, 84.4)

Mediana f-u 3 m

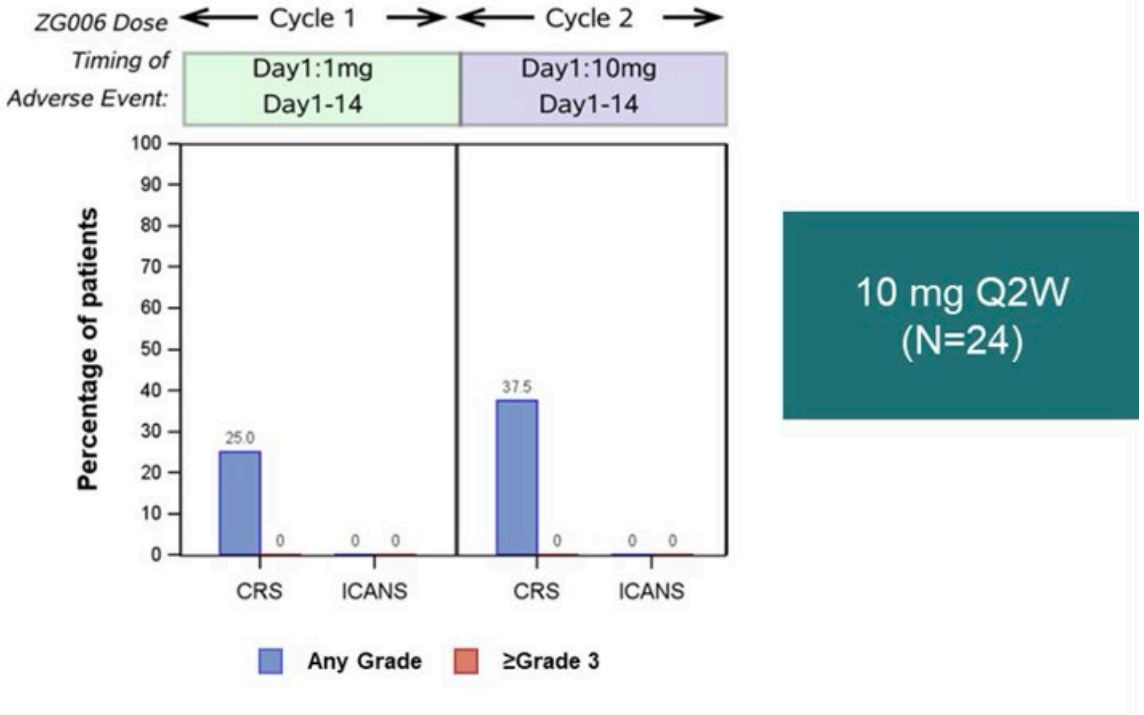


N: Negative; L: Low expression; M: Medium expression; H: High expression; /: NA.

