Dana-Farber
Cancer Institute

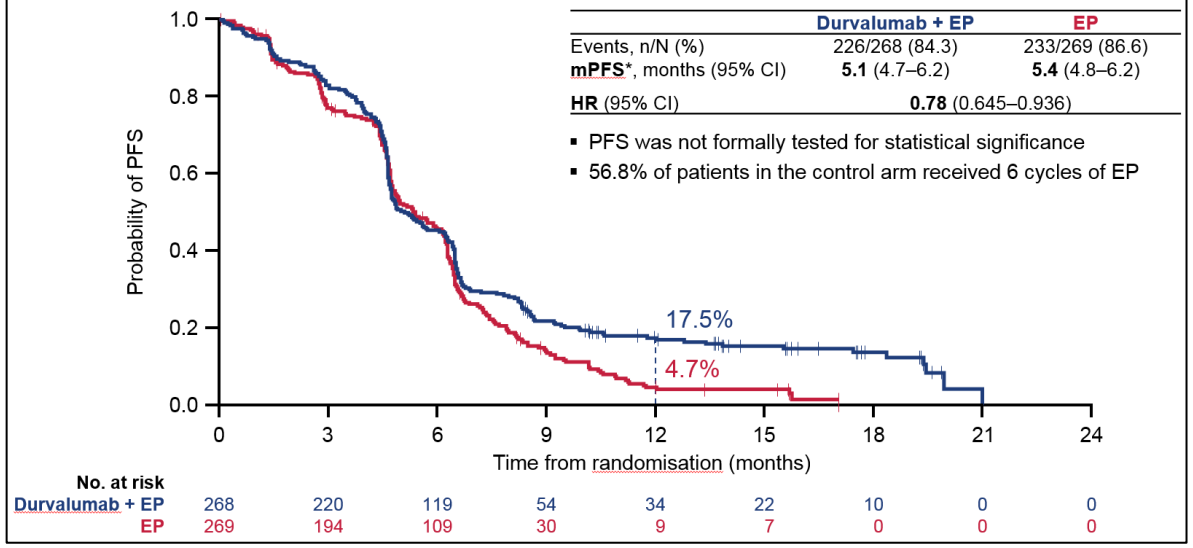
Updates In Small Cell Lung Cancer

Jacob Sands, MD

Oct 2025

CASPIAN

Progression-free Survival

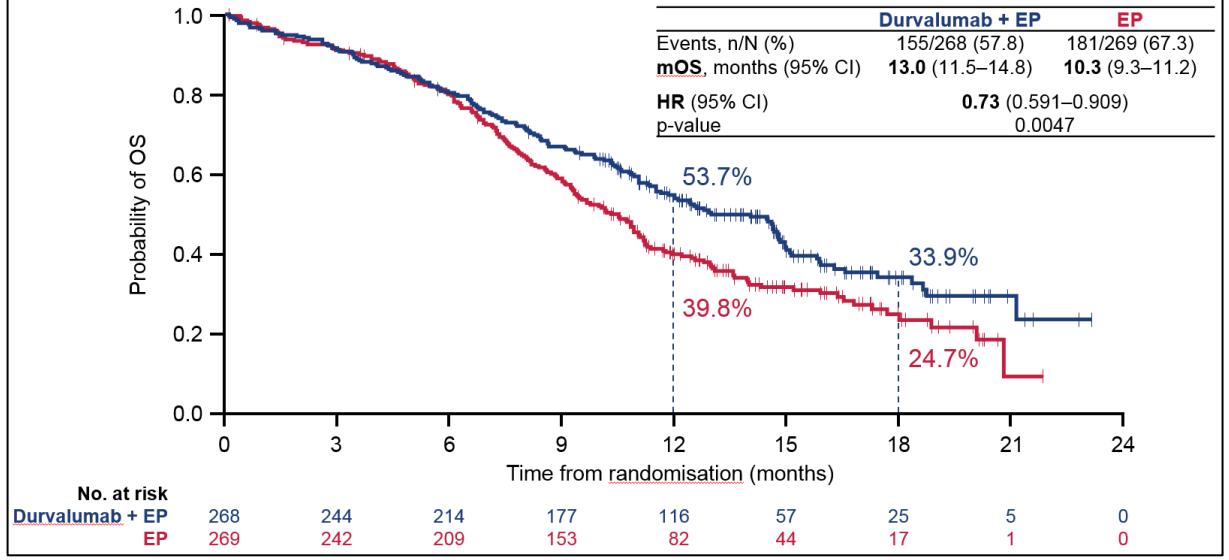


	Durvalumab + EP	EP
Events, n/N (%)	226/268 (84.3)	233/269 (86.6)
mPFS*, months (95% CI)	**5.1** (4.7–6.2)	**5.4** (4.8–6.2)
HR (95% CI)	**0.78** (0.645–0.936)	

- PFS was not formally tested for statistical significance
- 56.8% of patients in the control arm received 6 cycles of EP

No. at risk									
Durvalumab + EP	268	220	119	54	34	22	10	0	0
EP	269	194	109	30	9	7	0	0	0

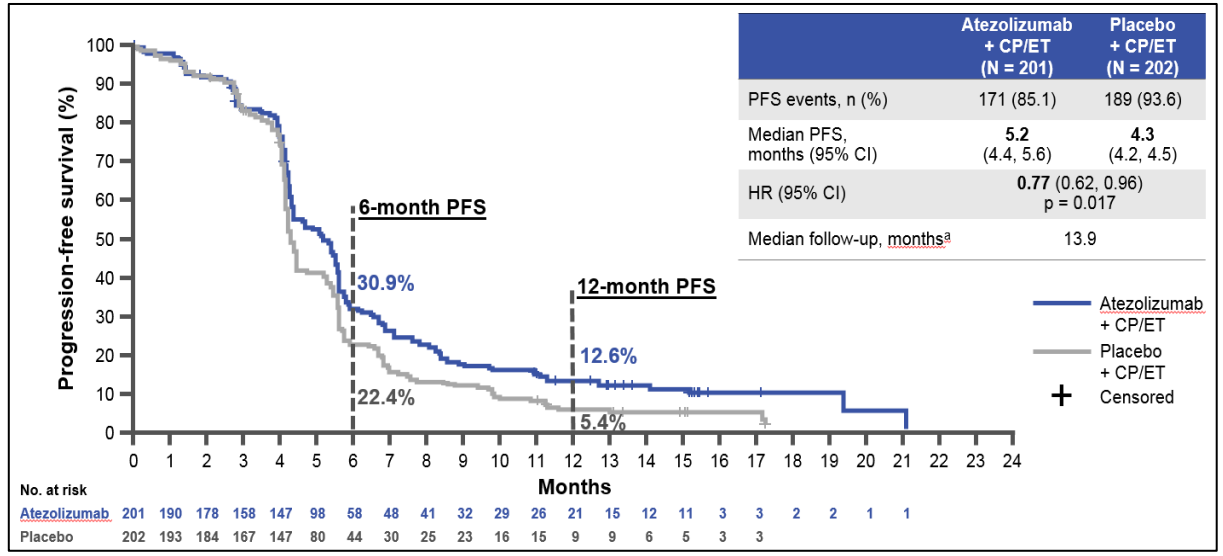
Overall Survival (Primary Endpoint)



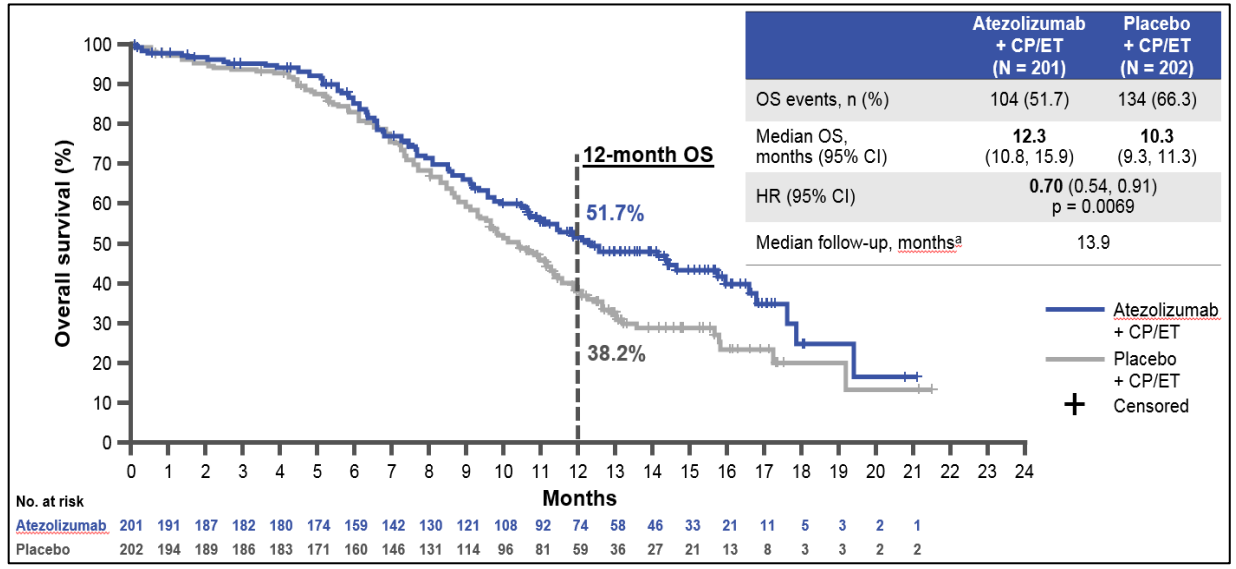
	Durvalumab + EP	EP
Events, n/N (%)	155/268 (57.8)	181/269 (67.3)
mOS, months (95% CI)	**13.0** (11.5–14.8)	**10.3** (9.3–11.2)
HR (95% CI)	**0.73** (0.591–0.909)	
p-value	0.0047	

No. at risk									
Durvalumab + EP	268	244	214	177	116	57	25	5	0
EP	269	242	209	153	82	44	17	1	0

IMpower-133

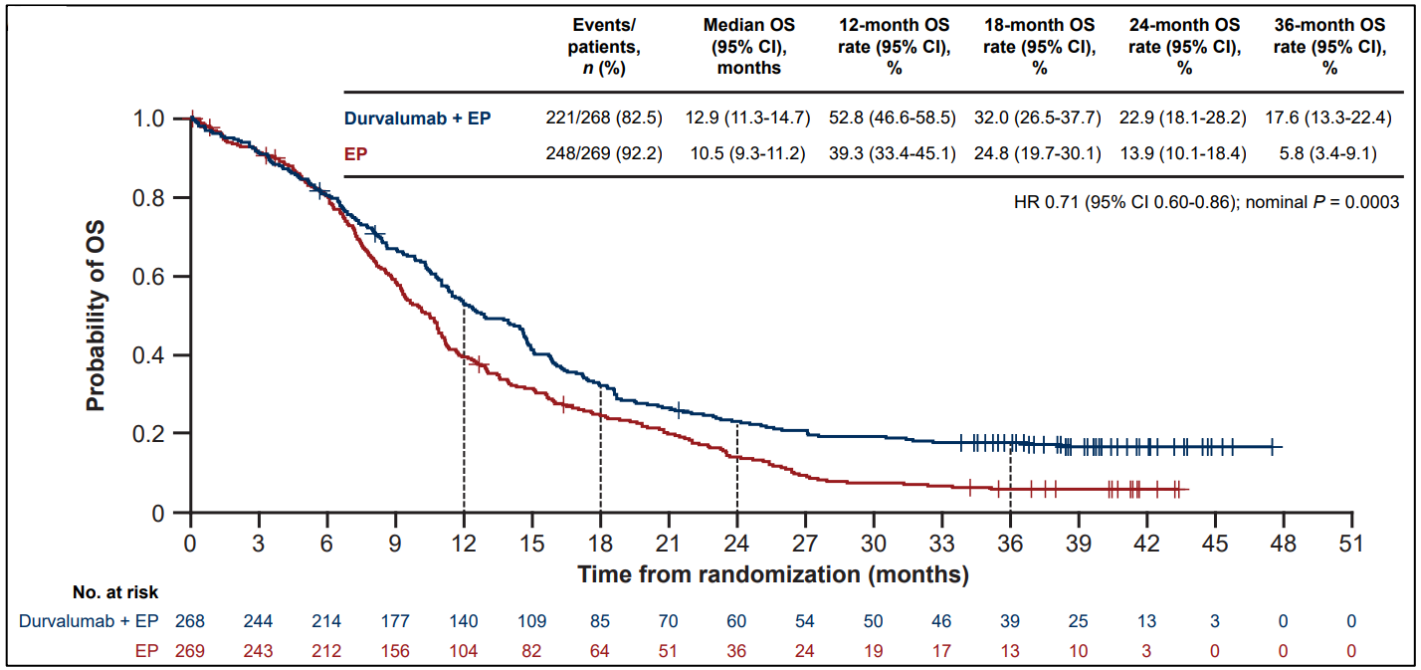


	Atezolizumab + CP/ET (N = 201)	Placebo + CP/ET (N = 202)
PFS events, n (%)	171 (85.1)	189 (93.6)
Median PFS, months (95% CI)	**5.2** (4.4, 5.6)	**4.3** (4.2, 4.5)
HR (95% CI)	**0.77** (0.62, 0.96) p = 0.017	
Median follow-up, months[a]	13.9	



