Integrating New Advances into the Care of Patients with Cancer

A Multitumor Symposium in Partnership with the American Oncology Network

CME/MOC, NCPD and ACPE Accredited

Saturday, November 8, 2025
10:00 AM – 3:00 PM CT

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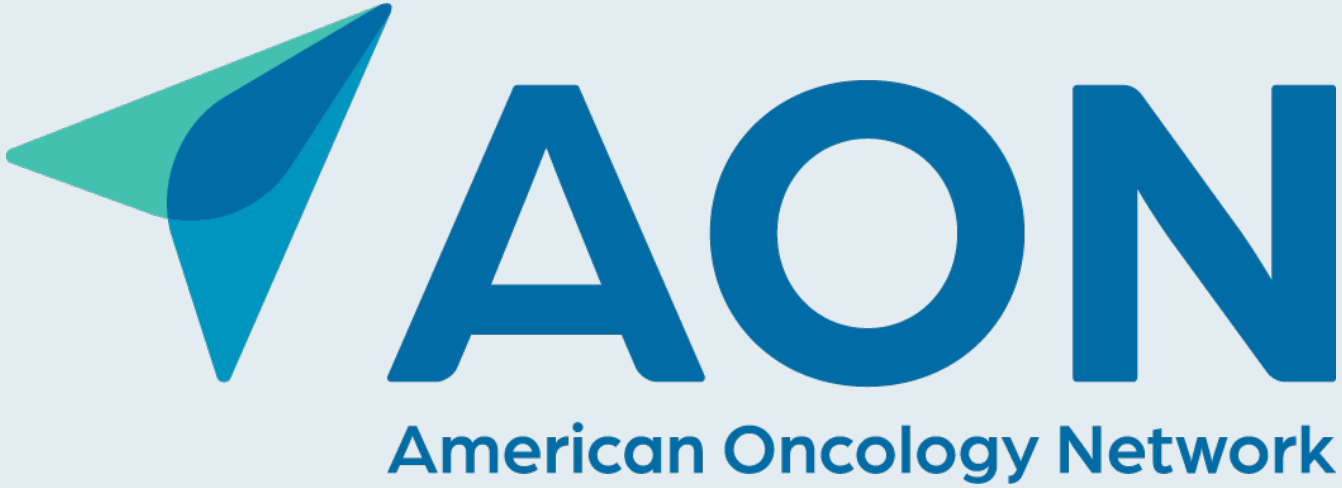

Welcome AON Members!

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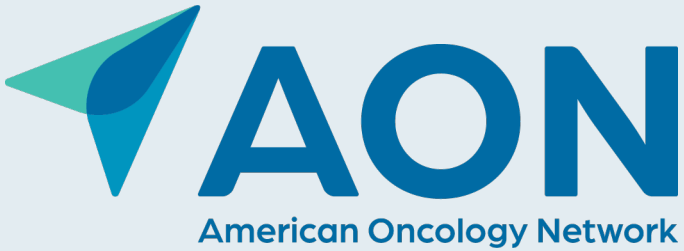

MiBA (Meaningful Insights Biotech Analytics) is not your average data company.

MiBA is a healthcare AI technology company launched with a mission to close the feedback loop between physicians, patients, and industry partners. The CME program is sponsored with MiBA data insights, from AON practices.

MiBA has a clear vision to improve data quality by unlocking the power of data to fuel decisions, education and improve patient care.

Commercial Support

This activity is supported by educational grants from AbbVie Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeOne, Corcept Therapeutics Inc, Daiichi Sankyo Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Lilly, Merck, and Nuvalent.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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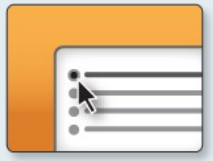
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the morning and afternoon premeeting surveys.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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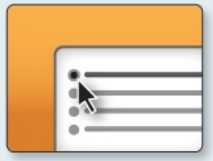
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the premeeting survey at the beginning of each module.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME/NCPD/ACPE Credit: A credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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Save The Date

Fifth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

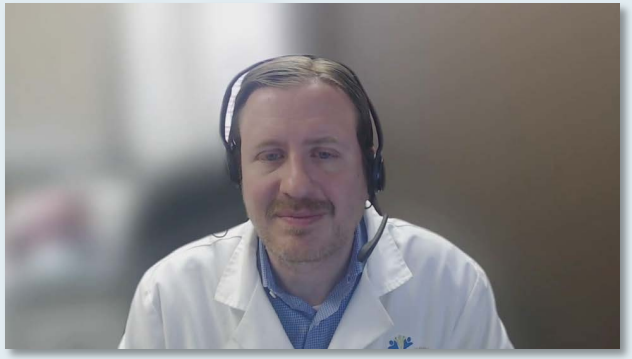
Contributing General Medical Oncologists

Sunil Babu, MD
Fort Wayne Medical Oncology and Hematology
Fort Wayne, Indiana

Sean Warsch, MD
Messino Cancer Centers
Asheville, North Carolina

Zanetta S Lamar, MD
Florida Oncology and Hematology
American Oncology Partners
Naples, Florida

Jennifer Yannucci, MD
Low Country Cancer Care
Savannah, Georgia



Brian P Mulherin, MD
American Oncology Network
Indianapolis, Indiana

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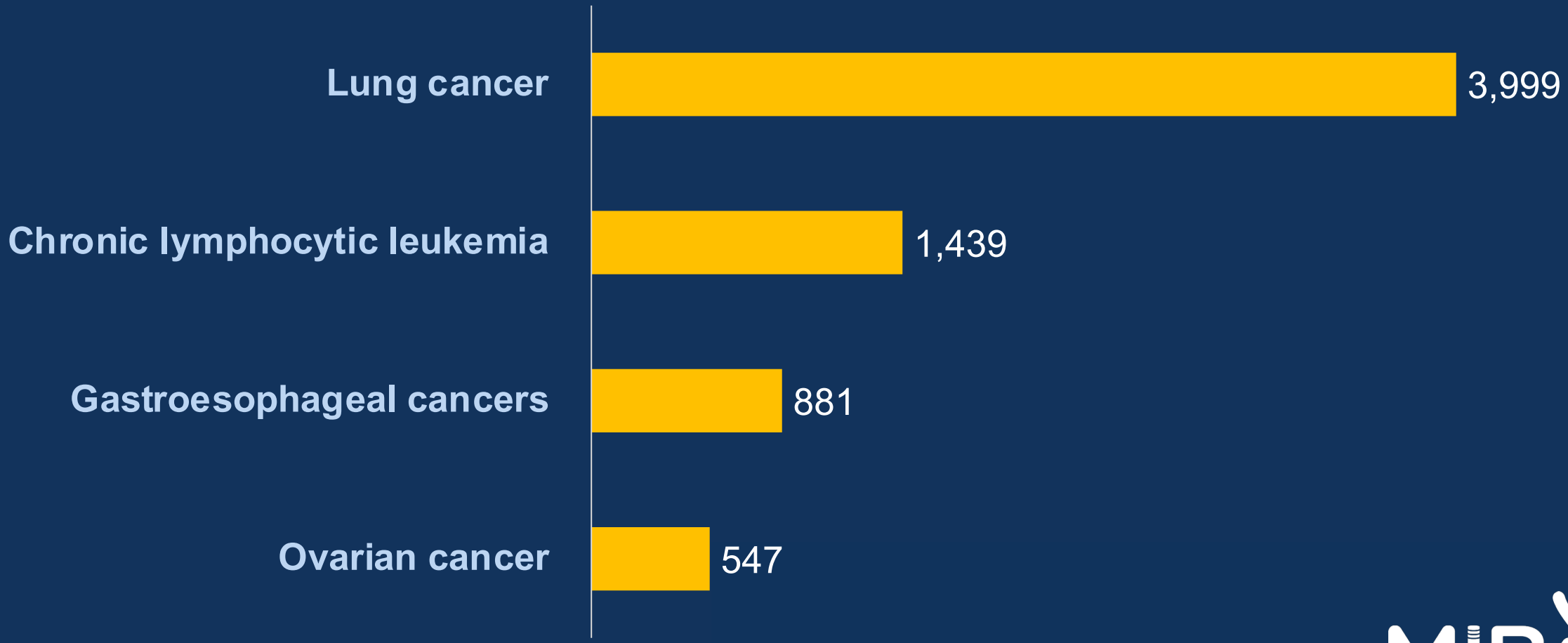
Snapshot of AON Practice
Patients Seen in the Last 12 Months



Agenda

Module 1 — Lung Cancer: *Drs Gainor, Langer and Shields*

Module 2 — Chronic Lymphocytic Leukemia: *Dr Rogers*

Module 3 — Ovarian Cancer: *Dr Konecny*

Module 4 — Gastroesophageal Cancers: *Dr Shah*

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Lung Cancer Faculty

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Indiana University School of Medicine
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Associate Member, Experimental and Developmental Therapeutics
Department of Medicine, Division of Hematology/Oncology, Thoracic Oncology
Indiana University Melvin and Bren Simon Comprehensive Cancer Center
Indianapolis, Indiana

MODERATOR
Stephen "Fred" Divers, MD
Chief Medical Officer
American Oncology Network
Hot Springs, Arkansas

