ETOP·IBCSG
PARTNERS FOUNDATION

Foundation for International
Cancer Research

ESMO Congress 2025

17–21 October 2025

Supported by Eli Lilly and Company, BeOne Medicines, GSK and Johnson&Johnson
None of these companies have influenced the content of this publication

GOLD SPONSOR Lilly

SILVER SPONSORS BeOne GSK Johnson&Johnson

Letter from Prof Rolf Stahel

Dear Colleagues

It is my pleasure to present this ETOP slide set which has been designed to highlight and summarise key findings in thoracic cancers from the major congresses in 2025. This slide set specifically focuses on the **ESMO Congress 2025** and is available in 3 languages – English, Chinese and Japanese.

The area of clinical research in oncology is a challenging and continually changing environment. Within this environment we all value access to scientific data and research which helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in thoracic cancers of benefit to you in your practice. If you would like to share your thoughts with us, we would welcome your comments. Please send any correspondence to etop@etop.eu-org.

I would like to thank our ETOP members Drs Enriqueta Felip, Solange Peters, Martin Reck and Egbert Smit for their roles as Editors – for prioritising abstracts and reviewing slide content. The slide set you see before you would not be possible without their commitment and hard work.

Finally, we are also very grateful to Lilly Oncology for their financial, administrative and logistical support in the realisation of this complex yet rewarding activity.

Yours sincerely,
Rolf Stahel
President, ETOP Foundation Council

ETOP Medical Oncology Slide Deck Editors 2025

Focus: biomarkers (all stages)

Dr Enriqueta Felip

Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain

Focus: early and locally advanced NSCLC (stages I–III)

Dr Egbert Smit

Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands

Focus: advanced NSCLC (not radically treatable stage III & stage IV)

Dr Solange Peters

Multidisciplinary Oncology Center, Lausanne Cancer Center, Lausanne, Switzerland

Focus: other malignancies, SCLC, mesothelioma, rare tumors

Dr Martin Reck

Department of Thoracic Oncology, Hospital Grosshansdorf, Grosshansdorf, Germany

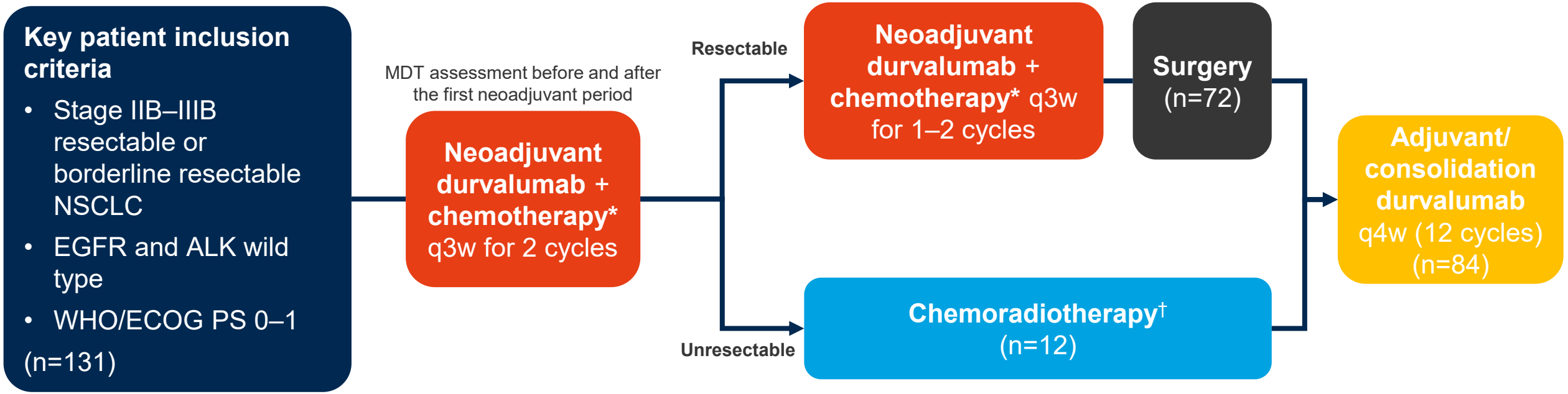
Contents

- Early stage and locally advanced NSCLC – Stages I, II and III
- Advanced NSCLC – Not radically treatable stage III and stage IV
  - Immunotherapy
  - Targeted therapies
  - ADCs and other therapies
- Other malignancies
  - SCLC, mesothelioma and thymic epithelial tumors

Early stage and locally advanced NSCLC – Stages I, II and III

LBA65: Neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D in patients (pts) with resectable or borderline resectable stage IIB–IIIB NSCLC: interim analysis (IA) of the phase 2 MDT-BRIDGE study – Reck M, et al

- **Study objective**
  - To evaluate the interim efficacy and safety of neoadjuvant durvalumab + chemotherapy followed by either surgery + adjuvant durvalumab or chemoradiotherapy + consolidation durvalumab in patients with resectable or borderline resectable stage IIB–IIIB NSCLC in the phase 2 MDT-BRIDGE study



Primary endpoints

- Resection rate (in patients who had definitive surgery)

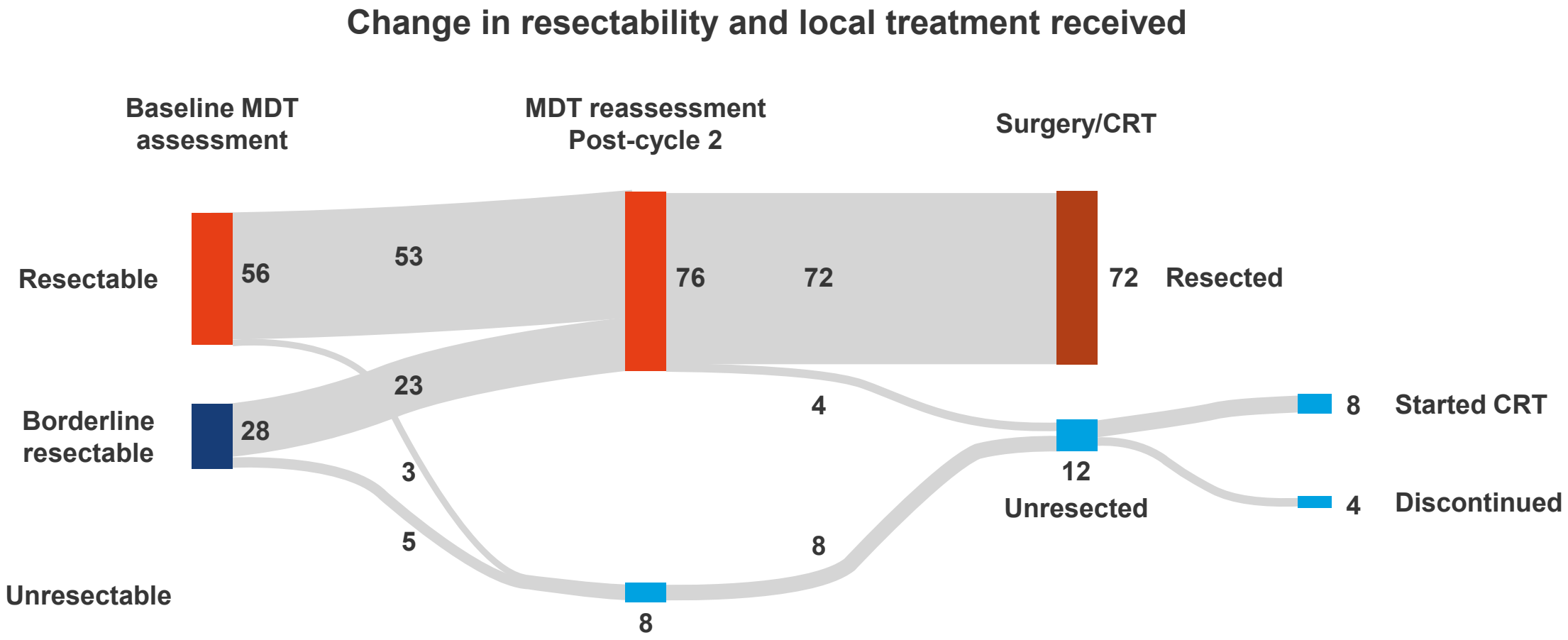
Secondary endpoints

- Resection rate (all patients), surgical outcomes, ORR, pCR, safety

*Investigator's choice platinum-based. †60 Gy ±10% (five fractions/week for 6 weeks).

LBA65: Neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D in patients (pts) with resectable or borderline resectable stage IIB–IIIB NSCLC: interim analysis (IA) of the phase 2 MDT-BRIDGE study – Reck M, et al

- Key **results** (cont.)



LBA65: Neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D in patients (pts) with resectable or borderline resectable stage IIB–IIIB NSCLC: interim analysis (IA) of the phase 2 MDT-BRIDGE study – Reck M, et al

- **Key results**

Resection rates and outcomes*

	All patients (n=84)	Baseline resectable (n=56)	Baseline borderline resectable (n=28)
Resection rate, % (95%CI)	85.7 (76.4, 92.4)	92.9 (82.7, 98.0)	71.4 (51.3, 86.8)
Resection outcomes, n	72	52	20
R0, % (95%CI)	94.4 (86.4, 98.5)	98.1 (89.7, 100)	85.0 (62.1, 96.8)
R1, % (95%CI)	1.4 (0, 7.5)	1.9 (0, 10.3)	0 (0, 16.8)
R2, % (95%CI)	1.4 (0, 7.5)	0 (0, 6.8)	5.0 (0.1, 24.9)
NE or missing, % (95%CI)	2.8 (0.3, 9.7)	0 (0, 6.8)	10.0 (1.2, 31.7)

ORR pre-surgery or pre-chemoradiotherapy

	Patients resectable after neoadjuvant therapy (n=76)	Patients unresectable after neoadjuvant therapy (n=8)
ORR, % (95%CI)	60.5 (48.6, 71.6)	12.5 (0.3, 52.7)
Response, %		
PR	60.5	12.5
SD	30.3	75.0
PD or death	1.3	0
NE	7.9	12.5

- pCR rate was 27.6% in the efficacy subset (76 resectable patients after neoadjuvant therapy)

*One patient did not complete surgical resection as intended.

LBA65: Neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D in patients (pts) with resectable or borderline resectable stage IIB–IIIB NSCLC: interim analysis (IA) of the phase 2 MDT-BRIDGE study – Reck M, et al

- **Key results (cont.)**

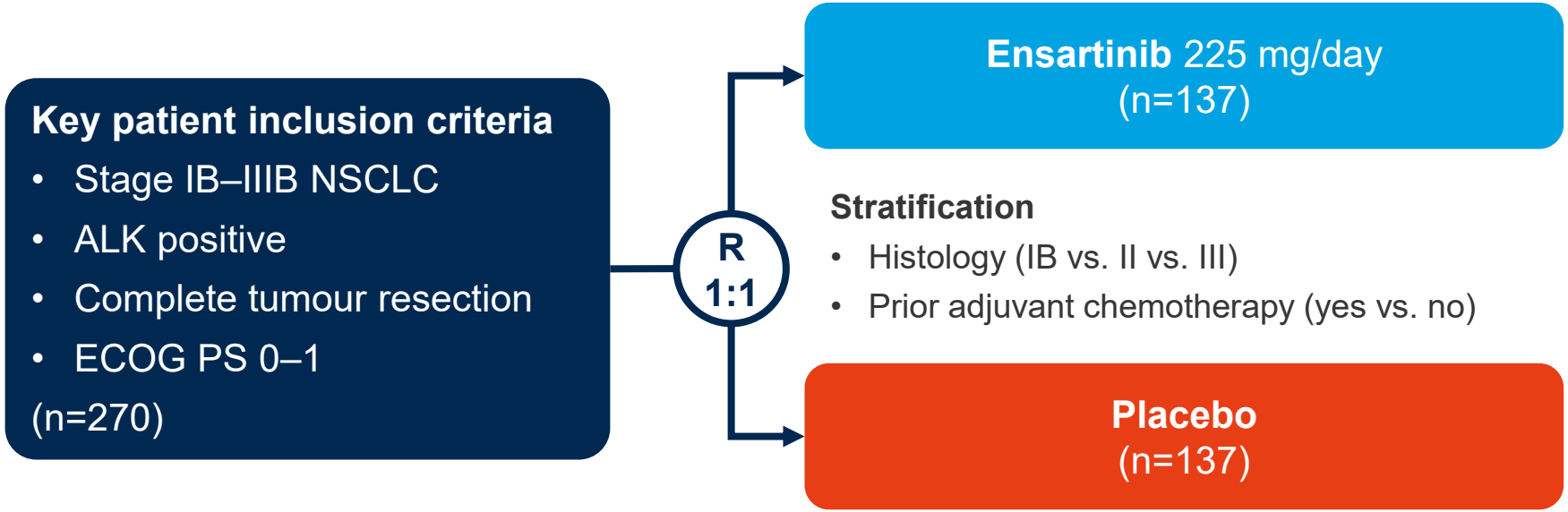
AEs, n (%)	All patients (n=131)
Any grade, all-cause	120 (91.6)
Grade ≤3–4	45 (34.4)
Serious	28 (21.4)
Led to death	2 (1.5)
Led to durvalumab discontinuation	8 (6.1)
Any grade, immune-mediated	15 (11.5)
Pneumonitis	2 (1.5)

AEs, n (%) (cont'd)	All patients (n=131)
Any grade, possibly related to study treatment	108 (82.4)
Grade ≤3–4	33 (25.2)
Serious	13 (9.9)
Led to death	1 (0.8)

- **Conclusions**
  - In patients with resectable or borderline resectable stage IIB–IIIB NSCLC, neoadjuvant durvalumab + chemotherapy enabled high resection rates and maintained chemoradiotherapy eligibility without introducing new safety concerns
  - Longer follow-up and a larger sample size are needed to evaluate feasibility, safety and efficacy of the strategy in patients with borderline resectable NSCLC

LBA66: Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB ALK-positive (ALK+) non-small cell lung cancer (NSCLC) after complete tumor resection: the phase III randomized ELEVATE trial – Yue D, et al

- **Study objective**
  - To evaluate the efficacy and safety of adjuvant ensartinib in patients with stage IB–IIIB ALK-positive NSCLC after complete tumor resection in the phase 3 ELEVATE study



Primary endpoints

- DFS in stage II–IIIB (investigator assessed)

Secondary endpoints

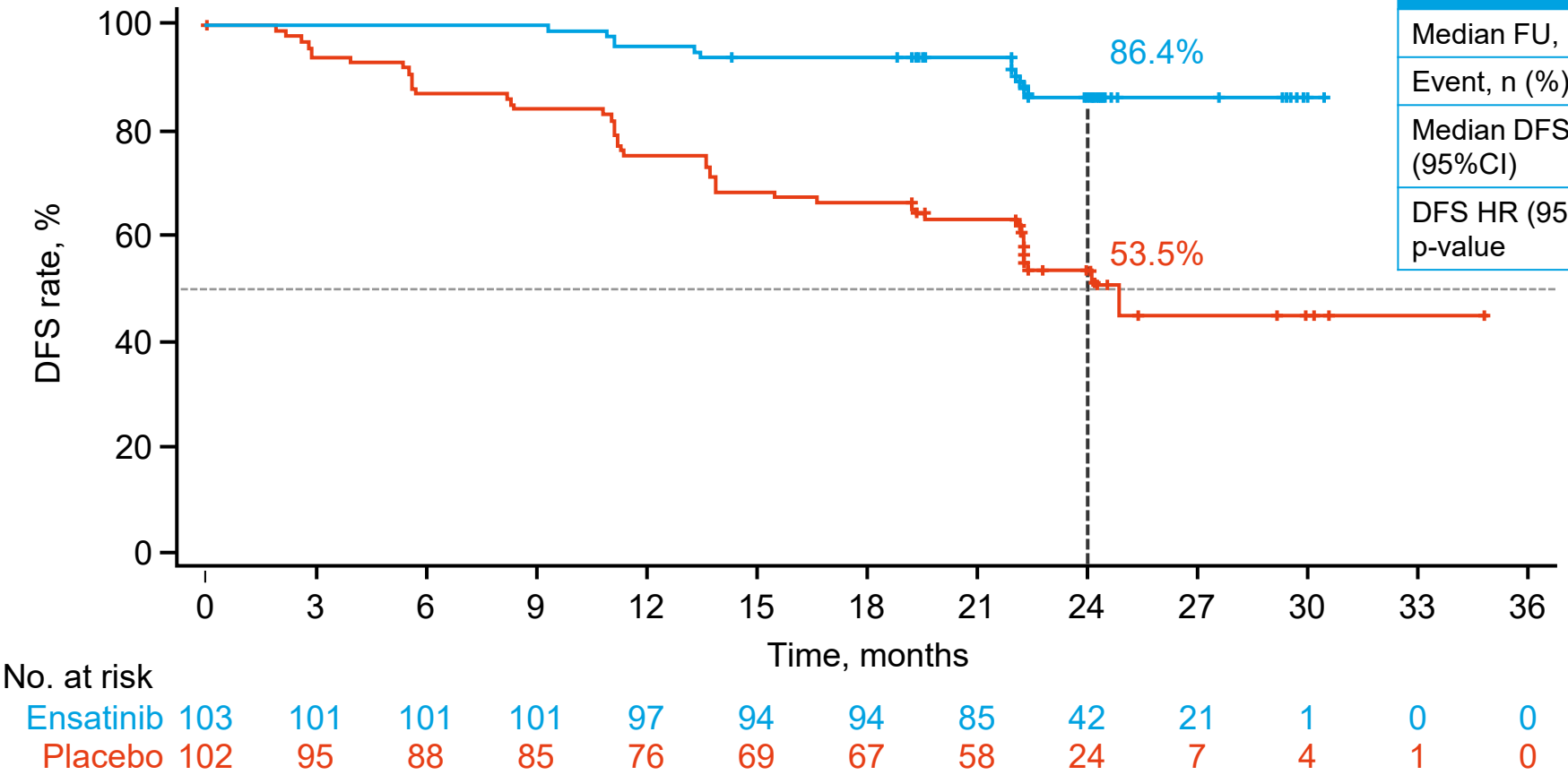
- DFS in stage IB–IIIB, 3–5-year DFS rate, OS, safety

Yue D, et al. Ann Oncol 2025;36(suppl):Abstr LBA66

LBA66: Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB ALK-positive (ALK+) non-small cell lung cancer (NSCLC) after complete tumor resection: the phase III randomized ELEVATE trial – Yue D, et al

- **Key results**

Investigator-assessed disease-free survival in stage II–IIIB



	Ensartinib (n=103)	Placebo (n=102)
Median FU, mo	24.0	24.0
Event, n (%)	12 (11.7)	46 (45.1)
Median DFS, mo (95%CI)	NE (NE, NE)	24.8 (22.2, NE)
DFS HR (95%CI); p-value	0.20 (0.11, 0.38); <0.0001	

LBA66: Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB ALK-positive (ALK+) non-small cell lung cancer (NSCLC) after complete tumor resection: the phase III randomized ELEVATE trial – Yue D, et al

- **Key results (cont.)**

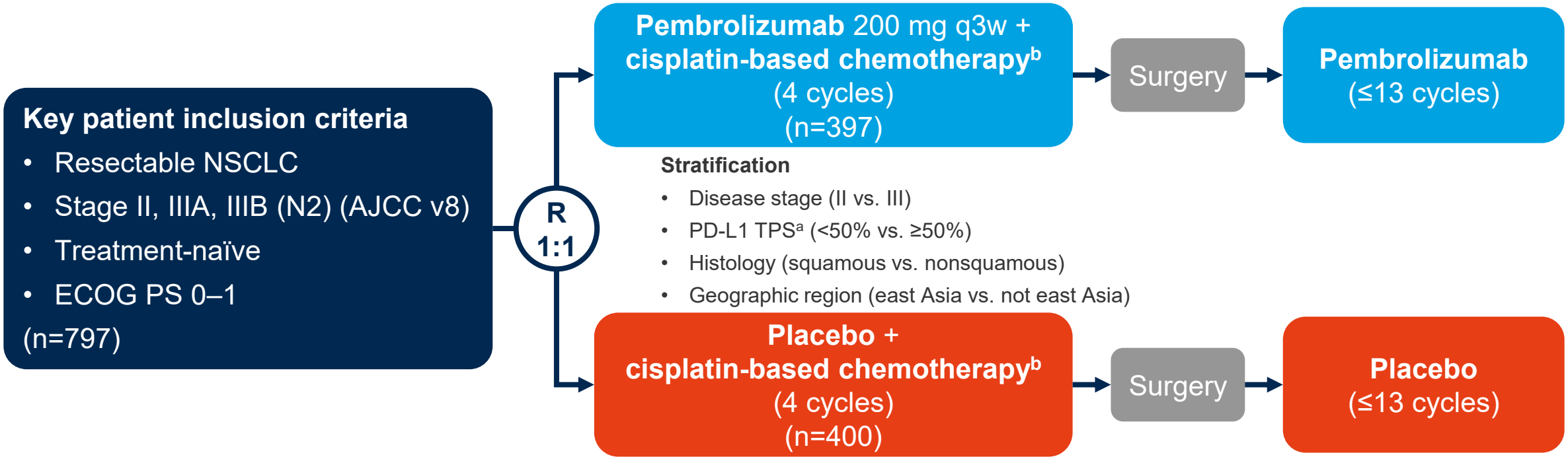
Outcomes in stage IB-IIIB	Ensartinib (n=137)	Placebo (n=137)
Median FU, mo	22.2	22.1
Event, n (%)	12 (8.8)	48 (35.0)
Median DFS, mo (95%CI)	NE (NE, NE)	24.8 (22.2, NE)
DFS HR (95%CI); p-value	0.20 (0.10, 0.37); <0.0001	
2-yeare DFS rate, %	87.3	57.2

	Ensartinib (n=137)	Placebo (n=137)
Median duration of treatment, mo	22.1	17.1
TEAEs, n (%)		
Any grade	135 (98.5)	126 (92.0)
Grade 3–4	48 (35.0)	23 (16.8)
Grade 5	1 (0.7)	2 (1.5)
SAEs	25 (18.2)	14 (10.2)
Led to dose reduction	41 (29.9)	2 (1.5)
Led to dose interruption	48 (35.0)	20 (14.6)
Led to discontinuation	3 (2.2)	2 (1.5)

- **Conclusions**
  - In patients with stage IB–IIIB ALK-positive NSCLC, ensartinib significantly improved DFS with no new safety concerns identified in the adjuvant setting

LBA67: Perioperative pembrolizumab in early-stage non–small-cell lung cancer (NSCLC): 5-year follow-up from KEYNOTE-671 – Wakelee H, et al

- **Study objective**
  - To evaluate the 5-year efficacy and safety of perioperative pembrolizumab in patients with early-stage NSCLC in the KEYNOTE-671 study



Dual primary endpoints

- EFS (investigator assessed), OS

Secondary endpoints

- MPR, pCR safety

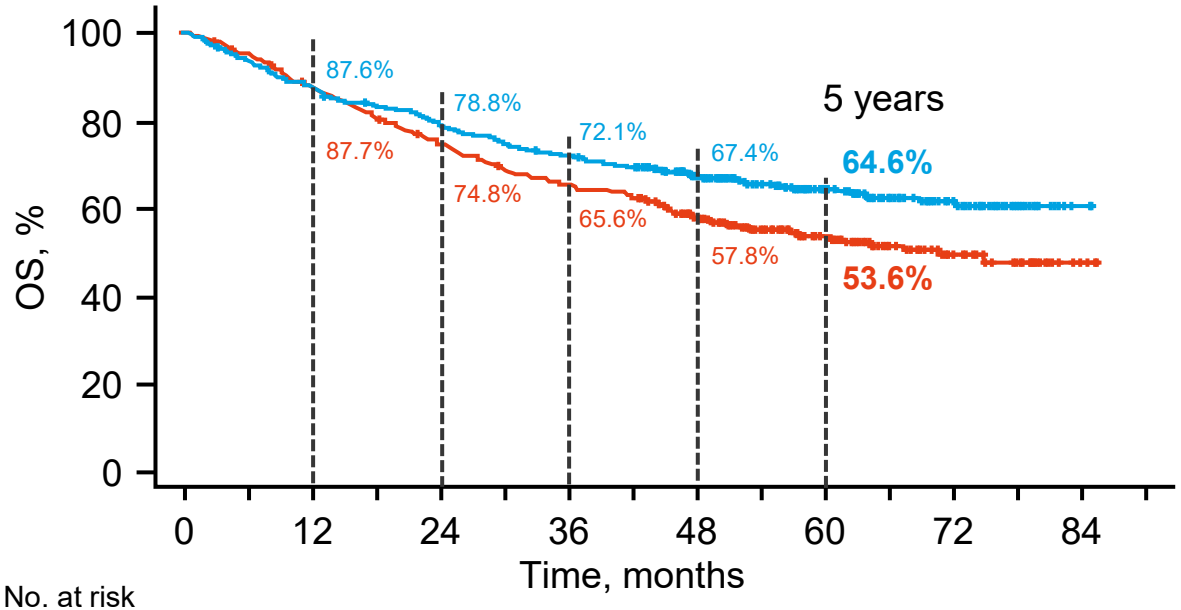
[a]Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx;
[b]squamous: cisplatin 75 mg/m^2 IV q3w + gemcitabine 1000 mg/m^2 IV D1, 8 q3w; nonsquamous: cisplatin 75 mg/m^2 IV q3w + pemetrexed 500 mg/m^2 IV q3w.