	Atezolizumab + CP/ET (N = 201)	Placebo + CP/ET (N = 202)
OS events, n (%)	104 (51.7)	134 (66.3)
Median OS, months (95% CI)	**12.3** (10.8, 15.9)	**10.3** (9.3, 11.3)
HR (95% CI)	**0.70** (0.54, 0.91) p = 0.0069	
Median follow-up, months[a]	13.9	

Updated OS data for CASPIAN



OS rate (95% CI), %	IMpower133 and IMbrella A Atezo + CP/ET (n=201)	IMpower133 only Placebo + CP/ET (n=202)
1-year	52% (45-59)	39% (32-46)
2-year	22% (16-28)	16% (11-21)
3-year	16% (11-21)	NE[a]
4-year	13% (8-18)	NE[a]
5-year	12% (7-17)	NE[a]

Limited Stage: ADRIATIC

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

N=730

R‡

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

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

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

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

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

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

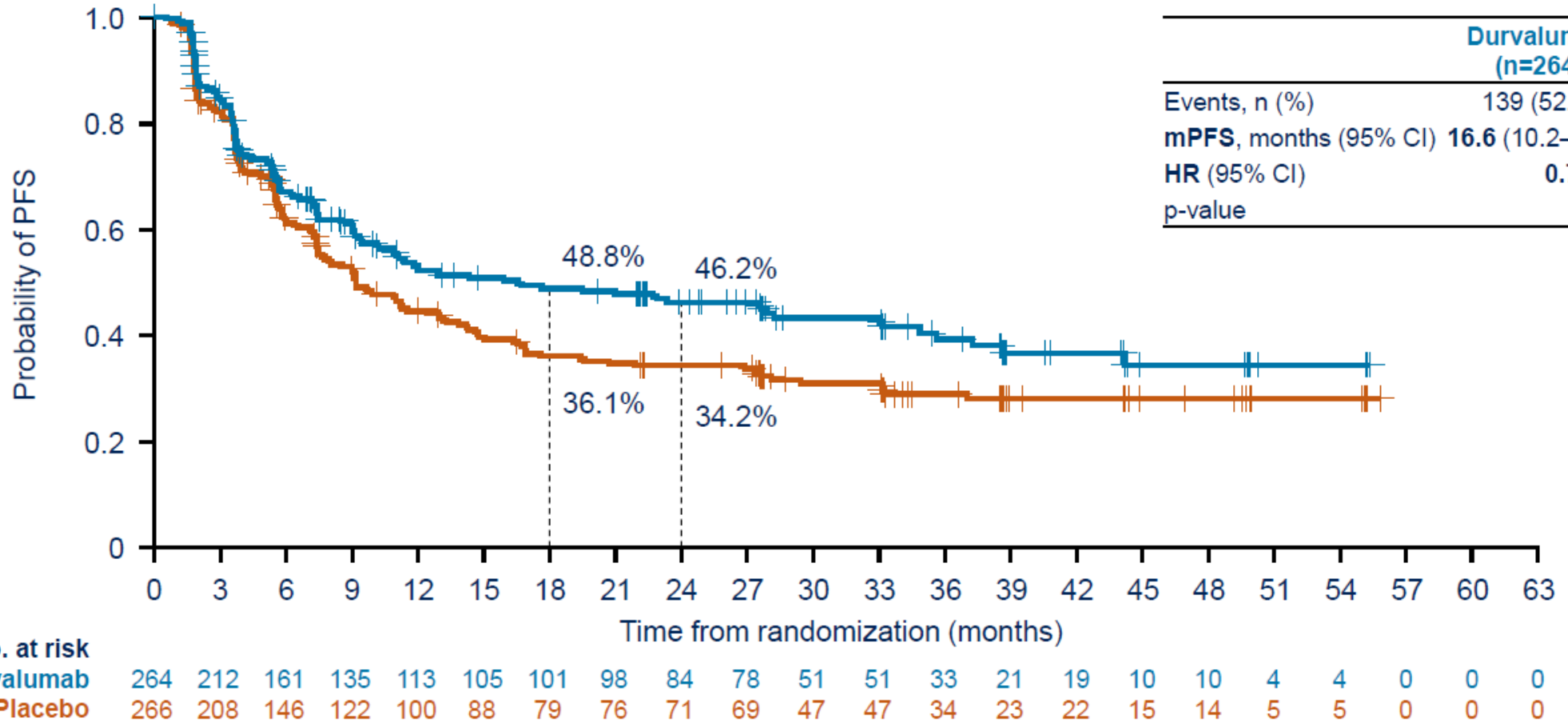
Key secondary endpoints:
- Durvalumab + tremelimumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

Other secondary endpoints:
- OS/PFS landmarks
- Safety

Spigel et al. ASCO 2024

Limited Stage: ADRIATIC

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

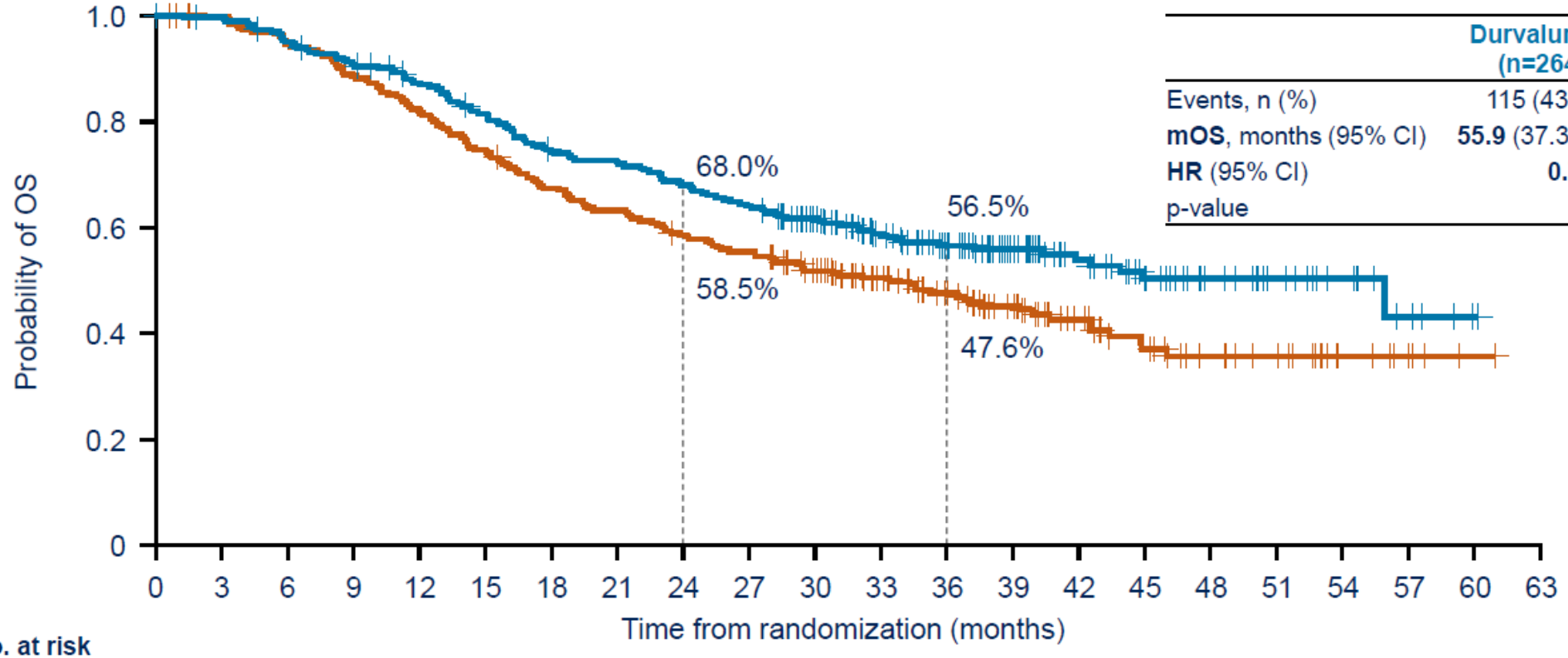


	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

Spigel et al. ASCO 2024

Limited Stage: ADRIATIC

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

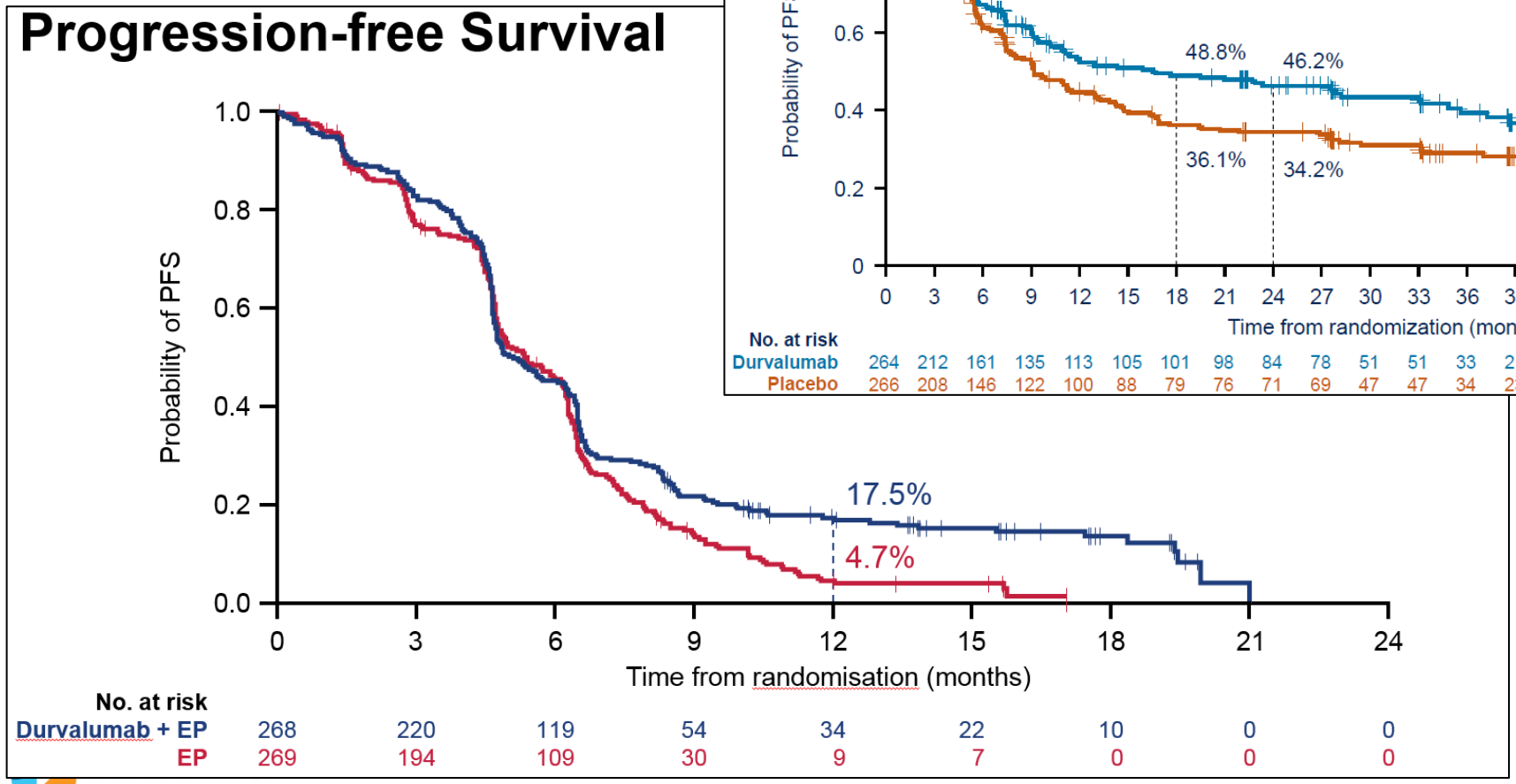


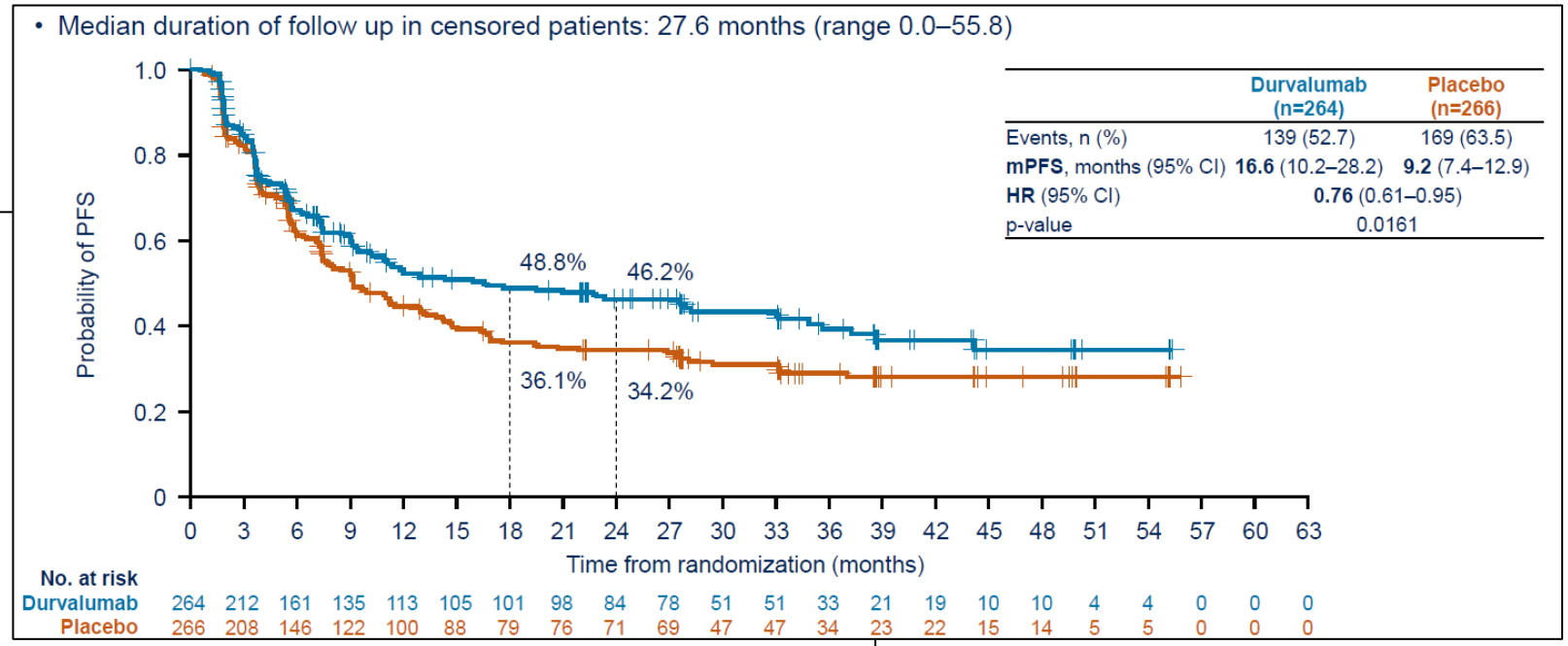
	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