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Dr Gainor — Disclosures

Advisory Committees	Amgen Inc, ARS Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Genentech, a member of the Roche Group, Gilead Sciences Inc, ITeos Therapeutics, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Mariana Oncology, Merck, Merus, Mirati Therapeutics Inc, Moderna, Novartis, Novocure Inc, Nuvalent, Pfizer Inc, Sanofi, Takeda Pharmaceuticals USA Inc
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Contracted Research	Adaptimmune, ALX Oncology, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Bristol Myers Squibb, Genentech, a member of the Roche Group, Jounce Therapeutics, Merck, Moderna, NextPoint Therapeutics, Novartis, Palleon Pharmaceuticals
Nonrelevant Financial Relationships	AI Proteins

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Dr Langer — Disclosures

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Contracted Research (Institutional Support for Clinical Research)	Amgen Inc, FUJIFILM Pharmaceuticals USA Inc, Novocure Inc
Data and Safety Monitoring Boards/Committees	Incyte Corporation, Summit Therapeutics
Nonrelevant Financial Relationships	Valor (VA)

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Dr Shields — Disclosures

Steering Committees	AstraZeneca Pharmaceuticals LP

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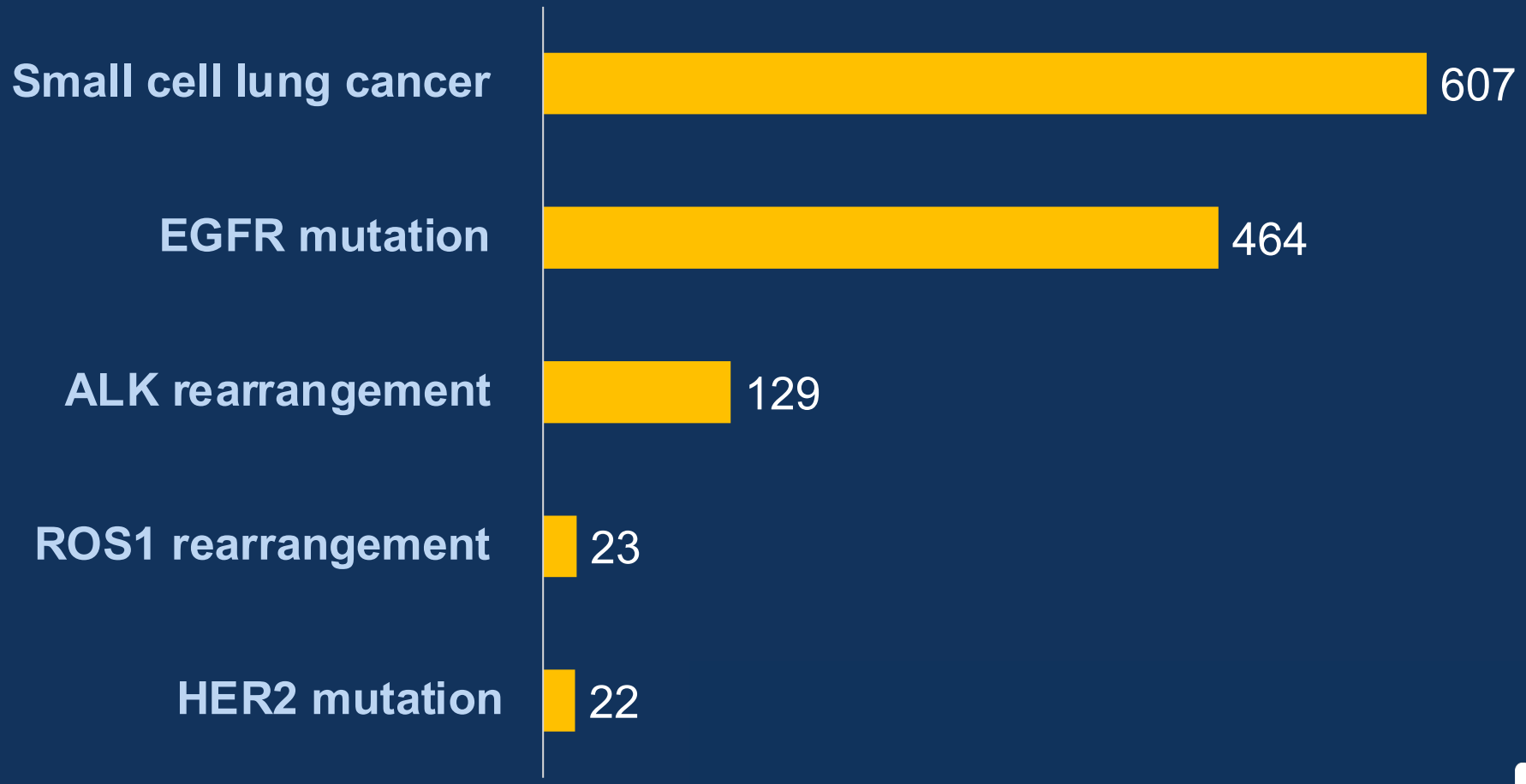
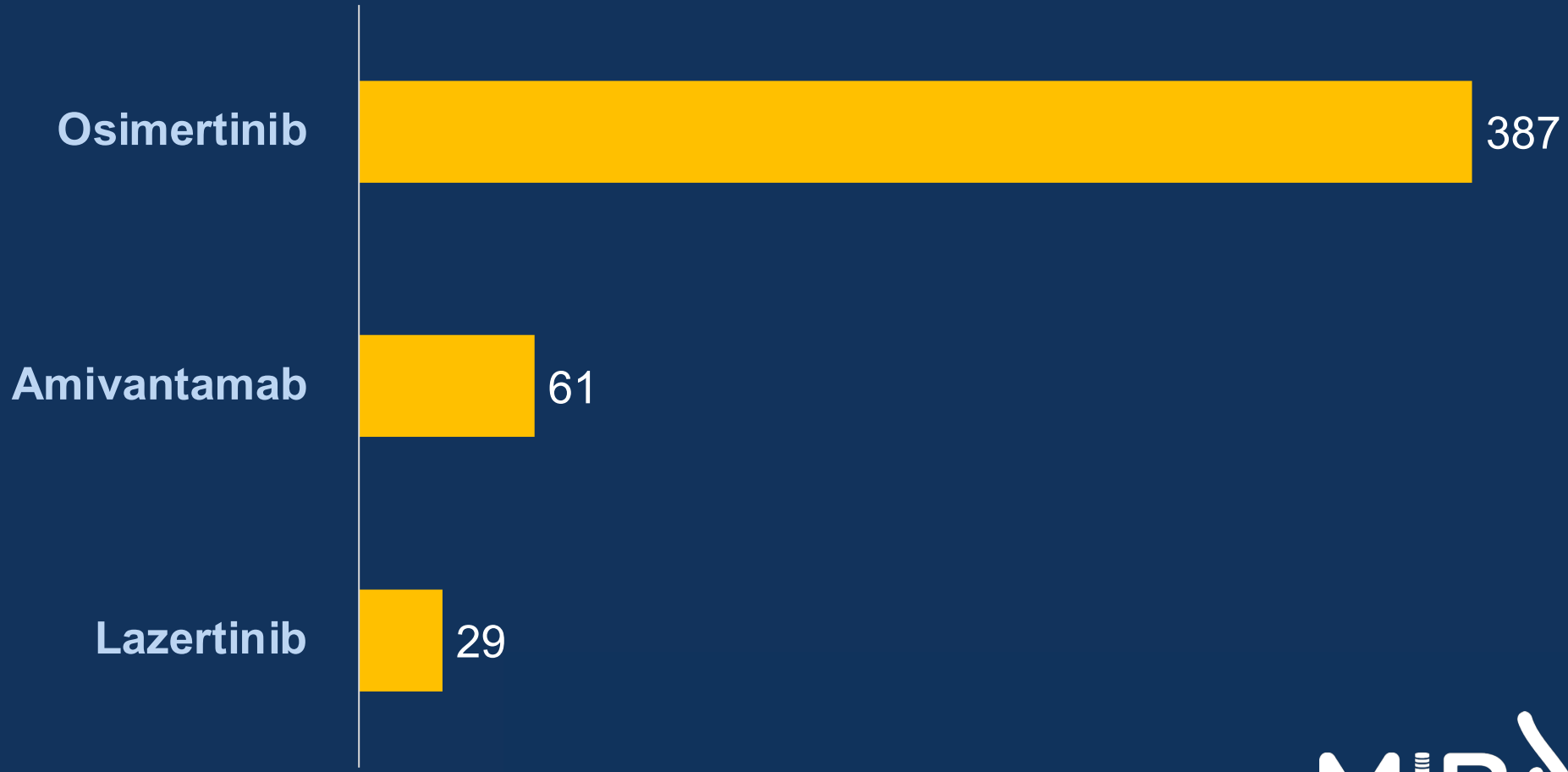
Dr Divers — Disclosures

