Lung Cancer UPDATES
ASCO HIGHLIGHTS
31 MAYO-04 JUNIO 2024
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Iniciativa científica de:
GECP lung cancer research

Otros tumores torácicos

Aitor Azkàrate Martínez

Hospital Universitari Son Espases

2024 ASCO ANNUAL MEETING

Abstract LBA5

ADRIATIC: durvalumab as consolidation treatment for patients with limited-stage small-cell lung cancer (LS-SCLC)

David R. Spigel, Ying Cheng, Byoung Chul Cho, Konstantin Laktionov, Jian Fang, Yuanbin Chen, Yoshitaka Zenke, Ki Hyeong Lee, Qiming Wang, Alejandro Navarro, Reyes Bernabe, Eva Buchmeier, John Wen-Cheng Chang, Isamu Okamoto, Sema Sezgin Goksu, Andrzej Badzio, Bethany Gill, Hema Gowda, Haiyi Jiang, Suresh Senan

PRESENTED BY: Dr David R. Spigel, Sarah Cannon Research Institute, Nashville, TN, USA

ADRIATIC study design

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

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

N=730

R‡

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

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

cCRT components

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

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

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

Dual primary endpoints:

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

Key secondary endpoints:

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

Other secondary endpoints:

- OS/PFS landmarks
- Safety

*cCRT and PCI treatment, if received per local standard of care, must have been completed within 1–42 days prior to randomization.
†If disease control was achieved and no additional benefit was expected with an additional cycle of chemotherapy, in the opinion of the investigator.
‡The first 600 patients were randomized in a 1:1:1 ratio to the 3 treatment arms; subsequent patients were randomized 1:1 to either durvalumab or placebo.

BICR, blinded independent central review; BID, twice daily; CT, chemotherapy; D, durvalumab; PCI, prophylactic cranial irradiation; PS, performance status; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; T, tremelimumab; WHO, World Health Organization.

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Baseline characteristics

		Durvalumab (n=264)	Placebo (n=266)
Age, years	Median (range)	62.0 (28–84)	62.0 (28–79)
Sex, %	Male / Female	67.4 / 32.6	70.7 / 29.3
Race, %	White / Asian / Other	49.2 / 49.6 / 1.1	51.5 / 45.5 / 3.0
WHO performance status, %	0 / 1	50.0 / 50.0	47.4 / 52.6
Smoking status, %	Current / Former / Never	23.9 / 67.4 / 8.7	20.7 / 69.5 / 9.8
AJCC disease stage at diagnosis, %	I / II / III	3.0 / 9.5 / 87.5	4.1 / 8.6 / 87.2
Prior chemotherapy regimen, %*	Cisplatin-etoposide / Carboplatin-etoposide	65.5 / 34.5	66.9 / 33.1
Prior radiation schedule, %	Once daily / Twice daily	73.9 / 26.1	70.3 / 29.7
Best response to prior cCRT, %	CR / PR / SD	11.7 / 72.3 / 15.9	12.8 / 75.2 / 12.0
Prior PCI, %	Yes / No	53.8 / 46.2	53.8 / 46.2

*Based on the first cycle of chemotherapy.

AJCC, American Joint Committee on Cancer; CR, complete response; PR, partial response; SD, stable disease.

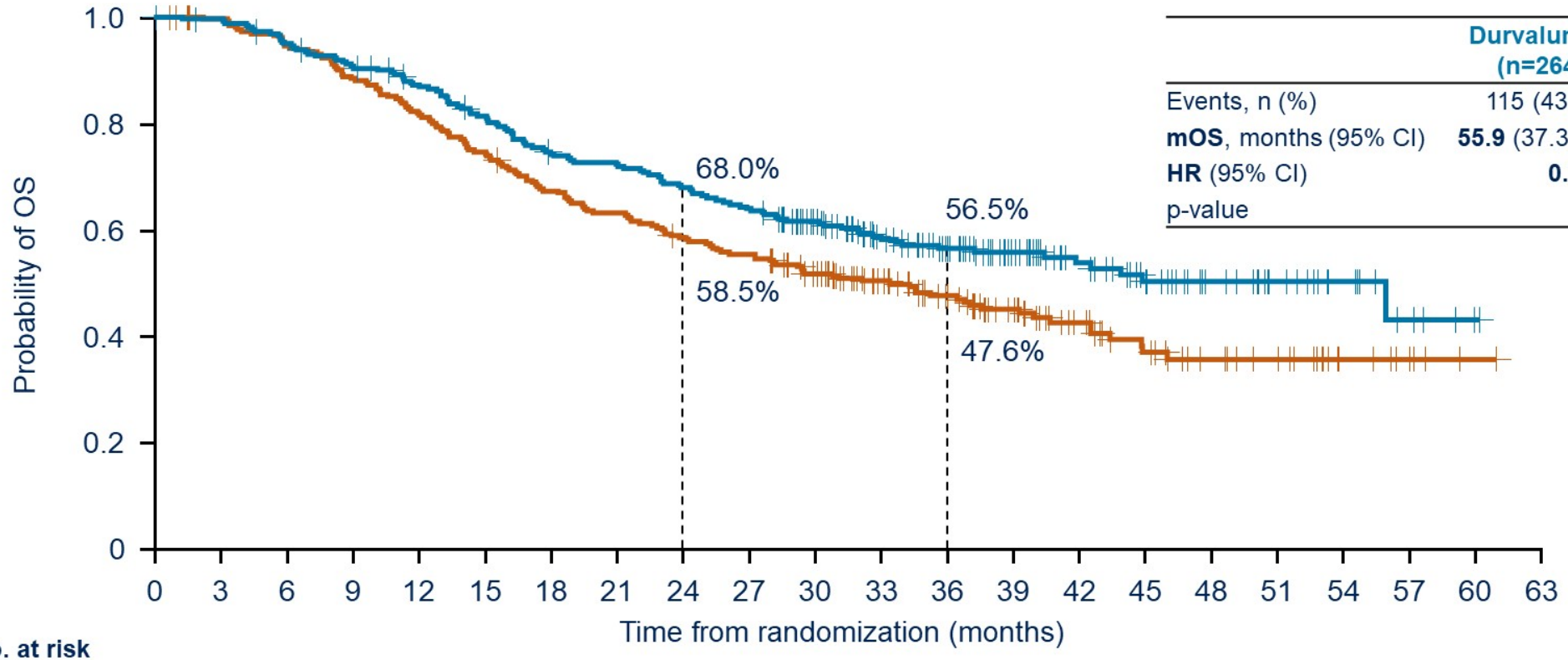
Patient disposition

	Durvalumab (n=264)	Placebo (n=266)
Received treatment, n (%)	263* (99.6)	265 (99.6)
Ongoing study treatment at data cut-off†, n (%)	0	0
Completed the maximum 24 months of treatment, n (%)	88 (33.5)	70 (26.4)
Discontinued study treatment, n (%)	175 (66.5)	195 (73.6)
Disease progression	121 (46.0)	154 (58.1)
Adverse event	43 (16.3)	29 (10.9)
Patient decision	10 (3.8)	11 (4.2)
Other reason	1 (0.4)	1 (0.4)
Ongoing study (in follow-up) at data cut-off†, n (%)	140 (53.0)	111 (41.7)
Received subsequent systemic anticancer therapy, n	95	127
Received immunotherapy as first subsequent treatment	17	31

*One patient randomized to the durvalumab arm received tremelimumab in addition to durvalumab and will be included in the durvalumab + tremelimumab arm of the safety population. †Jan 15, 2024.