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

Spigel et al. ASCO 2024

Progression free survival comparison with CASPIAN





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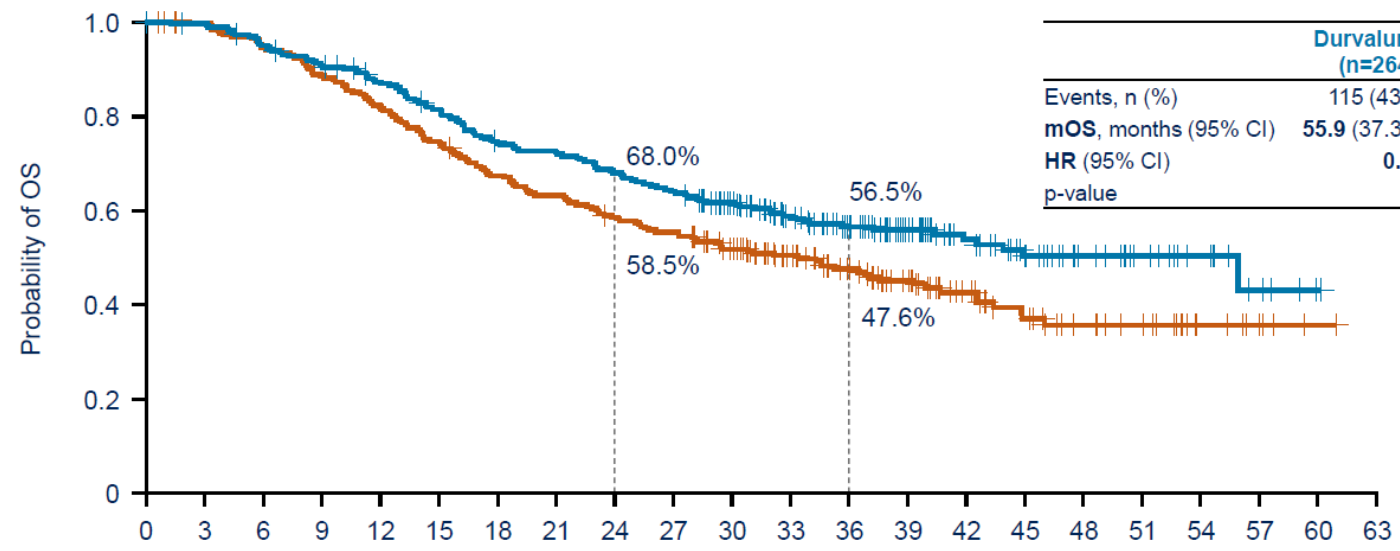
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

Overall Survival comparison with CASPIAN

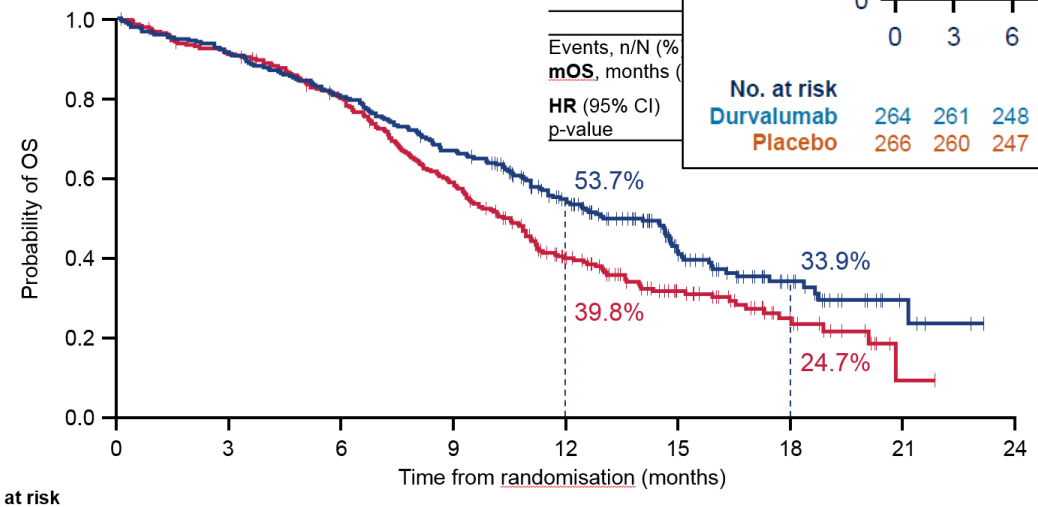
- Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



	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

Overall Survival (Primary Endpoint)



Events, n/N (%
mOS, months (
HR (95% CI)
p-value

No. at risk									
Durvalumab + EP	268	244	214	177	116	57	25	5	0
EP	269	242	209	153	82	44	17	1	0

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Lurbinectedin

- Single arm Phase 2 in second line SCLC
  - Sensitive disease = chemotherapy-free interval ≥90 days
  - Resistant disease = chemotherapy free interval <90 days and

	All patients (n=105)	Chemotherapy-free interval <90 days (n=45)	Chemotherapy-free interval ≥90 days (n=60)
RECIST responses			
Complete response	0	0	0
Partial response	37 (35%)	10 (22%)	27 (45%)
Stable disease*	35 (33%)	13 (29%)	22 (37%)
Progressive disease	28 (27%)	18 (40%)	10 (17%)
Not evaluable†	5 (5%)	4 (9%)	1 (2%)
Overall response, % (95% CI)	35·2% (26·2–45·2)	22·2% (11·2–37·1)	45·0% (32·1–58·4)
Disease control, % (95% CI)‡	68·6% (58·8–77·3)	51·1% (35·8–66·3)	81·7% (69·6–90·5)
Duration of response			
Disease progression, relapse, or death events in responding patients, n/N (%)	29/37 (78%)	9/10 (90%)	20/27 (74%)
Median duration of response, months	5·3 (4·1–6·4)	4·7 (2·6–5·6)	6·2 (3·5–7·3)
Patients still responding at 6 months	43·0% (25·6–60·5)	11·7% (0·0–33·1)	55·3% (34·5–76·0)
Progression-free survival			
Progression-free survival events, n (%)	90 (86%)	41 (91%)	49 (82%)
Median progression-free survival, months (95% CI)	3·5 (2·6–4·3)	2·6 (1·3–3·9)	4·6 (2·8–6·5)
4-month progression-free survival (95%CI)	46·6% (36·7–56·5)	29·1% (15·3–42·8)	59·9% (47·1–72·7)
6-month progression-free survival (95% CI)	32·9% (23·3–42·5)	18·8% (6·8–30·9)	43·5% (30·1–56·9)
Overall survival			
Deaths	66 (63%)	37 (82%)	29 (48%)
Median overall survival, months (95% CI)	9·3 (6·3–11·8)	5·0 (4·1–6·3)	11·9 (9·7–16·2)
6-month overall survival (95%CI)	67·1% (57·6–76·7)	45·8% (30·4–61·3)	83·6% (73·7–93·5)
12-month overall survival (95% CI)	34·2% (23·2–45·1)	15·9% (3·6–28·2)	48·3% (32·5–64·1)

RECIST=Response Evaluation Criteria in Solid Tumors. *Includes five patients with partial response not confirmed. †Five patients were not evaluable because they had no radiological assessment during treatment due to early death from malignant disease (n=2), symptomatic deterioration because of disease progression (n=2), and patient refusal (n=1). ‡Partial response or stable disease.

Table 2: **Overall efficacy of lurbinectedin treatment by investigator assessment and subgroup analyses by chemotherapy-free interval**

Trigo J et al. *Lancet Oncol.* 2020;21(5):645-654.

2025 ASCO ANNUAL MEETING

Lurbinectedin + atezolizumab as first-line maintenance treatment in patients with extensive-stage small cell lung cancer: Primary results of the Phase 3 IMforte trial

Luis Paz-Ares,[1] Hossein Borghaei,[2] Stephen V. Liu,[3] Solange Peters,[4] Roy S. Herbst,[5] Katarzyna Stencel,[6] Margarita Majem,[7] Grzegorz Czyżewicz,[8] Reyes Bernabé Caro,[9] Ki Hyeong Lee,[10] Melissa L. Johnson,[11] Nuri Karadurmuş,[12] Christian Grohé,[13] Vaikunth Cuchelkar,[14] Vilma Graupner,[15] Monika Kaul,[14] Ya-Chen Lin,[14] Debasis Chakrabarti,[16] Kamalnayan Bhatt,[16] Martin Reck[17]

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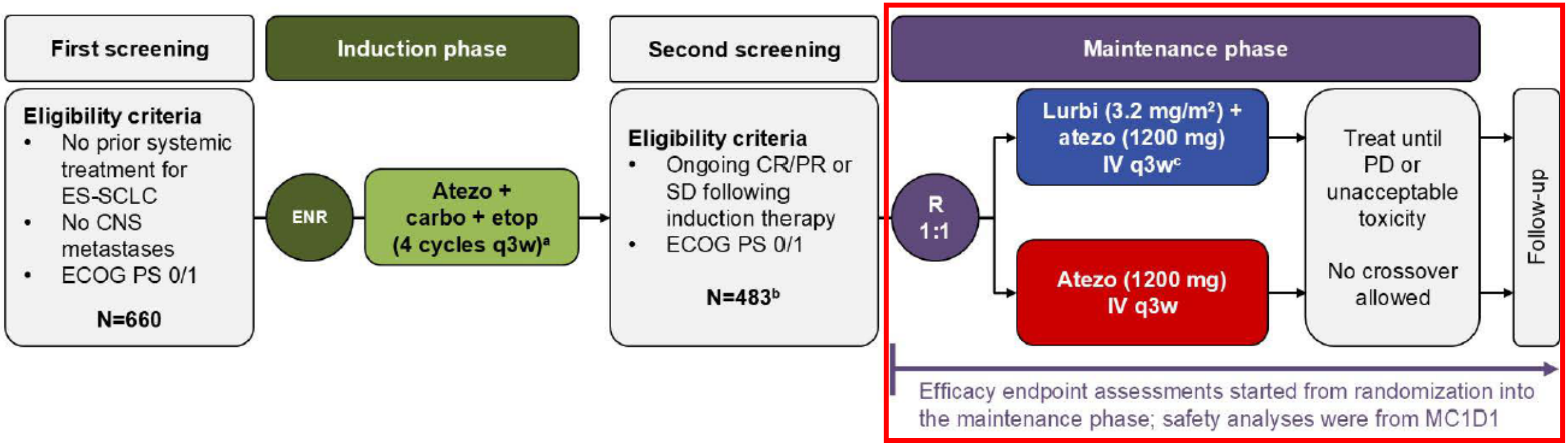
IMforte study design