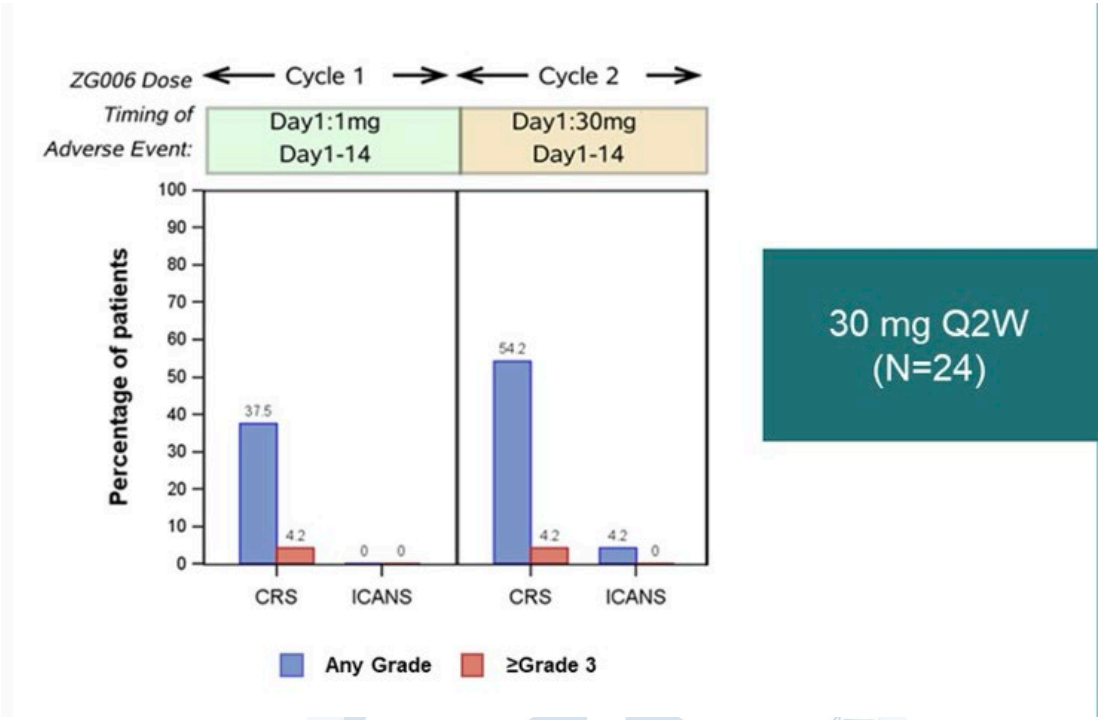




Alveltamig (TriTE; Biparatópico) Fase II / Ai X et al



10 mg Q2W
(N=24)



30 mg Q2W
(N=24)

Manejo efectos secundarios BITES DLL-3

Efficacy

- Median duration of follow–up (95% CI): 207 (106, 231) days and 30 of 42 patients experienced disease progression or death.
- Median progression free survival was 101 (62, 120) days. (Figure 2) Median overall survival was 215 (144, NA) days. (Figure 3)

Best Response	
PD	8 (19)
SD	10 (23.8)
PR	13 (31)
NE	11 (26.2)

Table 2: Response breakdown

Safety

- CRS and ICANs were reported in 29 (60%) patients, 3 (6.25%) experienced grade 3 CRS and 5 (10.4%) experienced grade 3 ICANS. (Table 3)
- Thirteen patients were directly admitted from the ICC for CRS/ICANS. (Figure 4)
- Patients were evaluated for infections, increased liver function tests (LFTs) and neutropenia.
  - Zero patients required dose holds or discontinuation of treatment due to neutropenia or elevated LFTs
  - Five patients were admitted for infection workup (2 Urinary tract infection, 1 sepsis, 2 pneumonia)
- Eighteen patients required dose holds, with four of those who reinitiated step up dosing.

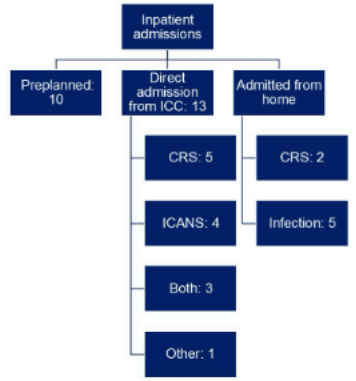


Figure 4: Admissions Breakdown

Grade	CRS	ICANS
1	12	9
2	9	8
3	3	5
4	0	0

Table 3: Breakdown of CRS and ICANS (n=48)

Conclusions

Outpatient administration of tarlatamab has higher rates of toxicity but is feasible and manageable with appropriate monitoring, including for patients with an ECOG performance status of 2.

A limitation is the need for education on guideline-directed management for CRS and ICANS.