Overall survival (dual primary endpoint)

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



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

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

OS was analyzed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints.

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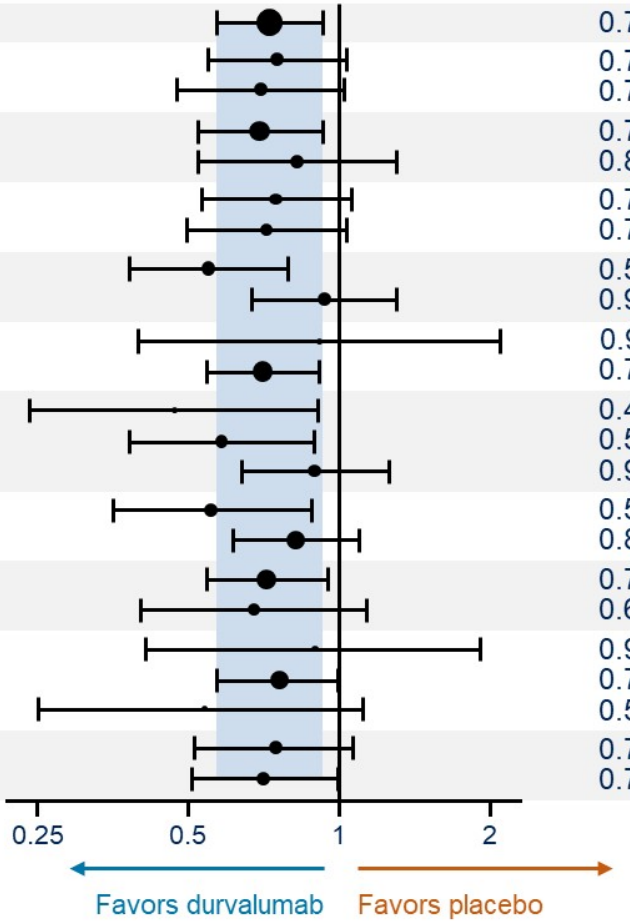
CI, confidence interval; mOS, median OS; NE, not estimable.

OS subgroup analysis

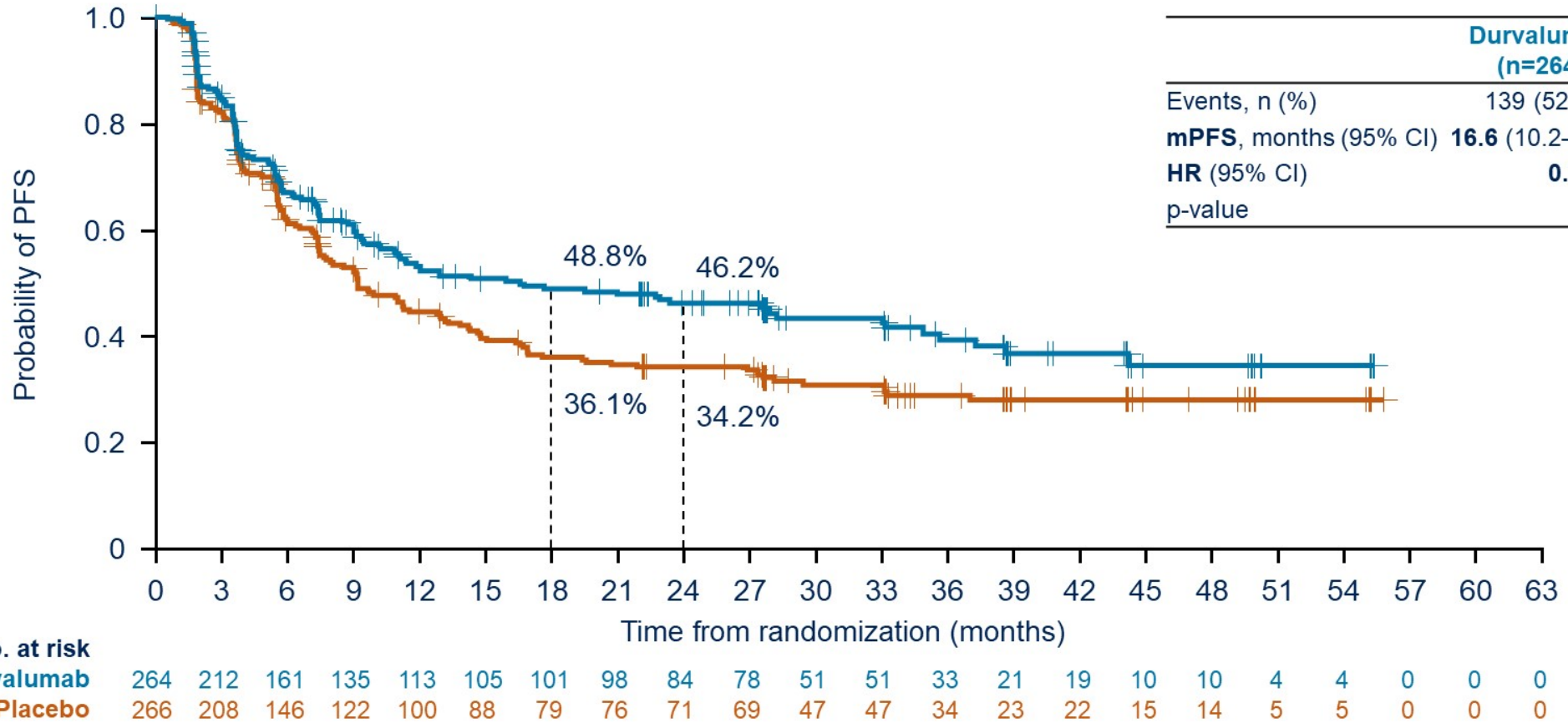
		Events/Patients n/N		HR (95% CI)
		Durvalumab	Placebo	
All patients		115/264	146/266	0.73 (0.57–0.93)
Age	<65 years	69/160	83/162	0.76 (0.55–1.04)
	≥65 years	46/104	63/104	0.70 (0.48–1.02)
Sex	Male	79/178	108/188	0.70 (0.52–0.93)
	Female	36/86	38/78	0.83 (0.52–1.31)
Race	White	60/130	77/137	0.75 (0.53–1.05)
	Asian	53/131	64/121	0.72 (0.50–1.04)
WHO performance status	0	48/133	74/131	0.55 (0.38–0.79)
	1	67/131	72/135	0.94 (0.67–1.31)
AJCC disease stage at diagnosis	I/II	11/33	12/34	0.92 (0.40–2.11)
	III	104/231	134/232	0.71 (0.55–0.91)
Time from end of cCRT* to randomization	<14 days	14/32	24/32	0.47 (0.24–0.91)
	≥14 days to <28 days	37/79	51/80	0.59 (0.38–0.90)
	≥28 days	64/153	71/154	0.90 (0.64–1.27)
Prior chemotherapy regimen	Carboplatin-etoposide	31/ 91	46/88	0.56 (0.35–0.89)
	Cisplatin-etoposide	84/173	100/178	0.82 (0.61–1.10)
Prior radiation schedule	Once daily	92/195	107/187	0.72 (0.55–0.95)
	Twice daily	23/69	39/79	0.68 (0.40–1.14)
Best response to prior cCRT	Complete response	12/31	15/34	0.90 (0.41–1.92)
	Partial response	88/191	116/200	0.76 (0.57–1.00)
	Stable disease	15/42	15/32	0.54 (0.25–1.13)
Prior PCI	Yes	53/142	67/143	0.75 (0.52–1.07)
	No	62/122	79/123	0.71 (0.51–0.99)



*End of chemotherapy or radiotherapy, whichever was latest.
Intention-to-treat analysis stratified, subgroup analyses unstratified. Not all prespecified subgroups are included in the plot.
Size of circle is proportional to number of events across both arms.