Wakelee H, et al. Ann Oncol 2025;36(suppl):Abstr LBA67

LBA67: Perioperative pembrolizumab in early-stage non–small-cell lung cancer (NSCLC): 5-year follow-up from KEYNOTE-671 – Wakelee H, et al

- **Key results**

Overall survival

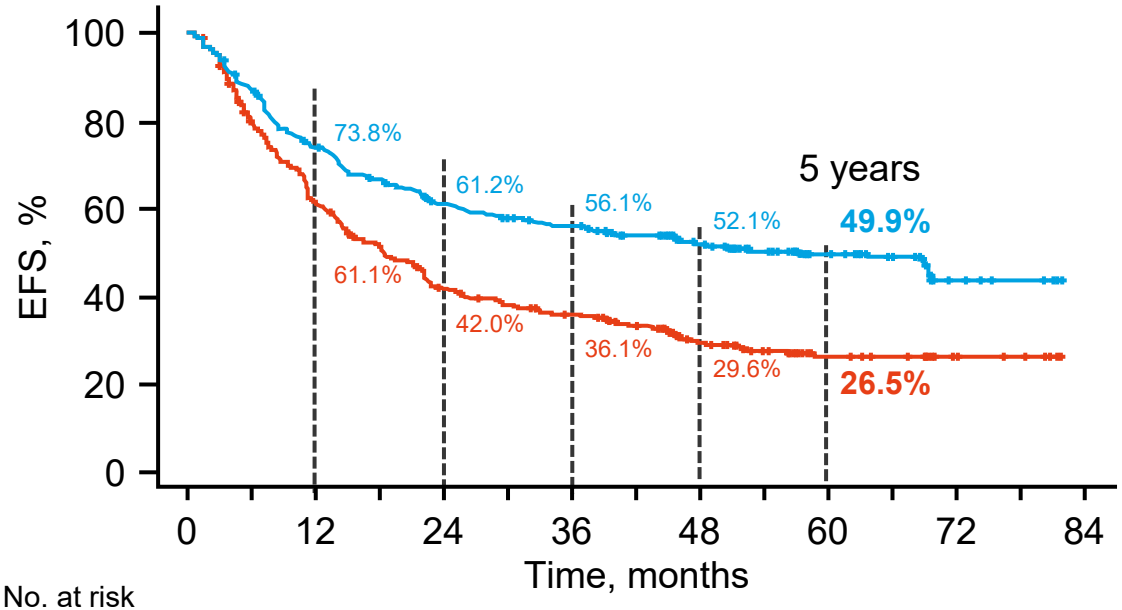


No. at risk

Pembro	397	371	347	328	310	295	283	272	236	179	128	90	61	26	2	0
Placebo	400	379	347	320	294	270	256	245	193	135	96	58	33	17	3	0

	Pembrolizumab (n=397)	Placebo (n=400)
Event, %	35.8	45.5
mOS, mo (95%CI)	NR (NR, NR)	70.7 (53.7, NR)
HR (95%CI)	0.74 (0.59, 0.92)	

Event-free survival



No. at risk

Pembro	397	340	284	255	229	214	205	185	143	113	62	52	10	6	0	
Placebo	400	310	236	196	158	143	131	112	79	58	28	22	9	6	0	

	Pembrolizumab (n=397)	Placebo (n=400)
Event, %	48.1	68.3
mEFS, mo (95%CI)	57.1 (38.0, NR)	18.4 (14.8, 22.1)
HR (95%CI)	0.58 (0.48, 0.69)	

Wakelee H, et al. Ann Oncol 2025;36(suppl):Abstr LBA67

LBA67: Perioperative pembrolizumab in early-stage non–small-cell lung cancer (NSCLC): 5-year follow-up from KEYNOTE-671 – Wakelee H, et al

- **Key results (cont.)**

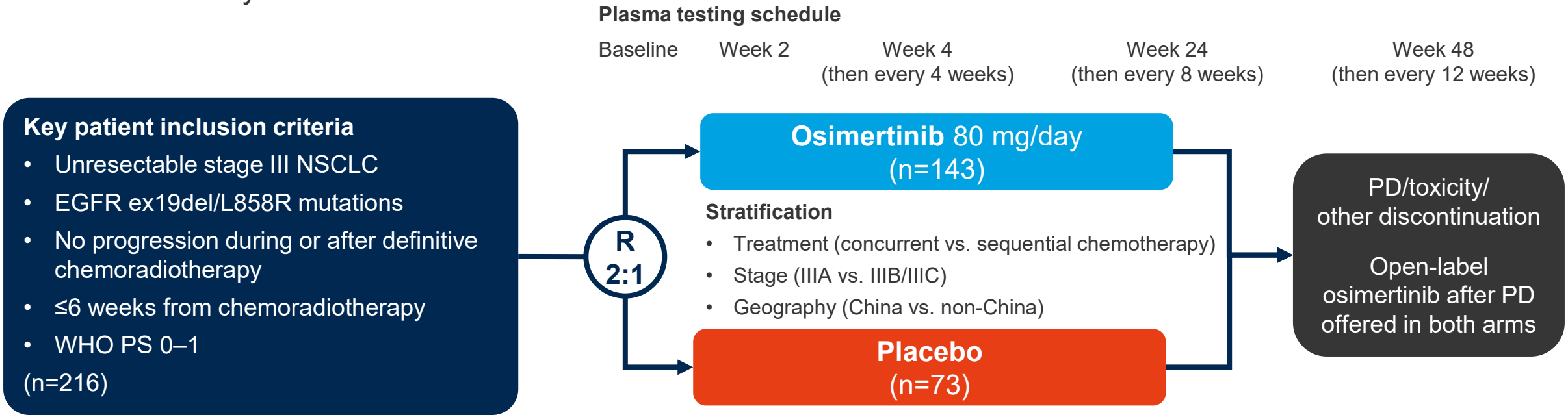
AEs, n (%)	Pembrolizumab (n=396)	Placebo (n=399)
TRAE	383 (96.7)	381 (95.5)
Grade 3–5	179 (45.2)	151 (37.8)
Serious	73 (18.4)	59 (14.8)
Led to death	4 (1.0)	3 (0.8)
Led to discontinuation of all study treatment	55 (13.9)	21 (5.3)
irAE and infusion reaction	103 (26.0)	37 (9.3)
Grade 3–5	25 (6.3)	7 (1.8)
Serious	24 (6.1)	7 (1.8)
Led to death	1 (0.3)	0
Led to discontinuation of all study treatment	22 (5.6)	3 (0.8)

- **Conclusions**
  - In patients with early-stage NSCLC, perioperative pembrolizumab combined with neoadjuvant chemotherapy provided sustained improvements in overall and event-free survival over 5 years, with no new safety signals observed

Wakelee H, et al. Ann Oncol 2025;36(suppl):Abstr LBA67

1817MO: Molecular residual disease (MRD) analysis from the LAURA study of osimertinib (osi) in unresectable (UR) stage III EGFR-mutated (EGFRm) NSCLC – Arriola E, et al

- **Study objective**
  - To evaluate MRD with osimertinib in patients with unresectable stage III EGFR-mutant NSCLC in the LAURA study



Primary endpoint

- PFS (BICR, RECIST v1.1)

Secondary endpoints

- OS, CNS PFS, safety

Exploratory analysis

- MRD clearance,* molecular progression/MRD event†

*MRD clearance: 10-fold ctDNA decrease from post-chemoradiotherapy levels or undetected MRD for 2 consecutive timepoints by week 12; †100% increase in ctDNA at a single timepoint or detected MRD above the lower limit of quantification. Plasma testing was done using Personalis Next Personal® assay.

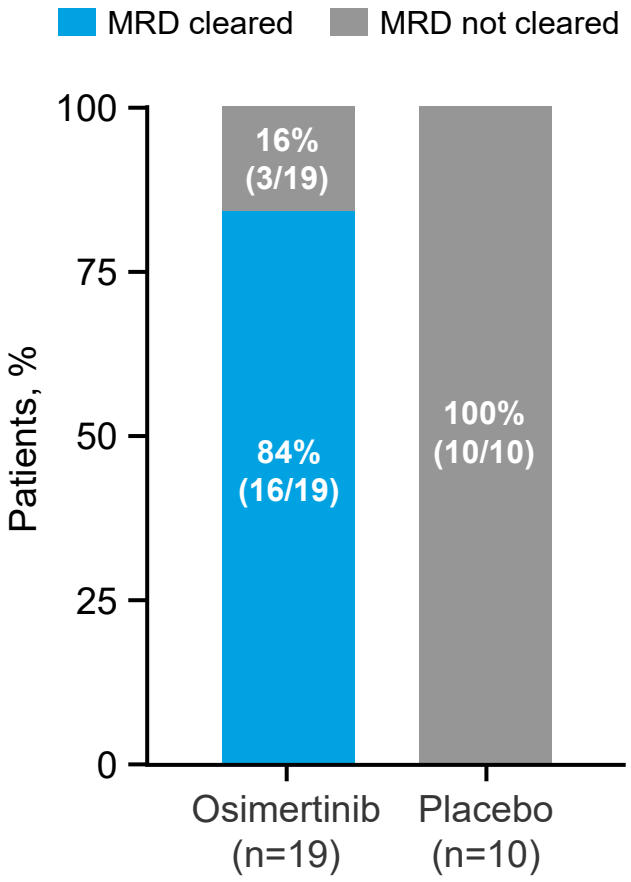
Arriola E, et al. Ann Oncol 2025;36(suppl):Abstr 1817MO

1817MO: Molecular residual disease (MRD) analysis from the LAURA study of osimertinib (osi) in unresectable (UR) stage III EGFR-mutated (EGFRm) NSCLC – Arriola E, et al

- **Key results**

Only 52/216 patients were included in the MRD analysis set

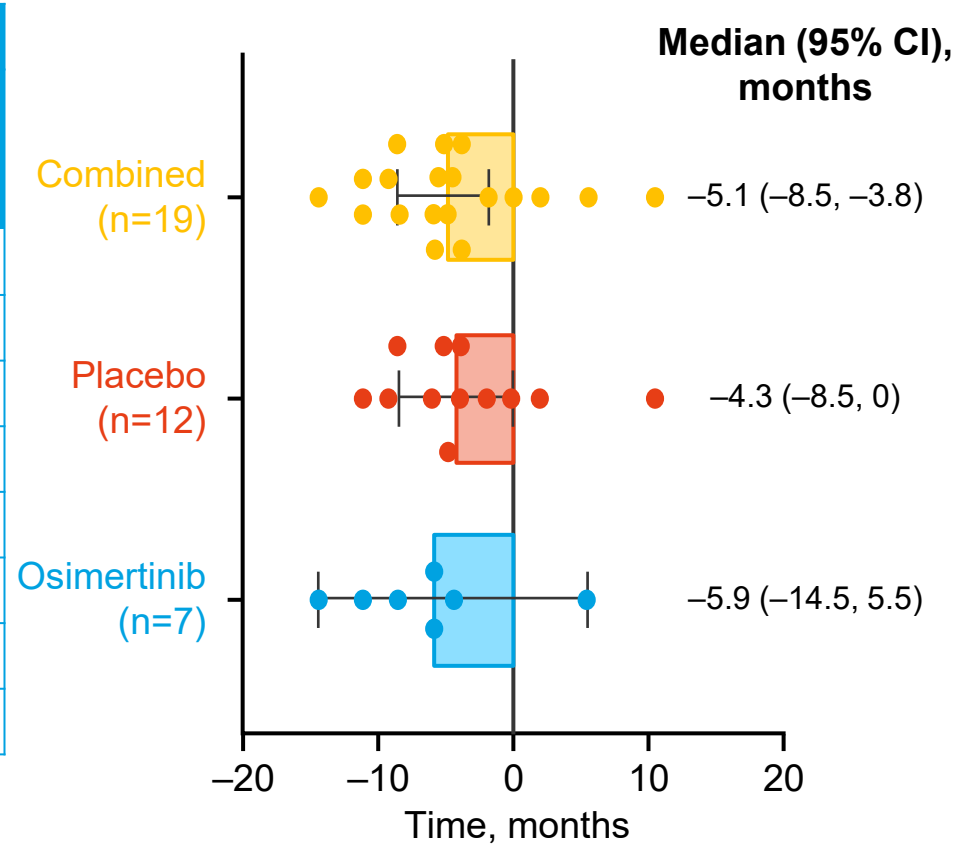
MRD clearance



MRD-based molecular progression

	MRD status, n	
	Molecular progression (n=22)	No molecular progression (n=30)
PFS, n/N		
Event	19/30	11/30
Censored	3/22	19/22
Concordance of MRD with PFS, % (95%CI)		
PPA (sensitivity)	63 (46, 81)	
NPA (specificity)	86 (72, 100)	
PPV	86 (72, 100)	
NPV	63 (46, 81)	

MRD lead time to PFS



Arriola E, et al. Ann Oncol 2025;36(suppl):Abstr 1817MO

1817MO: Molecular residual disease (MRD) analysis from the LAURA study of osimertinib (osi) in unresectable (UR) stage III EGFR-mutated (EGFRm) NSCLC – Arriola E, et al

- **Key results (cont.)**

	Osimertinib	Placebo
MRD detected post-CRT, n	19	10
mPFS, mo (95%CI)	38.8 (16.6, NC)	5.8 (1.9, 9.5)
MRD not detected post-CRT, n	15	7
mPFS, mo (95%CI)	39.3 (9.0, NC)	11.1 (3.5, 13.8)

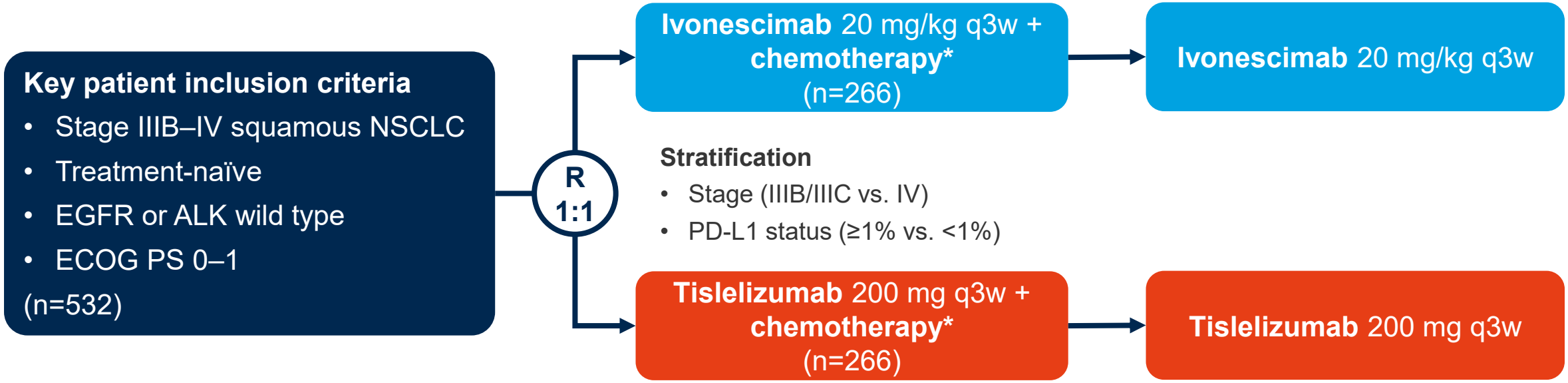
- **Conclusions**
  - In patients with unresectable stage III EGFR-mutant NSCLC, osimertinib improved PFS regardless of MRD status after chemoradiotherapy
  - MRD status after chemotherapy was prognostic but not predictive of osimertinib benefit, and MRD monitoring identified disease progression earlier than radiological assessment

Advanced NSCLC – Not radically treatable stage III and stage IV

Immunotherapy

LBA4: Phase III study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous non-small cell lung cancer (HARMONi-6) – Lu S, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L ivonescimab + chemotherapy vs tislelizumab + chemotherapy in patients with advanced squamous NSCLC in the phase 3 HARMONI-6 study



Primary endpoints

- PFS (IRRC, RECIST v1.1)

Secondary endpoints

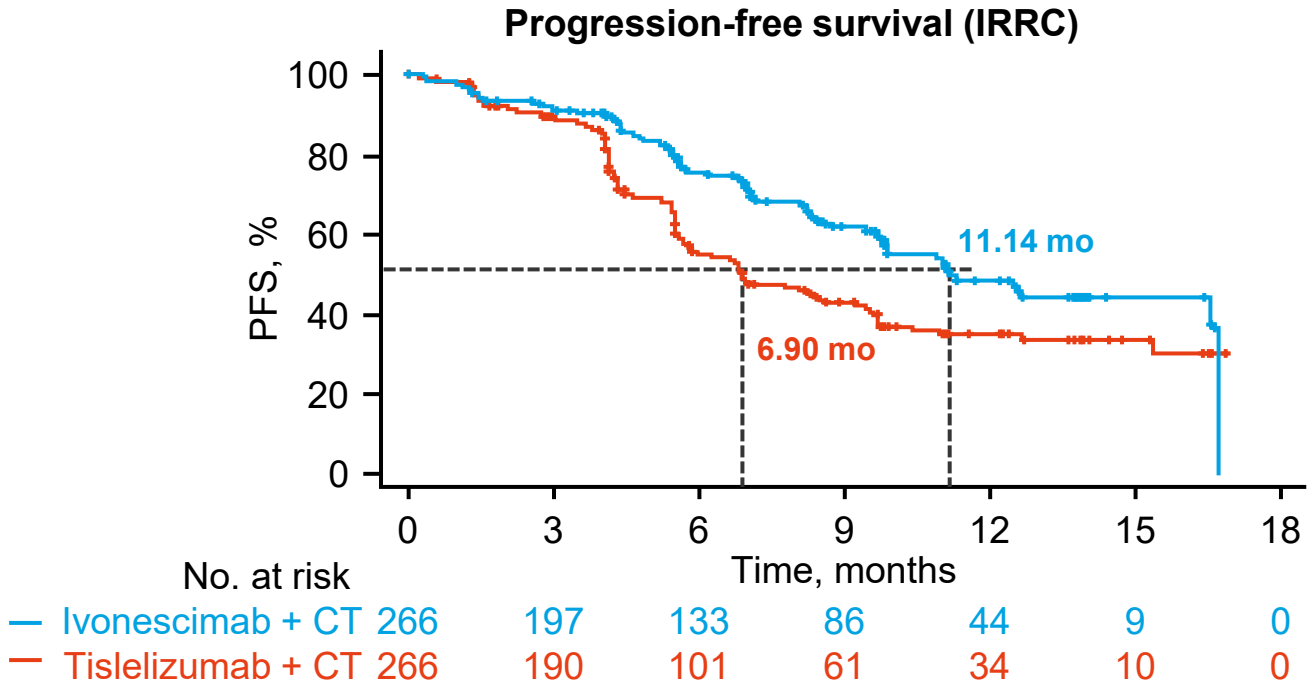
- OS, PFS (investigator), ORR, DCR, DoR, TTR, safety

*Carboplatin AUC5, q3w + paclitaxel 175 mg/m^2 q3w (up to 4 cycles).