Advisory Committees	Daiichi Sankyo Inc

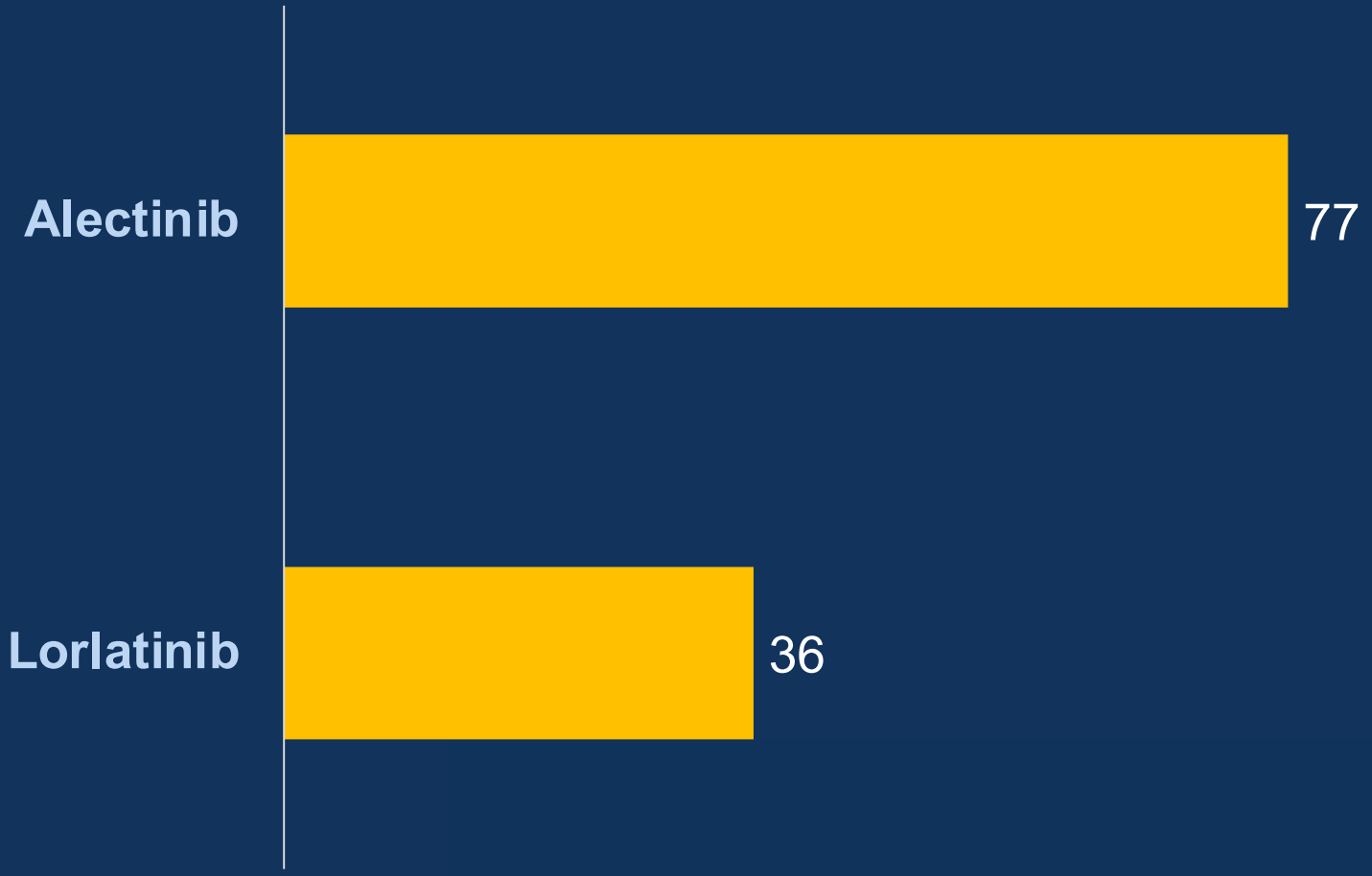
Snapshot of AON Practice
Lung Cancer



Snapshot of AON Practice
Lung Cancer with EGFR Mutation

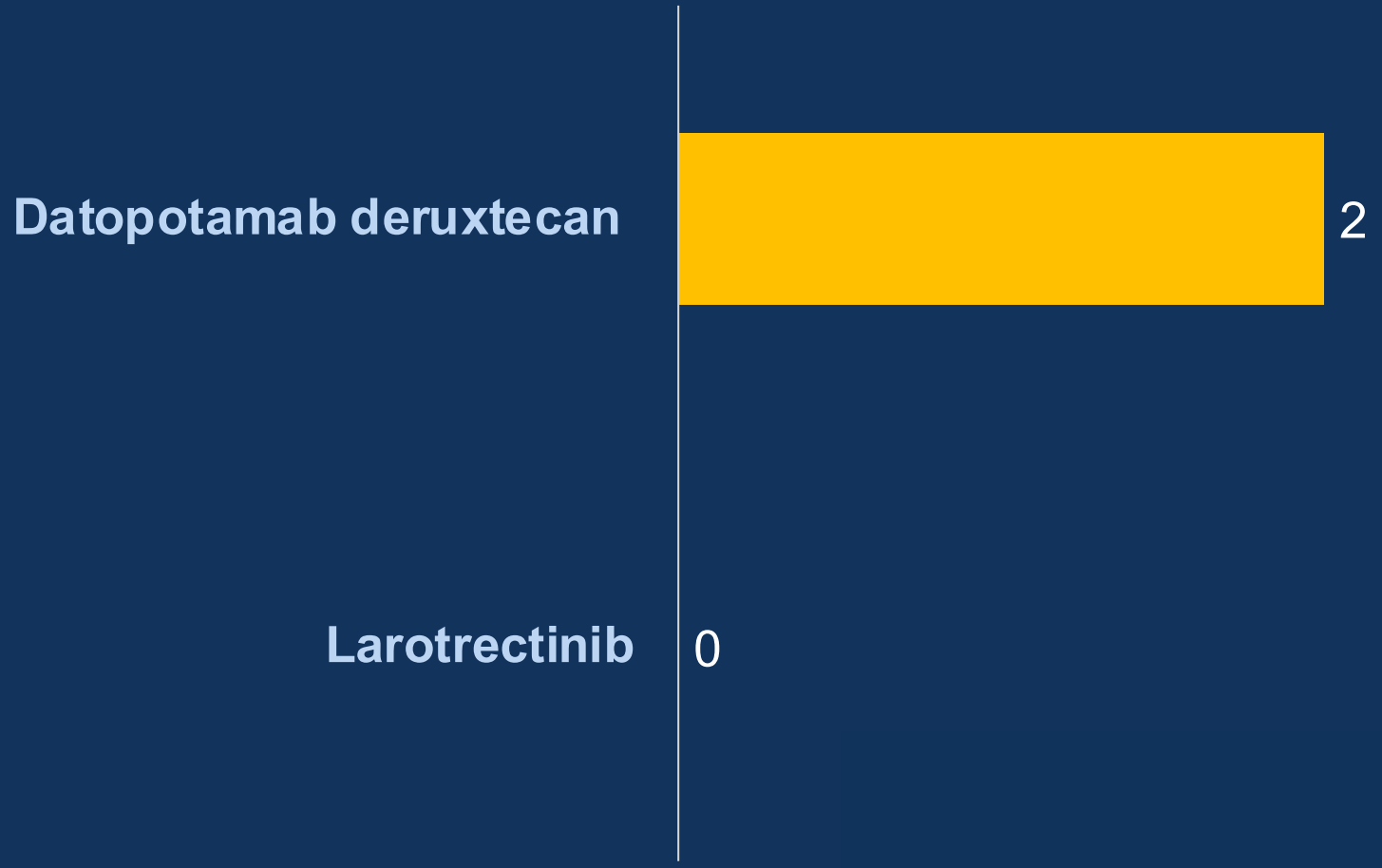


Snapshot of AON Practice
Lung Cancer with ALK Rearrangement

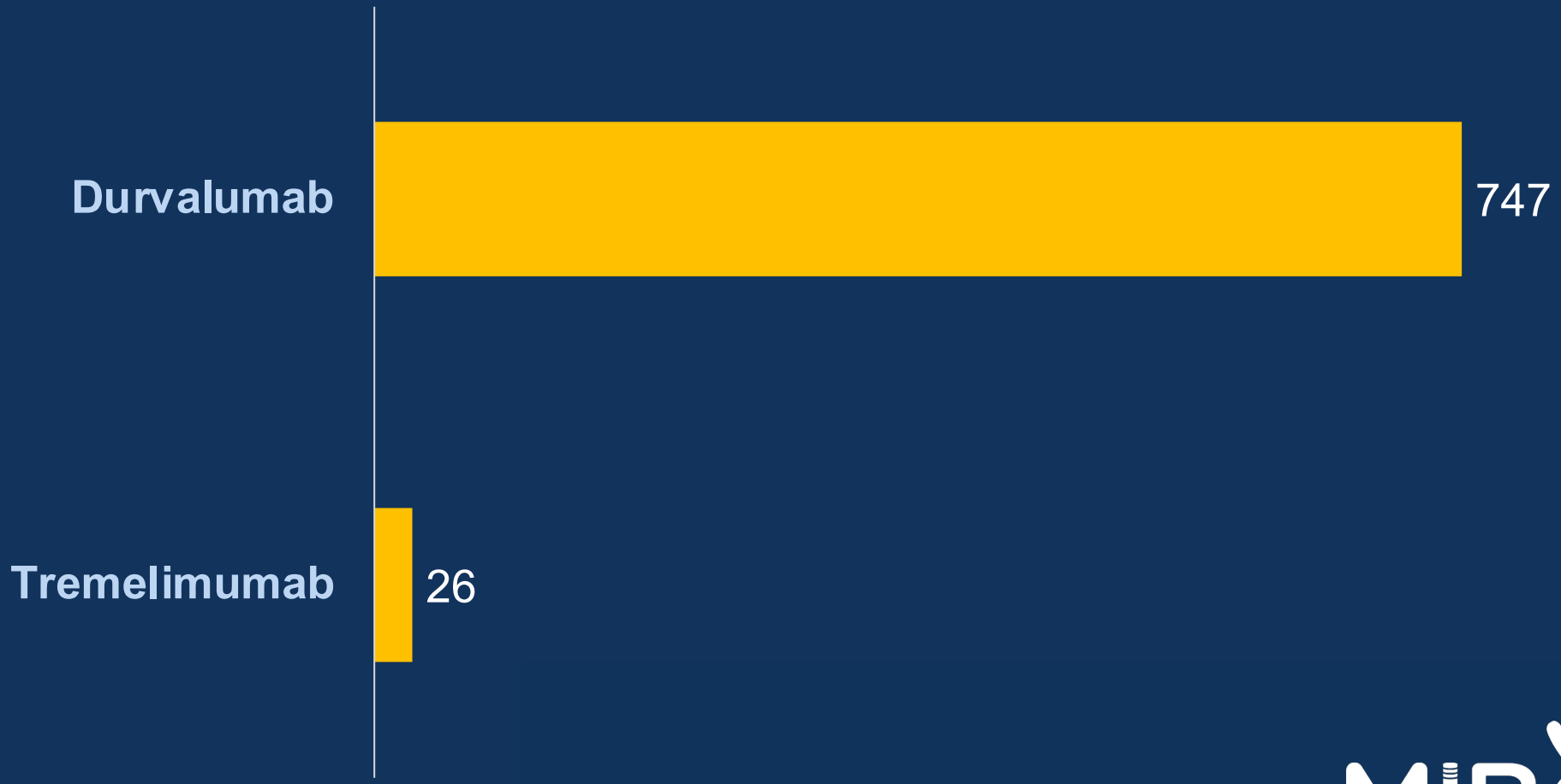


Snapshot of AON Practice
Lung Cancer with HER2 Mutation

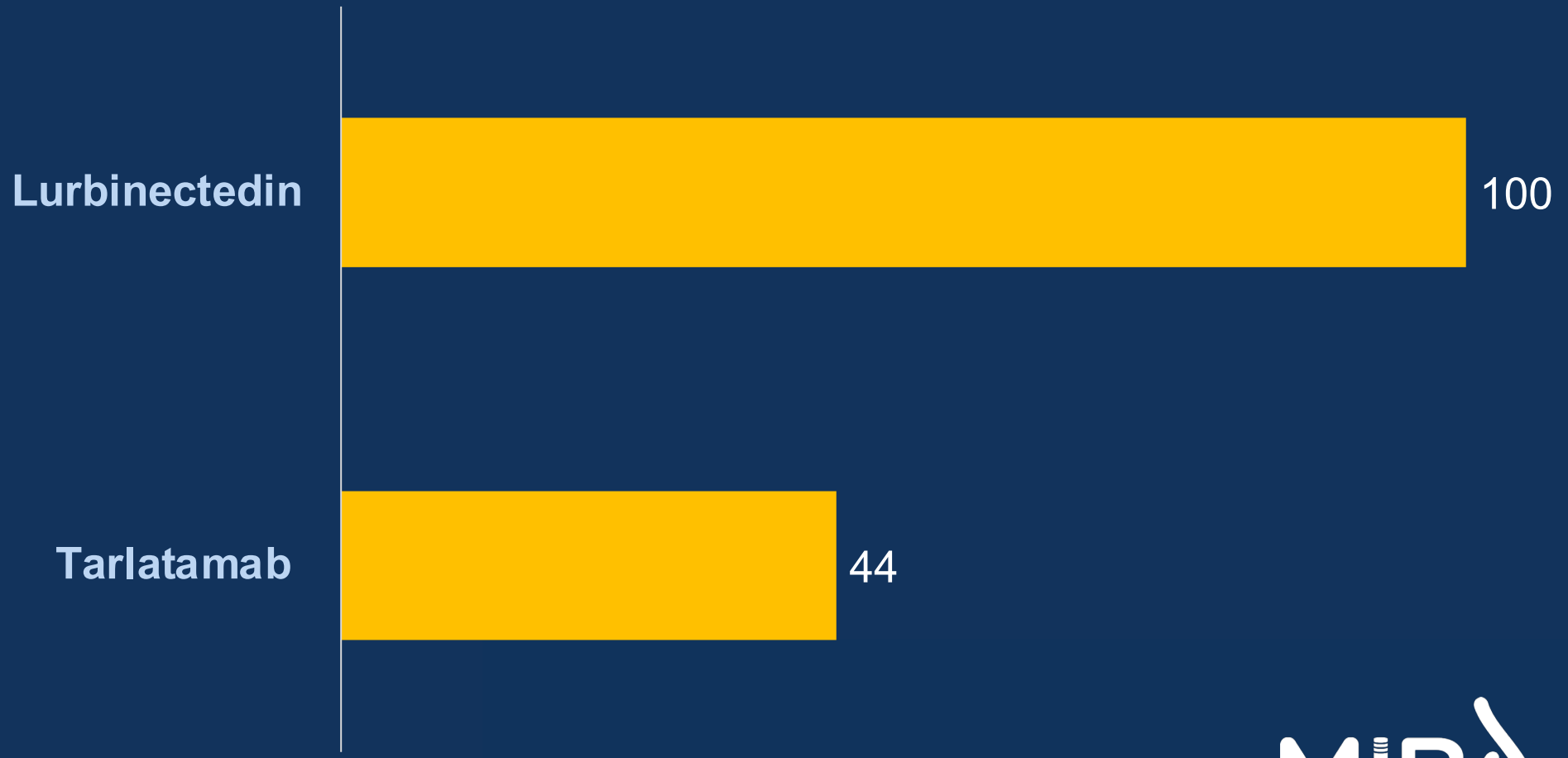
Snapshot of AON Practice
Lung Cancer — Other Targeted Agents



Snapshot of AON Practice
Lung Cancer — Immunotherapy



Snapshot of AON Practice
Small Cell Lung Cancer



Agenda

Module 1 — Lung Cancer: *Drs Gainor, Langer and Shields*

- **Targeted Therapy for Non-Small Cell Lung Cancer (NSCLC) —** *Dr Gainor*
- **Nontargeted Therapy for NSCLC; Small Cell Lung Cancer —** *Dr Langer*