Progression-free survival* (dual primary endpoint)

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



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

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

*By BICR per RECIST v1.1.

PFS was analyzed using a stratified log-rank test adjusted for disease stage (I/II vs III) and receipt of PCI (yes vs no). The significance level for testing PFS at this interim analysis was 0.00184 (2-sided) at the 0.5% level, and 0.02805 (2-sided) at the overall 5% level. Statistical significance for PFS was achieved through the recycling multiple testing procedure framework and testing at the 5% (2-sided) alpha level (adjusted for an interim and final analysis).

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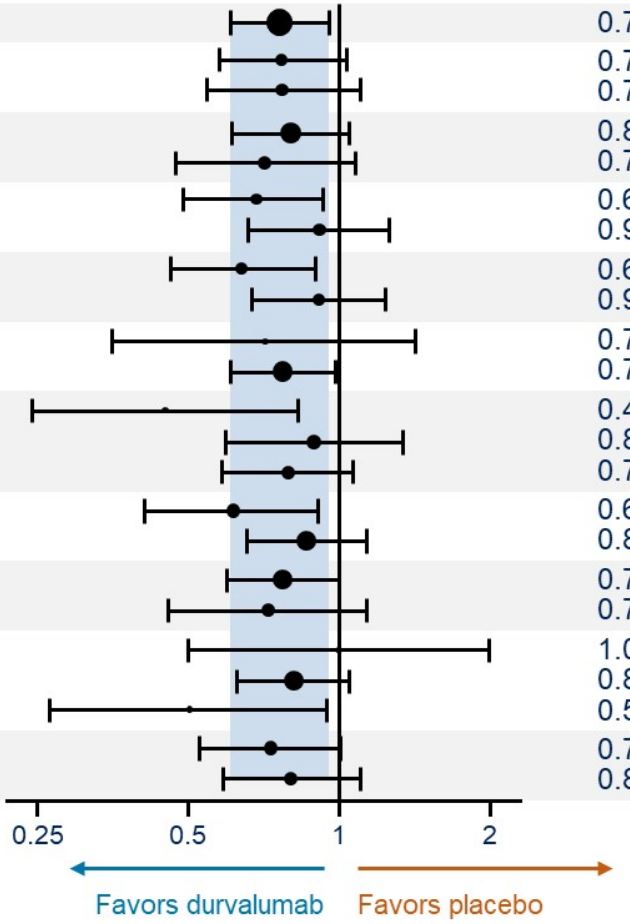
mPFS, median PFS.

PFS subgroup analysis

		Events/Patients n/N		HR (95% CI)
		Durvalumab	Placebo	
All patients		139/264	169/266	0.76 (0.61–0.95)
Age	<65 years	83/160	98/162	0.77 (0.58–1.03)
	≥65 years	56/104	71/104	0.77 (0.54–1.10)
Sex	Male	96/178	120/188	0.80 (0.61–1.04)
	Female	43/86	49/78	0.71 (0.47–1.08)
Race	White	65/130	90/137	0.68 (0.49–0.93)
	Asian	72/131	75/121	0.91 (0.66–1.26)
WHO performance status	0	60/133	82/131	0.64 (0.46–0.90)
	1	79/131	87/135	0.91 (0.67–1.24)
AJCC disease stage at diagnosis	I/II	14/33	19/34	0.71 (0.35–1.42)
	III	125/231	150/232	0.77 (0.61–0.98)
Time from end of cCRT* to randomization	<14 days	18/32	27/32	0.45 (0.24–0.83)
	≥14 days to <28 days	43/79	50/80	0.89 (0.59–1.34)
	≥28 days	78/153	92/154	0.79 (0.58–1.07)
Prior chemotherapy regimen	Carboplatin-etoposide	44/91	57/88	0.61 (0.41–0.90)
	Cisplatin-etoposide	95/173	112/178	0.86 (0.65–1.13)
Prior radiation schedule	Once daily	108/195	122/187	0.77 (0.60–1.00)
	Twice daily	31/69	47/79	0.72 (0.45–1.13)
Best response to prior cCRT	Complete response	15/31	18/34	1.00 (0.50–1.99)
	Partial response	106/191	130/200	0.81 (0.62–1.04)
	Stable disease	18/42	21/32	0.50 (0.26–0.94)
Prior PCI	Yes	65/142	84/143	0.73 (0.53–1.01)
	No	74/122	85/123	0.80 (0.59–1.09)