Lu S, et al. Ann Oncol 2025;36(suppl):Abstr LBA4

LBA4: Phase III study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous non-small cell lung cancer (HARMONi-6) – Lu S, et al

- **Key results**



	Ivonescimab + chemotherapy (n=266)	Tislelizumab + chemotherapy (n=266)
Median FU, mo	10.28	
mPFS, mo (95%CI)	11.14 (9.86, NE)	6.90 (5.82, 8.57)
Stratified HR (95%CI); p-value	0.60 (0.46, 0.78); <0.0001	

PFS in different PD-L1 expression subgroups

PD-L1 TPS	HR (95%CI)
<1%	0.55 (0.37, 0.82)
≥1%	0.66 (0.46, 0.95)
1–49%	0.63 (0.41, 0.98)
≥50%	0.71 (0.37, 1.33)

Lu S, et al. Ann Oncol 2025;36(suppl):Abstr LBA4

LBA4: Phase III study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous non-small cell lung cancer (HARMONi-6) – Lu S, et al

- **Key results (cont.)**

ORR (IRRC)

	Ivonescimab + chemotherapy (n=266)	Tislelizumab + chemotherapy (n=266)
BOR, n (%)		
CR	1 (0.4)	0
PR	201 (75.6)	177 (66.5)
SD	39 (14.7)	60 (22.6)
PD	6 (2.3)	15 (5.6)
ORR, %		
Any PD-L1	75.9	66.5
p-value	p=0.008	
PD-L1 TPS <1%	69.5	61.0
Any PD-L1 TPS ≥1%	80.1	70.2

DoR (IRRC)

	Ivonescimab + chemotherapy (n=202)	Tislelizumab + chemotherapy (n=177)
mDoR, mo (95%CI)	11.20 (8.54, NE)	8.38 (5.2, NE)
p-value	0.0219	

LBA4: Phase III study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous non-small cell lung cancer (HARMONi-6) – Lu S, et al

- **Key results (cont.)**

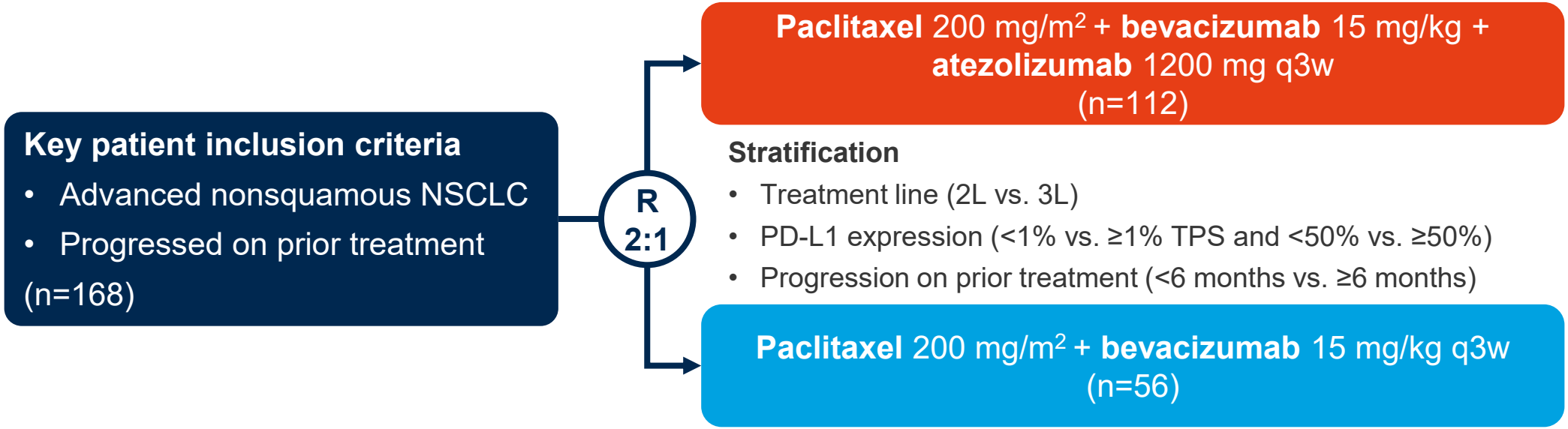
TRAE, n (%)	Ivonescimab + chemotherapy (n=266)	Tislelizumab + chemotherapy (n=265)
Any grade	264 (99.2)	261 (98.5)
Grade ≥3	170 (63.9)	144 (54.3)
Serious	86 (32.3)	80 (30.2)
Led to ivonescimab or tislelizumab discontinuation	9 (3.4)	11 (4.2)
Led to death	8 (3.0)	10 (3.8)

irAEs, n (%)	Ivonescimab + chemotherapy (n=266)	Tislelizumab + chemotherapy (n=265)
Any grade	73 (27.4)	67 (25.3)
Grade ≥3	24 (9.0)	27 (10.2)
Serious	23 (8.6)	26 (9.8)
Led to ivonescimab or tislelizumab discontinuation	3 (1.1)	6 (2.3)
Led to death	0	1 (0.4)

- **Conclusions**
  - In patients with advanced squamous NSCLC, 1L ivonescimab + chemotherapy significantly improved PFS compared with tislelizumab + chemotherapy, the benefit was consistent across all PD-L1 subgroups, and no new safety signals were observed
  - OS data are currently immature to be reported

LBA76: Paclitaxel-bevacizumab ± atezolizumab in advanced non-squamous NSCLC progressing after chemo-immunotherapy: IFCT-2201 ADAPTABLE randomized phase II trial – Scherpereel A, et al

- **Study objective**
  - To evaluate the efficacy and safety of paclitaxel-bevacizumab ± atezolizumab in patients with advanced nonsquamous NSCLC who have progressed after chemoimmunotherapy in the phase 2 ADAPTABLE study



Primary endpoints

- 6-month PFS (IRC)

Secondary endpoints

- ORR, OS, DCR, safety

LBA76: Paclitaxel-bevacizumab ± atezolizumab in advanced non-squamous NSCLC progressing after chemo-immunotherapy: IFCT-2201 ADAPTABLE randomized phase II trial – Scherpereel A, et al

- **Key results (cont.)**

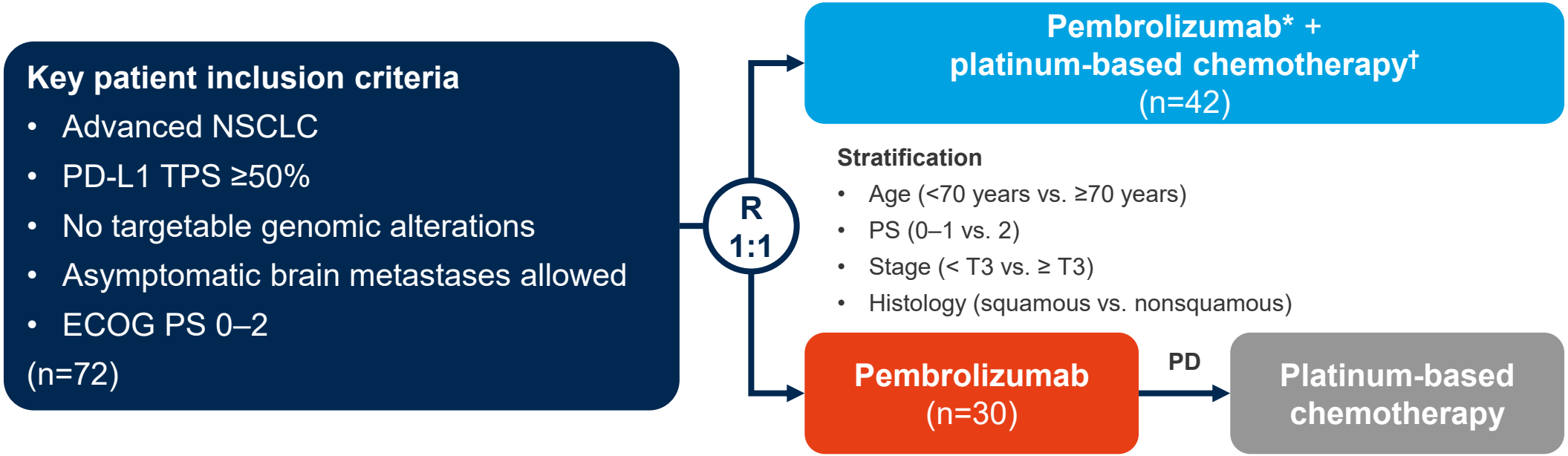
	Paclitaxel + bevacizumab + atezolizumab (n=103)	Paclitaxel + bevacizumab (n=50)
6-mo PFS rate, % (95%CI)		
IRC	40.8 (31.3, 50.3)	52.0 (38.2, 65.9)
Investigator	42.7 (33.2, 52.3)	52.0 (38.2, 65.9)
mPFS rate, mo (95%CI)	6.2 (5.5, 8.2)	7.5 (5.8, 9.8)
mOS rate, mo (95%CI)	16.6 (10.8, 19.3)	17.0 (10.9, NR)
ORR, %	41.7	42.0
DCR, %	76.7	82.0

TRAE, %	Paclitaxel + bevacizumab + atezolizumab (n=110)	Paclitaxel + bevacizumab (n=53)
Grade 3–4	48.2	54.7
Grade 5	1.8	3.8

- **Conclusions**
  - In patients with advanced nonsquamous NSCLC, the addition of atezolizumab to paclitaxel-bevacizumab + failed to provide survival benefit over paclitaxel-bevacizumab alone, and no new safety signals were observed

1851MO: Pembrolizumab plus chemotherapy (PEM + CT) versus pembrolizumab (PEM) as first-line therapy for advanced NSCLC with PD-L1 tumor proportion score (TPS) ≥50%: open-label, phase 3, randomized trial (PAULIEN) – Houda I, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L pembrolizumab ± chemotherapy in patients with advanced NSCLC and PD-L1 TPS ≥50% in the phase 3 PAULIEN study



Primary endpoints

- 6-week ORR (investigator assessed), 6-week DCR (investigator assessed)

Secondary endpoints

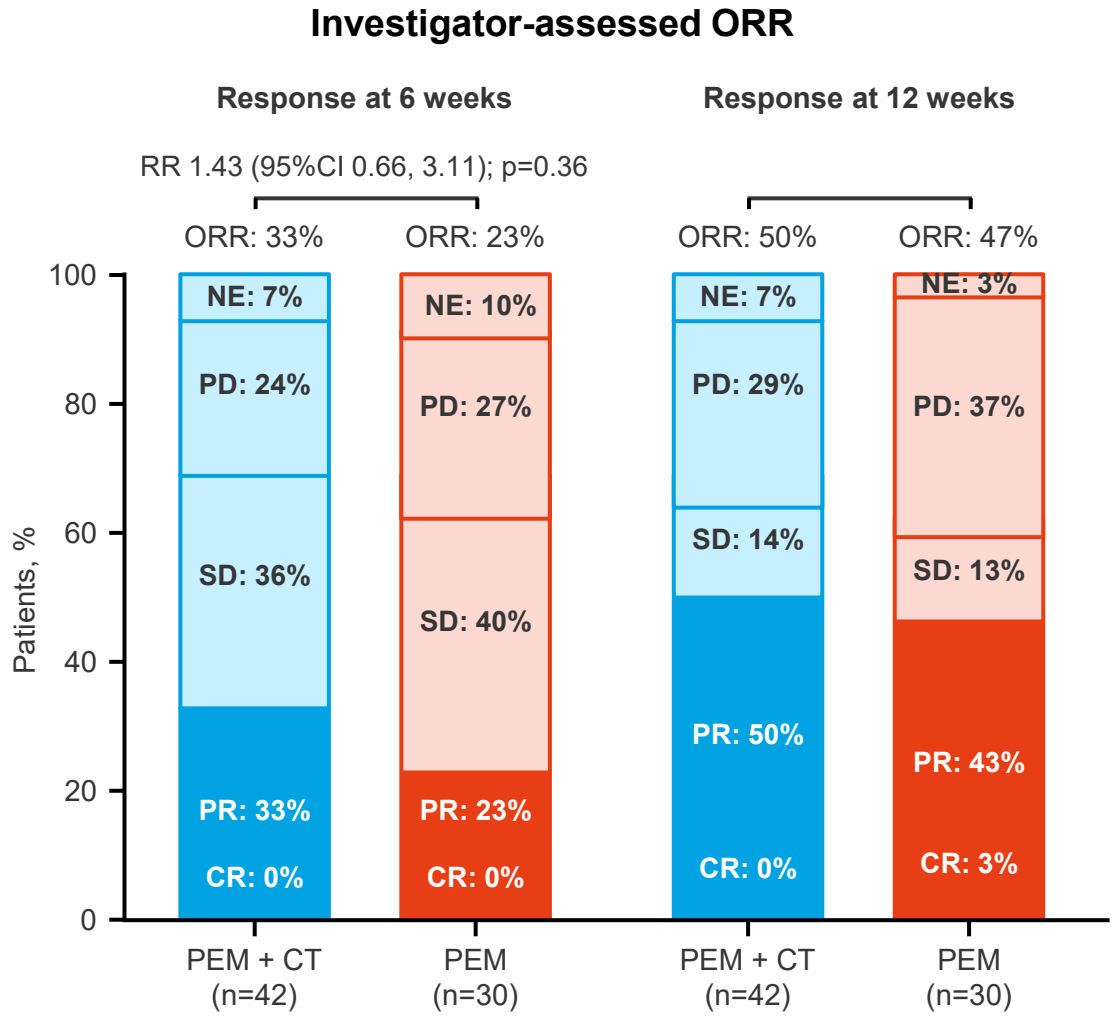
- 12-week ORR (investigator assessed), PFS, OS, safety

*Pembrolizumab every 3 or 6 weeks, depending on the local hospital guidelines. †Squamous NSCLC: platinum-paclitaxel q3w; nonsquamous NSCLC: platinum-pemetrexed q3w followed by pemetrexed q3w.

Houda I, et al. Ann Oncol 2025;36(suppl):Abstr 1851MO

1851MO: Pembrolizumab plus chemotherapy (PEM + CT) versus pembrolizumab (PEM) as first-line therapy for advanced NSCLC with PD-L1 tumor proportion score (TPS) ≥50%: open-label, phase 3, randomized trial (PAULIEN) – Houda I, et al

- **Key results**



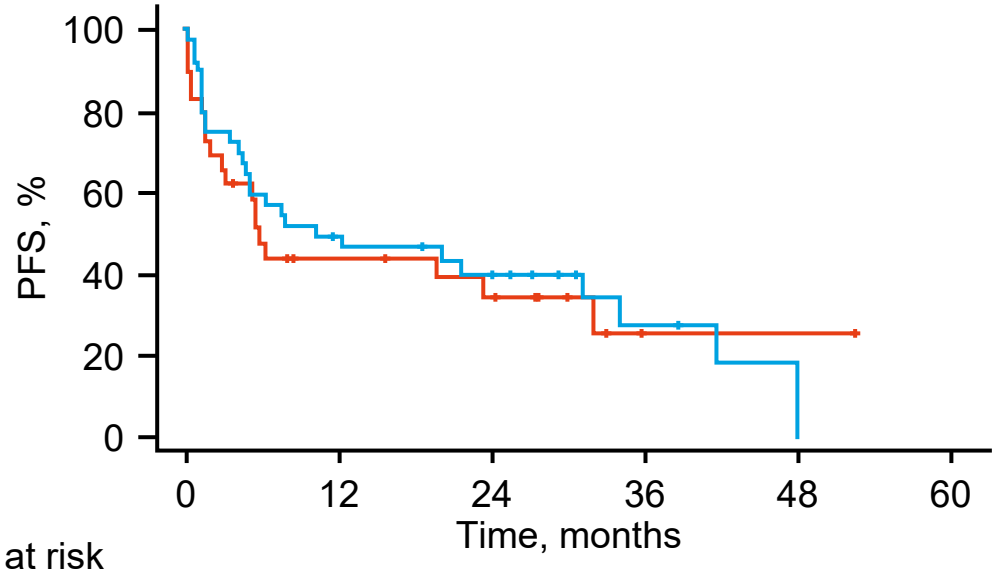
Response	Pembrolizumab + chemotherapy (n=42)	Pembrolizumab (n=30)
6-week ORR, n (%) [95%CI]	14 (33) [21, 48]	7 (23) [12, 41]
6-week DCR, n (%) [95%CI]	29 (69) [54, 81]	19 (63) [46, 78]
12-week ORR, n (%) [95%CI]	21 (50) [36, 64]	14 (47) [30, 64]
12-week DCR, n (%) [95%CI]	27 (64) [49, 77]	18 (60) [42, 75]
BOR, n (%)		
CR	0	1 (3)
PR	25 (60)	14 (47)
SD	4 (10)	5 (17)
PD	10 (24)	9 (30)
NE	3 (7)	1 (3)
DoR		
Responders, n (%)	25 (60)	15 (50)
Median, months (IQR)	11.3 (3.7–28.5)	14.1 (4.4–26.4)
Time to response		
Median, weeks (IQR)	6.0 (5.6–12.6)	11.3 (5.9–12.0)

1851MO: Pembrolizumab plus chemotherapy (PEM + CT) versus pembrolizumab (PEM) as first-line therapy for advanced NSCLC with PD-L1 tumor proportion score (TPS) ≥50%: open-label, phase 3, randomized trial (PAULIEN) – Houda I, et al

- **Key results (cont.)**

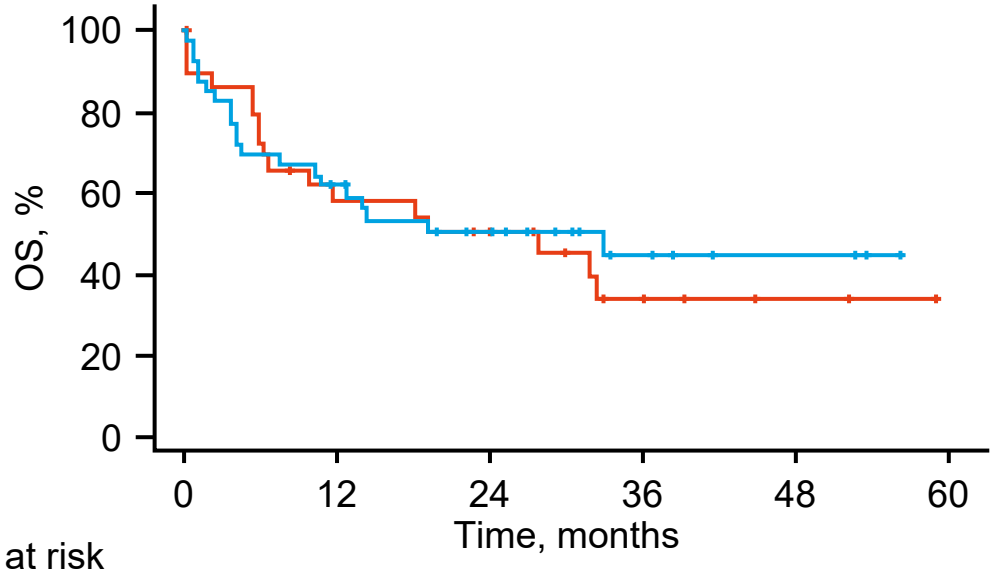
Progression-free survival

	Pembrolizumab + chemotherapy (n=42)	Pembrolizumab (n=30)
Events, n (%)	27 (64)	19 (63)
mPFS, mo (95%CI)	10 (5, NE)	6 (3, NE)
HR (95%CI)	0.91 (0.51, 1.64)	



Overall survival

	Pembrolizumab + chemotherapy (n=42)	Pembrolizumab (n=30)
Events, n (%)	20 (48)	17 (57)
mOS, mo (95%CI)	33 (11, NE)	28 (10, NE)
HR (95%CI)	0.89 (0.46, 1.70)	



1851MO: Pembrolizumab plus chemotherapy (PEM + CT) versus pembrolizumab (PEM) as first-line therapy for advanced NSCLC with PD-L1 tumor proportion score (TPS) ≥50%: Open-label, phase 3, randomized trial (PAULIEN) – Houda I, et al

- **Key results (cont.)**

n (%)	Pembrolizumab + chemotherapy (n=39)	Pembrolizumab (n=26)
Any grade AEs, any cause	39 (100)	26 (100)
Grade 3–4	27 (69)	15 (58)
Grade 5*	13 (33)	7 (27)
Any grade TRAEs	39 (100)	26 (100)
Grade 3–4	21 (54)	9 (35)
irAEs	15 (38)	16 (62)
Grade 3–4	4 (10)†	2 (8)‡
Serious AEs	28 (72)	15 (58)
TRAEs led to any treatment discontinuation	15 (38)§	5 (19)

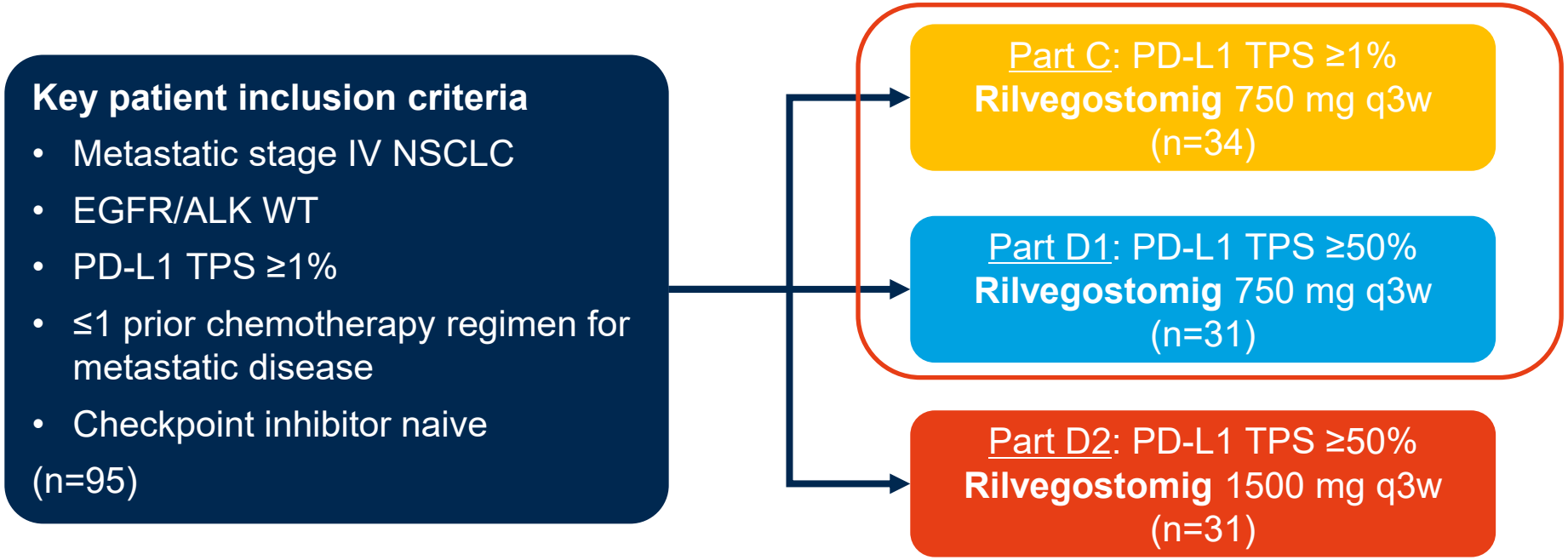
Grade 3–4 TRAEs, n (%)	Pembrolizumab + chemotherapy (n=39)	Pembrolizumab (n=26)
Leukopenia	18	0
Anemia	15	8
Fatigue	8	0
Electrolyte disorders	5	0
Appetite loss/nausea/vomiting	5	8
Renal function decreased	5	0
Transaminitis/hepatitis	5	0
GGT increased	5	0
Pneumonitis	3	8
Airway infection/pneumonia	3	4
Constipation	0	4
Cardiac disorders	0	4

- **Conclusions**
  - In patients with advanced PD-L1-positive NSCLC, pembrolizumab + chemotherapy did not improve tumor response, PFS, or OS compared with pembrolizumab alone
  - The trial was stopped early due to small sample size, and definitive conclusions are awaited from the results of larger ongoing controlled trials

Houda I, et al. Ann Oncol 2025;36(suppl):Abstr 1851MO

1853MO: Efficacy and safety of rilvegostomig, an anti-PD-1/TIGIT bispecific antibody, for checkpoint inhibitor (CPI)-naïve metastatic non-small-cell lung cancer (mNSCLC): ARTEMIDE-01 – Cho BC, et al

- **Study objective**
  - To evaluate the efficacy and safety of rilvegostomig, an anti-PD-1/TIGIT bispecific antibody, in checkpoint inhibitor-naïve patients with metastatic NSCLC in the ARTEMIDE-01 study



Primary endpoints

- ORR (investigator assessed, RECIST v1.1), safety

Secondary endpoints

- DoR, PFS

Part A was dose escalation and Part B dose expansion.