- **Neoadjuvant, Perioperative and Adjuvant Anti-PD-1/PD-L1 Antibody-Based Approaches for Patients with Localized NSCLC —** *Dr Shields*

Targeted Therapies for NSCLC

Justin F. Gainor, M.D.
Director, Center for Thoracic Cancers
Director, Targeted Immunotherapy
Massachusetts General Hospital
Harvard Medical School

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

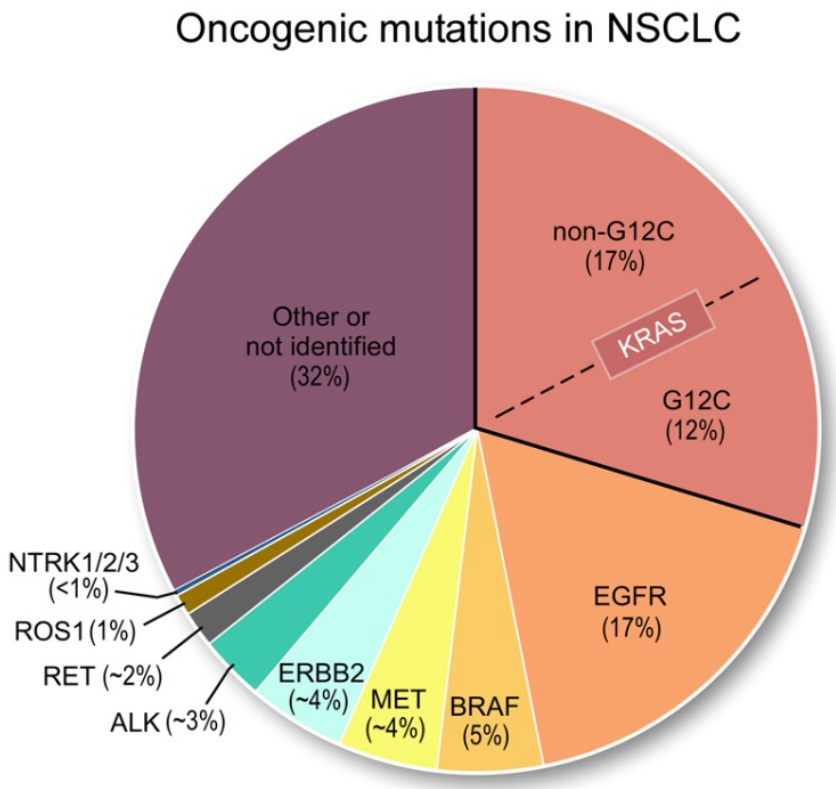
Targeted Therapies with Regulatory Approvals

NTRK
Larotrectinib
Entrectinib
Repotrectinib

ROS1
Crizotinib
Entrectinib
Repotrectinib
Taletrectinib

RET
Selpercatinib
Pralsetinib

ALK
Crizotinib
Alectinib
Brigatinib
Ceritinib
Ensartinib
Lorlatinib



KRAS G12C
Sotorasib
Adagrasib

Classical EGFR Mutations
Osimertinib
Erlotinib
Gefitinib
Afatinib
Dacomitinib
Lazertinib + Amivantamab