Carlisle JW et al Abstract 8106

FIGURE 1: Hospital based outpatient tarlatamab administration at Mayo Clinic

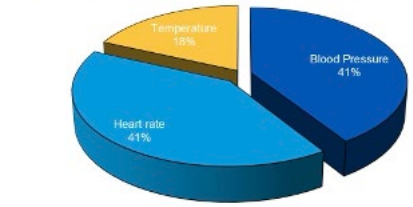


FIGURE 2: Distribution of RPM Alerts

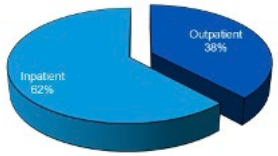
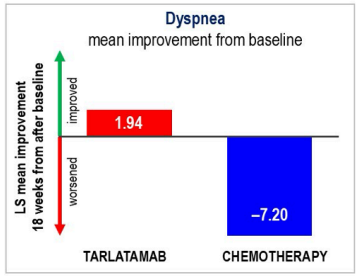
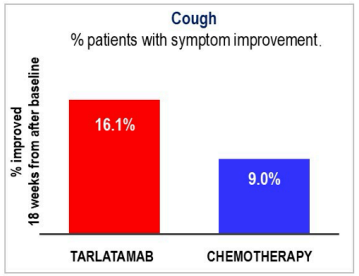


FIGURE 3: Patients treated Outpatient Vs Inpatient

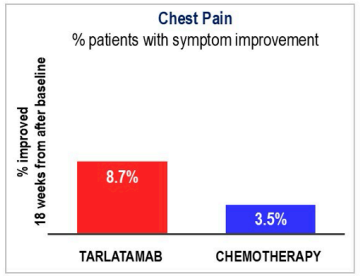
Potter A et al Abstract 1652



LS mean difference = -9.14*
95% CI (-12.64, -5.64)
$p < 0.001$



Odds ratio = 2.04*
95% CI (1.17, 3.55)
$p = 0.012$



Odds ratio = 1.84*
95% CI (0.89, 3.81)
$p = 0.1$
(Did not meet statistical significance)

Mesotelioma: MTAP Del; CAR-T

Maximum change in size of target lesions by mRECIST or RECIST among patients treated with immunotherapy

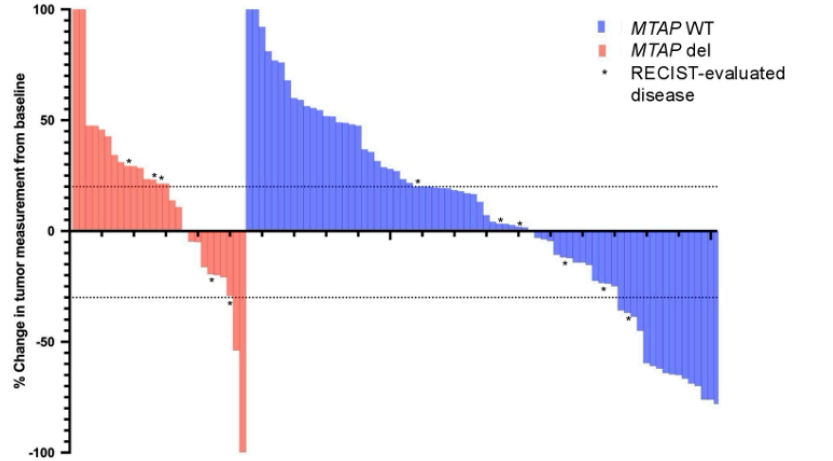


Figure 3. Unconfirmed maximum percentage change in size of target lesions from baseline by mRECIST or RECIST among patients treated with immunotherapy in any treatment line.