1853MO: Efficacy and safety of rilvegostomig, an anti-PD-1/TIGIT bispecific antibody, for checkpoint inhibitor (CPI)-naïve metastatic non-small-cell lung cancer (mNSCLC): ARTEMIDE-01 – Cho BC, et al

- **Key results**

Outcomes	PD-L1 TPS 1–49%		PD-L1 TPS ≥50%	
	CPI-naïve (n=31)	CPI + CTx-naïve (n=18)	CPI-naïve (n=34)	CPI + CTx-naïve (n=31)
ORR, % (95%CI)	29.0 (14.2, 48.0)	44.4 (21.5, 69.2)	61.8 (43.6, 77.8)	67.7 (48.6, 83.3)
Median DoR, mo (range)	9.9 (4.1–NC)	8.5 (4.1–NC)	NR (10.3–NC)	NR (10.3–NC)

TRAEs ≥5%, %	Any grade	Grade ≥3
Pruritus	12.3	1.5
AST increased	10.8	1.5
Myalgia	10.8	0
Hypercholesterolemia	10.8	0
Hypothyroidism	10.8	0
Lipase increased	9.2	1.5
Rash	9.2	0
Constipation	7.7	0
ALT increased	7.7	0
Fatigue	7.7	0
Diarrhea	7.7	3.1
Hypertriglyceridemia	7.7	3.1
Appetite decreased	6.2	0
GGT increased	6.2	3.1
Nausea	6.2	0

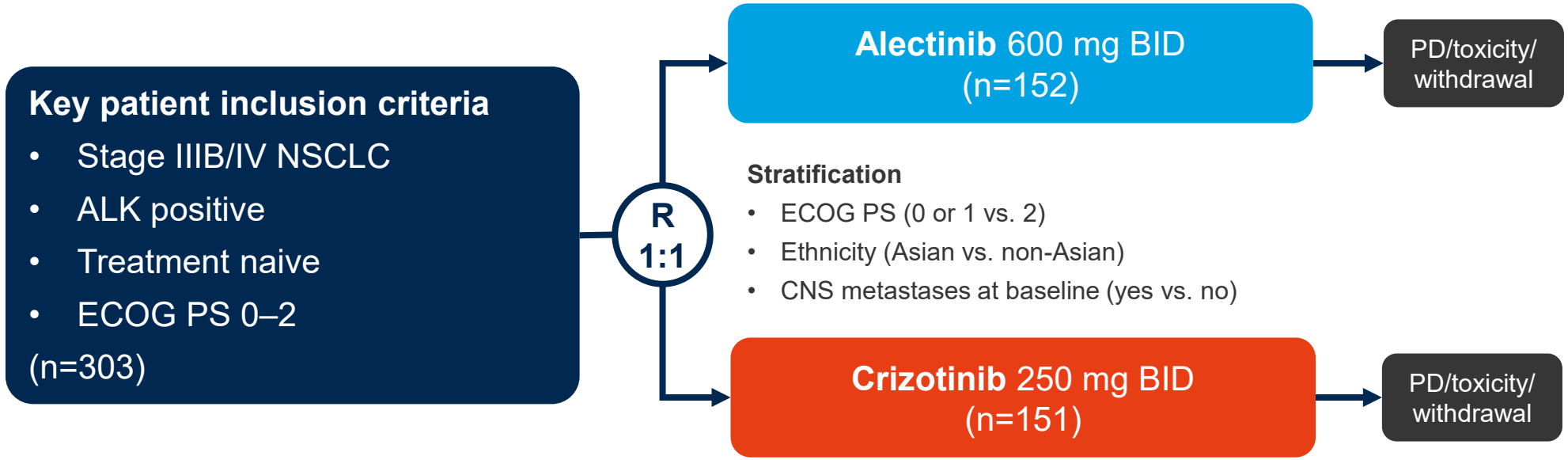
- **Conclusions**
  - In patients with metastatic NSCLC, rilvegostomig demonstrated antitumor activity with durable responses and promising PFS, while maintaining a manageable safety profile with no new safety signals observed

Advanced NSCLC – Not radically treatable stage III and stage IV

Targeted therapies

LBA73: Final overall survival (OS) and safety analysis of the phase 3 ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced ALK-positive (ALK+) non-small cell lung cancer (NSCLC) – Mok TSK, et al

- **Study objective**
  - To evaluate the final OS and safety of alectinib vs crizotinib in previously untreated patients with advanced ALK-positive NSCLC in the phase 3 ALEX study



Primary endpoint

- PFS (investigator assessed, RECIST v1.1)

Secondary endpoints

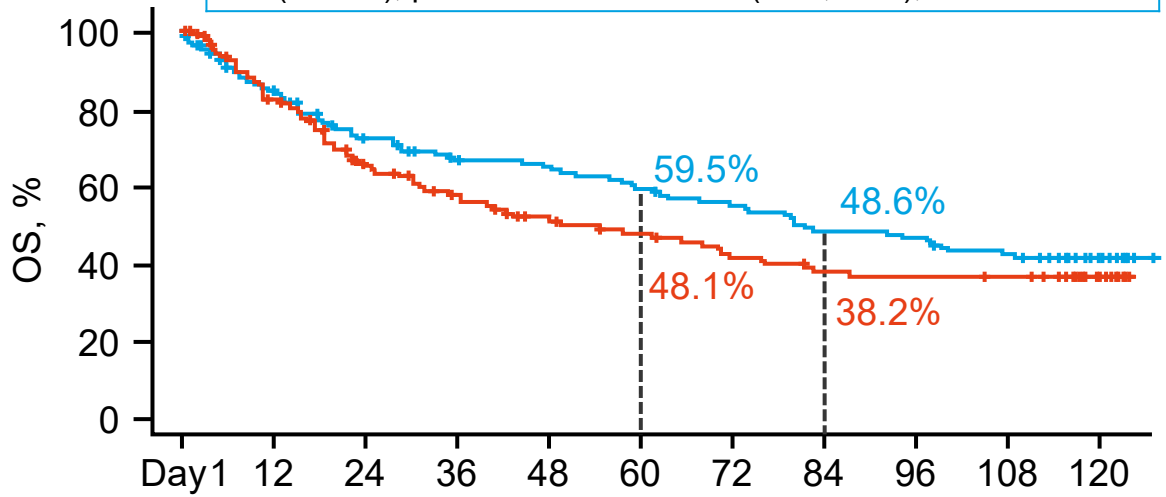
- PFS (IRC), ORR, time to CNS progression, DoR, OS, safety

LBA73: Final overall survival (OS) and safety analysis of the phase 3 ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced ALK-positive (ALK+) non-small cell lung cancer (NSCLC) – Mok TSK, et al

- **Key results**

Overall survival (ITT)

	Alectinib (n=152)	Crizotinib (n=151)
Events, n (%)	76 (50.0)	73 (48.3)
mOS, mo (95%CI)	81.1 (62.3, NE)	54.2 (34.6, 75.6)
HR (95%CI); p-value*	0.78 (0.56, 1.08); 0.1320	

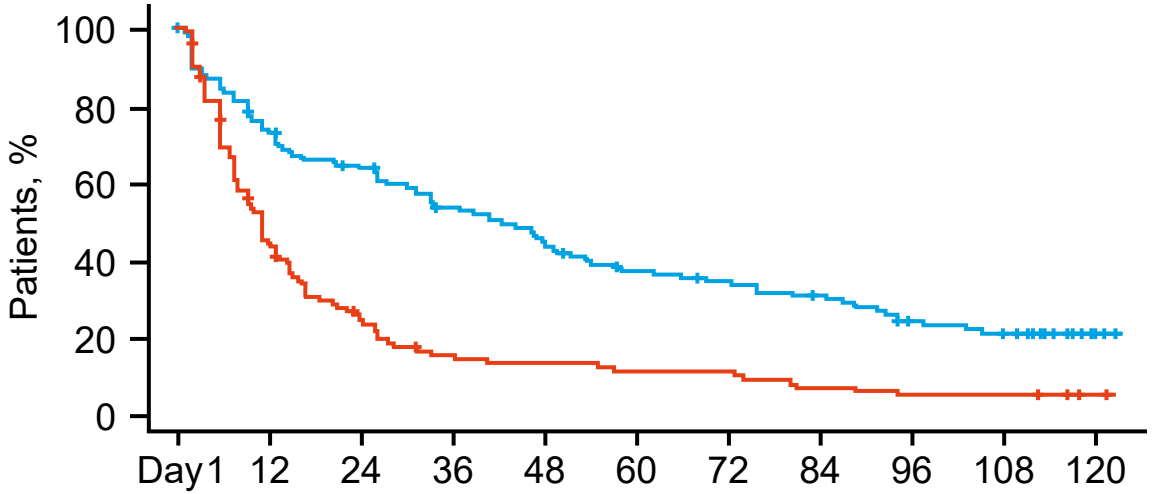


No. at risk

Alectinib	152	120	94	81	79	72	66	58	56	50	20
Crizotinib	151	104	73	60	50	45	38	34	33	32	9

DoR in responders† (Investigator-assessed)

	Alectinib (n=126)	Crizotinib (n=115)
mDoR, mo (95%CI)	42.3 (31.3, 51.3)	11.1 (7.9, 13.0)
HR (95%CI)	0.41 (0.30, 0.56)	



No. at risk

Alectinib	126	90	77	63	51	42	38	33	24	20	2
Crizotinib	115	47	25	14	13	11	11	7	5	5	1

*Stratified Log-rank; †patients with measurable disease at baseline.

Mok TSK, et al. Ann Oncol 2025;36(suppl):Abstr LBA73

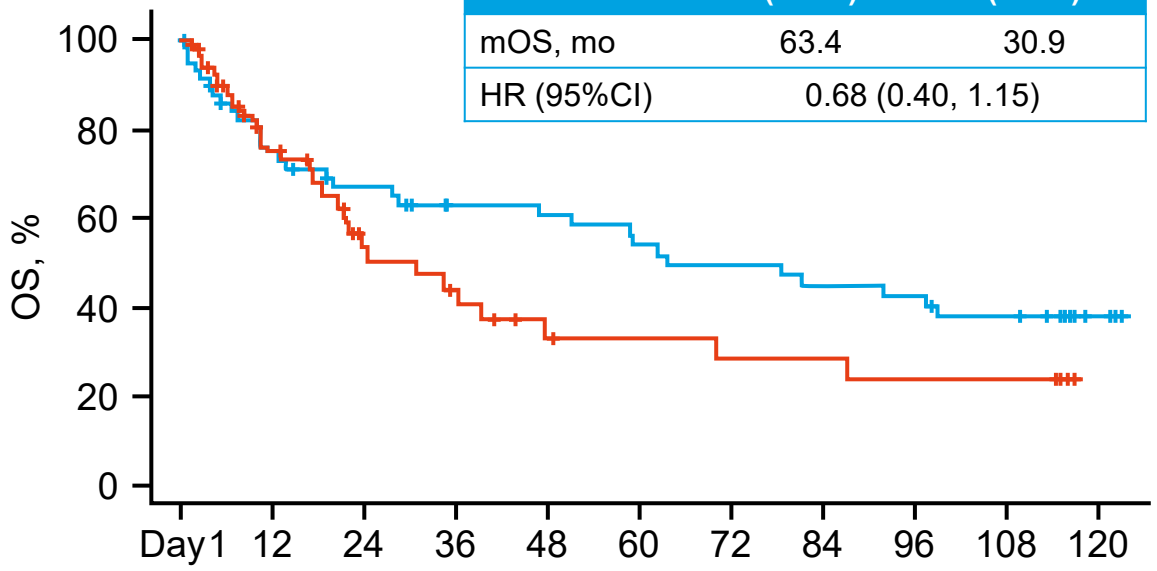
LBA73: Final overall survival (OS) and safety analysis of the phase 3 ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced ALK-positive (ALK+) non-small cell lung cancer (NSCLC) – Mok TSK, et al

- **Key results (cont.)**

Overall survival

Patients with CNS metastases at baseline

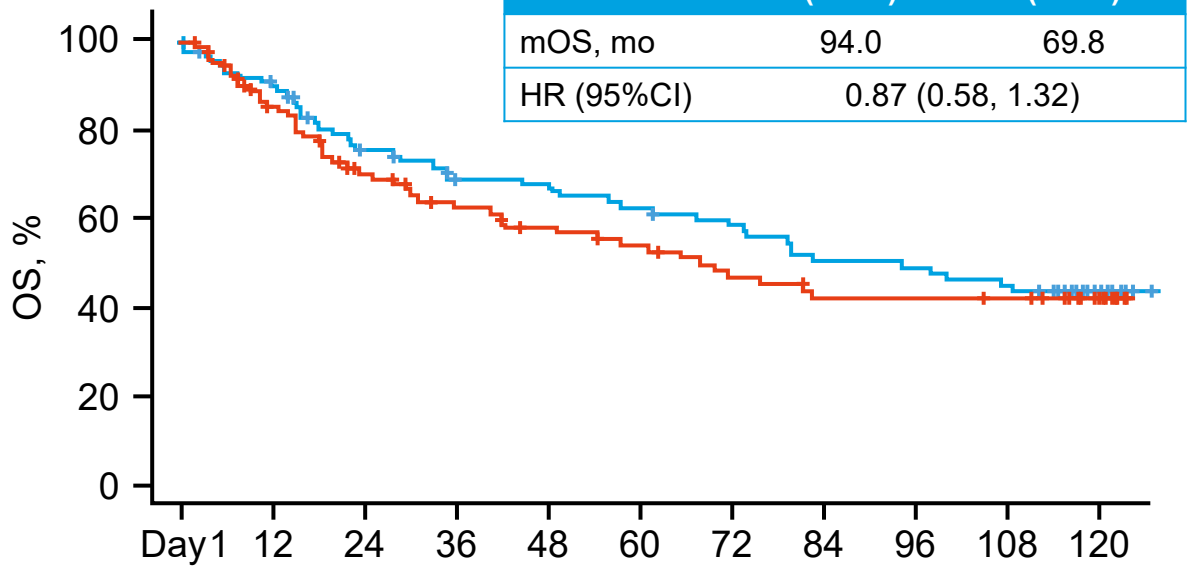
	Alectinib (n=59)	Crizotinib (n=53)
mOS, mo	63.4	30.9
HR (95%CI)	0.68 (0.40, 1.15)	



No. at risk											
Alectinib	59	40	33	28	27	24	22	20	19	16	5
Crizotinib	53	30	17	13	8	7	6	6	5	5	0

Patients without CNS metastases at baseline

	Alectinib (n=93)	Crizotinib (n=98)
mOS, mo	94.0	69.8
HR (95%CI)	0.87 (0.58, 1.32)	



No. at risk											
Alectinib	93	80	61	53	52	48	44	38	37	34	15
Crizotinib	98	74	56	47	42	38	32	28	28	27	9

LBA73: Final overall survival (OS) and safety analysis of the phase 3 ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced ALK-positive (ALK+) non-small cell lung cancer (NSCLC) – Mok TSK, et al

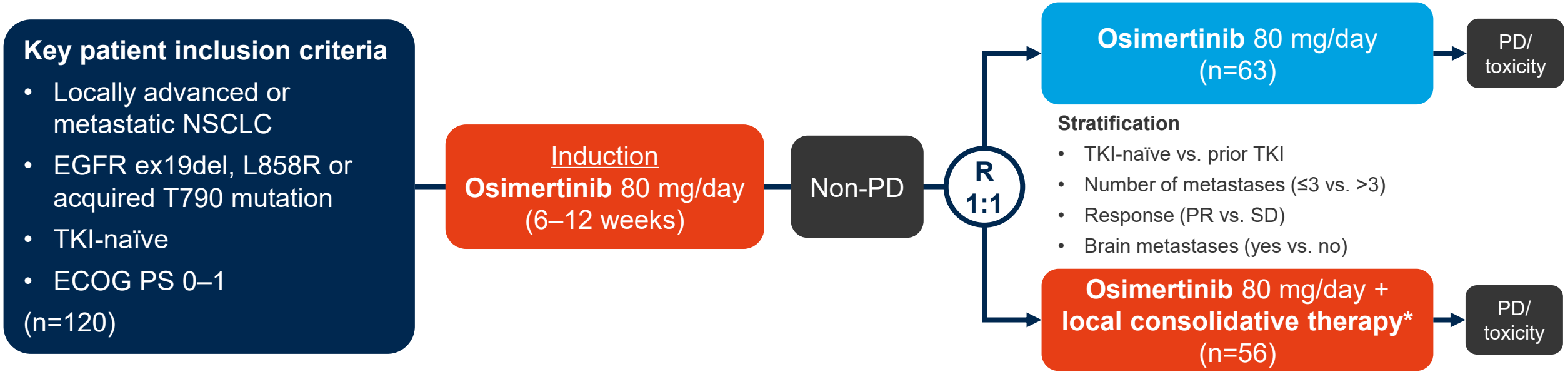
- **Key results (cont.)**

AEs, n (%)	Alectinib (n=152)	Crizotinib (n=151)
Any grade	147 (96.7)	148 (98.0)
Grade 3–5	88 (57.9)	87 (57.6)
Serious	70 (46.1)	48 (31.8)
Treatment-related	125 (82.2)	135 (89.4)
Led to treatment discontinuation	27 (17.8)	22 (14.6)
Led to dose reduction	35 (23.0)	30 (19.9)
Led to dose interruption	49 (32.2)	43 (28.5)
Led to death	10 (6.6)	7 (4.6)

- **Conclusions**
  - In previously untreated patients with advanced ALK-positive NSCLC, 1L alectinib provided a sustained clinical benefit over crizotinib, including patients with CNS metastases, and no new safety signals were observed

LBA72: NorthStar: a phase II randomized study of osimertinib (OSI) with or without local consolidative therapy (LCT) for metastatic EGFR-mutant non-small cell lung cancer (NSCLC) – Elamin YY, et al

- **Study objective**
  - To evaluate the efficacy and safety of osimertinib ± local consolidative therapy in patients with metastatic EGFR-mutant NSCLC in the phase 2 NorthStar study



Primary endpoints

- PFS

Secondary endpoints

- OS, PFS in ≤3 metastases, PFS in TKI-naïve, safety

*Radiation (VMAT or IMRT, SBRT or 3D/2D conformal; n=33); surgery (lobectomy, wedge resection, lobectomy and wedge resection, segmentectomy, or adrenalectomy; n=17); surgery and radiation (n=6).

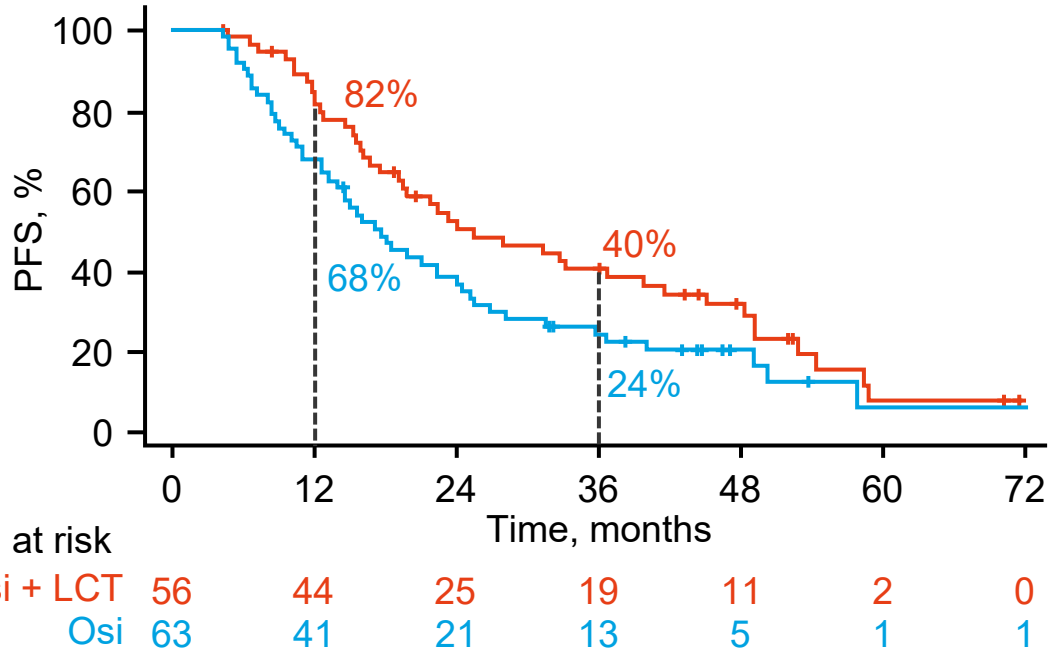
Elamin YY, et al. Ann Oncol 2025;36(suppl):Abstr LBA72

LBA72: NorthStar: a phase II randomized study of osimertinib (OSI) with or without local consolidative therapy (LCT) for metastatic EGFR-mutant non-small cell lung cancer (NSCLC) – Elamin YY, et al

- **Key results**

Progression-free survival

	Osimertinib (n=63)	Osimertinib + LCT (n=56)
PFS events, n (%)	50 (79.3)	42 (75.0)
mPFS, mo (95%CI)	17.5 (14.5, 24.3)	25.3 (19.4, 45.0)
HR (90%CI); p-value*	0.66 (0.50, 0.87); 0.025	



*One-sided Log rank.