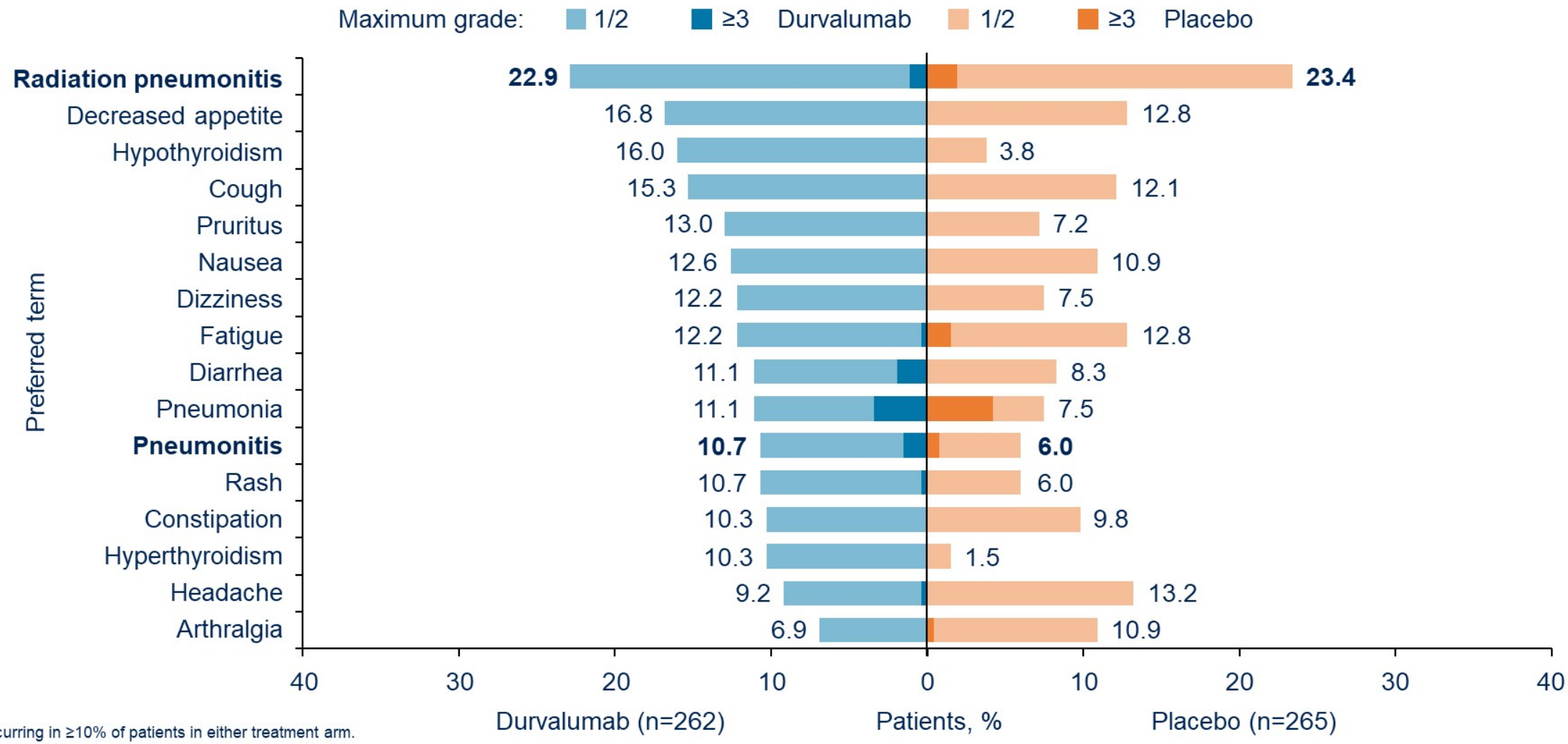
*End of chemotherapy or radiotherapy, whichever was latest.
Intention-to-treat analysis stratified, subgroup analyses unstratified. Not all prespecified subgroups are included in the plot.
Size of circle is proportional to number of events across both arms.

Exposure and safety summary

		Durvalumab (n=262)	Placebo (n=265)
Number of durvalumab or placebo doses	Median (range)	9.0 (1–26)	9.0 (1–26)
	Mean (standard deviation)	12.9 (9.6)	11.8 (9.2)
Any-grade all-cause AEs, n (%)		247 (94.3)	234 (88.3)
Maximum grade 3/4 AEs		64 (24.4)	64 (24.2)
Serious AEs		78 (29.8)	64 (24.2)
AEs leading to treatment discontinuation		43 (16.4)	28 (10.6)
AEs leading to death		7 (2.7)	5 (1.9)
Treatment-related* AEs leading to death		2 (0.8)‡	0
Any-grade immune-mediated AEs†		84 (32.1)	27 (10.2)
Maximum grade 3/4 immune-mediated AEs		14 (5.3)	4 (1.5)

Includes AEs with an onset date following first dose of study treatment, or pre-treatment AEs that increased in severity following first dose of study treatment, through to 90 days after last dose or until start of the first subsequent systemic anticancer therapy (whichever occurred first).
*Assessed by investigator. †Defined as an AE of special interest (excluding infusion related/hypersensitivity/anaphylactic reaction) that is consistent with an immune-mediated mechanism that required treatment with systemic corticosteroids, other immunosuppressants, or endocrine therapy. ‡Causes of death were encephalopathy and pneumonitis.

Most frequent AEs*



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

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Pneumonitis/radiation pneumonitis

Pneumonitis or radiation pneumonitis (grouped terms*), n (%)	Durvalumab (n=262)	Placebo (n=265)
Any grade	100 (38.2)	80 (30.2)
Maximum grade 3/4	8 (3.1)	7 (2.6)
Leading to death	1 (0.4)	0
Leading to treatment discontinuation	23 (8.8)	8 (3.0)

*Includes the preferred terms of immune-mediated lung disease, interstitial lung disease, pneumonitis, radiation fibrosis – lung, and radiation pneumonitis. Events are included irrespective of etiology and AE management.

Conclusions

- **Durvalumab as consolidation treatment after cCRT demonstrated statistically significant and clinically meaningful improvement in OS and PFS compared with placebo in patients with LS-SCLC**
  - **OS HR 0.73** (95% CI 0.57–0.93), p=0.0104; mOS 55.9 (95% CI 37.3–NE) vs 33.4 (95% CI 25.5–39.9) months
  - **PFS HR 0.76** (95% CI 0.61–0.95), p=0.0161; mPFS 16.6 (95% CI 10.2–28.2) vs 9.2 (95% CI 7.4–12.9) months
  - Treatment benefit was generally consistent across predefined patient subgroups for both OS and PFS
- **Durvalumab consolidation treatment for up to 2 years was well tolerated, and safety findings were consistent with the known safety profile of durvalumab monotherapy in the post-cCRT setting**

Consolidation durvalumab will become the new standard of care for patients with LS-SCLC who have not progressed after cCRT

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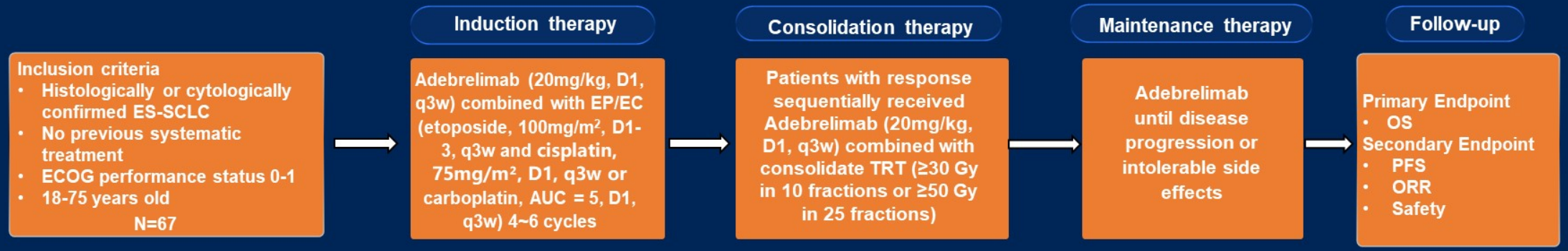
Cancer de pulmón microcítico

Primera línea: Abstract 8014

Iniciativa científica de: GECP lung cancer research

Overall survival of adebrelimab plus chemotherapy and sequential thoracic radiotherapy as first-line treatment for extensive-stage small cell lung cancer (ES-SCLC)

Study Design



Clinical trial information：NCT04562337

Baseline Characteristics

Characteristics	All patients (n = 67)
Age, years, median (range)	63 (38-75)
< 65 years, n (%)	42 (62.7)
≥ 65 years, n (%)	25 (37.3)
Gender, n (%)	
Male	56 (83.6)
Female	11 (16.4)
ECOG performance status, n (%)	
0	3 (4.5)
1	64 (95.5)
Disease stage, n (%)	
III	3 (4.5)
IV	64 (95.5)
Smoking status, n (%)	
Current or former smoker	44 (65.7)
Never smoked	23 (34.3)
Brain metastases, n (%)	
Yes	22 (32.8)
No	45 (67.2)
Liver metastases, n (%)	
Yes	21 (31.3)
No	46 (68.7)
ECOG, Eastern Cooperative Oncology Group;	

Data cutoff: December 22, 2023.