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

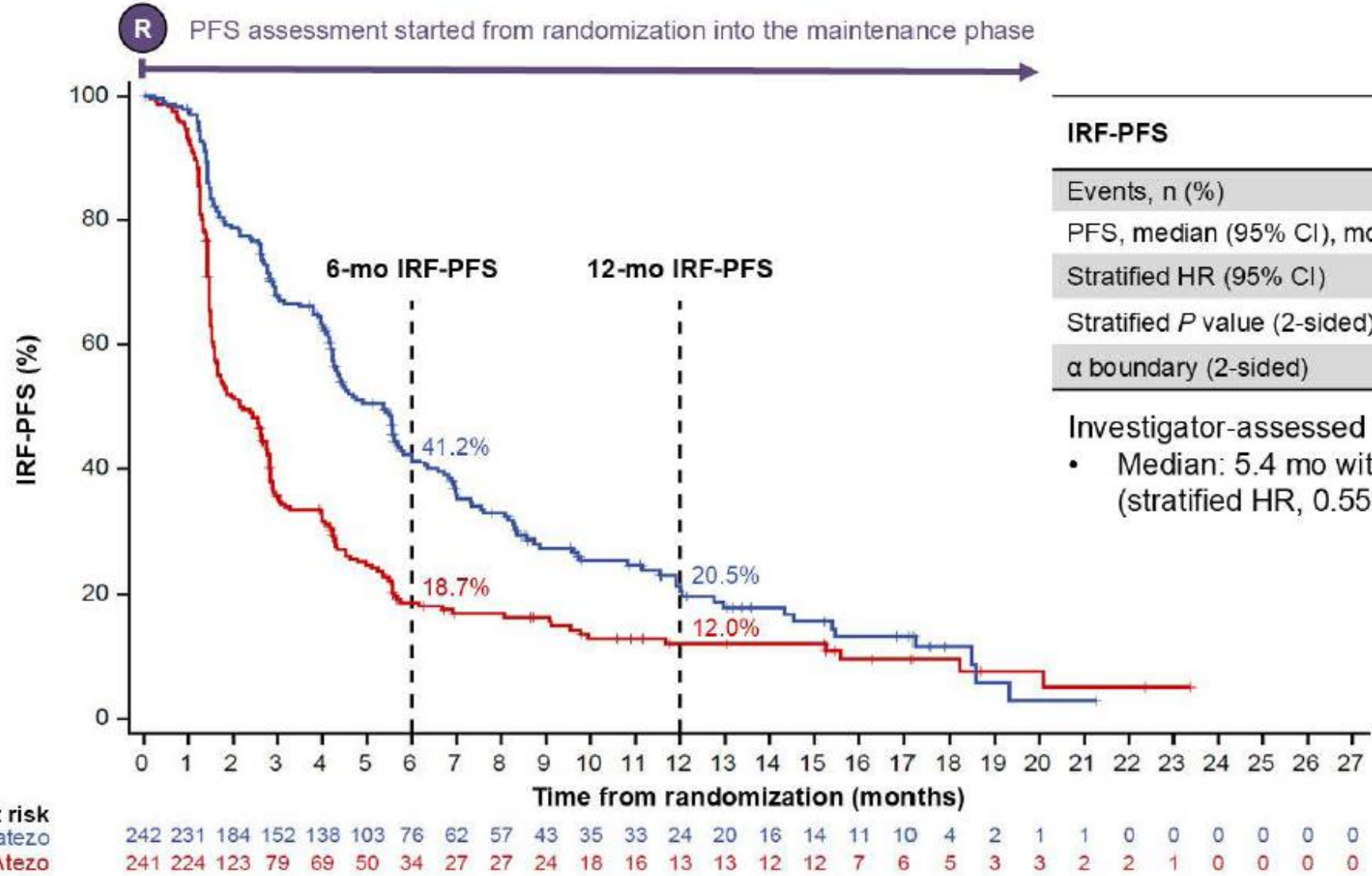
Primary endpoints
IRF-PFS and OS

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

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

ClinicalTrials.gov ID: NCT05091567.
[a] Administered per standard dose. [b] 73% of patients continued from induction to maintenance. [c] With **prophylactic granulocyte colony-stimulating factor** and anti-emetics.
atezo, atezolizumab; BL, baseline; carbo, carboplatin; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; ENR, enrollment; etop, etoposide; INV-PFS, investigator-assessed PFS; IRF-PFS, independent review facility-assessed PFS; IV, intravenously; LDH, lactate dehydrogenase; lurbi, lurbinectedin; MC1D1, maintenance Cycle 1 Day 1; PCI, prophylactic cranial irradiation; q3w, every 3 weeks; R, randomization; ULN, upper limit of normal; Y/N, yes/no.

IRF-PFS from randomization into maintenance phase



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	

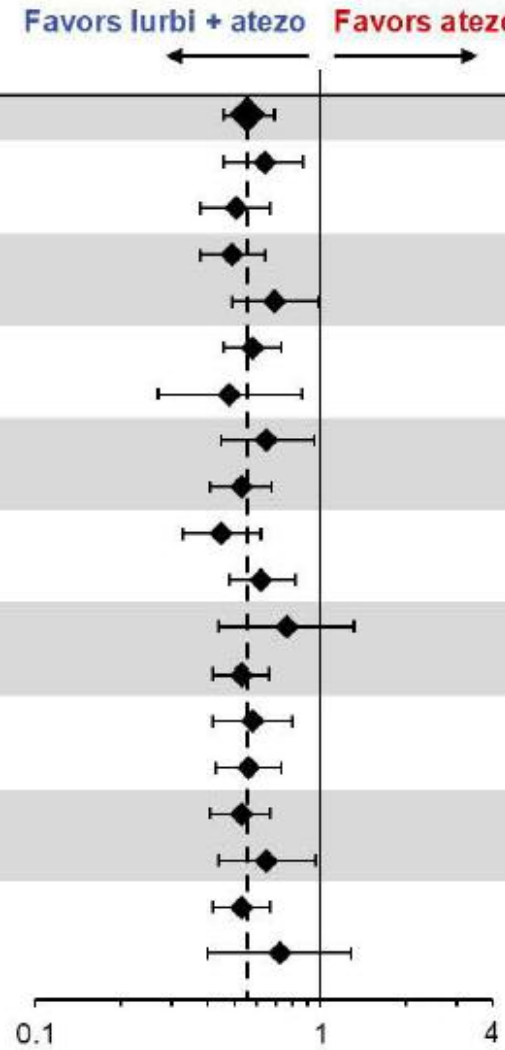
Investigator-assessed PFS was consistent with IRF-PFS

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

Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).
CI, confidence interval; HR, hazard ratio.

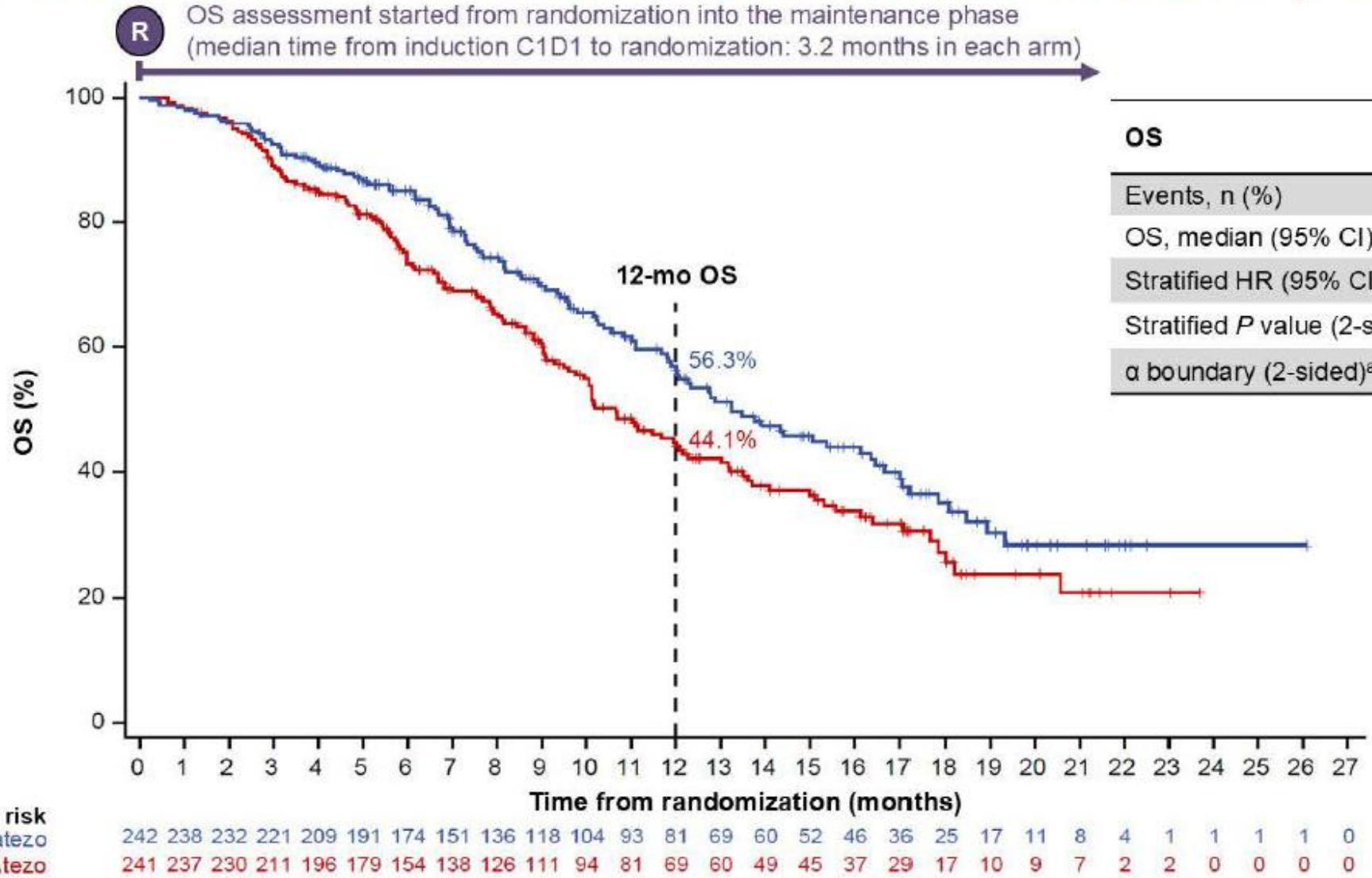
IRF-PFS subgroup analysis

Baseline risk factors		Events/patients, n/N		Unstratified IRF-PFS HR (95% CI)
		Lurbi + atezo	Atezo	
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)



Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).
[a] Data from subgroups with small numbers are not displayed. [b] Stratification factor for randomization; data determined from electronic case-report forms. [c] n=236 in the lurbi + atezo arm and n=240 in the atezo arm; 7 randomized patients did not have a maintenance screening tumor assessment.

OS from randomization into maintenance phase



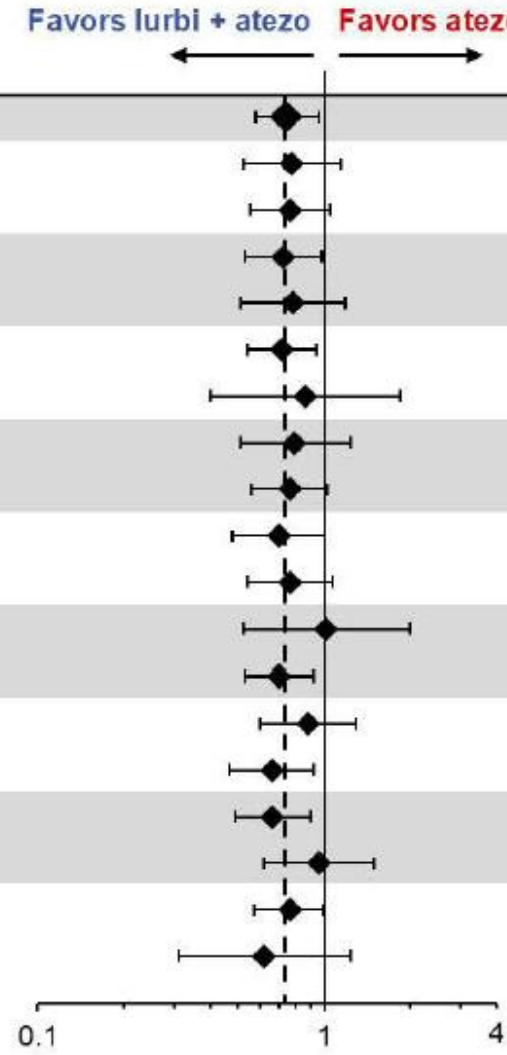
OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).

[a] As determined by the Hwang-Shih-Decani alpha spending function with the gamma parameter of −1.5.

OS subgroup analysis

Baseline risk factors		Events/patients, n/N		Unstratified OS HR (95% CI)
		Lurbi + atezo	Atezo	
All patients		113/242	136/241	0.74 (0.58, 0.96)
Age, years	<65	53/118	49/90	0.77 (0.52, 1.14)
	≥65	60/124	87/151	0.76 (0.55, 1.05)
Sex	Male	75/151	88/151	0.72 (0.53, 0.98)
	Female	38/91	48/90	0.78 (0.51, 1.19)
Race[a]	White	92/195	118/199	0.71 (0.54, 0.94)
	Asian	13/31	14/31	0.86 (0.40, 1.84)
Tobacco use history[a]	Current	38/88	39/73	0.79 (0.51, 1.24)
	Previous	72/147	94/163	0.76 (0.56, 1.03)
Liver metastases at induction BL[b]	Yes	55/100	63/94	0.70 (0.48, 1.00)
	No	58/142	73/147	0.76 (0.54, 1.07)
Prior PCI[b]	Yes	16/34	18/37	1.02 (0.52, 2.00)
	No	97/208	118/204	0.70 (0.53, 0.92)
ECOG PS[b]	0	51/105	53/102	0.88 (0.60, 1.29)
	1	62/137	83/139	0.66 (0.47, 0.92)
LDH[b]	≤ULN	72/176	97/179	0.66 (0.49, 0.90)
	>ULN	41/66	39/62	0.96 (0.62, 1.50)
Response to induction therapy[a,c]	CR/PR	92/206	115/213	0.76 (0.57, 0.99)
	SD	17/28	18/25	0.62 (0.31, 1.24)



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Follow-up systemic anticancer treatments

Patients, n (%)	Lurbi + atezo (n=242)	Atezo (n=241)
Patients who discontinued maintenance treatment	197	208
Patients with ≥1 follow-up systemic anticancer treatment	108 (44.6)	132 (54.8)
Chemotherapy	89 (36.8)	119 (49.4)
Immunotherapy	25 (10.3)	20 (8.3)
Targeted therapy	3 (1.2)	2 (0.8)
Other	3 (1.2)	3 (1.2)

At the time of clinical cutoff, no patient in the lurbi + atezo arm and 22 patients (9.1%) in the atezo arm had received follow-up lurbi treatment

Clinical cutoff: July 29, 2024.