PFS per EGFR mutation subtype

	Osimertinib	Osimertinib + LCT
Ex19del, n	44	34
mPFS, mo (95%CI)	22.4 (17.0, 35.7)	39.8 (25.4, 58.7)
HR (90%CI)	0.57 (0.40, 0.82)	
L858R, n	22	19
mPFS, mo (95%CI)	11.0 (6.4, 20.9)	19.0 (15.4, 36.6)
HR (90%CI)	0.60 (0.39, 0.92)	

PFS per number of metastases

	Osimertinib	Osimertinib + LCT
No. metastases ≤3, n	26	24
mPFS, mo (95%CI)	22.4 (12.5, NA)	33.1 (23.9, NA)
HR (90%CI)	0.67 (0.43, 1.03)	
No. metastases >3, n	37	32
mPFS, mo (95%CI)	15.9 (13.8, 23.9)	19.7 (15.4, 48.3)
HR (90%CI)	0.70 (0.50, 1.00)	

PFS in patients with polymetastatic disease

	Complete LCT	Partial LCT
mPFS, mo (95%CI)	27.9 (16.6, 48.3)	14.5 (10.2, 21.6)

LBA72: NorthStar: a phase II randomized study of osimertinib (OSI) with or without local consolidative therapy (LCT) for metastatic EGFR-mutant non-small cell lung cancer (NSCLC) – Elamin YY, et al

- **Key results (cont.)**

	Osimertinib (n=63)	Osimertinib + LCT (n=56)
Hyponatremia	3 (4.8)	4 (7.1)
Transaminitis	3 (4.8)	-
Pneumonitis	2 (3.2)	1 (1.8)
Diarrhea	-	2 (3.6)
Constipation		1 (1.8)
Leukopenia	-	1 (1.8)
Pleural effusion	-	1 (1.8)
Skin disorders	-	1 (1.8)
Thrombocytopenia	-	1 (1.8)

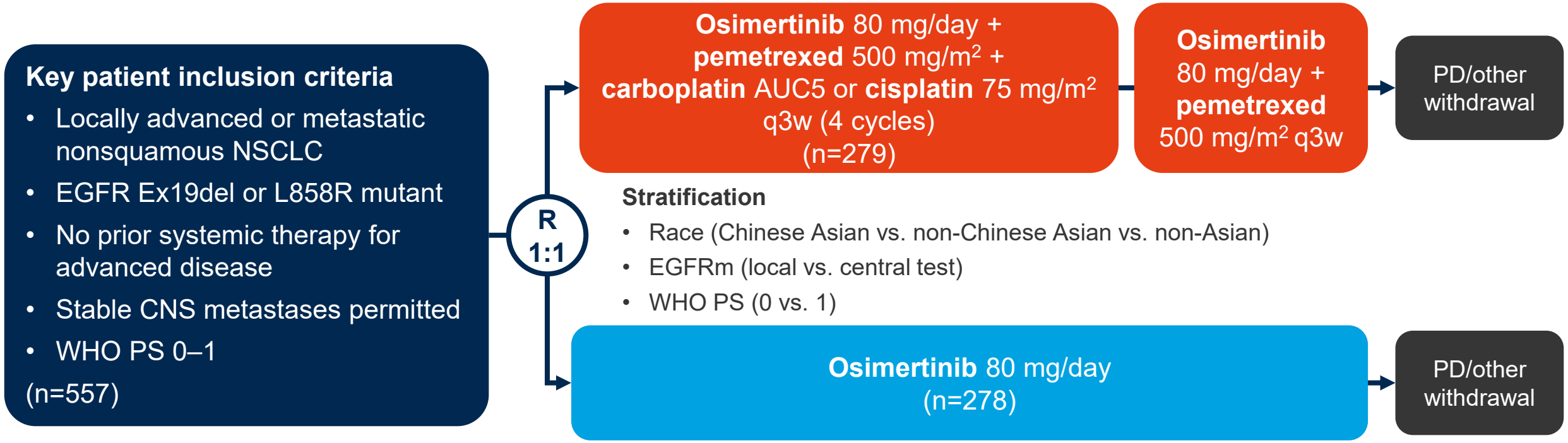
	Osimertinib + LCT (n=56)		
LCT-specific AEs, n (%)	Grade 1	Grade 2	Grade 3
Pneumonitis	1 (1.8)	5 (8.9)	1 (1.8)
Dyspnea	15 (26.8)	2 (3.6)	-
Arterial injury	-	-	1 (1.8)
Empyema	-	-	1 (1.8)
Esophagitis	1 (1.8)	1 (1.8)	-
Dysphagia	7 (12.5)	-	-

- **Conclusions**
  - In patients with metastatic EGFR-mutant NSCLC, osimertinib + local consolidative therapy significantly prolonged PFS over osimertinib alone, including in those with polymetastatic burden and no unexpected safety signals were observed

Elamin YY, et al. Ann Oncol 2025;36(suppl):Abstr LBA72

LBA77: FLAURA2: exploratory overall survival (OS) analysis in patients (pts) with poorer prognostic factors treated with osimertinib (osi) ± platinum-pemetrexed chemotherapy (CTx) as first-line (1L) treatment (tx) for EGFR-mutated (EGFRm) advanced NSCLC – Jänne PA, et al

- **Study objective**
  - To evaluate OS with 1L osimertinib ± platinum-pemetrexed chemotherapy in patients with advanced EGFR-mutant NSCLC and poorer prognostic factors in the FLAURA2 study



Primary endpoint

- PFS (investigator assessed, RECIST v1.1)

Secondary endpoints

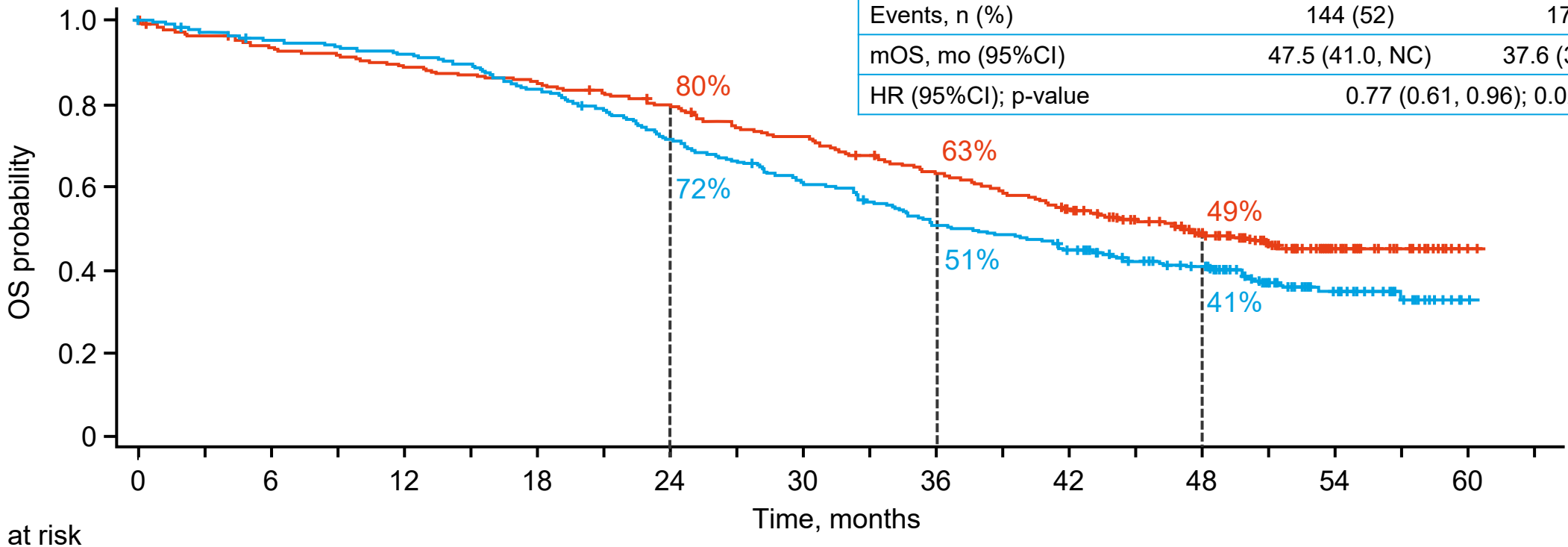
- OS, TFST, DoR, DCR, PFS2, TSST, safety

LBA77: FLAURA2: exploratory overall survival (OS) analysis in patients (pts) with poorer prognostic factors treated with osimertinib (osi) ± platinum-pemetrexed chemotherapy (CTx) as first-line (1L) treatment (tx) for EGFR-mutated (EGFRm) advanced NSCLC – Jänne PA, et al

- **Key results**

Overall survival

	Osimertinib + chemotherapy (n=279)	Osimertinib (n=278)
Median follow-up, mo (range)	51.2 (0.2–60.4)	51.3 (0.1–60.1)
Events, n (%)	144 (52)	171 (62)
mOS, mo (95%CI)	47.5 (41.0, NC)	37.6 (33.2, 43.2)
HR (95%CI); p-value	0.77 (0.61, 0.96); 0.02	



No. at risk

Osi + plat-pem	279	267	258	253	245	240	236	226	218	202	196	183	170	158	143	123	105	71	36	16	1	0
Osimertinib	278	267	260	257	252	245	229	214	195	180	165	152	137	131	118	103	93	61	38	16	1	0

Jänne PA, et al. Ann Oncol 2025;36(suppl):Abstr LBA77

LBA77: FLAURA2: exploratory overall survival (OS) analysis in patients (pts) with poorer prognostic factors treated with osimertinib (osi) ± platinum-pemetrexed chemotherapy (CTx) as first-line (1L) treatment (tx) for EGFR-mutated (EGFRm) advanced NSCLC – Jänne PA, et al

- **Key results (cont.)**

Prognostic factor	Osimertinib + chemotherapy	Osimertinib
With CNS metastases at baseline, n	116	110
3-year OS rate, %	57	40
mOS, mo (95%CI)	40.9 (35.2, 46.6)	29.7 (25.6, 35.8)
HR (95%CI)	0.72 (0.52, 0.99)	
Without CNS metastases at baseline, n	163	168
3-year OS rate, %	67	58
mOS, mo (95%CI)	NR (45.0, NC)	43.9 (37.8, 53.3)
HR (95%CI)	0.77 (0.57, 1.05)	
L858R mutation, n	106	107
3-year OS rate, %	54	42
mOS, mo (95%CI)	38.1 (33.4, 42.0)	32.4 (28.0, 37.6)
HR (95%CI)	0.76 (0.55, 1.07)	
Ex19 deletion, n	172	169
3-year OS rate, %	69	57
mOS, mo (95%CI)	NR (47.2, NC)	43.0 (35.7, 51.9)
HR (95%CI)	0.76 (0.56, 1.02)	

Prognostic factor (cont'd)	Osimertinib + chemotherapy	Osimertinib
Detected EGFRm, n	148	161
3-year OS rate, %	53	42
mOS, mo (95%CI)	38.4 (33.2, 46.6)	32.5 (28.8, 35.8)
HR (95%CI)	0.79 (0.60, 1.03)	
Non-detected EGFRm, n	65	48
3-year OS rate, %	83	77
mOS, mo (95%CI)	NR (50.8, NC)	NR (46.0, NC)
HR (95%CI)	0.79 (0.44, 1.44)	
With bone metastases, n	132	142
3-year OS rate, %	55	42
mOS, mo (95%CI)	40.2 (33.9, 47.2)	32.3 (26.7, 36.5)
HR (95%CI)	0.76 (0.56, 1.02)	
Without bone metastases, n	147	136
3-year OS rate, %	71	60
mOS, mo (95%CI)	NR (46.6, NC)	44.5 (38.3, NC)
HR (95%CI)	0.79 (0.57, 1.10)	

LBA77: FLAURA2: exploratory overall survival (OS) analysis in patients (pts) with poorer prognostic factors treated with osimertinib (osi) ± platinum-pemetrexed chemotherapy (CTx) as first-line (1L) treatment (tx) for EGFR-mutated (EGFRm) advanced NSCLC – Jänne PA, et al

- **Key results (cont.)**

Prognostic factor (cont'd)	Osimertinib + chemotherapy	Osimertinib
TP53 altered*, n	46	40
3-year OS rate, %	65	58
mOS, mo (95%CI)	51.1 (35.0, NC)	43.1 (34.0, 50.1)
HR (95%CI)	0.71 (0.40, 1.27)	
TP53 WT, n	33	34
3-year OS rate, %	85	76
mOS, mo (95%CI)	NR (46.6, NC)	NR (41.3, NC)
HR (95%CI)	0.70 (0.32, 1.54)	

- **Conclusions**
  - In patients with advanced EGFR-mutant NSCLC, osimertinib + platinum-pemetrexed chemotherapy significantly prolonged OS, and the benefit was consistent across all prognostic patient subgroups

*TP53 alterations excluding variants with unknown oncogenic significance.

Jänne PA, et al. Ann Oncol 2025;36(suppl):Abstr LBA77

1846MO: Intracranial efficacy of olomorasib, a second-generation KRAS G12C inhibitor, in patients with KRAS G12C-mutant NSCLC who have active, untreated brain metastases – Cassier P, et al

- **Study objective**
  - To evaluate the intracranial efficacy of olomorasib in patients with KRAS G12C-mutant NSCLC and active untreated brain metastases

Key patient inclusion criteria
- Advanced NSCLC
- KRAS G12C mutant
- No prior KRAS G12C inhibitor
- Active untreated brain metastases
- ECOG PS 0–1

(n=201)

→

Cohort B8: NSCLC
Olomorasib 150 mg BID
(n=21)

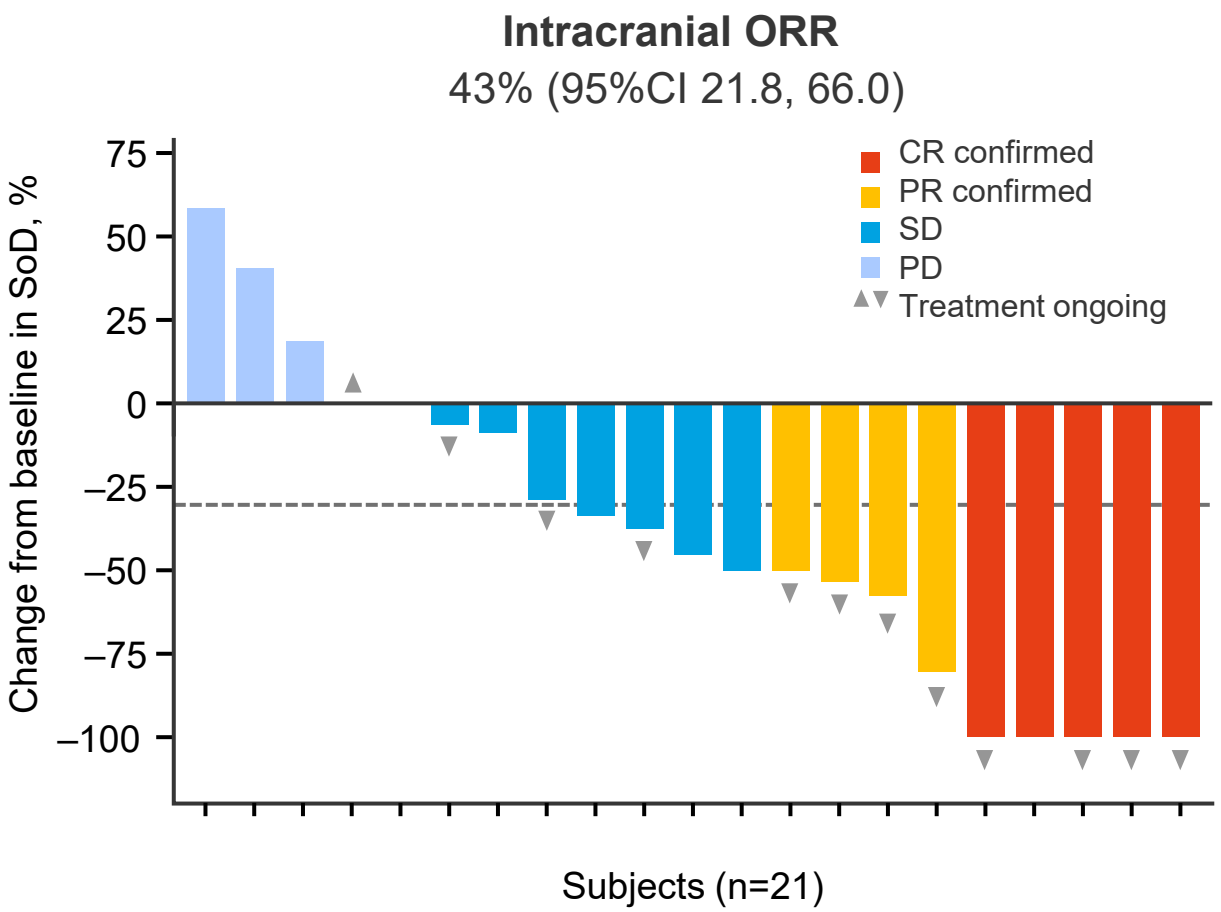
Primary endpoints
- Safety and tolerability

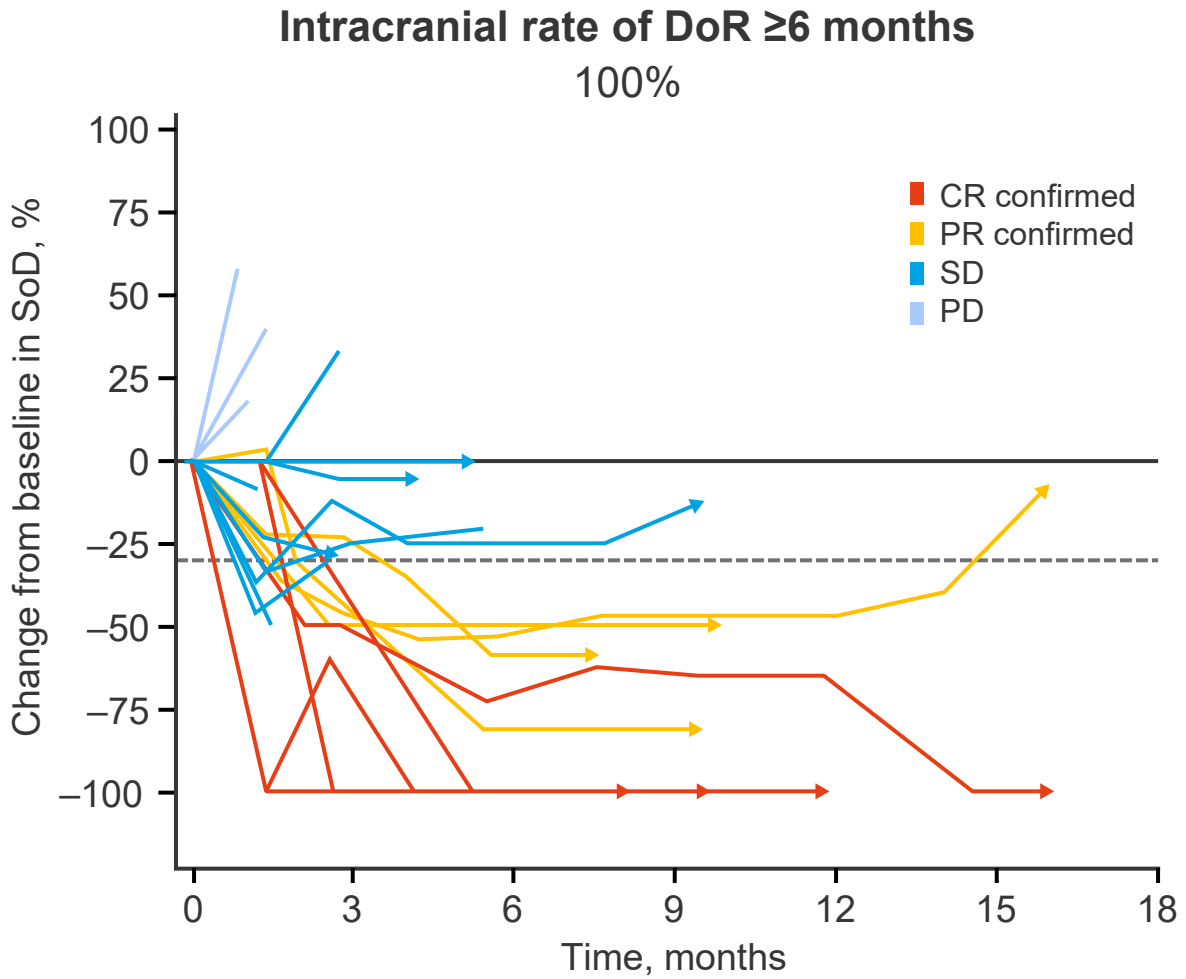
Secondary endpoints
- Pharmacokinetics, intracranial ORR, intracranial DoR, ORR, DoR, DCR, PFS

Cassier P, et al. Ann Oncol 2025;36(suppl):Abstr 1846MO

1846MO: Intracranial efficacy of olomorasib, a second-generation KRAS G12C inhibitor, in patients with KRAS G12C-mutant NSCLC who have active, untreated brain metastases – Cassier P, et al

- **Key results**





Cassier P, et al. Ann Oncol 2025;36(suppl):Abstr 1846MO

1846MO: Intracranial efficacy of olomorasib, a second-generation KRAS G12C inhibitor, in patients with KRAS G12C-mutant NSCLC who have active, untreated brain metastases – Cassier P, et al

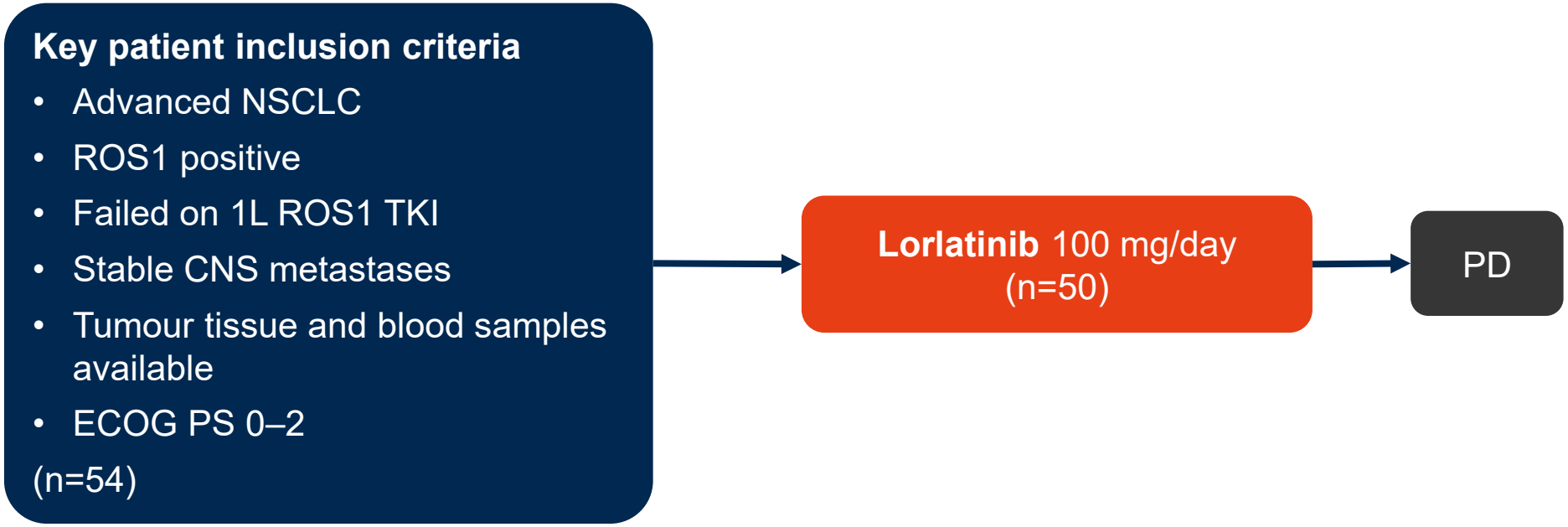
- **Key results (cont.)**

	Olomorasib (n=201)	
TRAEs, n (%)	**Any grade**	**Grade ≥3**
Any	140 (70)	14 (7)
Diarrhea	56 (28)	1 (1)
Nausea	24 (12)	-
Fatigue	19 (9)	1 (1)
ALT increased	19 (9)	2 (1)
AST increased	19 (9)	3 (2)