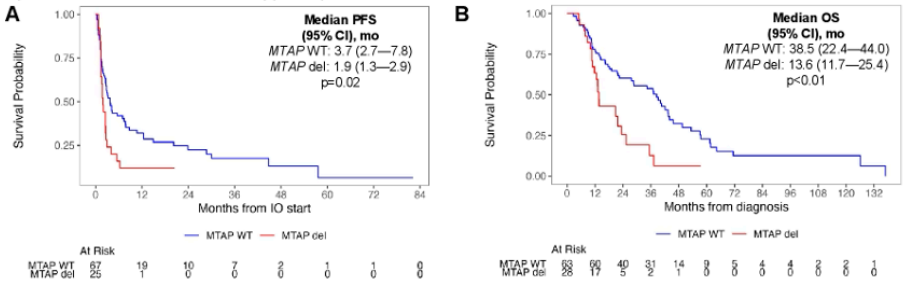


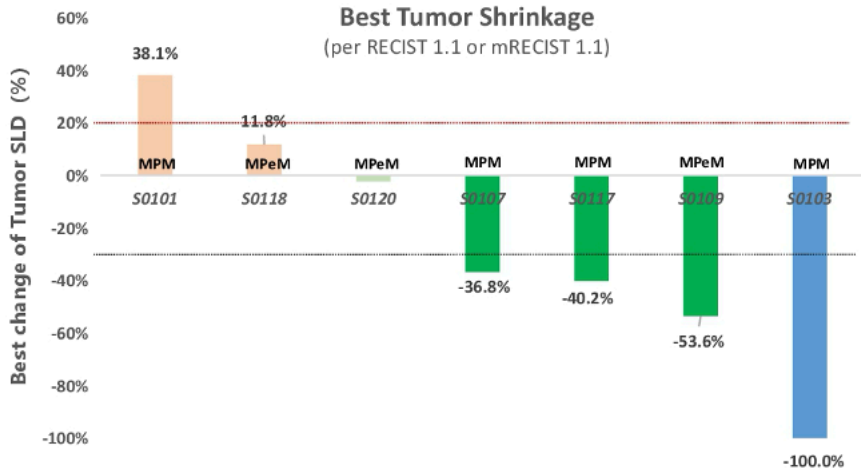
Figure 4 Kaplan-Meier estimates of **A)** progression-free survival on IO (immunotherapy) and **B)** overall survival between the *MTAP* del and *MTAP* wildtype cohorts.

Conclusions & Next Steps

- *MTAP* del (co-occurring with *CDKN2A* del) was identified in both epithelioid and non-epithelioid DPM.
- *MTAP* del was associated with a lower disease control rate and shorter progression-free survival on IO as well as shorter overall survival compared to *MTAP* WT.

Ross JS et al Abstract 8081

Clinical Response	DL 1 (0.5×10⁶/kg) (n=1)	DL 2 (1.0×10⁶/kg) (n=2)	DL3 (0.6-0.8×10⁶/kg) (n=4)
*ORR, n(%)	0	2 (100%)	2 (50%)
CR	0	1 (50%)	0
PR	0	1 (50%)	2 (50%)
SD	0	0	2 (50%)
PD	1 (100%)	0	0
DCR, n(%)	0	2 (100%)	4 (100%)



Sun Y et al Abstract 2534

BNT327/PM8002 Mesotelioma / Cheng Y et al

N=31 *

BNT327 (30 mg/kg) + pemetrexed (500 mg/m²) + platinum#, IV, Q3W for 4 to 6 cycles §

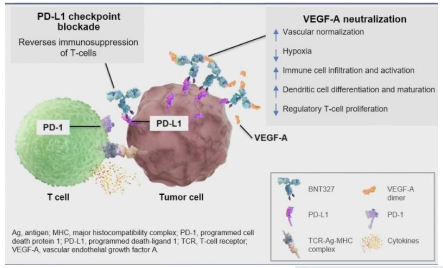
→

Maintenance: BNT327 (30 mg/kg), IV, Q3W until disease progression or unacceptable toxicity

Primary endpoints
- ORR per mRECIST v1.1 (pleural) and RECIST v1.1 (peritoneal)
- TRAEs per NCI-CTCAE v5.0

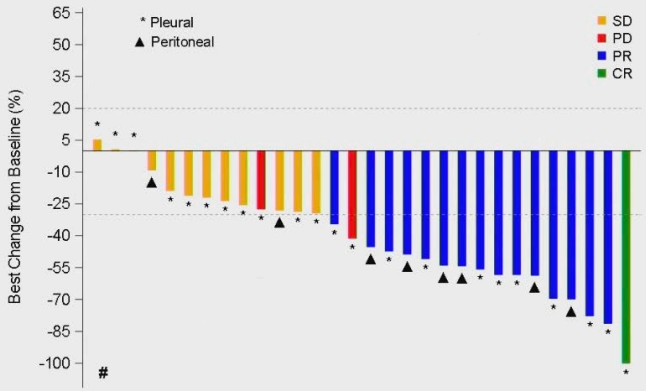
Secondary endpoints
- PFS, DCR, and DOR per mRECIST v1.1 (pleural) and RECIST v1.1 (peritoneal)
- OS