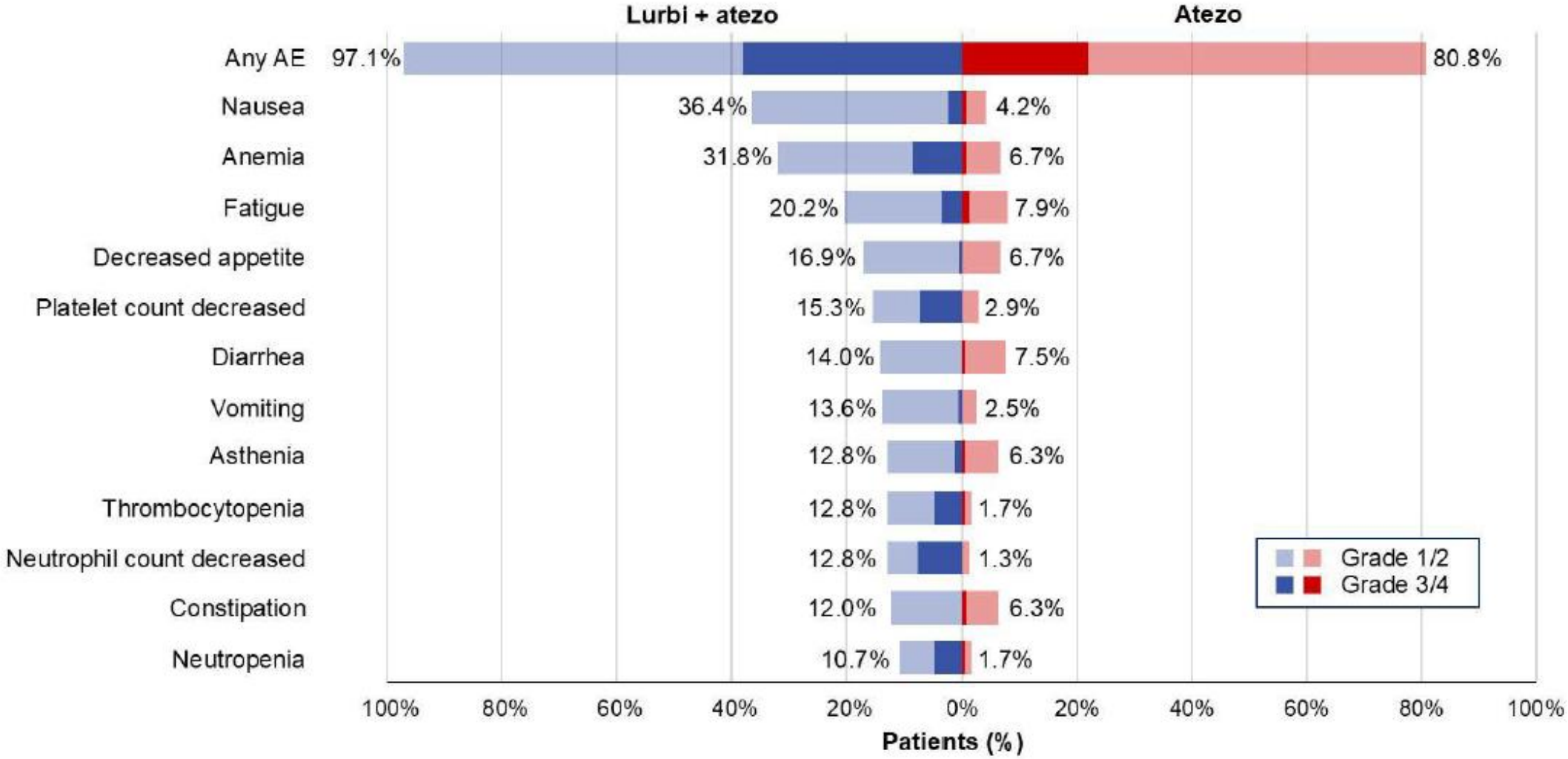
Safety summary during the maintenance phase

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

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

Clinical cutoff: July 29, 2024. One patient randomized to the atezo arm did not receive treatment and was not included in the safety analysis set.
[a] Sepsis and febrile neutropenia, both considered related to lurbi. [b] Sepsis considered related to atezo. [c] Atezo dose modifications were not permitted. [d] AESI for lurbi and atezo were pre-specified based on their mechanism of action and were independent of the causal relationship assigned by the investigator. AE, adverse event; AESI, adverse events of special interest.

All-cause AEs with incidence ≥10% in either arm



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

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

Clinical cutoff: July 29, 2024. Percentage labels represent all-grade AEs, including Grade 5 AEs. Grade 5 AEs occurred in 12 (5.0%) patients in the lurbi + atezo arm and 6 (2.5%) patients in the atezo arm.
[a] Includes 1 Grade 5 AE. [b] Grade 5 infections: lurbi + atezo arm (n=6 [2.5%]): COVID-19 pneumonia, pneumonia, pneumonia viral, sepsis, septic shock, and vascular device infection (n=1 each); atezo arm (n=4 [1.7%]): pneumonia (n=2), abscess intestinal, and sepsis (n=1 each).

Efficacy and safety of first-line maintenance therapy with lurbinectedin plus atezolizumab in extensive-stage small-cell lung cancer (IMforte): a randomised, multicentre, open-label, phase 3 trial

*Luis Paz-Ares, Hossein Borghaei, Stephen V Liu, Solange Peters, Roy S Herbst, Katarzyna Stencel, Margarita Majem, Mehmet Ali Nahit Şendur, Grzegorz Czyżewicz, Reyes Bernabé Caro, Ki Hyeong Lee, Melissa L Johnson, Nuri Karadurmuş, Christian Grohé, Sofia Baka, Tibor Csőszi, Jin Seok Ahn, Raffaele Califano, Tsung-Ying Yang, Yasemin Kemal, Marcus Ballinger, Vaikunth Cuchelkar, Vilma Graupner, Ya-Chen Lin, Debasis Chakrabarti, Kamalnayan Bhatt, George Cai, Robert Iannone, Martin Reck, for the IMforte investigators**

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2025 ASCO ANNUAL MEETING

Tarlatamab versus chemotherapy as second-line treatment for small cell lung cancer (SCLC): primary analysis of the phase 3 DeLLphi-304 study

Charles M. Rudin, Giannis S. Mountzios, Longhua Sun, Byoung Chul Cho, Umut Demirci, Sofia Baka, Mahmut Gumus, Antonio Lugini, Tudor-Eliade Ciuleanu, Myung-Ju Ahn, Pedro Rocha, Bo Zhu, Fiona Blackhall, Tatsuya Yoshida, Taofeek K. Owonikoko, Luis Paz-Ares, Shuang Huang, Diana Gauto, Gonzalo Recondo, Martin Schuler

Speaker: **Charles M. Rudin, MD, PhD,** Fiona and Stanley Druckenmiller Center for Lung Cancer Research, Memorial Sloan Kettering Cancer Center, New York, USA.

Randomized, controlled, phase 3 DeLLphi-304 study (NCT05740566)

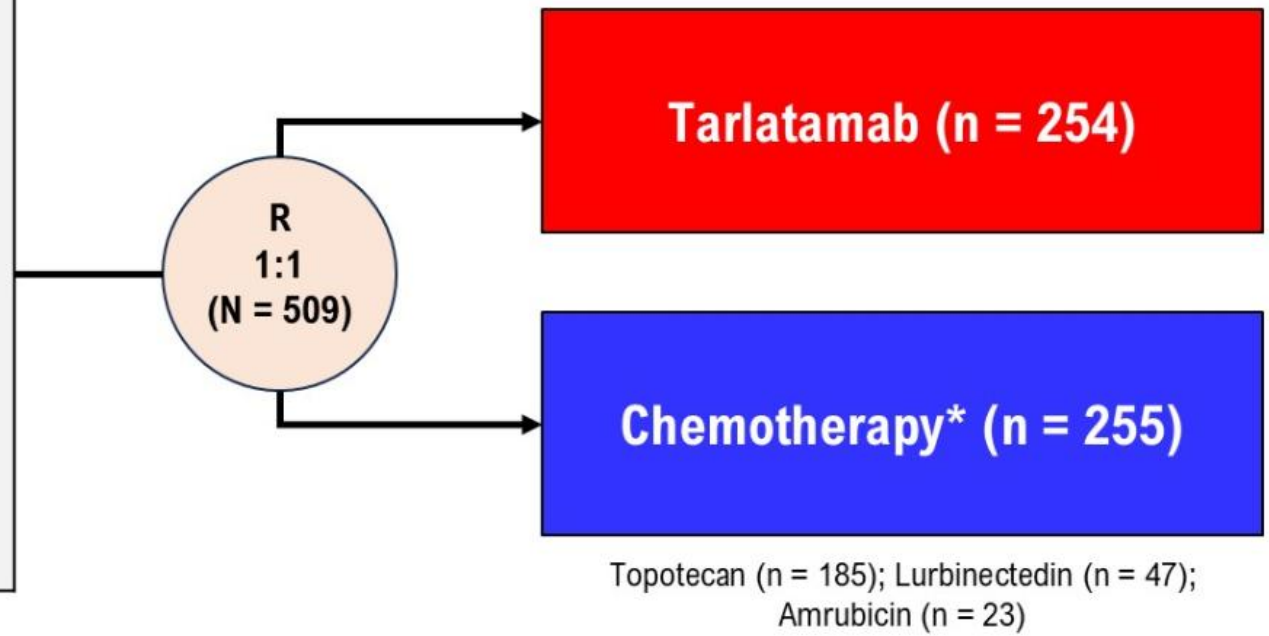
DeLLphi 304

Key inclusion criteria

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

Randomization stratified by

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

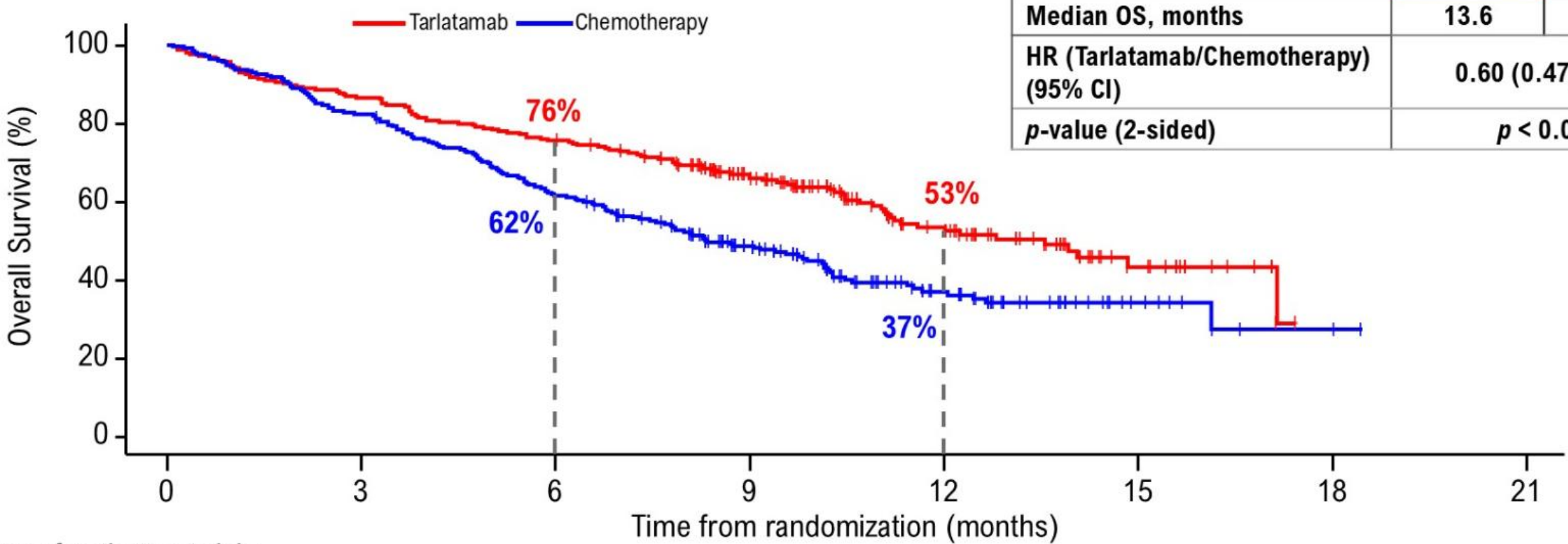


Primary Endpoint: Overall survival
Key Secondary Endpoints: Progression-free survival, patient-reported outcomes
Other Secondary Endpoints: Objective response, disease control, duration of response, safety

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

DeLLphi-304 met its primary endpoint with tarlatamab demonstrating superior overall survival over chemotherapy