- **Conclusions**
  - In patients with KRAS G12C-mutant NSCLC, olomorasib showed meaningful intracranial antitumor activity and disease control, with durable responses and a manageable safety profile

1987MO: Efficacy of lorlatinib after failure of a first-line ROS1 tyrosine kinase inhibitor (ROS1 TKI) in patients (pts) with advanced ROS1-positive non-small cell lung cancer (ROS1+ NSCLC) (IFCT-2003 ALBATROS) – Duruisseaux M, et al

- **Study objective**
  - To evaluate the efficacy and safety of lorlatinib after failure of 1L ROS1 TKI in patients with advanced ROS1-positive NSCLC in the ALBATROS study



Primary endpoints

- Confirmed ORR (investigator assessed)

Secondary endpoints

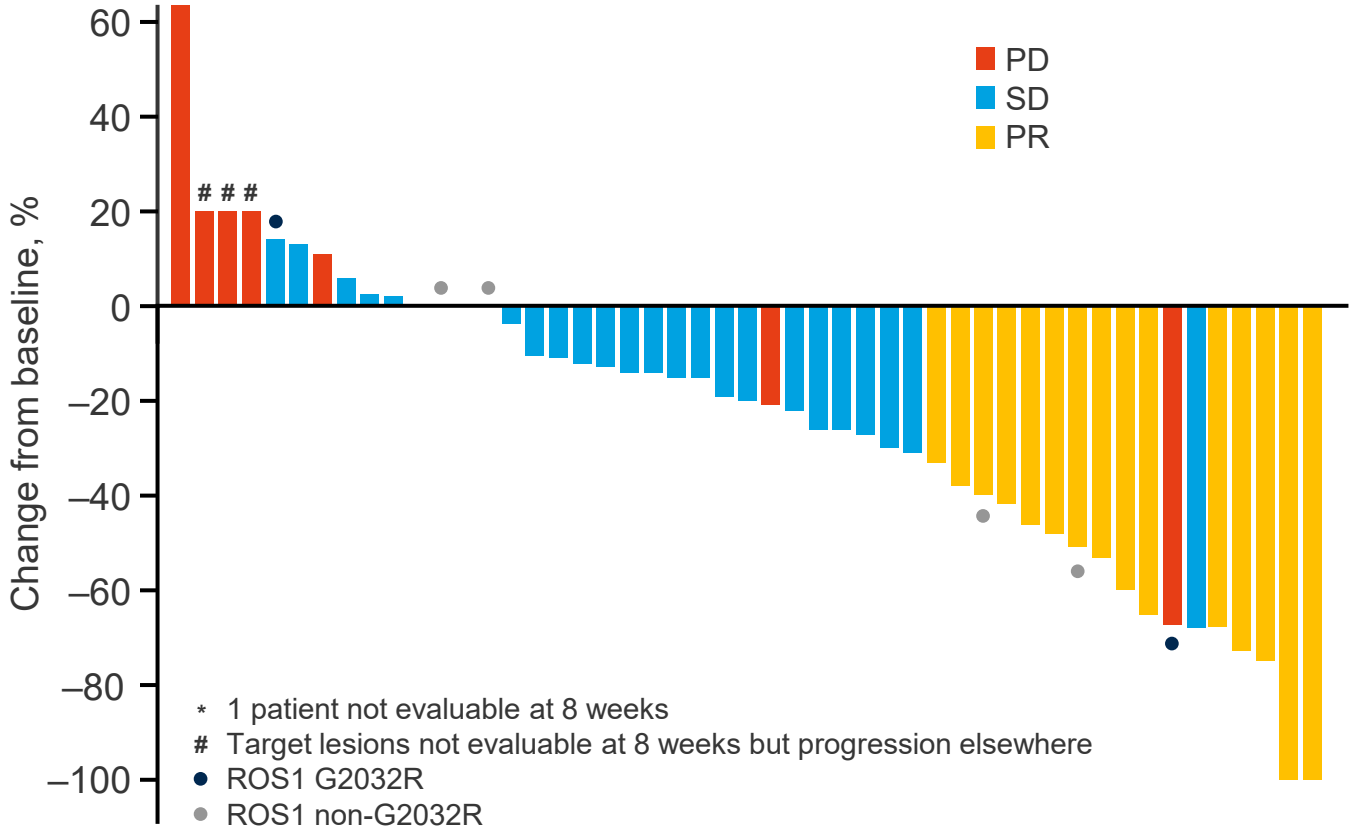
- Confirmed ORR (BICR), DCR, PFS, DoR, OS, CNS ORR, safety

1987MO: Efficacy of lorlatinib after failure of a first-line ROS1 tyrosine kinase inhibitor (ROS1 TKI) in patients (pts) with advanced ROS1-positive non-small cell lung cancer (ROS1+ NSCLC) (IFCT-2003 ALBATROS) – Duruisseaux M, et al

- **Key results**

Response, n (%) [95%CI]	Investigator assessed (n=50)	BICR assessed (n=50)
ORR	15 (30.0) [17.3,42.7]	17 (34.0) [20.9, 47.1]
CR	0	0
PR	15 (30.0) [17.3,42.7]	17 (34.0) [20.9, 47.1]
DCR	42 (84.0) [73.8, 94.3]	37 (74.0) [61.8, 86.2]

Investigator assessed CNS ORR, n (%) [95%CI]	Lorlatinib (n=13)
ORR	12 (92.3) [77.8, 100]
CR	7 (53.8) [26.7, 80.9]
PR	5 (38.5) [12.0, 64.9]
SD	1 (7.7) [0, 22.2]
PD	0
DCR	13 (100) [100, 100]



Duruisseaux M, et al. Ann Oncol 2025;36(suppl):Abstr 1987MO

1987MO: Efficacy of lorlatinib after failure of a first-line ROS1 tyrosine kinase inhibitor (ROS1 TKI) in patients (pts) with advanced ROS1-positive non-small cell lung cancer (ROS1+ NSCLC) (IFCT-2003 ALBATROS) – Duruisseaux M, et al

- **Key results (cont.)**

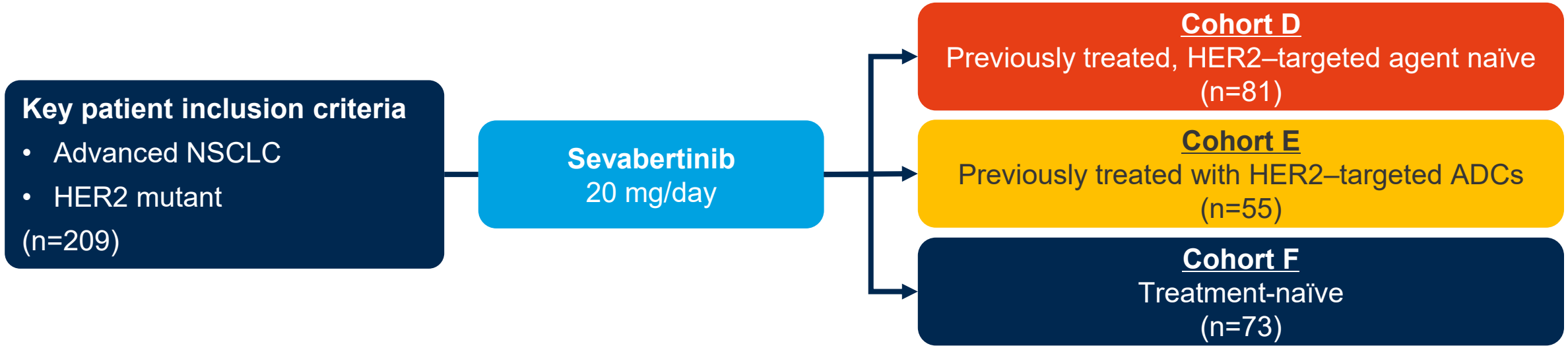
Secondary endpoints	Lorlatinib (n=50)
Investigator assessed PFS	
Events, n (%)	36 (72.0)
mPFS, mo (95%CI)	7.4 (4.1, 14.6)
Investigator assessed DoR	
Events, n (%)	14 (56)
mDoR, mo (95%CI)	20.4 (3.9, 34.5)
OS	
Events, n (%)	23 (46.0)
mOS, mo (95%CI)	42.3 (14.5, NR)

	Lorlatinib (n=530)	
TRAEs occurring in ≥10%, %	All grades	Grade 3–5
Any	90.6	45.3
Blood cholesterol increased	81.1	37.7
Hypertriglyceridemia	64.2	9.5
Peripheral edema	43.4	0
Diarrhea	18.9	0
AST increased	17.0	0
ALT increased	15.1	0
Fatigue	15.1	0
Weight increased	15.1	1.9
Anemia	13.2	0

- **Conclusions**
  - In patients with advanced ROS1-positive NSCLC, lorlatinib demonstrated durable antitumor activity and CNS efficacy with a manageable safety profile

LBA75: Sevabertinib (BAY 2927088) in advanced HER2-mutant non-small cell lung cancer (NSCLC): results from the SOHO-01 study – Le X, et al

- **Study objective**
  - To evaluate the efficacy and safety of sevabertinib in patients with advanced HER2-mutant NSCLC in the SOHO-01 study



Primary endpoints (extension phase)

- ORR (BICR, RECIST v1.1)

Secondary endpoints

- DoR, DCR, PFS, safety

Le X, et al. Ann Oncol 2025;36(suppl):Abstr LBA75

LBA75: Sevabertinib (BAY 2927088) in advanced HER2-mutant non-small cell lung cancer (NSCLC): results from the SOHO-01 study – Le X, et al

- **Key results**

ORR (BICR)

	Cohort D (n=81)	Cohort E (n=55)	Cohort F (n=73)
Median FU, mo (range)	13.8 (1–32)	11.6 (2–22)	9.9 (<1 –15)
BOR, n (%)			
CR	2 (2)	3 (5)	3 (4)
PR	50 (62)	18 (33)	49 (67)
SD	20 (25)	23 (42)	16 (22)
PD	6 (7)	7 (13)	2 (3)
NE	3 (4)	4 (7)	1 (1)
NA	-	-	2 (3)
ORR,* n (%) [95%CI]	52 (64) [53, 75]	21 (38) [25, 52]	52 (71) [59, 81]
DCR,† n (%) [95%CI]	66 (81) [71, 89]	39 (71) [57, 82]	65 (89) [80, 95]
mDoR, mo (95%CI)	9.2 (6.3, 13.5)	8.5 (5.6, 16.4)	11.0 (81, NE)
mPFS, mo (95%CI)	8.3 (6.9, 12.3)	5.5 (4.3, 8.3)	NE (9.6, NE)

*Confirmed CR and PR; †confirmed CR, PR, or SD for ≥12 week.

Le X, et al. Ann Oncol 2025;36(suppl):Abstr LBA75

LBA75: Sevabertinib (BAY 2927088) in advanced HER2-mutant non-small cell lung cancer (NSCLC): results from the SOHO-01 study – Le X, et al

- **Key results (cont.)**

ORR (RECIST, v1.1) in patients with and without brain metastases at baseline

	Cohort D	Cohort E	Cohort F	Total
Brain metastases at baseline, n/N (%)	18/81 (22)	15/55 (27)	9/73 (12)	42/209 (20)
Post-progression in brain	4/18 (22)	3/15 (20)	0/9 (0)	7/42 (17)
ORR, n/N (%)				
All patients	52/81 (64)	21/55 (38)	52/73 (71)	125/209 (60)
Brain metastases	11/18 (61)	4/15 (27)	7/9 (78)	22/42 (52)
No brain metastases	41/63 (65)	17/40 (43)	45/64 (70)	103/167 (62)
No brain metastases at baseline, n/N (%)	63/81 (78)	40/55 (73)	64/73 (88)	167/209 (80)
Post-progression in brain	4/63 (6)	2/40 (5)	2/64 (3)	8/167 (5)

LBA75: Sevabertinib (BAY 2927088) in advanced HER2-mutant non-small cell lung cancer (NSCLC): results from the SOHO-01 study – Le X, et al

- **Key results (cont.)**

Mot frequent TRAEs (≥10% of total), %	Cohort D (n=81)		All cohorts (n=209)	
	Grade 1–2	Grade 3	Grade 1–2	Grade 3
Diarrhea	63	23	73	14
Rash	49	1	48	1
Paronychia	27	0	26	0
Stomatitis	17	1	18	1
Nausea	19	3	16	2
Hypokalemia	12	4	14	6
Vomiting	14	4	11	4
Anemia	15	1	16	1
Weight decreased	17	0	14	0

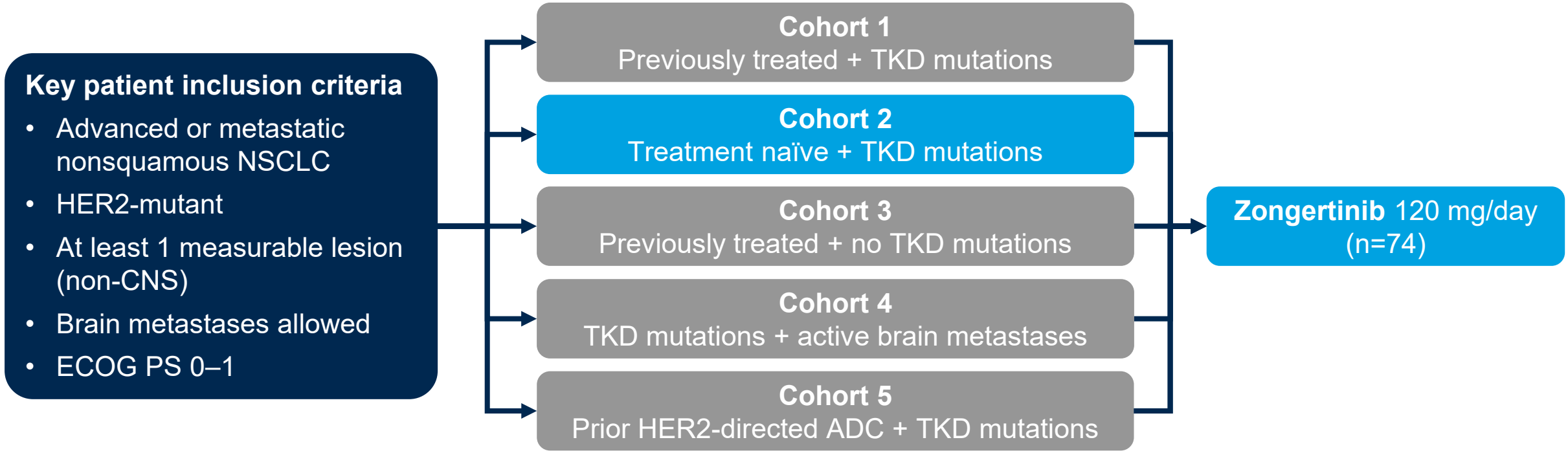
Mot frequent TRAEs (≥10% of total), % (cont'd)	Cohort D (n=81)		All cohorts (n=209)	
	Grade 1–2	Grade 3	Grade 1–2	Grade 3
ALT increased	15	1	13	1
Dry skin	17	0	14	0
AST increased	16	1	13	1
Pruritus	17	3	13	1
Appetite decreased	11	4	13	2
Amylase increased	15	0	14	1
Lipase increased	12	0	16	0

- **Conclusions**
  - In patients with advanced HER2-mutant NSCLC, sevabertinib demonstrated a durable response regardless of the prior treatment, with high efficacy observed in treatment-naïve patients
  - Previously treated patients with baseline brain metastases achieved a similar ORR to those without brain metastases
  - The safety profile was manageable but included a high proportion of patients experiencing GI toxicities

Le X, et al. Ann Oncol 2025;36(suppl):Abstr LBA75

LBA74: Zongertinib as first-line treatment in patients with advanced HER2-mutant NSCLC: Beamion LUNG 1 – Popat S, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L zongertinib in patients with advanced HER2-mutant NSCLC in the Beamion LUNG 1 study



Primary endpoint

- ORR (BICR, RECIST v1.1)

Secondary endpoints

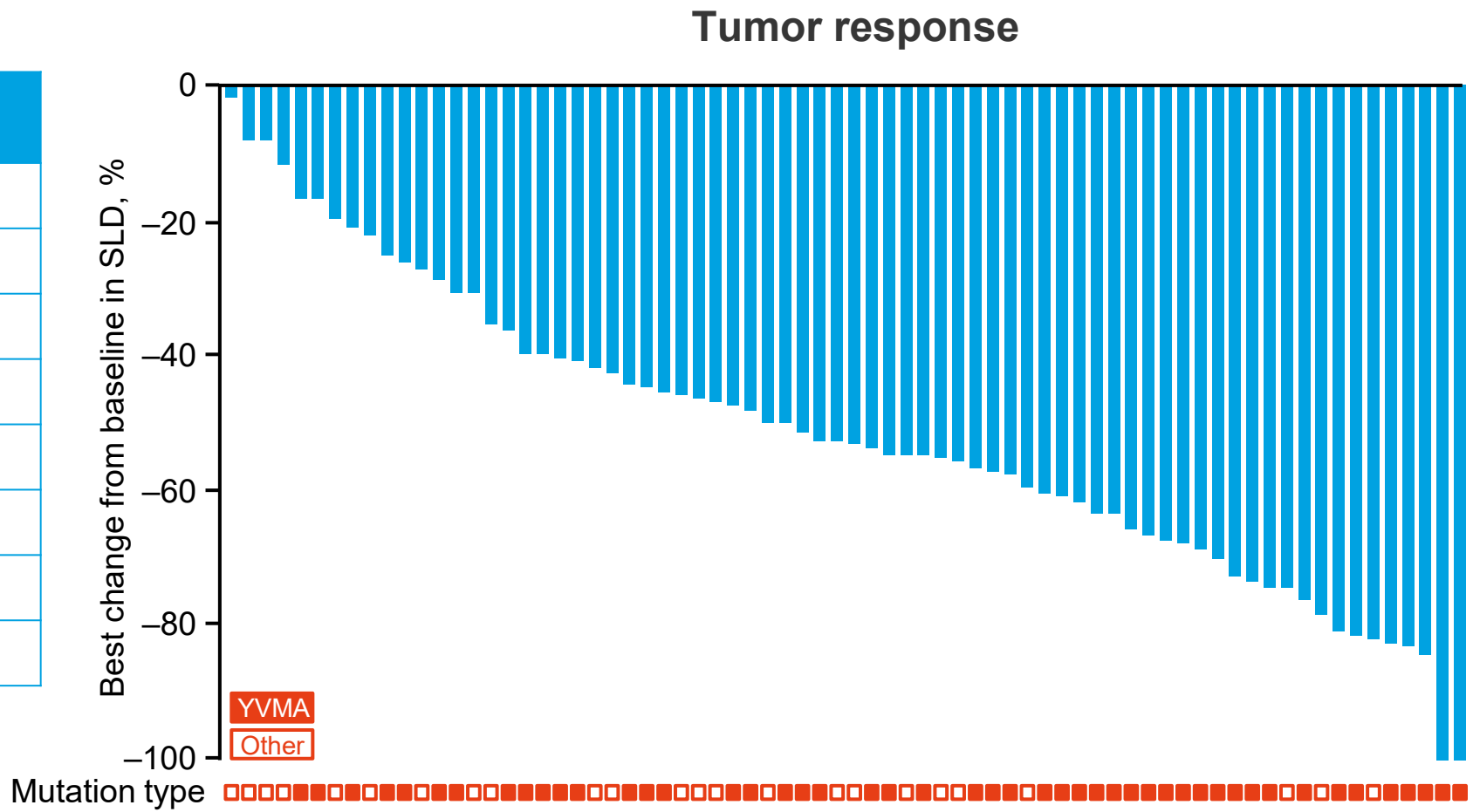
- DoR, DCR, PFS, safety

Popat S, et al. Ann Oncol 2025;36(suppl):Abstr LBA74

LBA74: Zongertinib as first-line treatment in patients with advanced HER2-mutant NSCLC: Beamion LUNG 1 – Popat S, et al

- **Key results**

Confirmed response by BICR (RECIST, v1.1)	Cohort 2 (n=74)*
ORR, % (95%CI)	77 (66, 85)
p-value	<0.0001
BOR, n (%)	
CR	6 (8)
PR	51 (69)
SD	14 (19)
PD	1 (1)†
DCR, % (95%CI)	96 (89, 99)



*Two patients were not evaluable for response; †PD due to non-target lesion progression.