Exon 20 Mutations
Amivantamab
Sunvozertinib

NRG1
Zenocutuzumab

HER2
T-DXd
Zongertinib

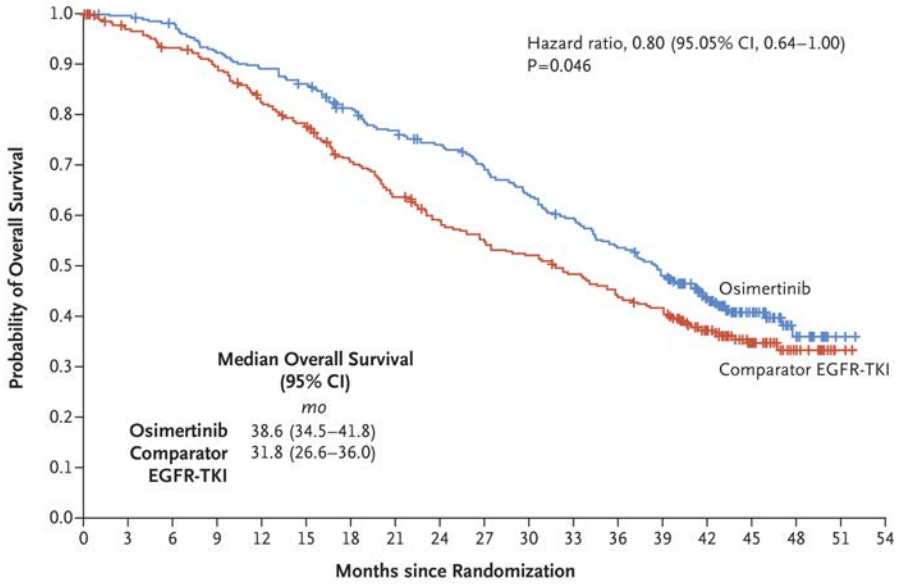
MET
Capmatinib
Tepotinib

BRAF
Dab/Trametinib
Enco/Binimetinib

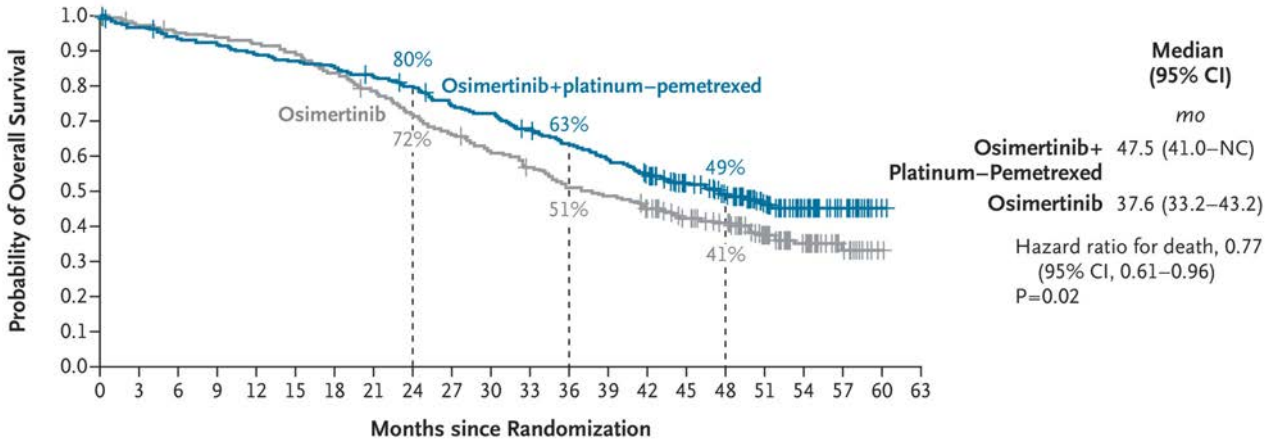
Adapted from Thai A, et al. Lancet 2021

EGFR-Mutant NSCLC: 1st Line

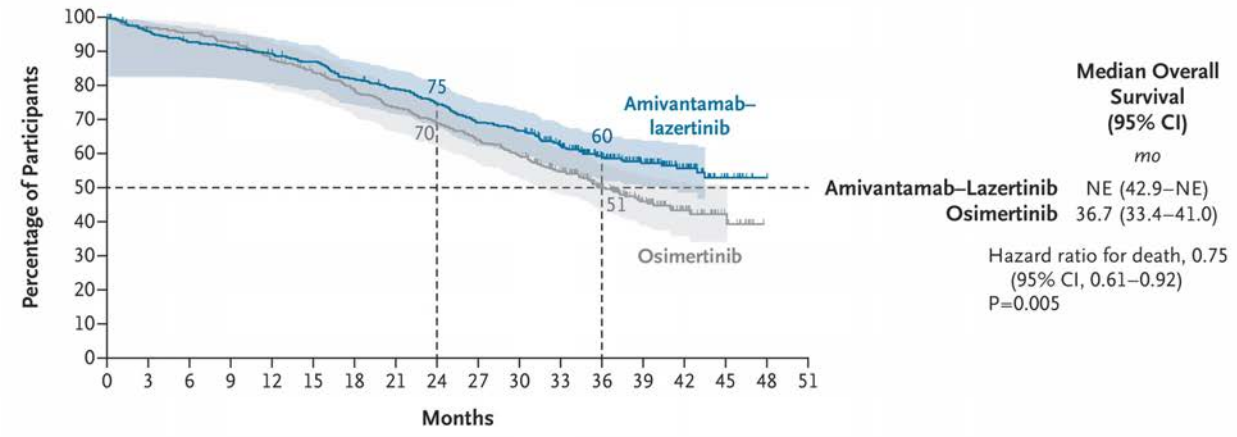
FLAURA



FLAURA2



MARIPOSA



Ramalingam S, et al. NEJM 2020; Janne P, et al. NEJM 2025; Yang JC, et al. NEJM 2025

MARIPOSA-2

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1
- Stable brain metastases were allowed; radiation/definitive therapy was not required (untreated)

Stratification Factors

- Osimertinib line of therapy (1st vs 2nd)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=657)

Serial brain MRIs were required for all patients[a]

- **Amivantamab-Lazertinib-Chemotherapy (n=263)**
- **Chemotherapy (n=263)**
- **Amivantamab-Chemotherapy (n=131)**

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at Cycle 3 (week 7)

Lazertinib: 240 mg daily starting after completion of carboplatin[b]

Chemotherapy administered at the beginning of every cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m² until disease progression

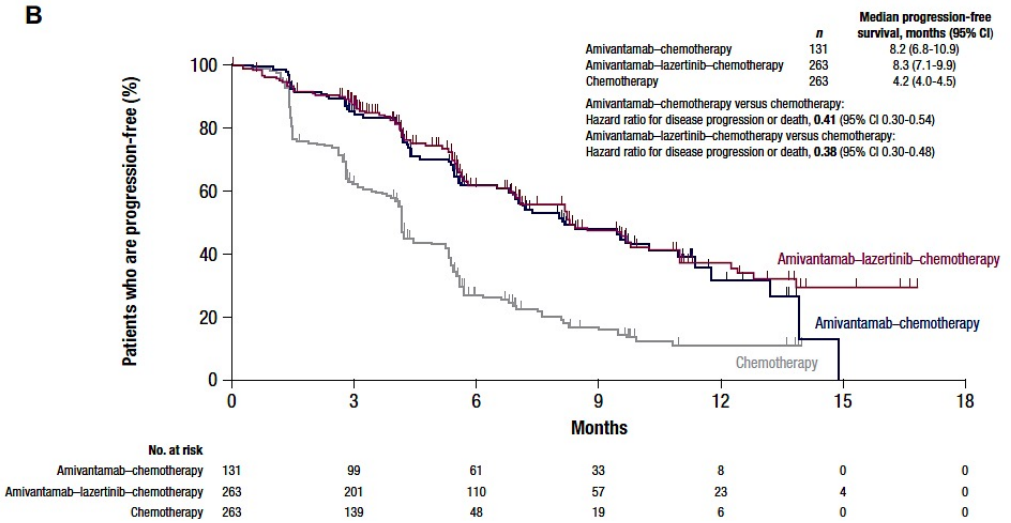
Dual primary endpoint of PFS[c] by BICR per RECIST v1.1:

- **Amivantamab-Lazertinib-Chemotherapy** vs **Chemotherapy**
- **Amivantamab-Chemotherapy** vs **Chemotherapy**

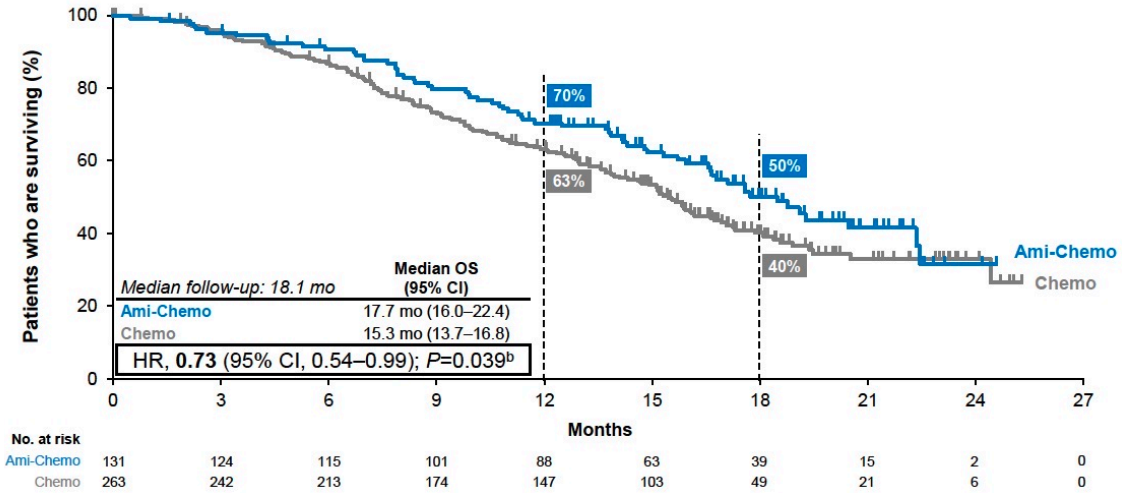
Secondary endpoints:

- Objective response rate (ORR)[c]
- Duration of response (DoR)
- Overall survival (OS)[c]
- Intracranial PFS
- Time to subsequent therapy[d]
- PFS after first subsequent therapy (PFS2)[d]
- Symptomatic PFS[d]
- Safety

PFS

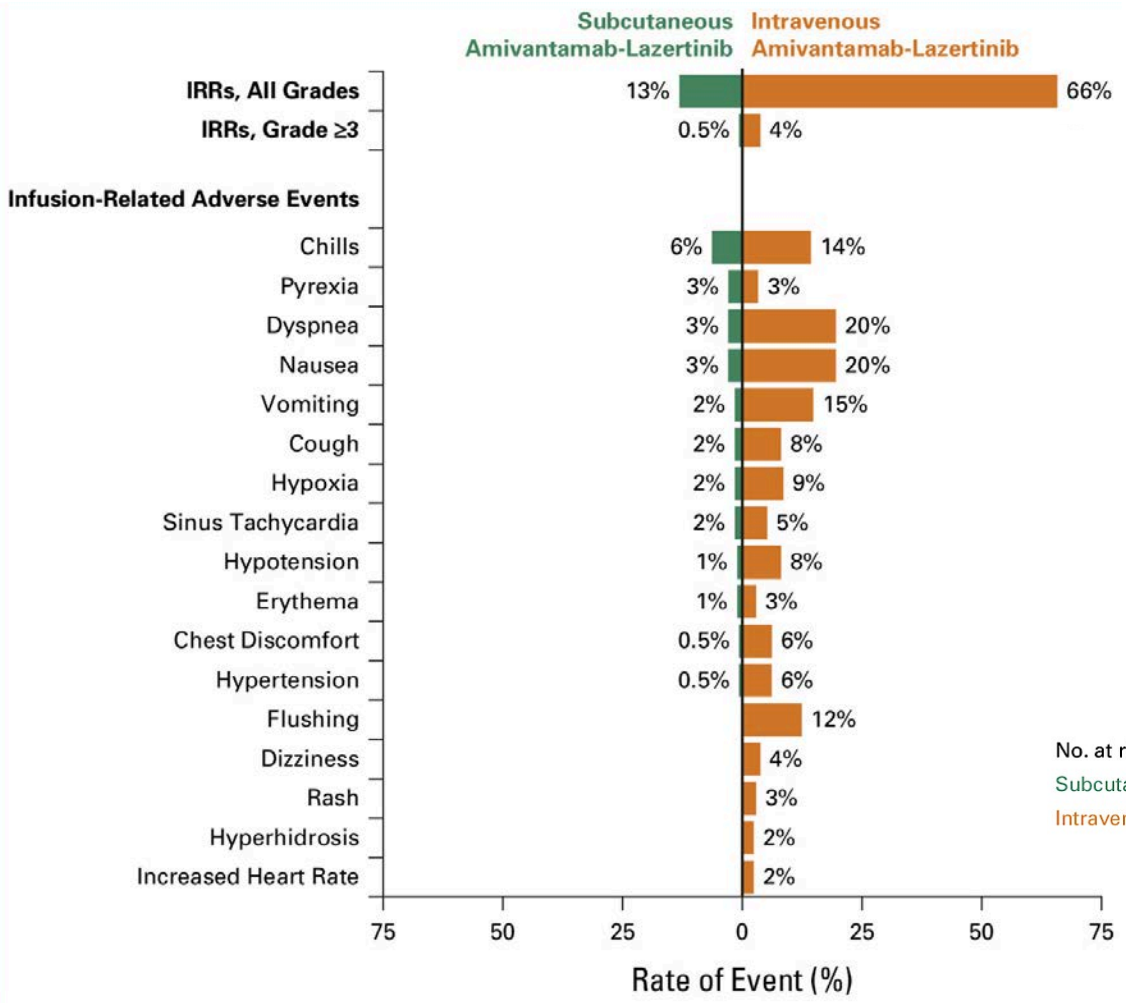


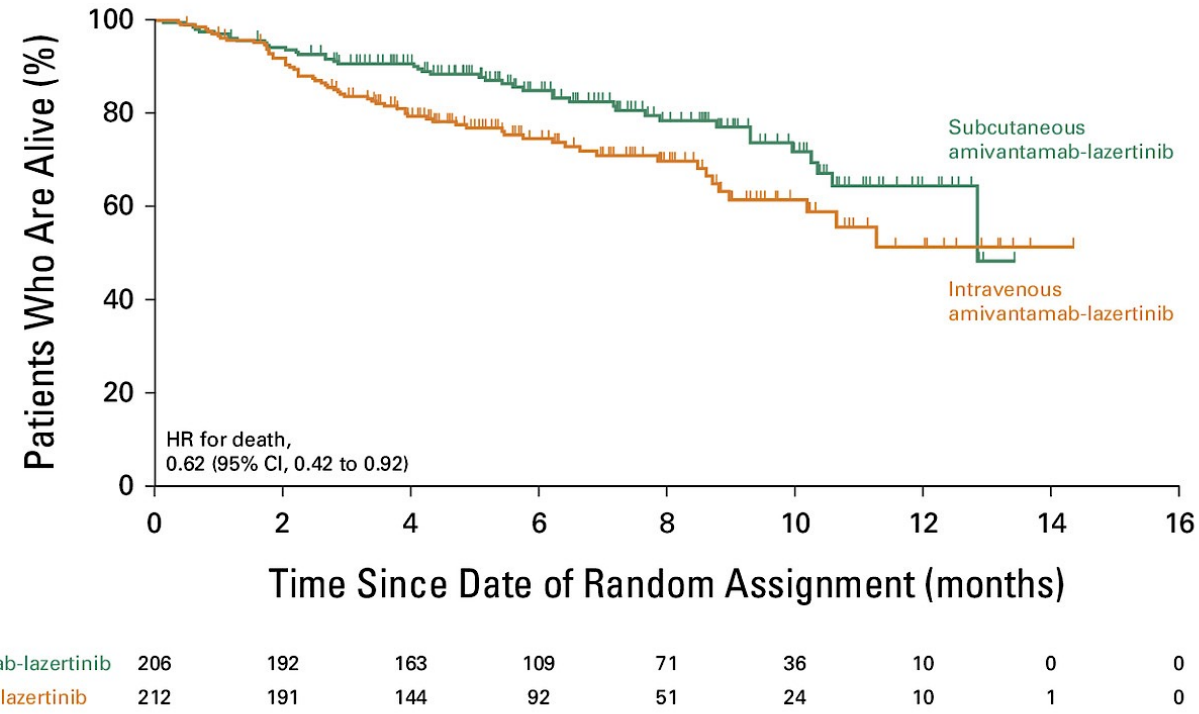
OS



Passaro A, et al. ESMO 2023; Passaro A, et al. Ann Oncol 2023; Popat S, et al. ESMO 2024

PALOMA-3: Subcutaneous Amivantamab





No. at risk

Subcutaneous amivantamab-lazertinib	206	192	163	109	71	36	10	0	0
Intravenous amivantamab-lazertinib	212	191	144	92	51	24	10	1	0

Leighl N, et al. JCO 2024

Datopotamab Deruxtecan

TROPION-Lung05 (Phase II study)

- **Presence of ≥1 actionable genomic alteration** (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
  - ≥1 line of targeted therapy
  - 1–2 prior cytotoxic agent–containing therapies including Pt-CT in the metastatic setting
  - Radiographic disease progression after most recent therapy

TROPION-Lung01 (Phase III study)

- **In those with actionable genomic alterations** (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
  - 1–2 prior approved targeted therapies + Pt-CT, and ≤1 anti–PD-(L)1 mAb
  - No prior docetaxel

R 1:1

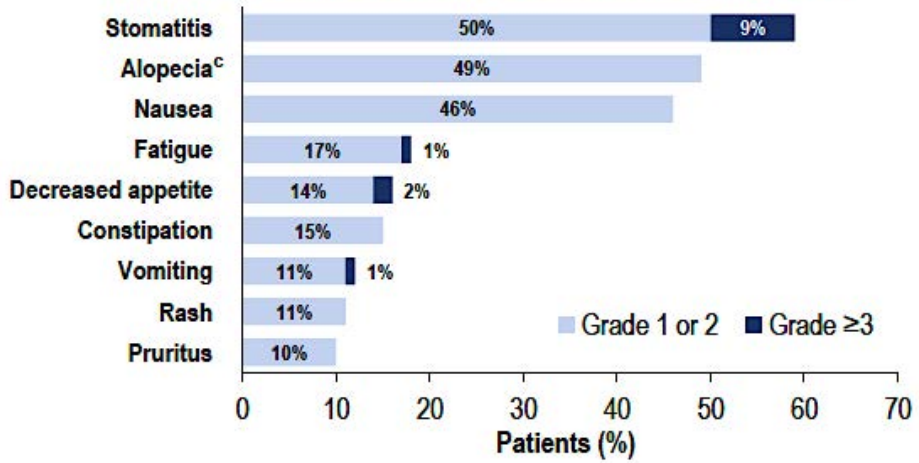
- Dato-DXd 6 mg/kg Q3W[a] (N=137)
- Dato-DXd 6 mg/kg Q3W[b] (N=299)
- Docetaxel 75 mg/m² Q3W[b] (N=305)