- The median age was 63 years (range, 38-75 years) and 56 patients (83.6%) were male.
- 22 (32.8%) patients were diagnosed with brain metastasis and 21 (31.3%) patients had liver metastasis at baseline.
- 45 patients received sequential TRT as planned.

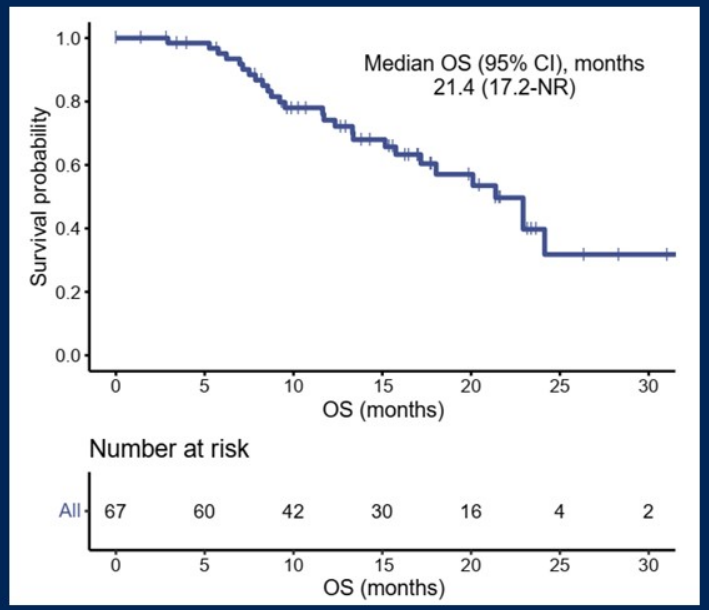
Antitumor Activity

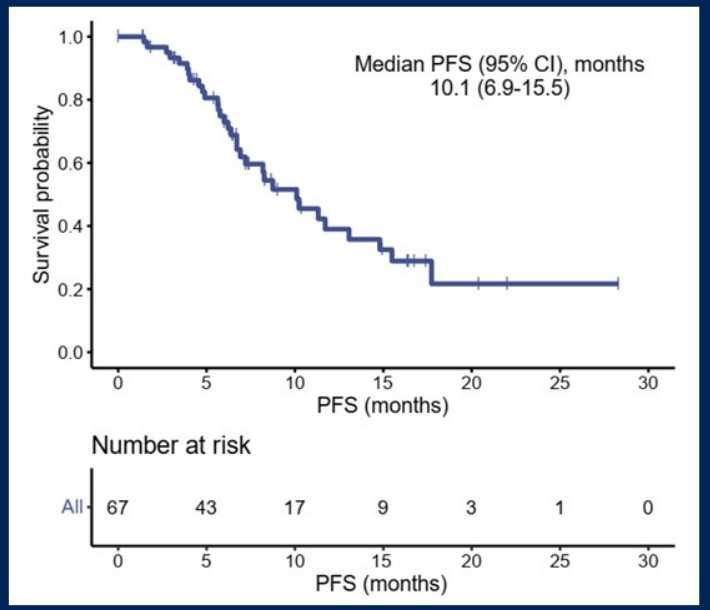
Variables	All patients (n = 67)
Best overall response, n (%)	
Complete response (confirmed)	3 (4.5)
Partial response (confirmed)	45 (67.2)
Stable disease	12 (17.9)
Progressive disease	2 (3.0)
Not evaluable*	5 (7.5)
Confirmed ORR, n (%; 95% CI)	48 (71.6; 59.3-82.0)
DCR, n (%; 95% CI)	60 (89.6; 79.7-95.7)

- 3 (4.5%) patients achieved CR.
- 45 (67.2%) patients achieved PR.
- The confirmed ORR was 71.6% (95% CI: 59.3-82.0%).
- DCR was 89.6% (95% CI: 79.7-95.7%).

Data cutoff: December 22, 2023.

OS and PFS





- The median OS was 21.4 months (95% CI: 17.2–not reached months).
- 1-year and 2-year OS rate were 74.1% (95% CI: 63.6-86.4%) and 39.7% (95% CI: 25.5-61.9%), respectively.

- The median PFS was 10.1 months (95% CI: 6.9–15.5 months).

Data cutoff: December 22, 2023.

Treatment-related Adverse Events (>10%)

Adverse events	All patients, n (%)	
	Any grade	≥ Grade 3
Any TRAE	60 (89.6)	39 (58.2)
Hematological toxicities		
Neutrophil count decreased	48 (71.6)	28 (41.8)
Anemia	46 (68.7)	3 (4.5)
White blood cell count decreased	43 (64.2)	13 (19.4)
Lymphocyte count decreased	29 (43.3)	9 (13.4)
Platelet count decreased	16 (23.9)	2 (3.0)
Non-hematological toxicities		
Nausea	23 (34.3)	1 (1.5)
Vomiting	19 (28.4)	2 (3.0)
Pneumonitis	17 (25.4)	4 (6.0)
Asthenia	8 (11.9)	0 (0.0)

- TRAEs occurred in 60 (89.6%) patients.
- Grade 3 or higher TRAEs occurred in 39 (58.2%) patients.
- The most commonly reported TRAEs were neutrophil count decreased (71.6%), anemia (68.7%), white blood cell count decreased (64.2%), lymphocyte count decreased (43.3%) and nausea (34.3%).

Data cutoff: December 22, 2023.

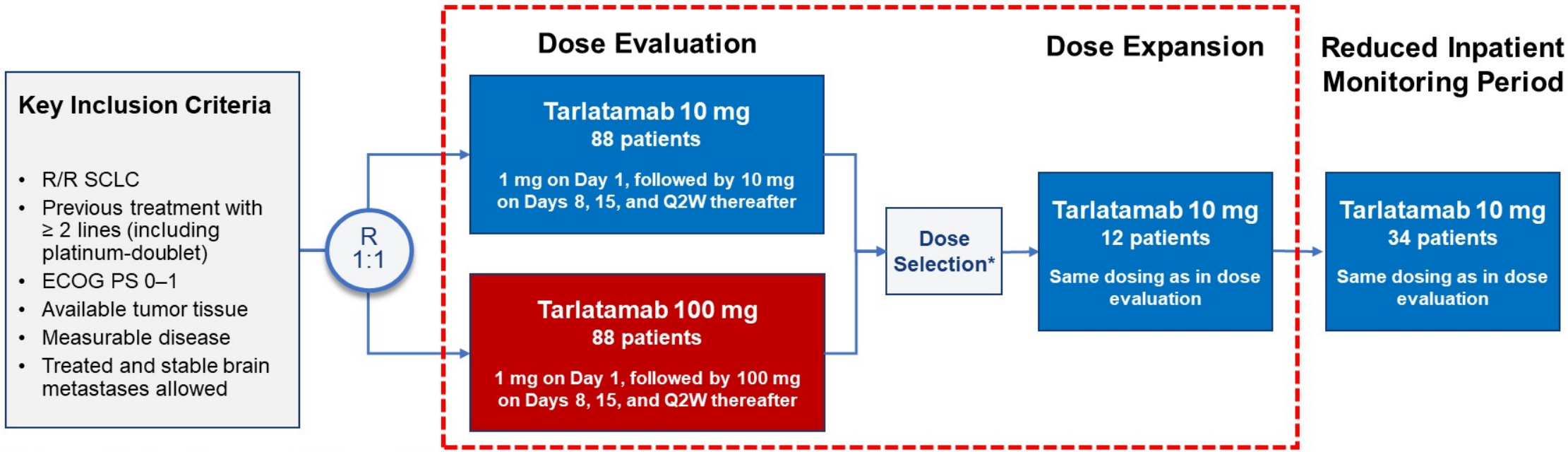
Cancer de pulmón microcítico

Abstract 8014

Iniciativa científica de: GECP

DeLLphi-301: Tarlatamab phase 2 trial in small cell lung cancer (SCLC)—Efficacy and safety analyzed by presence of brain metastases