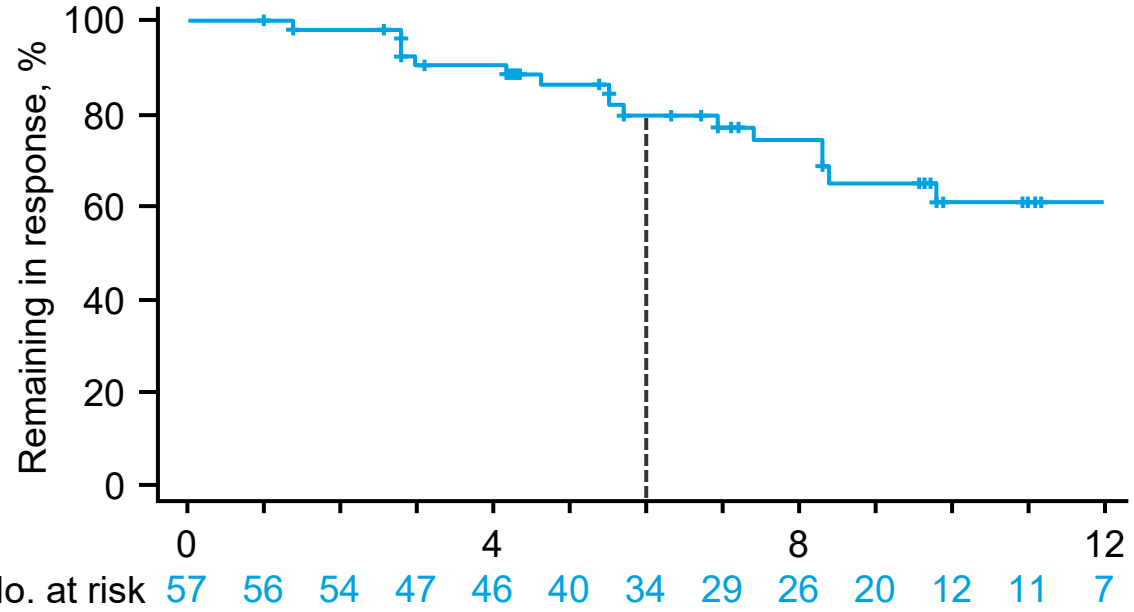
Popat S, et al. Ann Oncol 2025;36(suppl):Abstr LBA74

LBA74: Zongertinib as first-line treatment in patients with advanced HER2-mutant NSCLC: Beamion LUNG 1 – Popat S, et al

- **Key results (cont.)**

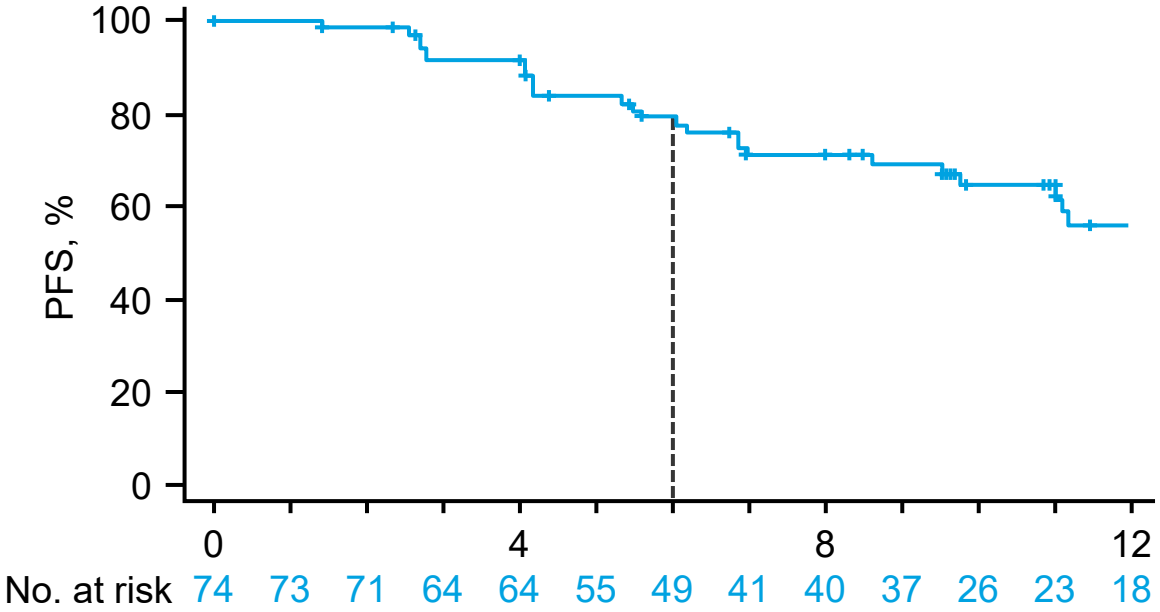
6-month DoR

	Cohort 2
Median FU, mo (95%CI)	9.7 (7.1, 9.9)
DoR, % (95%CI)	80 (65, 89)



6-month PFS

	Cohort 2
Median FU, mo (95%CI)	11.0 (9.7, 12.4)
6-month PFS, % (95%CI)	79 (68, 87)



Popat S, et al. Ann Oncol 2025;36(suppl):Abstr LBA74

LBA74: Zongertinib as first-line treatment in patients with advanced HER2-mutant NSCLC: Beamion LUNG 1 – Popat S, et al

- **Key results (cont.)**

TRAEs, n (%)	Cohort 2
Any	67 (91)
Grade 3	13 (18)
Led to dose reduction	11 (15)
Led to dose discontinuation	7 (9)

	Cohort 2	
AEs, n, %	All	Grade 3
Diarrhea	40 (54)	2 (3)
Rash	17 (23)	0
ALT increased	13 (18)	3 (4)
AST increased	12 (16)	2 (3)
Dysgeusia	12 (16)	0
Nausea	12 (16)	0
Dry skin	10 (14)	0
Pruritus	10 (14)	0
Paronychia	9 (12)	1 (1)
Stomatitis	8 (11)	0

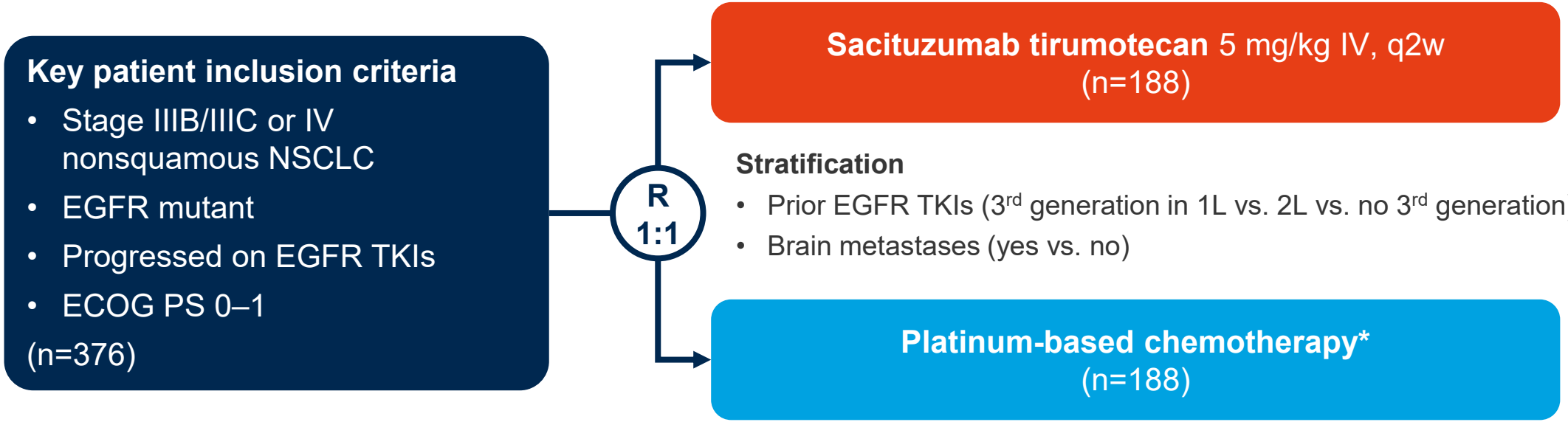
- **Conclusions**
  - In patients with advanced HER2-mutant NSCLC, 1L zongertinib demonstrated a significant ORR benefit with durable responses, and was generally well tolerated, although around half of the patients experienced diarrhea but this was rarely grade 3

Advanced NSCLC – Not radically treatable stage III and stage IV

ADCs and other therapies

LBA5: Sacituzumab tirumotecan (sac-TMT) vs platinum-based chemotherapy in EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC) following progression on EGFR-TKIs: results from the randomized, multi-center phase 3 OptiTROP-Lung04 study – Zhang L, et al

- **Study objective**
  - To evaluate the efficacy and safety of sacituzumab tirumotecan vs platinum-based chemotherapy in patients with EGFR-mutant NSCLC who have progressed on EGFR TKIs in the phase 3 OptiTROP-Lung04 study



Primary endpoints

- PFS (BICR)

Secondary endpoints

- OS, PFS (investigator assessed), ORR, DCR, DoR, safety

*Pemetrexed 500 mg/m^2 + carboplatin AUC5 or cisplatin 75 mg/m^2 q3w (up to 4 cycles), followed by pemetrexed 500 mg/m^2 q3w (maintenance).

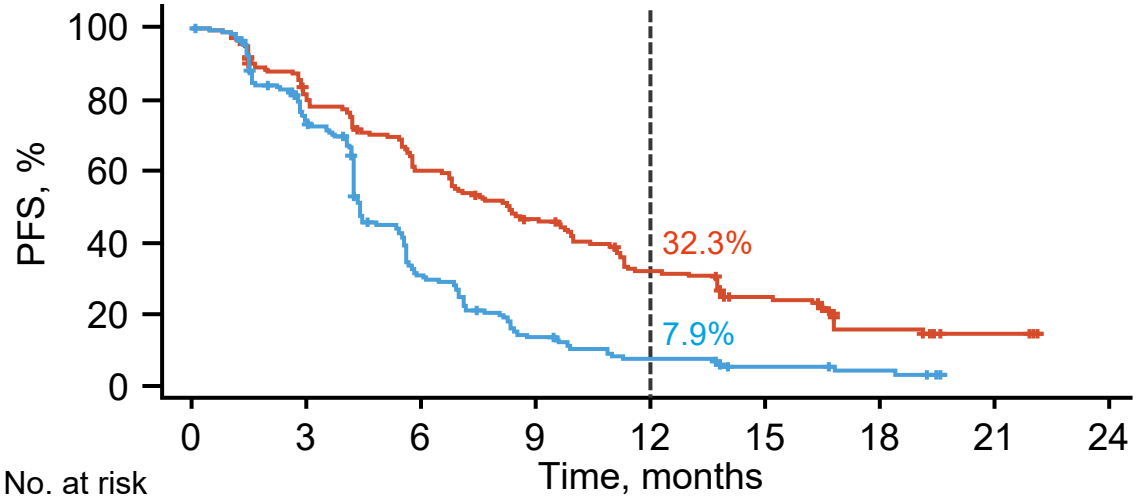
Zhang L, et al. Ann Oncol 2025;36(suppl):Abstr LBA5

LBA5: Sacituzumab tirumotecan (sac-TMT) vs platinum-based chemotherapy in EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC) following progression on EGFR-TKIs: results from the randomized, multi-center phase 3 OptiTROP-Lung04 study – Zhang L, et al

- **Key results**

Progression-free survival (BICR)

	Sacituzumab tirumotecan (n=188)	Chemotherapy (n=188)
PFS events, n (%)	144 (76.6)	159 (84.6)
mPFS, mo (95%CI)	8.3 (6.7, 9.9)	4.3 (4.2, 5.5)
12-mo PFS, mo (95%CI)	32.3 (25.5, 39.2)	7.9 (4.4, 12.8)
HR (95%CI); p-value	0.49 (0.39, 0.62); <0.0001	

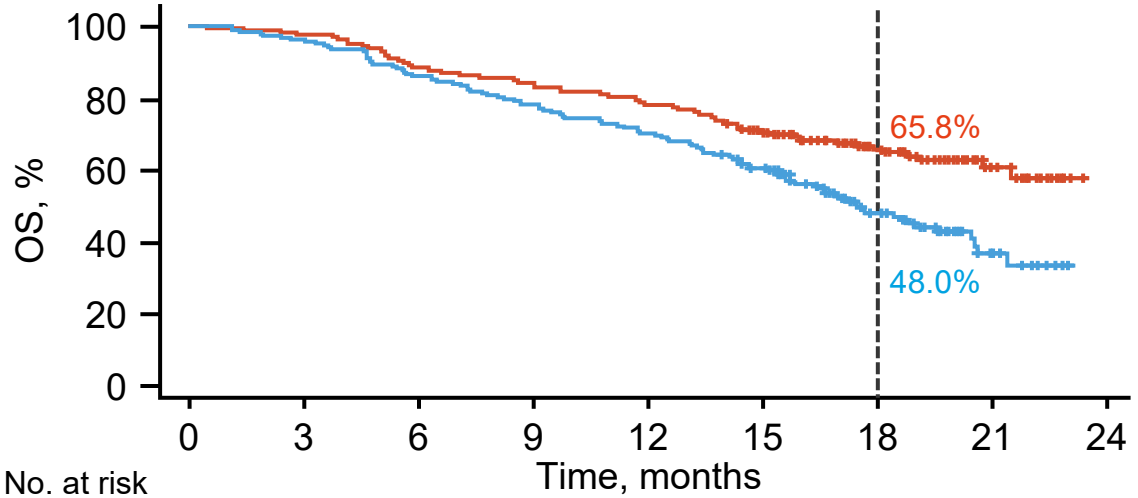


No. at risk

Sac-TMT	188	144	108	82	55	35	14	5	0
Chemotherapy	188	125	51	22	12	6	4	0	0

Overall survival

	Sacituzumab tirumotecan (n=188)	Chemotherapy (n=188)
OS events, n (%)	67 (35.6)	101 (53.7)
mOS, mo (95%CI)	NR (21.5, NE)	17.4 (15.7, 20.4)
18-mo OS, mo (95%CI)	65.8 (58.3, 72.3)	48.0 (40.2, 55.4)
HR (95%CI); 2-sided p-value*	0.60 (0.44, 0.82); 0.001*	



No. at risk

Sac-TMT	188	184	167	158	147	127	75	25	0
Chemotherapy	188	180	162	147	132	110	57	13	0

*Determined by the O'Brien-Fleming alpha spending function. Based on pre-specified OS IA, it was less than pre-specified efficacy boundary.

Zhang L, et al. Ann Oncol 2025;36(suppl):Abstr LBA5

LBA5: Sacituzumab tirumotecan (sac-TMT) vs platinum-based chemotherapy in EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC) following progression on EGFR-TKIs: results from the randomized, multi-center phase 3 OptiTROP-Lung04 study – Zhang L, et al

- **Key results (cont.)**

	Sacituzumab tirumotecan (n=188)	Chemotherapy (n=182)
ORR, % (95%CI)	60.6 (53.3, 67.7)	43.1 (35.9, 50.5)
Difference,* % (95%CI)	17.0 (7.0, 27.1)	
DCR, % (95%CI)	87.2 (81.6, 91.6)	80.3 (73.9, 85.7)
Median DoR, mo (95%CI)	8.3 (6.2, 10.0)	4.2 (3.0, 4.4)
12-mo DoR rate, % (95%CI)	36.3 (27.3, 45.3)	8.1 (3.3, 15.8)

TRAEs, n (%)	Sacituzumab tirumotecan (n=188)	Chemotherapy (n=182)
Any	188 (100)	179 (98.4)
Grade ≥3	109 (58.0)	98 (53.8)
Serious	17 (9.0)	32 (17.6)
Led to dose reduction	57 (30.3)	41 (22.5)
Led to dose interruption	69 (36.7)	60 (33.0)
Led to dose discontinuation	0	1 (0.5)
Led to death	0	1 (0.5)†

- **Conclusions**
  - In patients with EGFR-mutant NSCLC who had progressed on EGFR TKIs, sacituzumab tirumotecan significantly improved PFS and OS compared with platinum-based chemotherapy, with a manageable safety profile and no unexpected safety concerns

*Cochran-Mantel-Haenszel test; †cardiorespiratory arrest chemotherapy-related.

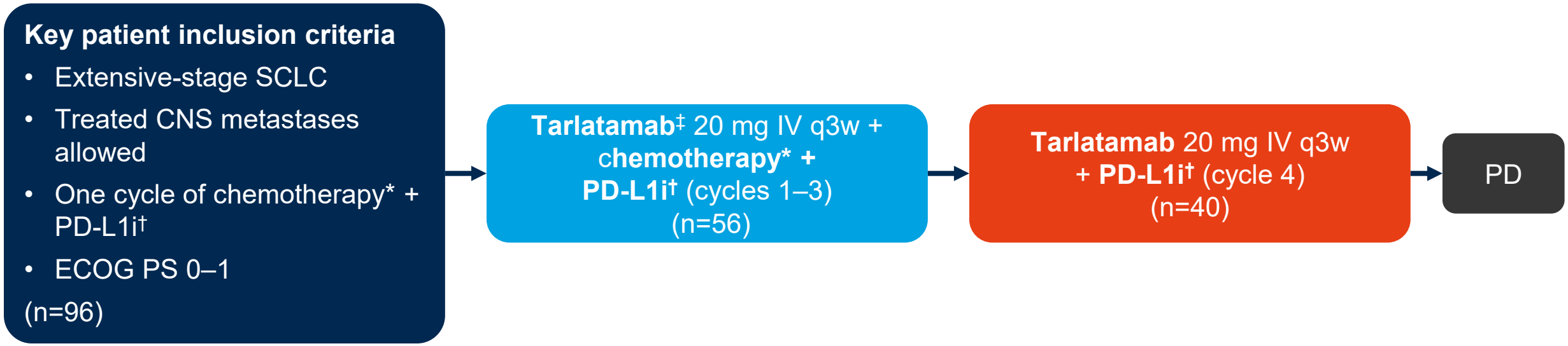
Zhang L, et al. Ann Oncol 2025;36(suppl):Abstr LBA5

Other malignancies

SCLC, mesothelioma and thymic epithelial tumors

2757O: Tarlatamab with first-line chemoimmunotherapy for extensive stage small cell lung cancer (ES-SCLC): DeLLphi-303 study – Wermke M, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L tarlatamab + chemoimmunotherapy after 1 cycle of chemotherapy + immunotherapy in patients with extensive-stage SCLC in the DeLLphi-303 study



Primary endpoints

- DLT, safety

Secondary endpoints

- ORR, DoR, DCR, PFS, OS

*Carboplatin AUC5 IV (D1) + etoposide 100 mg/m^2 (D1–3); †atezolizumab 1200 mg IV q3w OR durvalumab 1500 mg IV q3w; ‡tarlatamab was administered with step dosing: 1 mg (Cycle 1, D1), followed by 20 mg q3w.

Wermke M, et al. Ann Oncol 2025;36(suppl):Abstr 2757O

2757O: Tarlatamab with first-line chemoimmunotherapy for extensive stage small cell lung cancer (ES-SCLC): DeLLphi-303 study – Wermke M, et al

- **Key results**

Safety	Tarlatamab + EP + atezolizumab (n=56)	Tarlatamab + EP + durvalumab (n=40)	Overall (n=96)
Median duration of treatment, weeks (IQR)	46 (16–60)	30 (12–62)	46 (14–60)
Median study FU, mo (95%CI)	12.5 (11.3, 14.7)	14.8 (13.2, 15.0)	13.8 (12.5, 15.0)
Dose-limiting toxicities,* n (%)	3 (5)	0	3 (3)
Treatment-emergent AEs, n (%)	56 (100)	40 (100)	96 (100)
TRAEs, n (%)	56 (100)	40 (100)	96 (100)
Grade 3	26 (46)	15 (38)	41 (43)
Grade 4	21 (38)	13 (33)	34 (35)
Fatal TRAEs	0	1 (3)	1 (1)

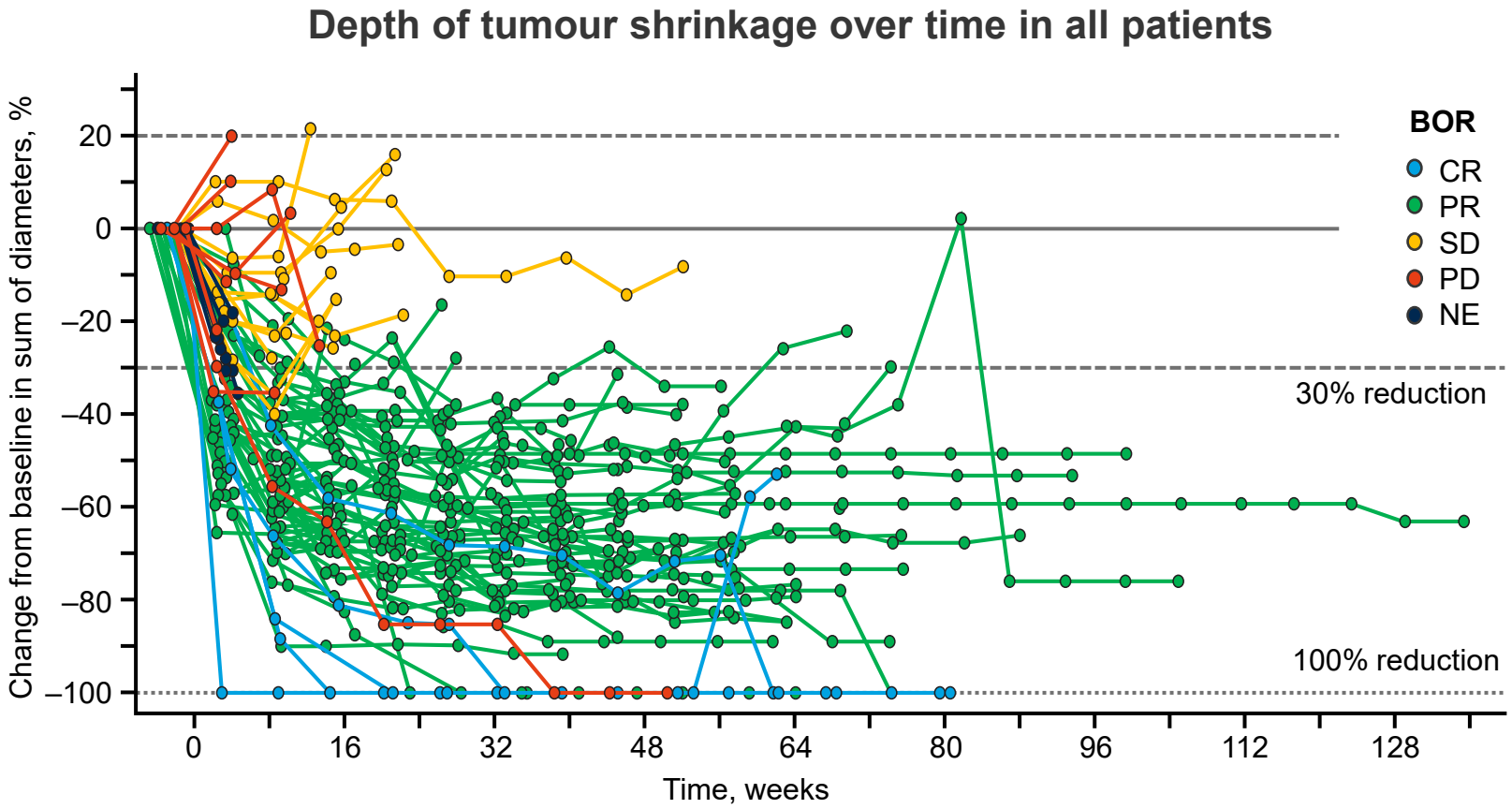
*Included ICANS (n=1), platelet count decrease (n=1), and thrombocytopenia (n=1).