	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)	$p < 0.001$	



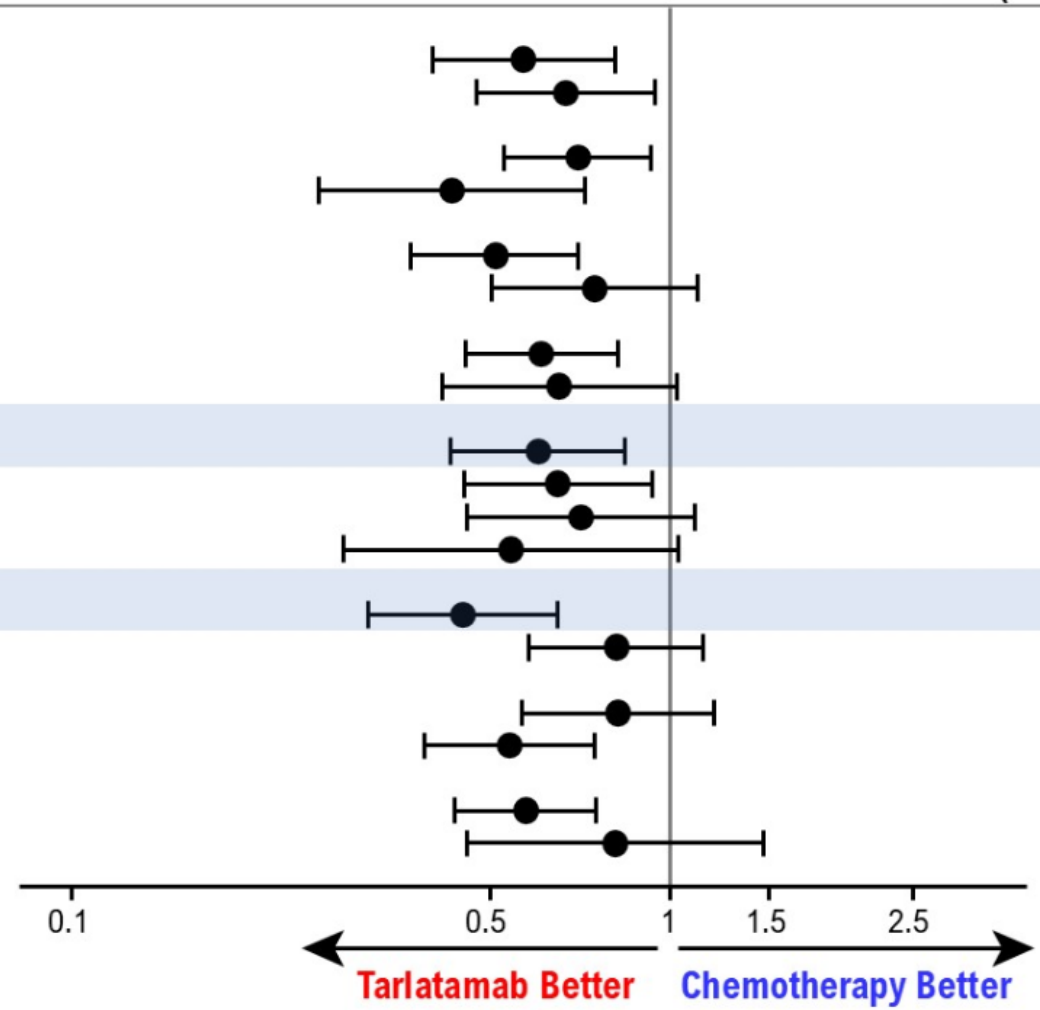
Number of patients at risk:

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

Median follow-up time: 11.2 months for the tarlatamab group and 11.7 months for the chemotherapy group. *p*-value was calculated using a stratified log-rank test.
HR, hazard ratio; **OS**, overall survival.

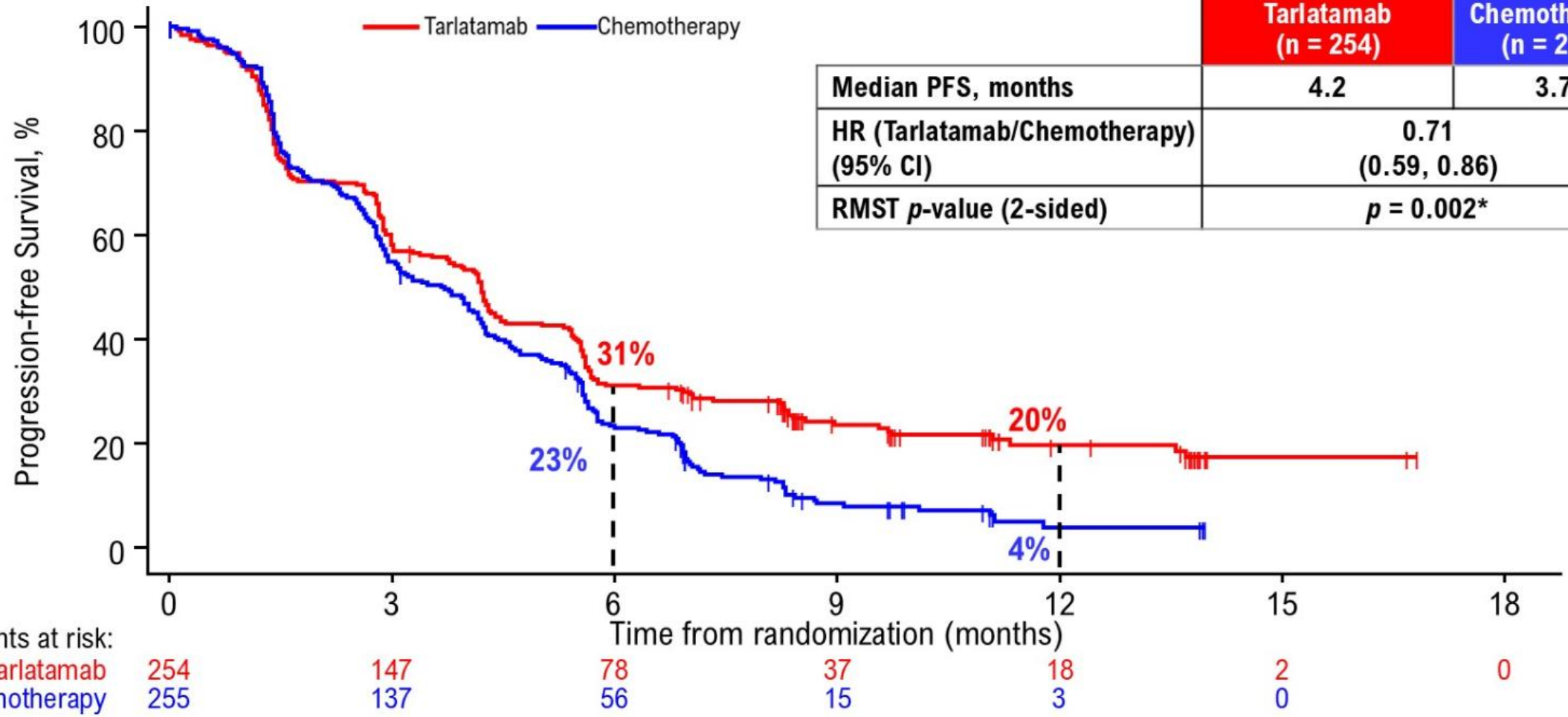
Survival benefit with tarlatamab was consistent across prespecified patient subgroups

Subgroup	Tarlatamab (no. of patients)	Chemotherapy (no. of patients)	Hazard Ratio for Death (95% CI)
Age			
< 65 years	129	115	0.57 (0.40, 0.81)
≥ 65 years	125	140	0.67 (0.48, 0.94)
Sex			
Male	182	169	0.70 (0.53, 0.93)
Female	72	86	0.43 (0.26, 0.72)
Race			
White	152	139	0.51 (0.37, 0.70)
Asian	97	107	0.75 (0.50, 1.11)
Prior anti-PD-(L)1 exposure			
Yes	180	180	0.61 (0.45, 0.82)
No	74	75	0.65 (0.42, 1.03)
Chemotherapy-free interval			
< 90 days	109	114	0.60 (0.43, 0.84)
≥ 90 days	145	141	0.65 (0.45, 0.93)
≥ 90 to <180 days	85	78	0.71 (0.46, 1.10)
≥ 180 days	60	63	0.54 (0.29, 1.03)
Presence (previous or current) of brain metastases			
Yes	113	115	0.45 (0.31, 0.65)
No	141	140	0.81 (0.58, 1.13)
Liver metastases			
Yes	84	95	0.82 (0.57, 1.18)
No	170	160	0.54 (0.39, 0.75)
Chemotherapy			
Topotecan/Amrubicin	209	208	0.57 (0.44, 0.75)
Lurbinectedin	45	47	0.81 (0.46, 1.44)



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

Progression-free survival was significantly longer with tarlatamab vs chemotherapy



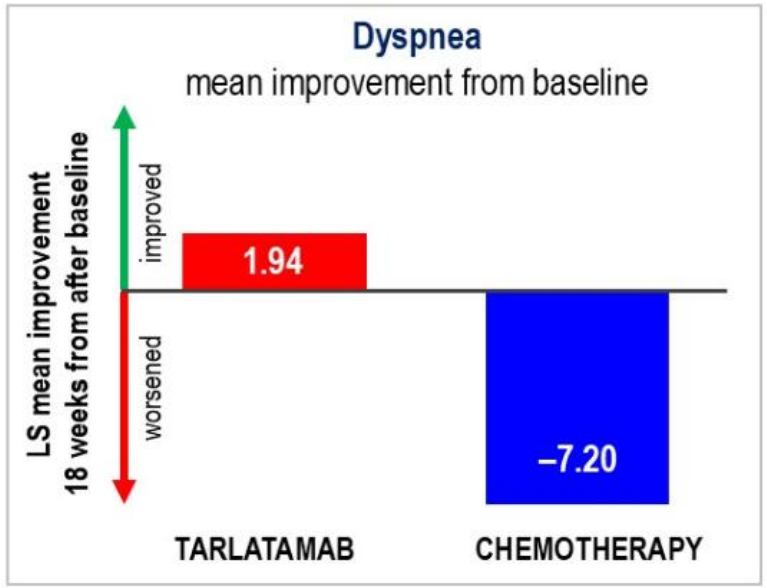
	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median PFS, months	4.2	3.7
HR (Tarlatamab/Chemotherapy) (95% CI)	0.71 (0.59, 0.86)	
RMST *p*-value (2-sided)	*p* = 0.002*	

Median follow-up time: 11.0 months for the tarlatamab and the chemotherapy group. *The restricted mean PFS time in the tarlatamab and the chemotherapy group was 5.3 months and 4.3 months at 12 months respectively, resulting in statistically significant improvement of the tarlatamab group over the chemotherapy group.

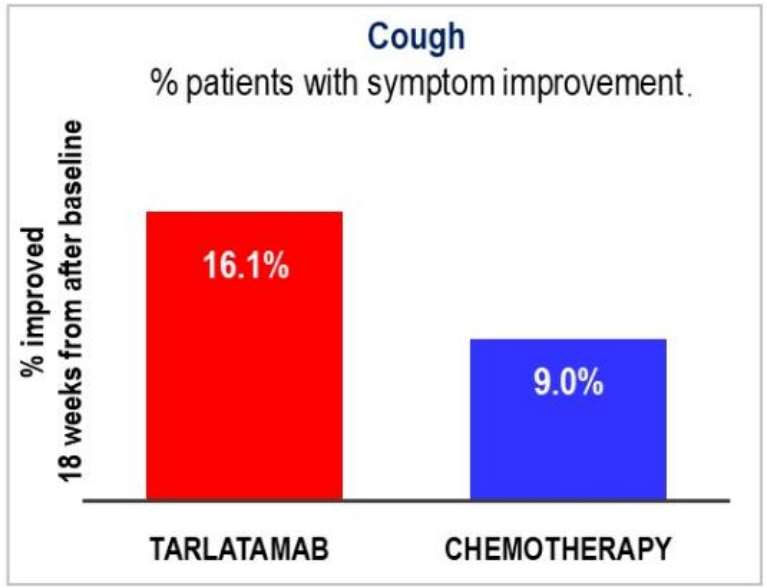
HR: hazard ratio; **PFS**, progression-free survival.

PRESENTED BY: Charles M. Rudin, MD, PhD

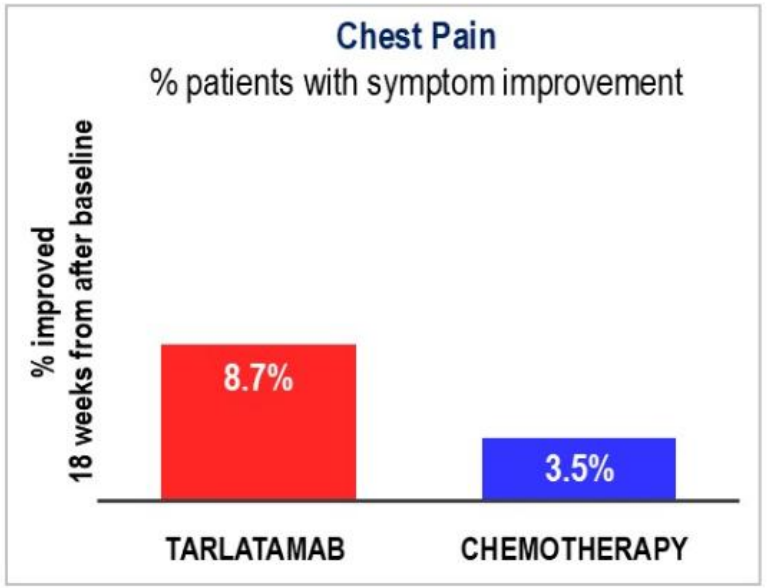
Tarlatamab improved symptoms of dyspnea and cough after 18 weeks from baseline



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)

The mean difference in the change after 18 weeks in the physical functioning score (10.35 points [95% CI: 6.00 to 14.69]) and the global health status score (8.93 points [95% CI: 5.04 to 12.83]) trended in favor of tarlatamab. *Similar results were observed when the sensitivity analyses were carried out incorporating a more conservative estimand (i.e., treatment policy strategy) for change from baseline after 18 weeks in **dyspnea** (mean difference, -6.19; [95% CI, -8.88 to -3.49]), **cough** (odds ratio, 1.48 [95% CI, 1.08 to 2.02]), **chest pain** (odds ratio, 1.21 [95% CI, 0.80 to 1.82]).