*EGFR*m Pool: N=117
- TROPION-Lung05 (n=78)
- TROPION-Lung01 (n=39)

Endpoints:
- ORR per BICR
- BOR per BICR
- DCR per BICR
- DOR per BICR
- PFS per BICR
- OS
- Safety

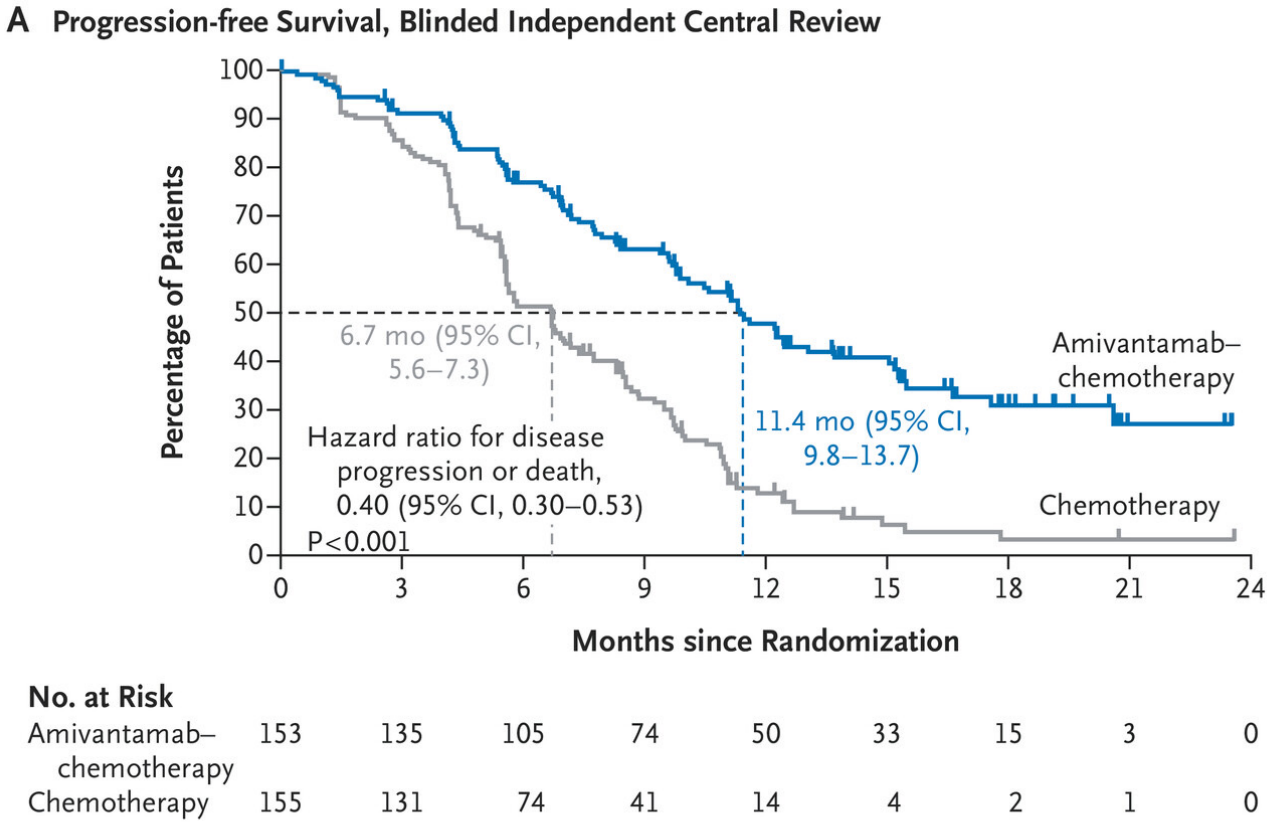
Response	*EGFR*m Pool (N=117)	Prior Osimertinib (N=96)
Confirmed ORR,[a] n (%) [95% CI]	50 (**42.7**) [33.6–52.2]	43 (**44.8**) [34.6–55.3]
BOR, n (%)		
CR	5 (**4.3**)	4 (**4.2**)
PR	45 (**38.5**)	39 (**40.6**)
SD	48 (41.0)	37 (38.5)
Non-CR/Non-PD	3 (2.6)	2 (2.1)
PD	12 (10.3)	10 (10.4)
NE	4 (3.4)	4 (4.2)
Median DOR, months (95% CI)	**7.0** (4.2–9.8)	**6.9** (4.2–9.8)
DCR,[b] n (%) [95% CI]	101 (**86.3**) [78.7–92.0]	82 (**85.4**) [76.7–91.8]
Median PFS, months (95% CI)	**5.8** (5.4–8.2)	**5.7** (5.4–7.9)
Median OS, months (95% CI)	**15.6** (13.1–19.0)	**14.7** (13.0–18.3)

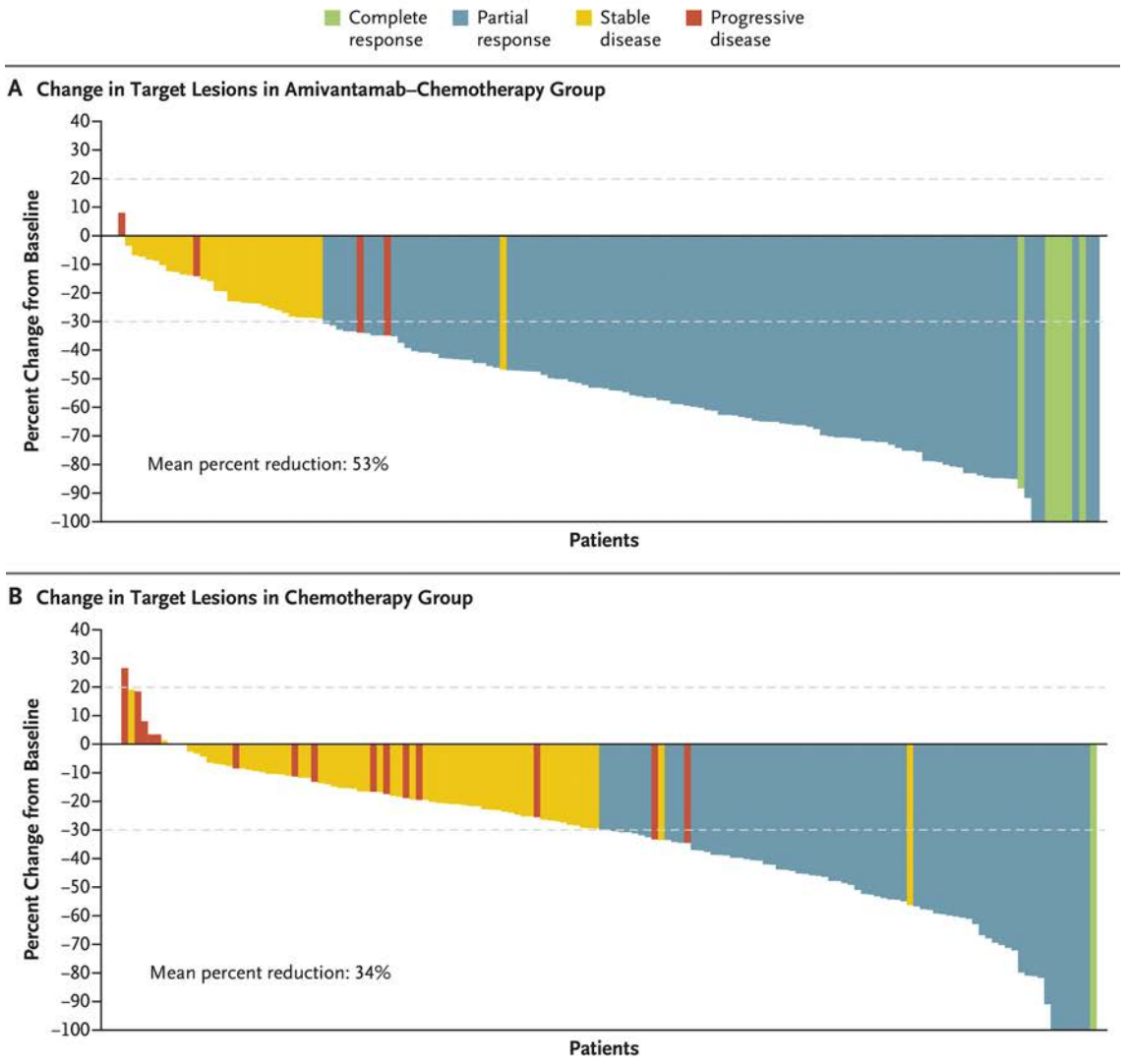
TRAEs Occurring in ≥10% of *EGFR*m Pool (N=117)