Wermke M, et al. Ann Oncol 2025;36(suppl):Abstr 2757O

2757O: Tarlatamab with first-line chemoimmunotherapy for extensive stage small cell lung cancer (ES-SCLC): DeLLphi-303 study – Wermke M, et al

- **Key results (cont.)**

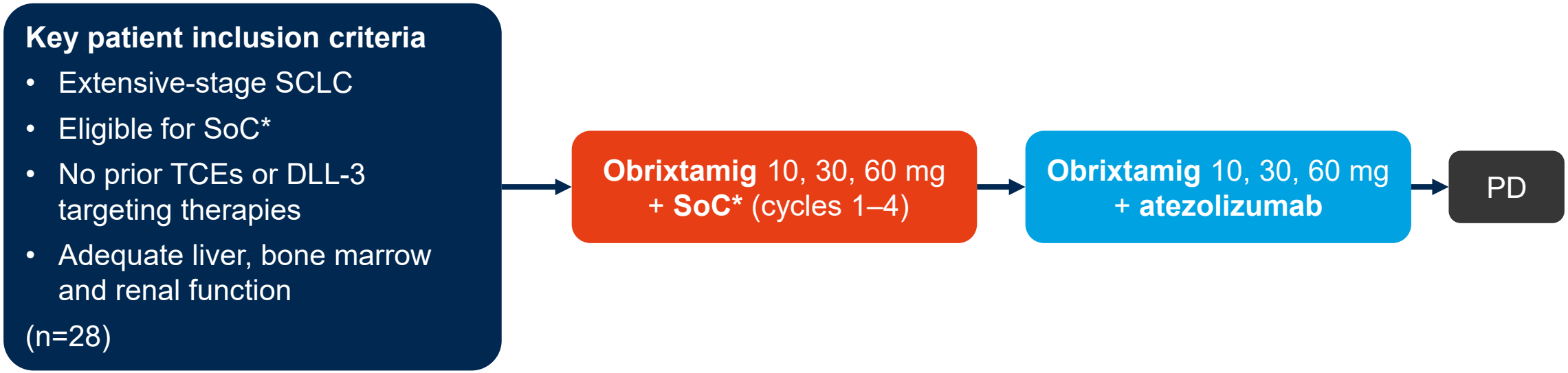
	Overall (n=96)
ORR, n (%) [95%CI]	68 (71) [61, 80]
BOR, n (%)	
CR	5 (5)
PR	63 (66)
SD	11 (11)
PD	8 (8)
NE	9 (9)
mDoR, mo (95%CI)	11.0 (8.5, NE)
DCR, % (95%CI)	82 (73, 89)
mDoDC, mo (95%CI)	10.7 (7.7, 18.8)
12-mo OS, %	80.6



- **Conclusions**
  - In patients with extensive-stage SCLC, 1L tarlatamab + chemoimmunotherapy provided durable response with a manageable safety profile

2759O: DAREON®-8: a phase I trial of first-line obrixtamig plus standard of care (SoC) in extensive-stage small cell lung carcinoma (ES-SCLC) – Peters S, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L obrixtamig + SoC in patients with extensive-stage SCLC in the phase 1 DAREON-8 study



Primary endpoints

- DLT (evaluation period)

Secondary endpoints

- DLT (on-treatment period), ORR, DoR, safety

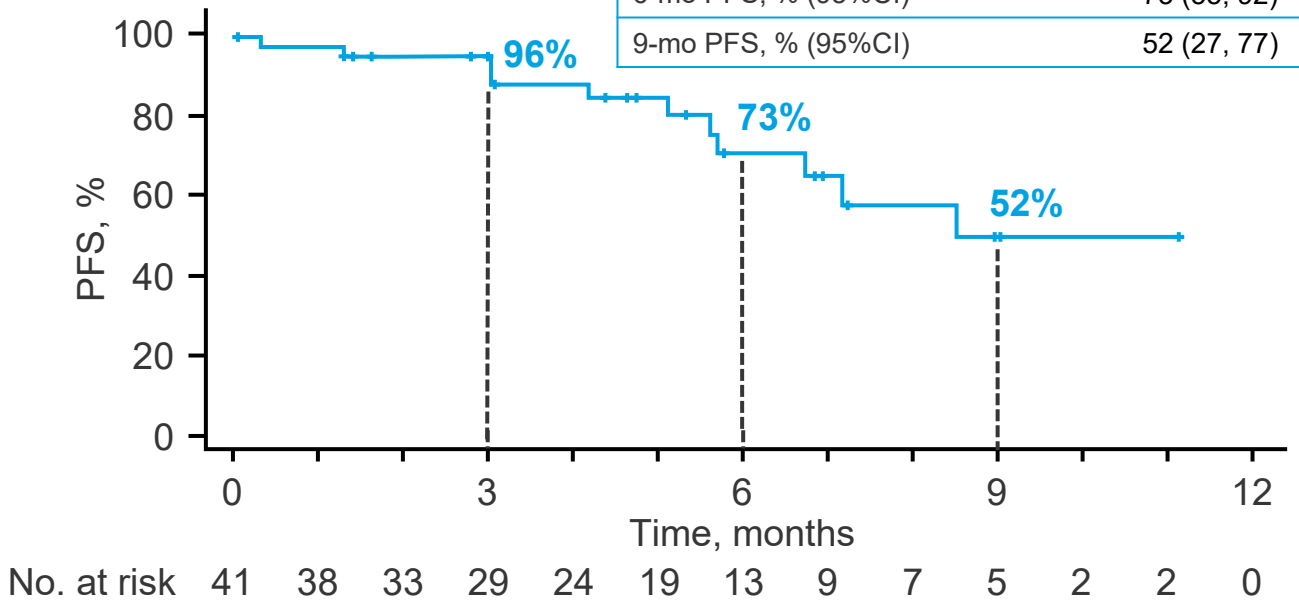
*Carboplatin + etoposide + atezolizumab.

2759O: DAREON®-8: a phase I trial of first-line obrixtamig plus standard of care (SoC) in extensive-stage small cell lung carcinoma (ES-SCLC) – Peters S, et al

- **Key results**

Progression-free survival

	Obrixtamig + SoC
Median follow-up, mo (range)	6.9 (5.8–9.0)
mPFS, mo (95%CI)	NR
3-mo PFS, % (95%CI)	96 (89, 100)
6-mo PFS, % (95%CI)	73 (55, 92)
9-mo PFS, % (95%CI)	52 (27, 77)



	Obrixtamig + SoC (n=28)
Confirmed ORR, % (95%CI)	68 (49, 82)
Confirmed DCR, % (95%CI)	89 (73, 96)
mDoR, mo (95%CI)	7.3 (4.4, NC)
BOR, n (%)	
CR	1 (4)
PR	18 (64)
SD	6 (21)
PD	1 (4)
NE/missing	2 (7)

Peters S, et al. Ann Oncol 2025;36(suppl):Abstr 2759O

2759O: DAREON®-8: a phase I trial of first-line obrixtamig plus standard of care (SoC) in extensive-stage small cell lung carcinoma (ES-SCLC) – Peters S, et al

- **Key results (cont.)**

Obrixtamig-related AEs in ≥25% of patients, n (%)	All (n=28)	
	All grade	Grade ≥3
Any	27 (96)	11 (39)
CRS	14 (50)	0
Dysgeusia	11 (39)	0
Appetite decreased	9 (32)	0
Neutropenia	8 (29)	6 (21)*
Pyrexia	8 (29)	0
Anemia	7 (25)	0
Fatigue	7 (25)	1 (4)

TEAEs, %	Grade ≥3	Grade ≥3 attributed to chemotherapy
Any	79	75
Neutropenia	54	54
Anemia	18	18
Appetite decreased	14	14
Asthenia	11	4
Thrombocytopenia	7	7

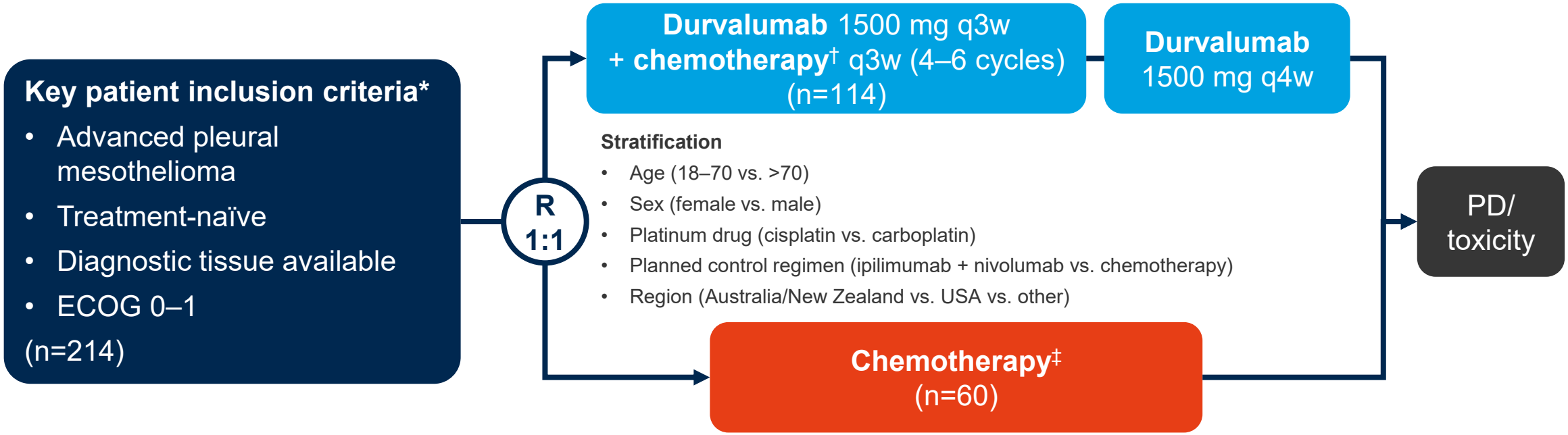
- **Conclusions**
  - In patients with extensive-stage SCLC , 1L obrixtamig combined with SoC chemo-immunotherapy showed favorable tolerability with no unexpected toxicities and delivered encouraging efficacy

*7 of 8 cases of neutropenia were attributed to chemotherapy.

Peters S, et al. Ann Oncol 2025;36(suppl):Abstr 2759O

LBA104: Primary results of DREAM3R: DuRvalumab (MEDI4736) with chEmotherapy as first line treAtment in advanced pleural Mesothelioma - a phase 3 Randomised trial – Nowak AK, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L durvalumab + chemotherapy in patients with advanced pleural mesothelioma in the phase 3 DREAM3R study



Primary endpoints

- OS

Secondary endpoints

- PFS, ORR, safety

*Key changes: protocol v3, choice of chemotherapy (cisplatin or carboplatin); protocol v4, investigator choice of control (chemotherapy or nivolumab + ipilimumab), randomization from 2:1 to 1:1, and limiting recruiting to epithelioid subtype; †cisplatin 75 mg/m^2 or carboplatin AUC5 + pemetrexed 500 mg/m^2; ‡ipilimumab 1 mg/kg q6w + nivolumab 360 mg q3w or 3 mg/kg q2w OR chemotherapy.

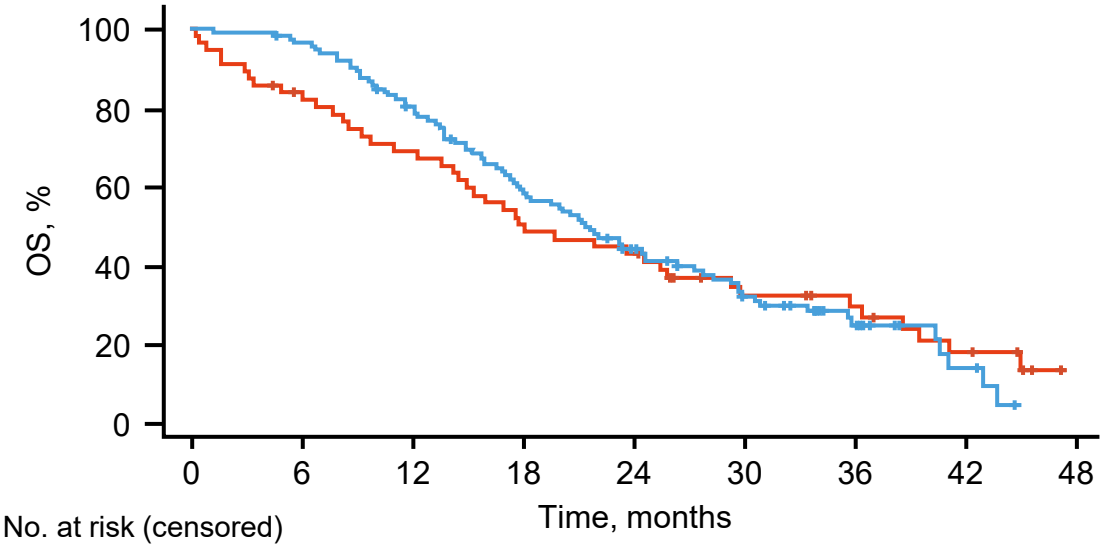
Nowak AK, et al. Ann Oncol 2025;36(suppl):Abstr LBA104

LBA104: Primary results of DREAM3R: DuRvalumab (MEDI4736) with chEmotherapy as first line treAtment in advanced pleural Mesothelioma - a phase 3 Randomised trial – Nowak AK, et al

- **Key results**

Overall survival

	Durvalumab + chemotherapy	Chemotherapy
mOS, mo (95%CI)	21 (18, 27)	18 (14, 30)
Adjusted HR (95%CI); p-value*	0.92 (0.63, 1.36); 0.9	

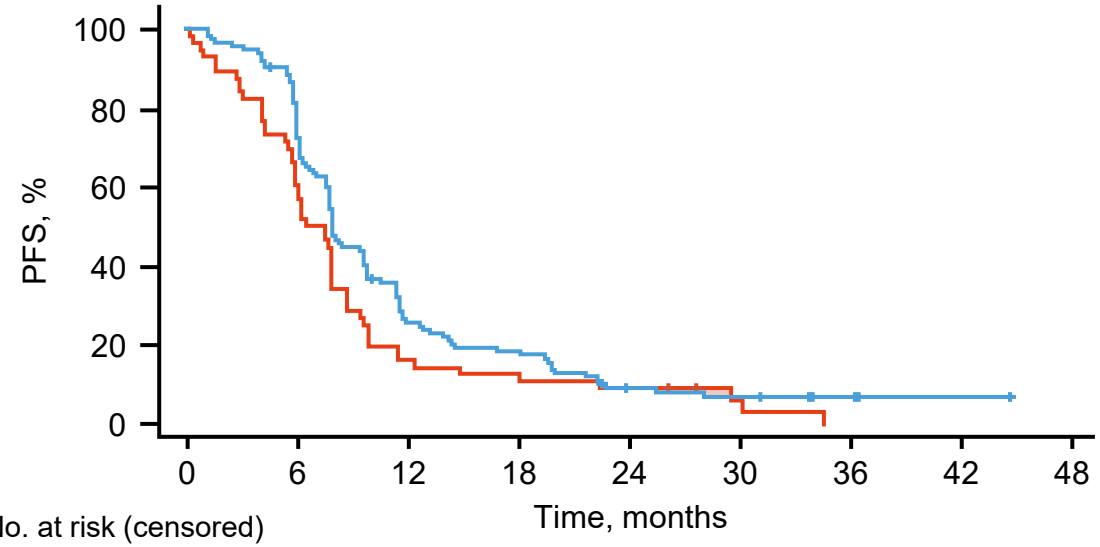


No. at risk (censored)

D + CT	114 (0)	108 (2)	88 (4)	63 (5)	44 (9)	28 (14)	13 (24)	4 (30)	0 (32)
CT alone	60 (3)	45 (6)	37 (6)	27 (6)	23 (6)	14 (10)	11 (12)	6 (13)	0 (18)

Progression-free survival

	Durvalumab + chemotherapy	Chemotherapy
mPFS, mo (95%CI)	8 (8, 10)	7 (6, 8)
Adjusted HR (95%CI); p-value*	0.70 (0.5, 0.98); 0.20	



No. at risk (censored)

D + CT	114 (0)	85 (2)	28 (3)	20 (3)	8 (5)	6 (5)	3 (8)	1 (10)	0 (0)
CT alone	60 (3)	34 (4)	9 (4)	7 (4)	5 (4)	2 (6)	0 (6)	0 (6)	0 (0)

*Stratified Log-rank test.

Nowak AK, et al. Ann Oncol 2025;36(suppl):Abstr LBA104

LBA104: Primary results of DREAM3R: DuRvalumab (MEDI4736) with chEmotherapy as first line treAtment in advanced pleural Mesothelioma - a phase 3 Randomised trial – Nowak AK, et al

- **Key results (cont.)**

Objective tumor response	Durvalumab + chemotherapy (n=113)	Chemotherapy (n=60)
iCR/iPR, n (%)	65 (58)	21 (35)
iSD/iPD/Unknown, n (%)	48 (42)	39 (65)

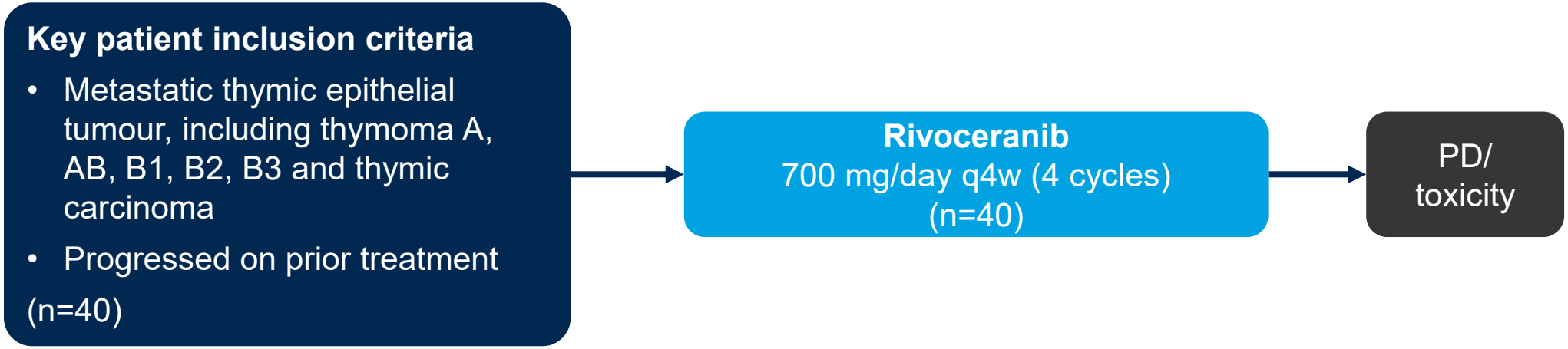
AEs occurring in ≥5% of patients, %	Durvalumab + chemotherapy (n=112)			Chemotherapy (n=60)		
	Grade 1–2	Grade 3–5	Any	Grade 1–2	Grade 3–5	Any
Fatigue	66	7	73	22	3	25
Nausea	61	2	63	27	2	29
Anemia	28	15	43	12	1	13
Neutrophil count decreased	19	12	31	4	2	6
Mucositis oral	15	1	16	6	1	7
Platelet count decreased	8	5	13	1	1	2
Pain	8	2	10	1	1	2
Thromboembolic event	6	3	9	0	3	3
Pleural effusion	6	3	9	1	1	2
Skin infection	6	1	7	1	1	2
Hypertension	5	1	6	2	1	3

- **Conclusions**
  - In patients with advanced pleural mesothelioma, durvalumab + chemotherapy showed safety and efficacy outcomes consistent with prior phase 2 trials, but early trial closure limited definitive conclusions

Nowak AK, et al. Ann Oncol 2025;36(suppl):Abstr LBA104

LBA105: A phase II, open-label, single-arm, multi-center study of rivoceranib in patients with metastatic thymic epithelial tumor, KCSG LU23-09 (THRIVE) – Ahn M-J, et al

- **Study objective**
  - To evaluate the efficacy and safety of rivoceranib (an anti-VEGFR2 TKI) in patients with metastatic thymic epithelial tumour in the phase 2 THRIVE study



Primary endpoints

- ORR

Secondary endpoints

- PFS, DCR, DoR, safety

Ahn M-J, et al. Ann Oncol 2025;36(suppl):Abstr LBA105

LBA105: A phase II, open-label, single-arm, multi-center study of rivoceranib in patients with metastatic thymic epithelial tumor, KCSG LU23-09 (THRIVE) – Ahn M-J, et al

- **Key results**

	Total (n=40)*	Thymoma (n=16)	Thymic carcinoma (n=24)
ORR, %	35.0	-	-
DCR, %	85.0	-	-
BOR, n (%)			
PR	14 (35.0)	5 (31.2)	9 (37.5)
SD	20 (50.0)	10 (62.5)	10 (41.7)
PD	2 (5.0)	0	2 (8.3)
NE	4 (10.0)	1 (6.3)	3 (12.5)
Median reduction in tumor size, %	−19.8 (−69.7, 50.7)	−21.0 (−69.7, −3.3)	−14.1 (−59.6, 50.7)
mPFS, mo	NR	-	-
mOS, mo	NR	-	-

*Four patients were not radiologically evaluable (treatment discontinuation, n=3; disease progression, n=1).

Ahn M-J, et al. Ann Oncol 2025;36(suppl):Abstr LBA105

LBA105: A phase II, open-label, single-arm, multi-center study of rivoceranib in patients with metastatic thymic epithelial tumor, KCSG LU23-09 (THRIVE) – Ahn M-J, et al

- **Key results (cont.)**

	Total (n=40)			
Safety, n (%)	**Any**	**Grade 1–2**	**Grade 3**	**Grade 4**
Dose modification	25 (62.5)	-	-	-
Treatment discontinuation	6 (15.0)	-	-	-
TRAE ≥20%				
Proteinuria	17 (42.5)	12 (30.0)	4 (10.0)	1 (2.5)
Hypertension	19 (47.5)	12 (30.0)	7 (17.5)	0
Stomatitis	14 (35.0)	10 (25.0)	4 (10.0)	0
Palmar-plantar erythrodysesthesia syndrome	10 (25.0)	9 (22.5)	1 (2.5)	0
Nausea	9 (22.5)	9 (22.5)	0	0
Headache	8 (20.0)	8 (20.0)	0	0
Fatigue	8 (20.0)	8 (20.0)	0	0

- **Conclusions**
  - In patients with metastatic thymic epithelial tumour, rivoceranib showed encouraging efficacy and had a manageable safety profile

Ahn M-J, et al. Ann Oncol 2025;36(suppl):Abstr LBA105