The change from baseline after 18 weeks in symptoms of chest pain, cough, and dyspnea were measured by European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30) and the supplementary symptom scores for Lung Cancer (QLQ-LC13). Change from baseline after 18 weeks in chest pain and cough were analyzed using generalized linear mixed model (GLMM) with a cumulative logit link. Change from baseline after 18 weeks in dyspnea was analyzed using mixed effects model with repeated measures (MMRM) with a restricted maximum likelihood estimator method (REML). A hypothetical estimand strategy was pre-specified for these key secondary PRO endpoints. Clinically meaningful improvement in chest pain and cough was defined as improving at least 1 level in the response categories. Difference in dyspnea score between groups with more than 9 points is considered clinically meaningful.
LS, least squares.

Tarlatamab had a more favorable safety profile

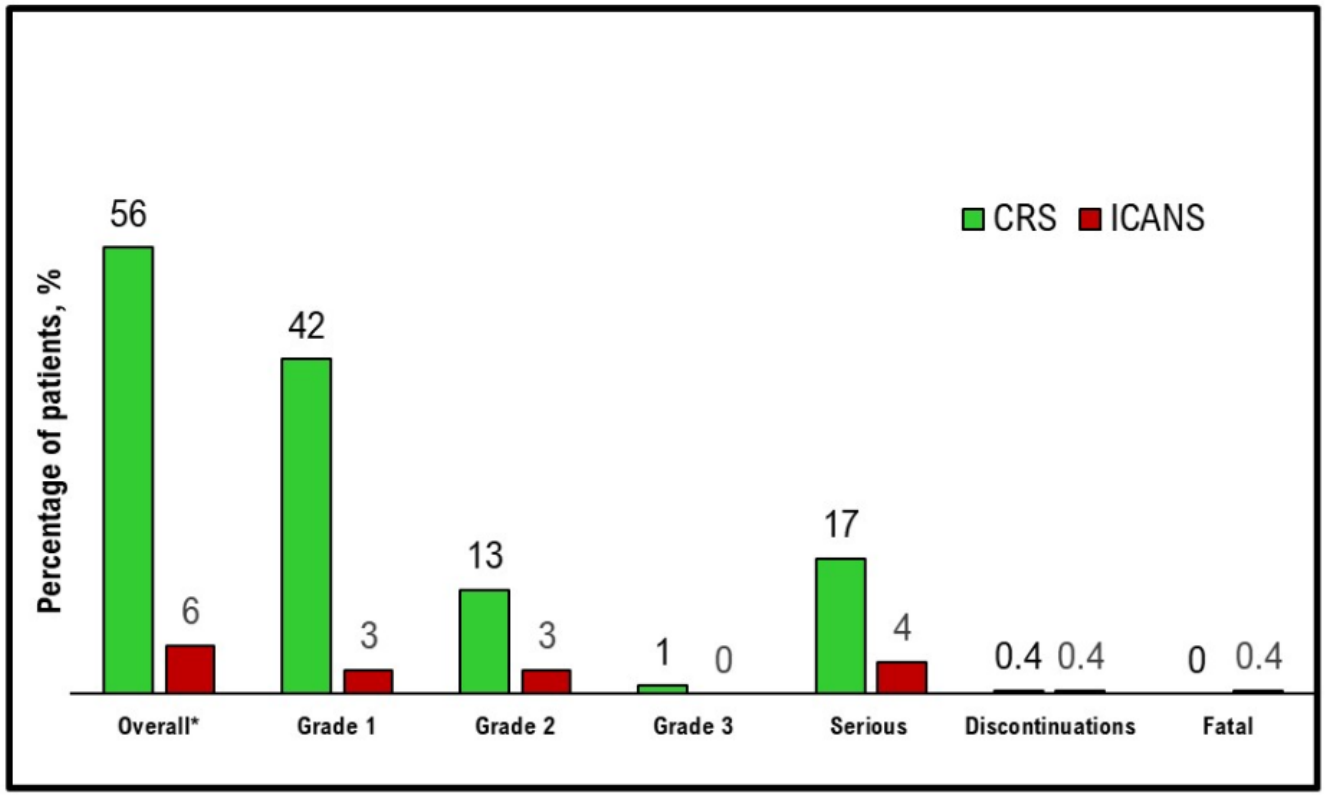
	Tarlatamab (n = 252)*	Chemotherapy (n = 244)*
Median duration of treatment, months, (range)	4.2 (< 1–17)	2.5 (< 1–15)
All grade, TEAEs, n (%)	249 (99)	243 (100)
All grade, TRAEs n (%)	235 (93)	223 (91)
Grade ≥ 3 TRAEs, n (%)	67 (27)	152 (62)
Serious TRAEs, n (%)	70 (28)	75 (31)
TRAEs leading to dose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

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

ICANS, immune effector cell-associated neurotoxicity syndrome; **TEAE,** treatment-emergent adverse event; **TRAE,** treatment-related adverse event.

CRS and ICANS events were consistent with tarlatamab's established safety profile

Treatment-emergent CRS and ICANS with tarlatamab



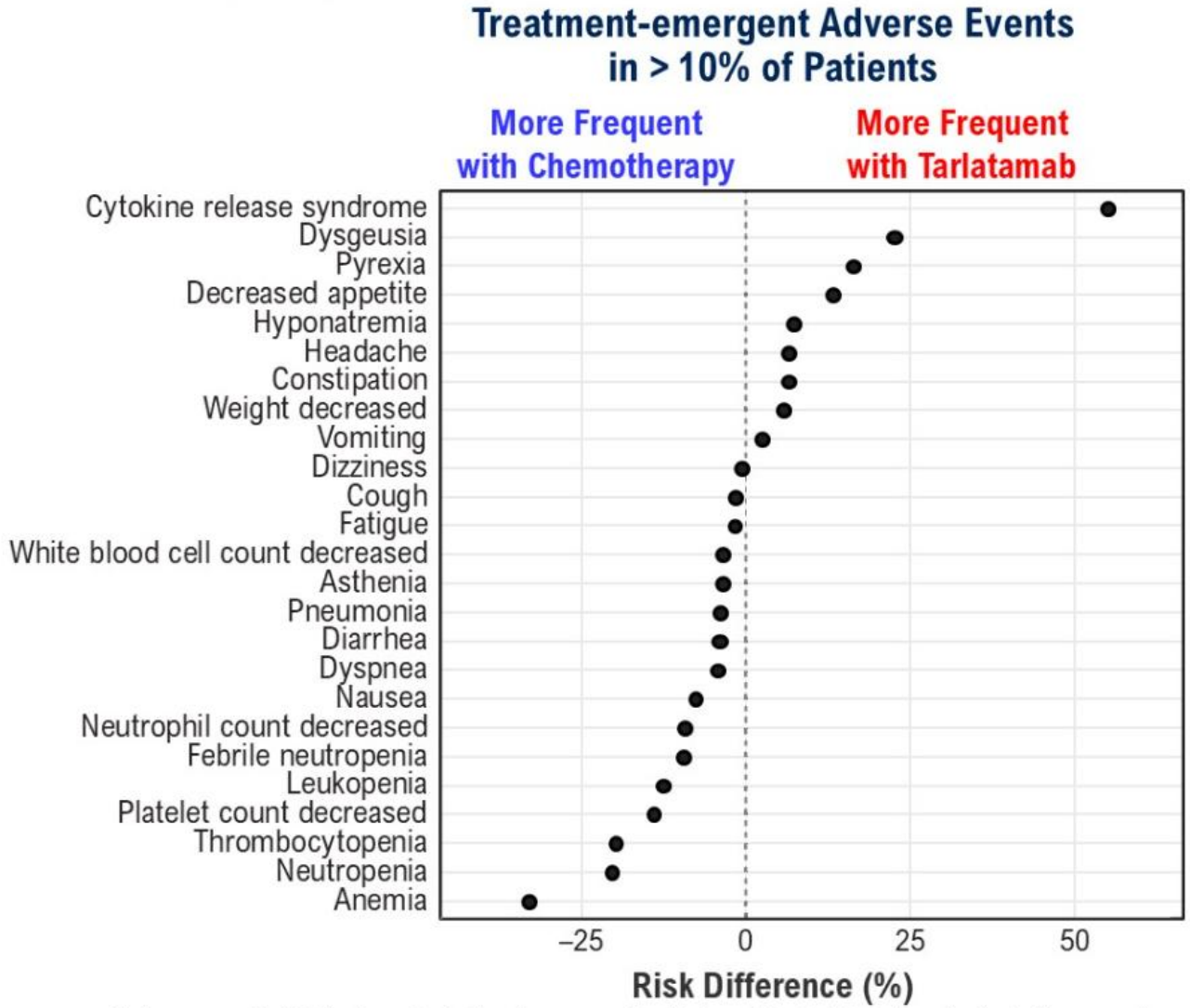
CRS with first two infusions

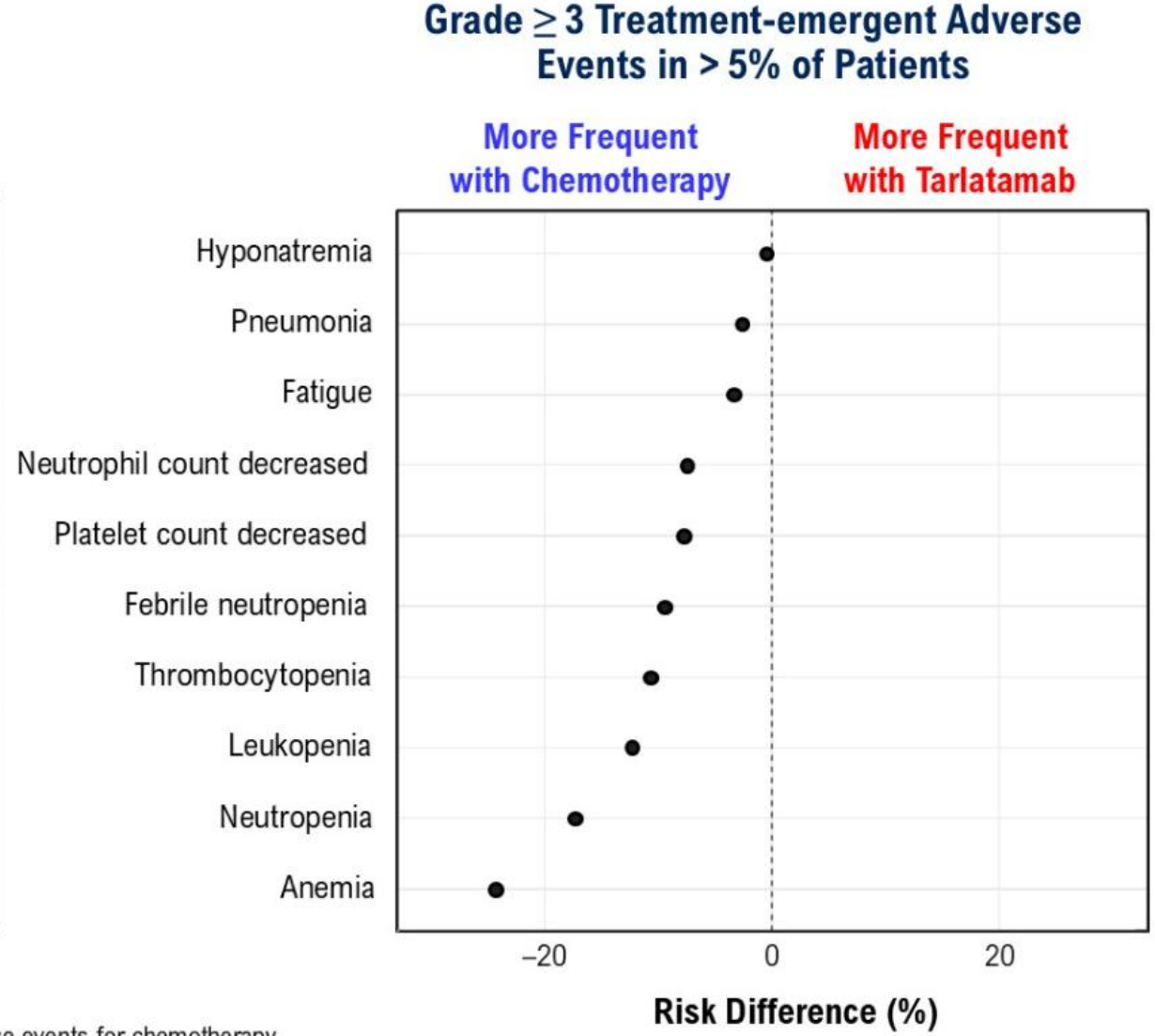
Tarlatamab (N = 252)	Minimum required monitoring duration	
	6 - 8 Hours (n = 43)	48 Hours (n = 209)
Treatment emergent CRS, n (%)*	16 (37)	125 (60)
Grade 1	12 (28)	94 (45)
Grade 2	4 (9)	28 (13)
Grade 3	0 (0)	3 (1)
Serious adverse events	3 (7)	39 (19)
Leading to discontinuation of IP	0 (0)	1 (0.5)
Median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

*Grade 4 CRS or ICANS events were not observed. A single grade 5 treatment-related adverse event observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension.