Phase 2 DeLLphi-301 Study Design



Primary Endpoint: ORR per RECIST v1.1 by BICR, TEAEs, tarlatamab serum concentrations
Secondary Endpoints: DOR, DCR, PFS per RECIST v1.1 by BICR, OS

Subgroup Analysis: Efficacy by BICR and safety, by presence or absence of baseline brain metastases
Post-hoc Analysis: Intracranial activity

NCT05060016. Post-enrollment, brain imaging was performed if clinically indicated. *Once 30 patients per dose level had the opportunity to confirm an objective response after the first post-treatment scan or up to 13 weeks of follow-up, whichever occurred first. **BICR**, blinded independent central review; **DCR**, disease control rate; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **R**, randomization; **RECIST**, Response Evaluation Criteria in Solid Tumors; **R/R SCLC**, relapsed/refractory small cell lung cancer; **TEAE**, treatment-emergent adverse event.
Ahn MJ, et al. *N Engl J Med*. 2023;389:2063-2075.

Patient Baseline Clinical Characteristics

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 100)†	
	Yes (n = 23)	No (n = 77)
ECOG PS 0 / 1, n (%)	4 (17) / 19 (83)	22 (29) / 55 (71)
Median prior lines of therapy, n (range)	2 (2–5)	2 (1–6)
Prior anti-PD-(L)1 treatment, n (%)	19 (83)	55 (71)
DLL3 expression (> 0% of tumor cells), x/X (%)	21/22 (95)	59/61 (97)

Median follow-up period: 10.6 months‡

*Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383. †The intention-to-treat analysis set consists of all patients who were randomized and enrolled according to assigned treatment dose levels. ‡OS data yet to mature. **DLL3,** delta-like ligand 3; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PD-(L)1**, programmed cell death 1 protein/programmed cell death ligand-1 protein; **Q2W**, every 2 weeks.

Efficacy Summary

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 100)†	
	Yes (n = 23)	No (n = 77)
ORR, % (95% CI)	52 (31–73)	38 (27–49)
Median DOR, months (range)	NE (3–12+)	NE (2–12+)
DOR probability at 12 months, KM estimate, % (95% CI)	55 (22–78)	50 (29–68)
Median PFS, months (95% CI)	6.7 (3–NE)	4.0 (3–6)
Median OS‡, months (95% CI)	14.3 (14–NE)	NE (9–NE)

Tarlatamab demonstrated durable response with promising survival regardless of the presence of treated, stable brain metastases at baseline

Data cutoff, June 27, 2023. Median follow-up: 10.6 months. *Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383. †The intention-to-treat analysis set consists of all patients who were randomized and enrolled according to assigned treatment dose levels. ‡OS data yet to mature. **CI,** confidence interval; **DOR**, duration of response; **KM**, Kaplan-Meier; **NE**, not estimable; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks.

Treatment-Related Adverse Events (TRAEs)

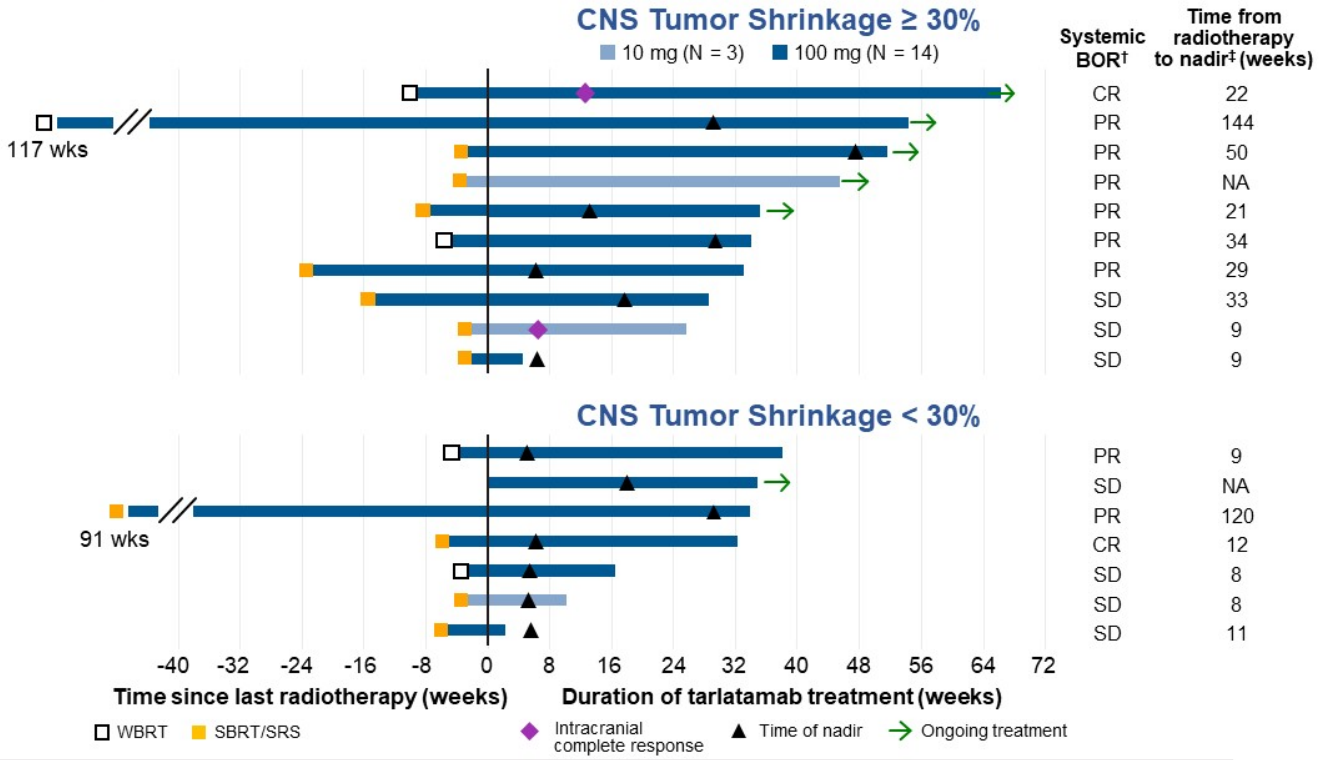
Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 99)†	
	Yes (n = 22)	No (n = 77)
TRAEs, n (%)	21 (95)	71 (92)
Grade ≥3	8 (36)	25 (32)
Fatal (grade 5)§	0	0
Leading to dose interruption and / or reduction of tarlatamab	3 (14)	11 (14)
Leading to discontinuation of tarlatamab	1 (5)	3 (4)
TRAEs of interest		
CRS‡	12 (55)	39 (51)
Grade ≥3	0	0
Leading to discontinuation of tarlatamab	0	0
ICANS and associated neurological events§	3 (14)	5 (6)
Grade ≥3	0	0
Leading to discontinuation of tarlatamab	0	1 (1)

*Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383. †The safety analysis includes all patients who received ≥ 1 dose of tarlatamab. One patient in the tarlatamab 10 mg group did not receive tarlatamab. Coded using MedDRA version 26.1. CRS and ICANS events were graded using American Society for Transplantation and Cellular Therapy 2019 Consensus Grading. ‡CRS based on AMQ narrow search. §ICANS and associated neurological events based on 61 selected preferred terms with AMQ broad search. §One patient (1%) in the tarlatamab 10 mg group died during part 3 from respiratory failure assessed by the investigator to be related to the trial treatment; contributing factors include baseline chronic obstructive pulmonary disease requiring supplemental oxygen, baseline compromised functional reserve, concurrent Grade 3 CRS and pneumonitis after cycle 1 day 1 treatment, and a decision against escalation to ICU-level care. This patient did not have brain metastases at baseline screening. **AMQ**, Amgen MedDRA query; **CRS**, cytokine release syndrome; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **MedDRA**, Medical Dictionary for Regulatory Activities; **Q2W**, every 2 weeks; **TRAE**, treatment-related adverse event.

Intracranial Activity*

Tarlatamab 10 mg (n = 3) or 100 mg (n = 14) Q2W with baseline CNS lesion ≥ 10 mm

- **mRANO BM§ analyses (N = 17)**
  - CNS tumor shrinkage ≥ 30% in 10 of 17 patients (59%)
  - Intracranial disease control in 94% (16 of 17) patients (95% CI, 71.3–99.9)
  - Median duration of intracranial disease control was NE (range, 2.6–13.9+ months)
  - CNS disease progression per modified RANO-BM occurred in 3 of 17 patients (18%)



CNS tumor shrinkage was observed in patients with previously treated brain metastases

*The CNS measurable analysis set included patients who had ≥ 2 brain scans (baseline and post-baseline) and were identified per modified RANO-BM by BICR as having ≥ 1 brain lesion ≥ 10 mm at baseline. †Systemic BOR was determined using RECIST v1.1 by BICR. ‡Minimum percentage change from baseline (smallest SLD) before disease progression. Median follow-up: 11.8 months. §mRANO BM represents RANO BM criteria with the following modifications: (1) corticosteroid data and clinical status were not incorporated into imaging reads; (2) diffusion weighted imaging MRI sequences were not required but were made available to the independent reviewer if received. **BICR**, blinded independent central review; **BOR**, best overall response; **CNS**, central nervous system; **CR**, complete response; **mRANO BM**, modified response assessment in neuro-oncology criteria for brain metastases; **MRI**, magnetic resonance imaging; **NA**, not available; **NE**, not estimable; **PR**, partial response; **RECIST**, Response Evaluation Criteria in Solid Tumors; **RT**, radiotherapy; **SBRT**, stereotactic body radiation therapy; **SD**, stable disease; **SLD**, sum of longest diameter; **SRS**, stereotactic radiosurgery; **WBRT**, whole brain radiation therapy.

PRESENTED BY: Anne-Marie C. Dingemans, MD, PhD

Limitations

- Interpretation of intracranial results may be confounded by prior radiotherapy
- Sample sizes for patients with brain metastases ≥ 10 mm at baseline were small
- Only patients with confirmed brain metastases at baseline had mandated surveillance CNS imaging

Conclusions

- Tarlatamab 10 mg Q2W demonstrated a favorable benefit-risk profile in patients with previously treated SCLC irrespective of the presence of treated and stable brain metastases (BM) at baseline
  - ORR was 52% in patients with BM (n = 23) and 38% in patients without BM (n = 77)
  - In patients with BM, median PFS was 6.7 months and median OS was 14.3 months
  - The safety profile of tarlatamab in patients with BM was manageable and consistent with the overall safety profile from the tarlatamab program
- CNS tumor shrinkage was observed after radiotherapy in some patients treated with tarlatamab

Results support further study of tarlatamab in patients with previously treated SCLC irrespective of the presence of brain metastases at baseline

CNS, central nervous system; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **SCLC**, small-cell lung cancer.

Mesothelioma

Abstract 8017

Iniciativa científica de:

GECP lung cancer

Niraparib and Dostarlimab efficacy in patients with platinum-sensitive relapsed mesothelioma: MIST5, a phase IIa clinical trial

Study Design

Key inclusion criteria

- Histologically confirmed pleural or peritoneal mesothelioma
- ECOG PS1
- Prior platinum-based systemic therapy >6 months PFS, (max 2 lines),
- Measurable disease by mRECIST1.1
- Adequate hematological and biochemical status
- Willingness to undergo a re-biopsy (optional)

Treatment

Niraparib 300mg po od every 3 weeks**
(if weight >77kg and platelets >1500,000/μl)

Dostarlimab 500mg IV day 1 every 3 weeks

Treatment until disease progression

Endpoints

Primary:

Disease control rate at 12 weeks (DCR12w).*

Secondary:

DCR at 24 weeks (DCR24w),

Best objective response rate (ORR) and toxicity (NCI CTCAE 4.03).

Re-biopsy on progression

Correlative Research

- Gut 16s RNA sequencing
- Tissue microarray for
  - ultradeep multiplex immunofluorescence
  - Spatial transcriptomics
- Tumour and germline whole exome sequencing
- Optional re-biopsy at the time of disease progression for omic-analyses

**200mg if weight <77kg and/or platelets <1500,000/μl
*minimum 11/26 patients with DCR needed to meet threshold for further evaluation

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Patient Characteristics

Characteristics (n=26)		N (%)
Age (years)	Median (range)	69.5 (35-85)
Gender	Male	21 (80.8)
	Female	5 (19.2)
Mesothelioma subtype	Epithelioid	21 (80.8)
	Biphasic	1(3.8)
	Sarcomatoid	2 (7.7)
	NOS	2 (7.7)
History of asbestos	Yes	18(69.2%)
	No	8 (30.8%)
ECOG status	0	2 (7.7)
	1	24 (92.3)
Metastases	No	21(80.8%)
	Yes	4 (15.4%)
	Not available	1 (3.9%)
Primary tumour site	Thoracic	18 (69.2%)
	Abdominal	1 (3.9%)
	Missing	7 (26.9%)

Between September 2021 and November 2022, **26 patients** with MM.

All 26 patients received at least one dose of Niraparib and Dostarlimab.

The median cycles of N dosing was 5 (IQR, 3-8) and D dosing was 5 (IQR, 3-7).