Patients
- Age ≥18 years, life expectancy of ≥12 weeks, adequate organ function, and ECOG PS: 0 or 1
- Histologically confirmed, unresectable malignant mesothelioma
- No prior systemic anti-tumor therapy
- ≥ 1 measurable lesion (pleural mesothelioma per mRECIST v1.1; peritoneal mesothelioma per RECIST v1.1)

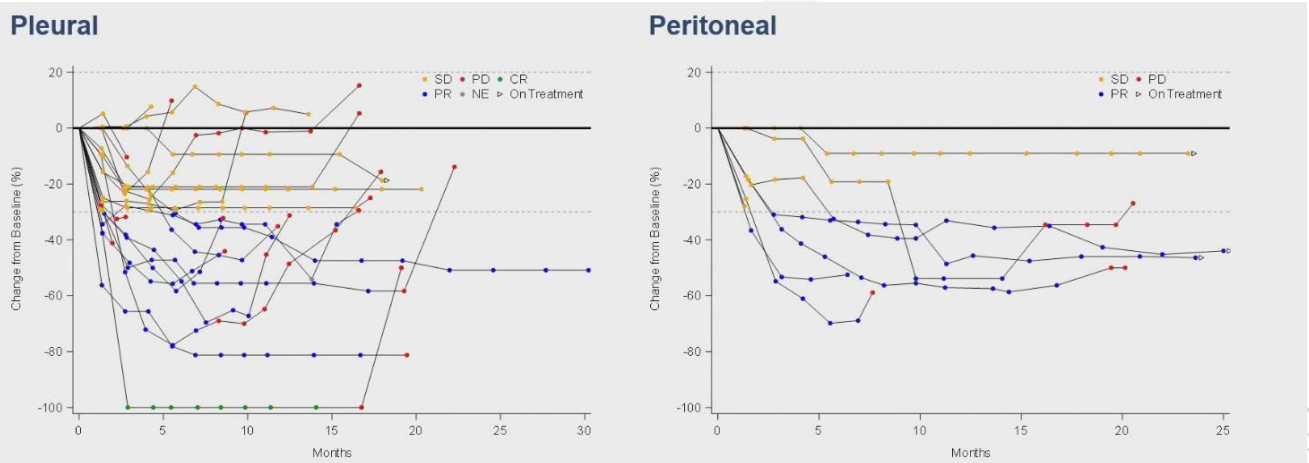


Patients, (N=31)	TEAE n (%)	TRAE n (%)
AE	31 (100)	31 (100)
AE (Grade 3 or 4)	29 (93.5)	29 (93.5)
AE (Grade 5)	0	0
SAE	14 (45.2)	10 (32.3)
SAE (Grade 3 or 4)	9 (29.0)	5 (16.1)
AE leading to dose interruption	22 (71.0)	15 (48.4)
AE leading to dose discontinuation	6 (19.4)	6 (19.4)
AE leading to dose reduction	7 (22.6)	6 (19.4)

Patients, (N=31)	Any grade n (%)	Grade 3 n (%)
irAE	7 (22.6)	1 (3.2)



Response assessed by investigator	Total N=31	Pleural N=23	Peritoneal N=8
Best overall response, n			
CR	1	1	0
PR	15	9	6
SD	12	10	2
PD	2	2	0
Non-CR/Non-PD	1	1	0
cORR %, (95% CI)	**51.6 (33.1, 69.9)**	**43.5 (23.2, 65.5)**	**75.0 (34.9, 96.8)**
Epithelioid histology, n cORR %, (95% CI)	19 47.4 (24.5, 71.1)	13 30.8 (9.1, 61.4)	6 83.3 (35.9, 99.6)
DCR %, (95% CI)	**90.3 (74.3, 98.0)**	**87.0 (66.4, 97.2)**	**100 (63.0, 100)**
Epithelioid histology, n DCR %, (95% CI)	19 89.5 (66.9, 98.7)	13 84.6 (54.6,98.1)	6 100 (54.1, 100)



- Responses were durable with median duration of response of 15.2 months (95% CI: 5.8, 17.8).
  - Pleural mesothelioma: 11.8 months (5.6, 17.8).
  - Peritoneal mesothelioma: 16.3 months (4.8, --).