CRS, cytokine release syndrome; **ICANS,** immune effector cell-associated neurotoxicity syndrome; **IP**, investigational product.

Patients treated with tarlatamab experienced lower incidence of high-grade AEs





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

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tarlatamab in Small-Cell Lung Cancer after Platinum-Based Chemotherapy

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Charles M. Rudin, M.D., Ph.D.,[24] for the DeLLphi-304 Investigators*

Phase 1b study of tarlatamab with anti-PD-L1 as 1L maintenance for ES-SCLC: DeLLphi 303 Study[a]

DeLLphi 303

1L Chemo-IO

Platinum-etoposide + anti-PD-L1[c]

(4-6 cycles)

Enrollment

Key Inclusion Criteria

- ✓ No disease progression following 4–6 cycles of 1L chemo-IO
- ✓ ECOG PS 0 or 1
- ✓ Patients with treated and asymptomatic brain metastases were permitted
- ✓ No active autoimmune disease or disease requiring immunosuppressive therapy[d]

Non-randomized[e]

Switching to a different anti-PD-L1 than that received in 1L chemo-IO was permitted

1L Maintenance[b]

Tarlatamab (10 mg IV Q2W) + Atezolizumab (1680 mg IV Q4W) n = 48

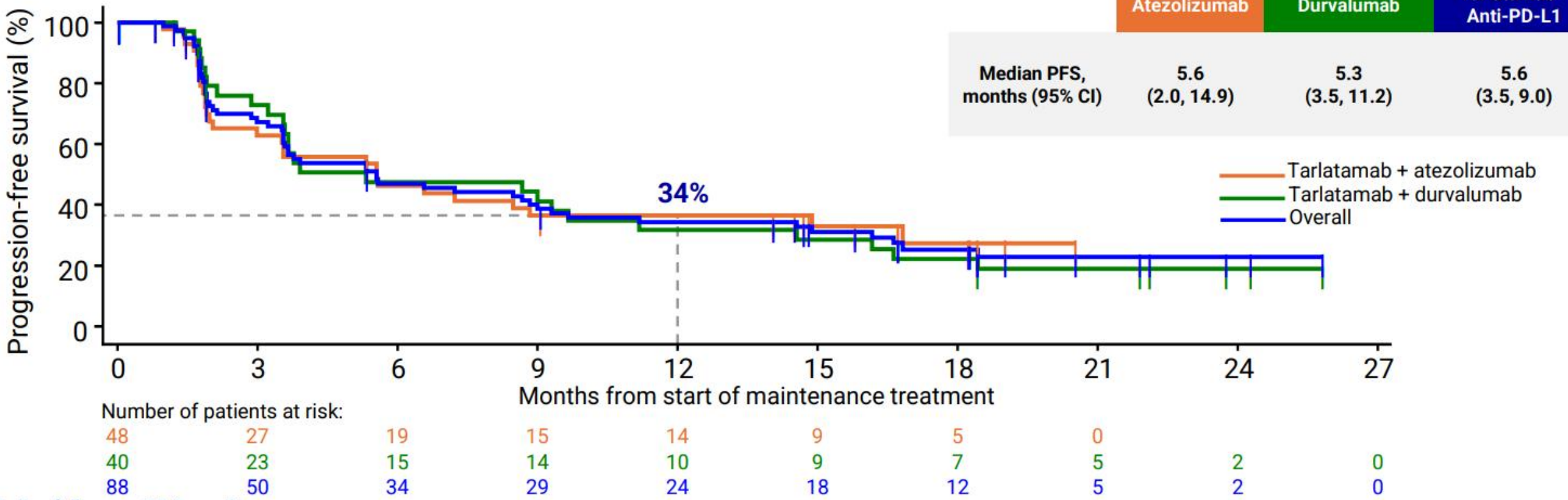
Tarlatamab (10 mg IV Q2W) + Durvalumab (1500 mg IV Q4W) n = 40

Primary Endpoints[f]: Dose-limiting toxicities[g], treatment-emergent and treatment-related adverse events
Secondary Endpoints[h]: Progression-free survival, overall survival, objective response rate, duration of response, and disease control

[a]Cohorts 5, 6, and 8; NCT05361395. [b]Maintenance therapy commenced within 8 weeks of the start of the last cycle of 1L chemo-IO. [c]Patients without access to 1L anti-PD-L1 were allowed. [d]Patients with active autoimmune disease requiring systemic treatment (except replacement therapy) within the past 2 years were excluded. [e]Patients were allocated to treatment arms in a non-randomized manner based on slot availability. [f]Also included vital signs, electrocardiograms, and clinical laboratory tests [g]Dose-limiting toxicities were assessed for cohort 5 only. [h]Also included serum concentrations of tarlatamab, quantification of biomarker expression, and incidence of anti-tarlatamab antibody formation. **1L:** first-line; **chemo-IO:** chemo-immunotherapy; **ECOG PS**: Eastern Cooperative Oncology Group performance status; **ES-SCLC:** extensive-stage small cell lung cancer; **IV:** intravenous; **PD-L1:** programmed death-ligand 1; **Q2W:** once every 2 weeks; **Q4W**: once every 4 weeks.

Progression free survival with addition of tarlatamab to anti-PD-L1 as 1L maintenance therapy

	Tarlatamab+ Atezolizumab	Tarlatamab+ Durvalumab	Overall Tarlatamab + Anti-PD-L1
Median PFS, months (95% CI)	5.6 (2.0, 14.9)	5.3 (3.5, 11.2)	5.6 (3.5, 9.0)



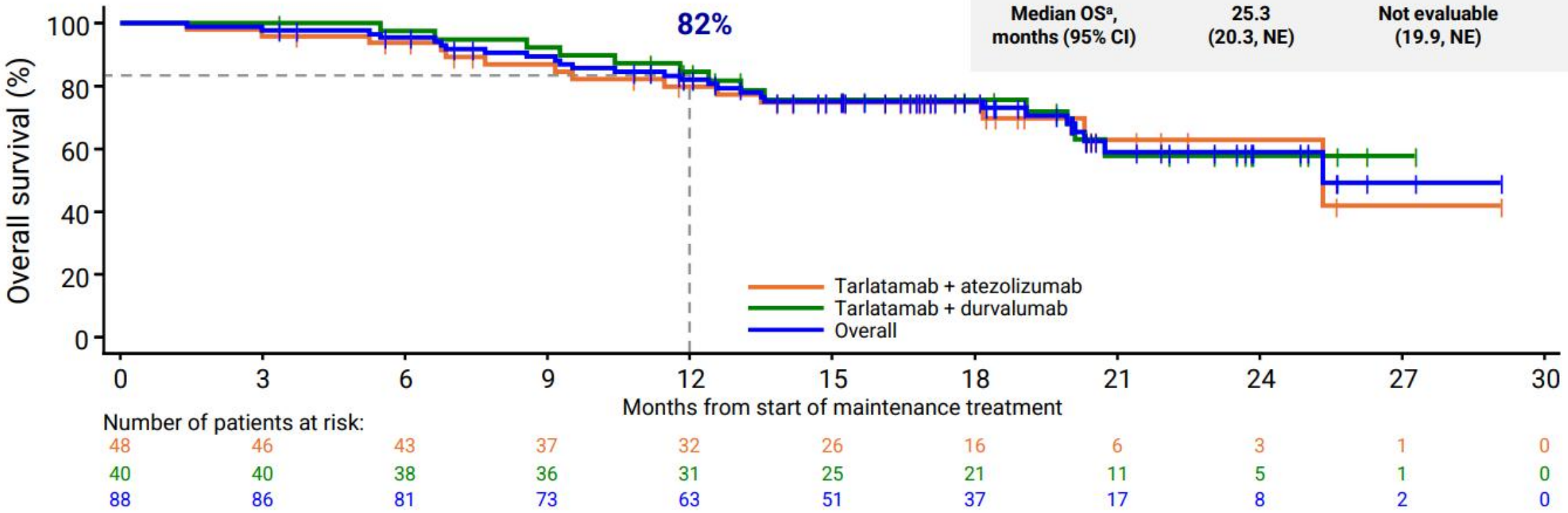
Median follow-up: 18.4 months

Tarlatamab with anti-PD-L1 as 1L maintenance therapy led to a median PFS of 5.6 months (95% CI, 3.5, 9.0).

1L: first-line; **CI:** confidence interval; **PD-L1:** programmed death-ligand 1; **PFS:** progression-free survival.

Overall survival with addition of tarlatamab to anti-PD-L1 as 1L maintenance therapy

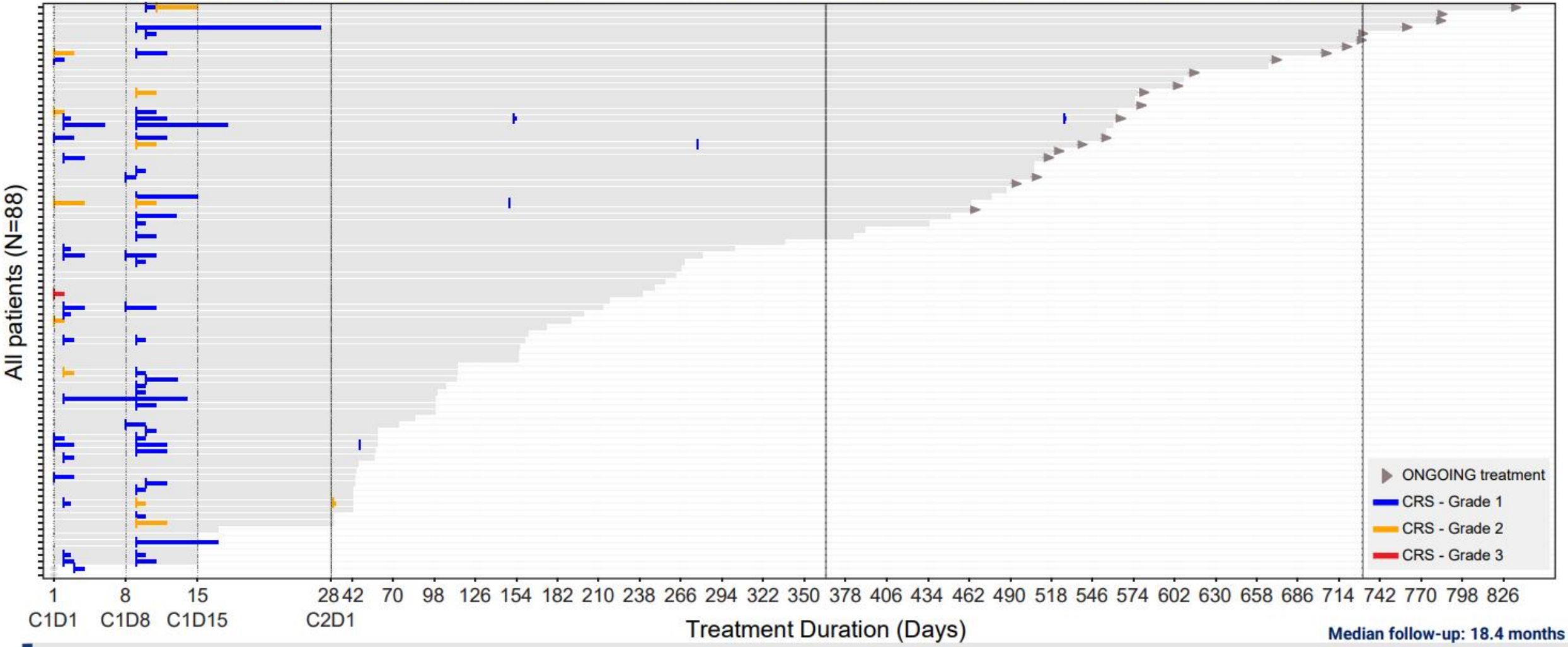
	Tarlatamab+ Atezolizumab	Tarlatamab+ Durvalumab	Overall Tarlatamab + Anti-PD-L1
Median OS[a], months (95% CI)	25.3 (20.3, NE)	Not evaluable (19.9, NE)	25.3 (20.3, NE)



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

[a]The median OS is immature and will continue to evolve with longer follow-up time. **1L:** first-line; **CI:** confidence interval; **NE:** not evaluable; **OS:** overall survival; **PD-L1:** programmed death-ligand 1.

CRS primarily occurred after the first or second tarlatamab dose in cycle 1



Median follow-up: 18.4 months

CRS occurred in 49 (56%) of patients, with most events grade 1 (43%) or grade 2 (11%); all CRS events resolved.

CRS (grade 1) led to tarlatamab interruption in one patient . Tarlatamab dose was reduced (i.e., repeat step dosing) in one patient with grade 3 CRS. No CRS events of grade 4 or 5 occurred. The four CRS events after 3 months occurred with tarlatamab rechallenge. **CRS**: cytokine release syndrome.

The Long Road Ahead

Photo credit: Steven Schild