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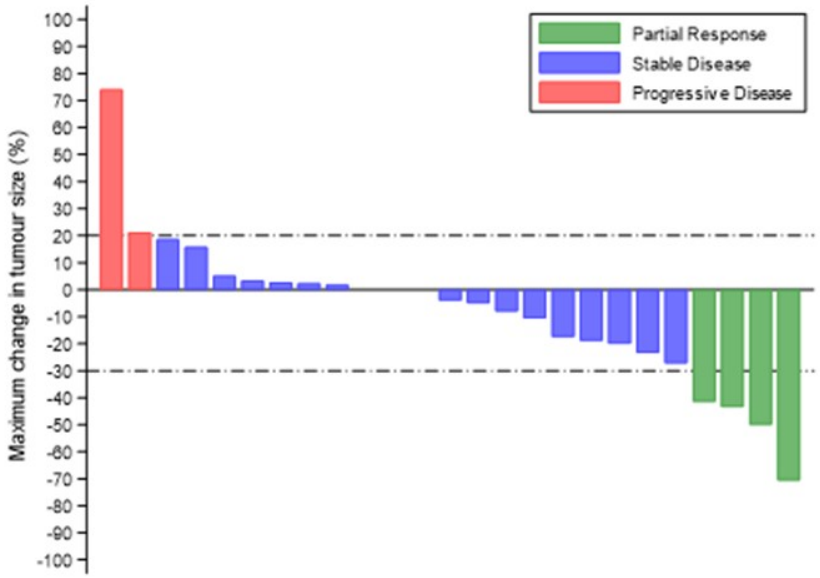
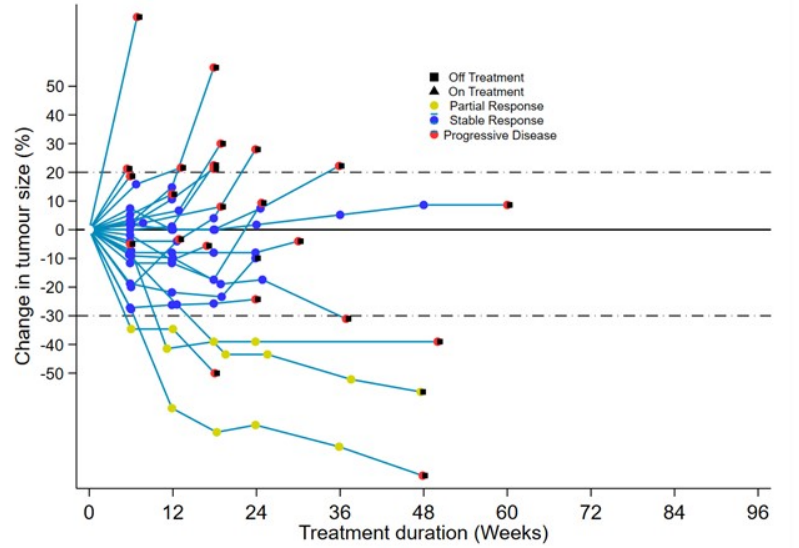
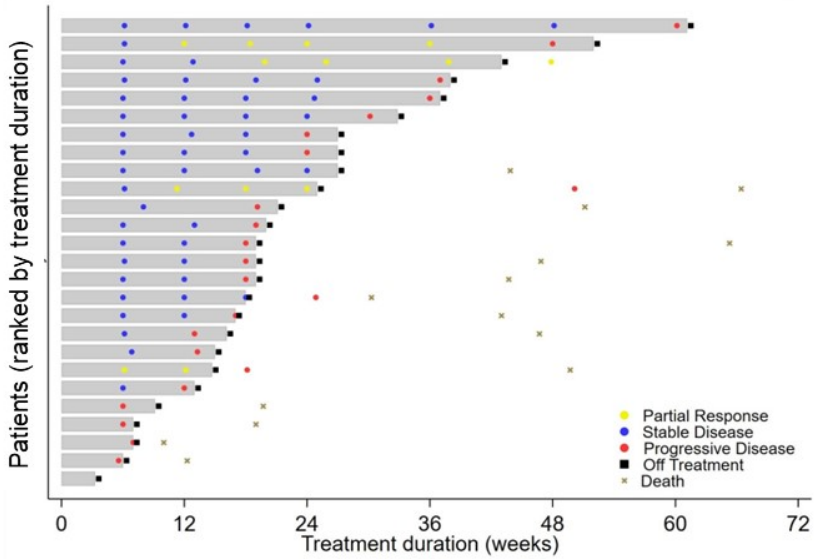
Efficacy



Outcome	n (%)
DCR12weeks	17/26 (**65.4%**)
DCR24weeks	8/26 (30.8%)
Best ORR *(Evaluable cohort, N=25)*	
Partial response	4/25 (16%)
Stable disease	17/25 (68%)
Progressive disease	4/25 (16%)
Overall DCR (best)	21/25 **(84%)**





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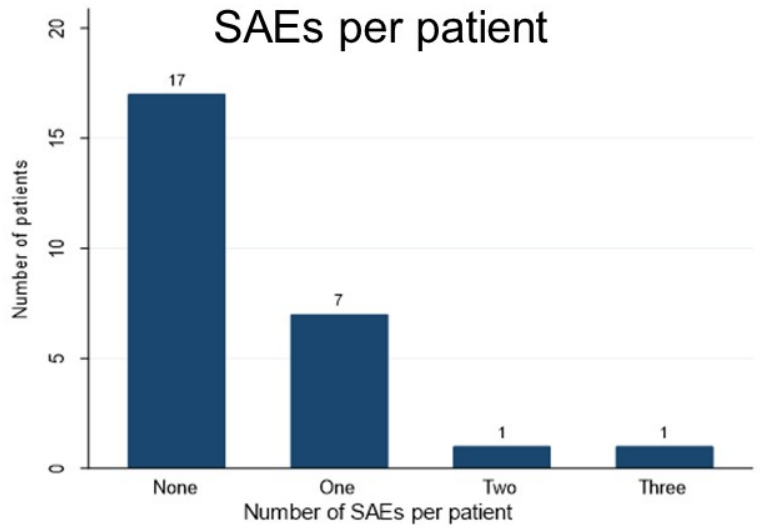
Safety – Adverse Events

	Adverse Events by CTCAE 4.03					
	Any grade	Grade 1	Grade 2	**Grade 3**	**Grade 4**	**Grade 5**
Any AEs	**24 (92.3%)**	**9 (34.6%)**	**6 (23.1%)**	**7 (26.9%)**	**1 (3.8%)**	**1 (3.8%) ***
AEs by preferred term (for AEs experienced by ≥10% of patients or with at least one event of CTCAE ≥3)						
Fatigue	9 (34.6%)	9 (34.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nausea	8 (30.8%)	8 (30.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Constipation	7 (26.9%)	6 (23.1%)	1 (3.8%)	0 (0%)	0 (0%)	0 (0%)
Decreased appetite	5 (19.2%)	5 (19.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dyspnoea	5 (19.2%)	5 (19.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

- Due to sepsis.



G3-5 TRAEs N(%)

Dolstarlimab 1(**3.9%**) participant *possibly related* and 2 (7.7%) participants *definitely* related

Niraparib 2(**7.7%**) *possibly* related and 1 (3.9%) participant *definitely* related

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Iniciativa científica de:

GECP lung cancer research

Gracias