Data cut: 28th March 2025; median follow-up: 22.3 months overall, 24.0 months peritoneal mesothelioma, 20.3 months pleural mesothelioma
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease

BNT327/PM8002 Mesotelioma / Cheng Y et al

Single arm, open label Phase 2 trial conducted in China (NCT05918107 / CTR20221048)

N=31 *

BNT327 (30 mg/kg) + pemetrexed (500 mg/m²) + platinum#, IV, Q3W for 4 to 6 cycles §

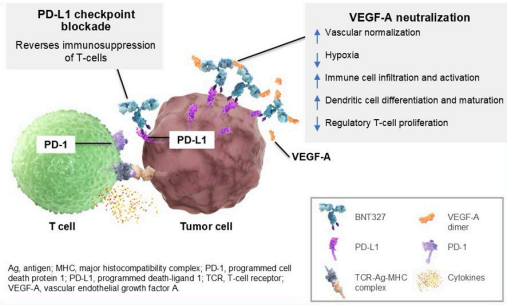
→

Maintenance: BNT327 (30 mg/kg), IV, Q3W until disease progression or unacceptable toxicity

Primary endpoints
- ORR per mRECIST v1.1 (pleural) and RECIST v1.1 (peritoneal)
- TRAEs per NCI-CTCAE v5.0

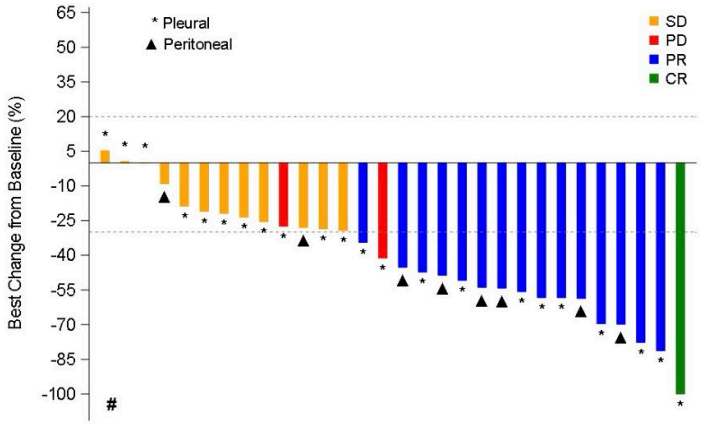
Secondary endpoints
- PFS, DCR, and DOR per mRECIST v1.1 (pleural) and RECIST v1.1 (peritoneal)
- OS

Patients
- Age ≥18 years, life expectancy of ≥12 weeks, adequate organ function, and ECOG PS: 0 or 1
- Histologically confirmed, unresectable malignant mesothelioma
- No prior systemic anti-tumor therapy
- ≥ 1 measurable lesion (pleural mesothelioma per mRECIST v1.1; peritoneal mesothelioma per RECIST v1.1)



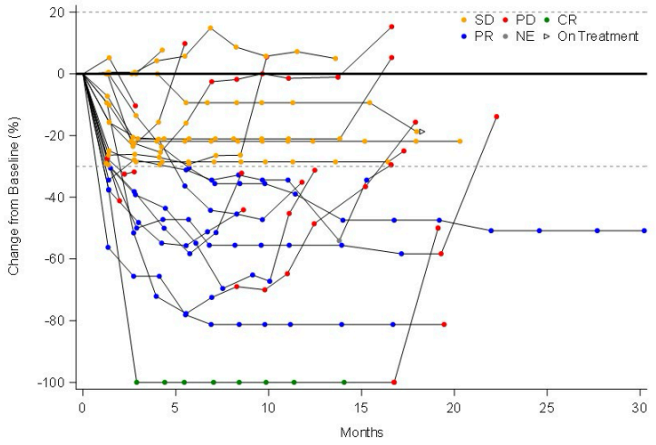
Patients, (N=31)	Any causality n (%)	Related n (%)
TEAE	31 (100)	31 (100)
TEAE (Grade 3 or 4)	29 (93.5)	29 (93.5)
TEAE (Grade 5)	0	0
SAE	14 (45.2)	10 (32.3)
SAE (Grade 3 or 4)	9 (29.0)	5 (16.1)
TEAE leading to dose interruption	22 (71.0)	15 (48.4)
TEAE leading to dose discontinuation	6 (19.4)	6 (19.4)
TEAE leading to dose reduction	7 (22.6)	6 (19.4)

Patients, (N=31)	Any grade n (%)	Grade 3 n (%)
irAE	7 (22.6)	1 (3.2)

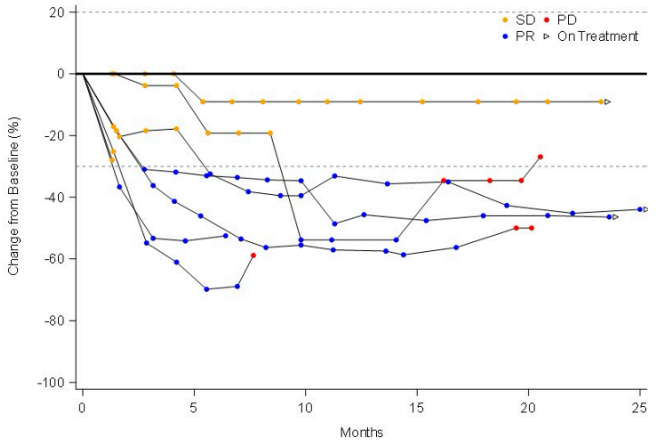


Response assessed by investigator	Total N=31	Pleural N=23	Peritoneal N=8
Best overall response#, n			
CR	1	1	0
PR	15	9	6
SD	12	10	2
PD	2	2	0
cORR %, (95% CI)	**51.6 (33.1, 69.9)**	**43.5 (23.2, 65.5)**	**75.0 (34.9, 96.8)**
Epithelioid histology, n	19	13	6
cORR %, (95% CI)	47.4 (24.5, 71.1)	30.8 (9.1, 61.4)	83.3 (35.9, 99.6)
DCR %, (95% CI)	**90.3 (74.3, 98.0)**	**87.0 (66.4, 97.2)**	**100 (63.0, 100)**
Epithelioid histology, n	19	13	6
DCR %, (95% CI)	89.5 (66.9, 98.7)	84.6 (54.6,98.1)	100 (54.1, 100)

Pleural



Peritoneal



Mediana Duración Respuesta: 15.,2 meses

Tumores tímicos: NIVOTHYM / Girard N et al

Advanced/relapsed thymic tumor

Type B3 thymoma or thymic carcinoma

No more than one line of platinum-based chemotherapy

No autoimmune disorder

Cohort 1:

Nivolumab
(240 mg IV Q2 weeks)

n=55

Previously published

Cohort 2:
Nivolumab
(240 mg IV Q2 weeks)
+ Ipilimumab
(1 mg/kg IV Q6 weeks)
n=56

Imaging at week 8 and then every 6 weeks

Primary endpoint :
PFS rate at 6 months per BICR (RECIST 1.1)

H0: PFSR-6 ≤ 40%
H1: PFSR-6 = 60%

Alpha = 0.1 (one-sided)
Power = 94%

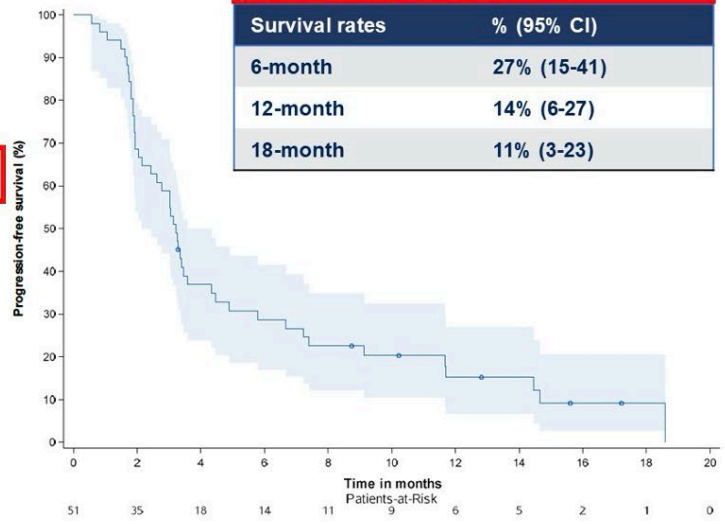
Secondary endpoints: PFSR-6 per local investigator, PFS, Response, OS, Safety

	Cohort 2 (n=56) n (%)
Maximal grade of adverse events	
1-2	29 (52)
3-4	27 (48)
Grade ≥3 Treatment-Related Adverse Events	16 (29)
Myocarditis	2 (4)
Colitis	4 (8)
Infusion-related reaction/allergy	2 (4)
Skin rash	2 (4)
Other: heart failure, immune-related hepatitis, arthritis, myositis, hypophysitis, Gougerot-Sjögren syndrome, pharyngitis, fatigue, fever, infusion-related reaction	1 patient each
Death related to Treatment-Related Adverse Events	0 (0)

PFSR-6 by central review	Nivolumab + Ipilimumab (n=51) Per protocol population n (%)
PFSR-6	
Failure	40 (78%)
Success	11 (22%)
Reason failure at 6 months	
Progressive disease (PD)	27 (68)
Death before PD	3 (8)
Start further therapy before PD	4 (10)
Missing disease evaluation at 6 months	6 (15)

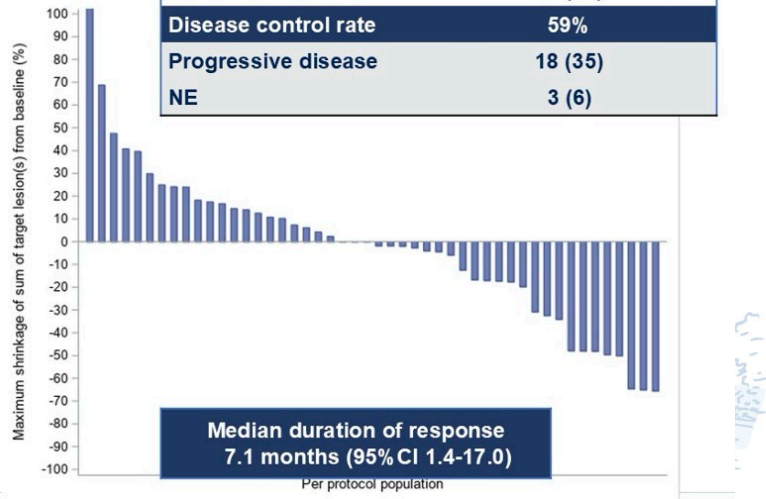
Median Follow-up 16.1 months

Median PFS: 3.1 (2.0-3.6) months	
Survival rates	**% (95% CI)**
6-month	27% (15-41)
12-month	14% (6-27)
18-month	11% (3-23)



Objective response

	Nivolumab + Ipilimumab (n=51) n (%)
Partial response	8 (16)
Stable disease	22 (43)
Disease control rate	59%
Progressive disease	18 (35)
NE	3 (6)



Median duration of response
7.1 months (95% CI 1.4-17.0)

Resumen

- Modificaciones en la práctica clínica en Ca Microcítico
  - Lurbinectedina en 2L y mantenimiento en asociación a Atezolizumab
  - Tarlatamab en 2L y con desarrollo en 1L
- Continua investigación factores predictivos y tratamientos más allá de la Inmunoterapia en Mesotelioma (ADCs, CAR-T)
- Limitados resultados con efectos secundarios significativos de la inmunoterapia en tumores tímicos