Ahn MJ, et al. ESMO Asia 2024

EGFR Exon 20 Mutations: PAPILLON





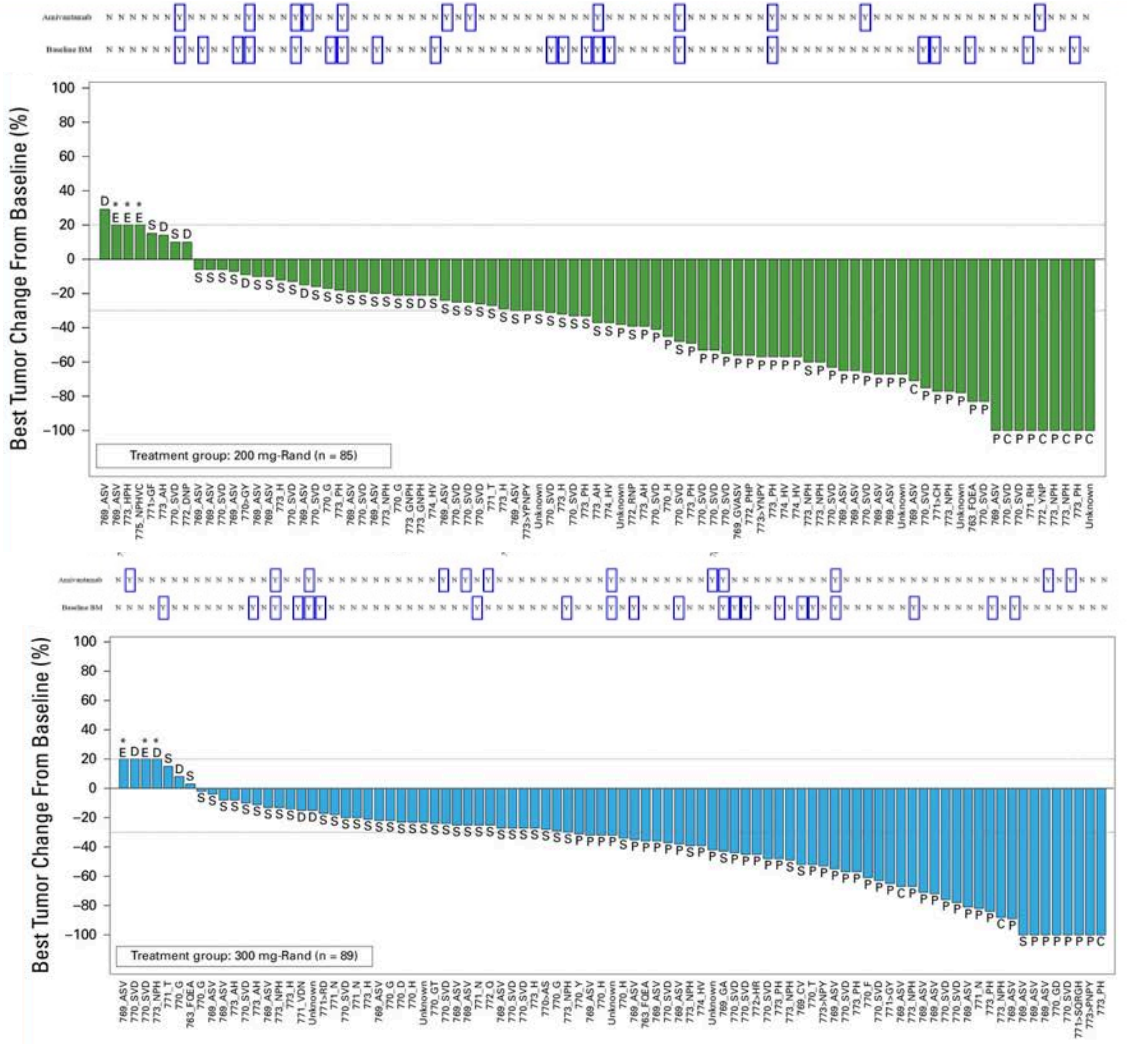
Zhou C, et al. NEJM 2023

Sunvozertinib: Anti-Tumor Efficacy

Anti-tumor Efficacy

Tumor Response Per BICR		200 mg (N = 85)	300 mg (N = 89)
Confirmed ORR (%, 97.5% CI)		45.9 (33.6, 58.5)	47.2 (35.1, 59.5)
Disease Control Rate (%, 97.5% CI)		89.4 (79.6, 95.6)	92.1 (83.3, 97.2)
Best Overall Response (n, %)			
Complete Response		5 (5.9)	3 (3.4)
Partial Response		34 (40.0)	39 (43.8)
Stable Disease		37 (43.5)	40 (44.9)
Progressive Disease		6 (7.1)	5 (5.6)
Not Evaluable		3 (3.5)	2 (2.2)
Median DoR (months, 95% CI)		11.1 (8.2, NE)	13.8 (8.3, NE)
Median PFS (months, 95% CI)		8.4 (6.8, 13.9)	7.7 (6.0, 9.8)
Subgroup Analysis of Confirmed ORR (%)			
Prior Amivantamab Treatment	With	25.0	41.7
	Without	49.3	48.1
Baseline Brain Metastasis	With	28.6	52.4
	Without	51.6	45.6

Data cut-off date: December 2, 2024.
BICR: Blinded Independent Central Review; ORR: Objective Response Rate; DoR: duration of response; PFS: Progression Free Survival, CI: Confidence Interval; NE: Not Estimable.



C: Complete Response; P: Partial Response; S: Stable Disease; D: Progressive Disease; E: Not Evaluable; BM: Brain Metastasis. For the patient with tumor size missing, the best change from baseline was reported as 20% increase if the patient had objective progression, discontinued treatment due to PD or died. Such patient was flagged *.

Janne P, WCLC 2025 and Yang JCH, JCO 2025

Sunvozertinib: Treatment-Related Adverse Events

TABLE A4. The Common (≥20%) TRAE by Maximum CTCAE Grade

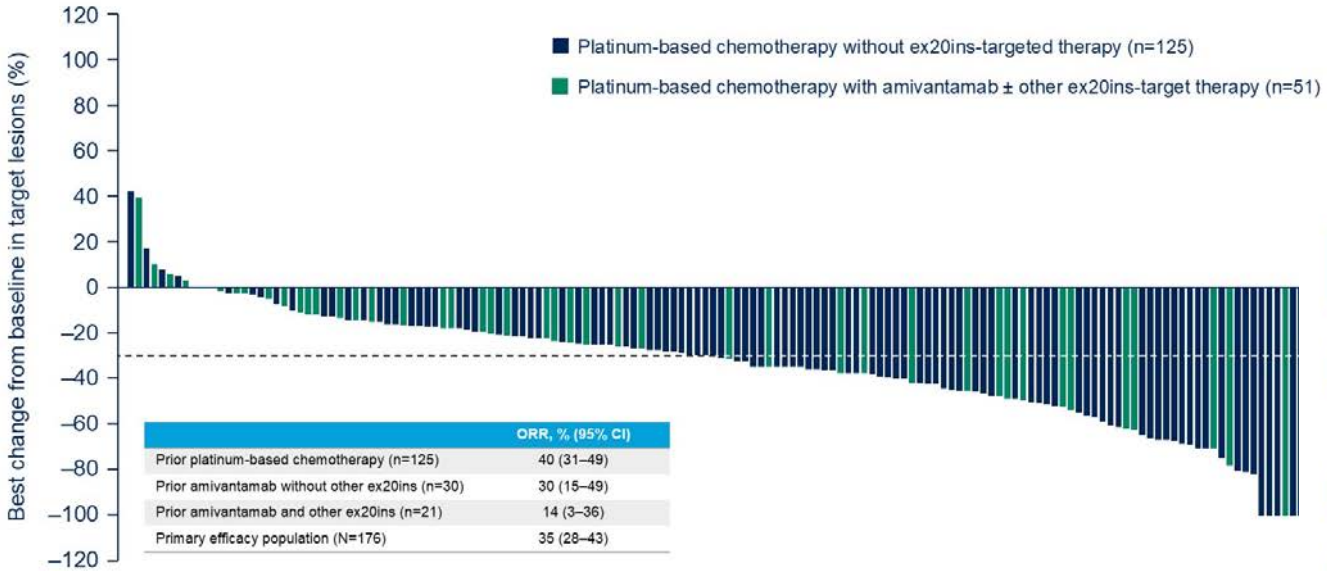
	200 mg-Rand (n = 91), No. (%)					300 mg-All (n = 111), No. (%)				
Preferred Term	All Grades	Grade 1	Grade 2	Grade 3	Grade 4	All Grades	Grade 1	Grade 2	Grade 3	Grade 4
Patients with any TRAE	86 (94.5)	12 (13.2)	37 (40.7)	34 (37.4)	3 (3.3)	108 (97.3)	8 (7.2)	35 (31.5)	56 (50.5)	9 (8.1)
Diarrhea	62 (68.1)	44 (48.4)	16 (17.6)	2 (2.2)	0 (0.0)	92 (82.9)	51 (45.9)	21 (18.9)	20 (18.0)	0 (0.0)
Blood creatine phosphokinase increased	32 (35.2)	14 (15.4)	12 (13.2)	6 (6.6)	0 (0.0)	58 (52.3)	28 (25.2)	16 (14.4)	12 (10.8)	2 (1.8)
Rash	37 (40.7)	26 (28.6)	7 (7.7)	4 (4.4)	0 (0.0)	53 (47.7)	33 (29.7)	15 (13.5)	5 (4.5)	0 (0.0)
Nausea	25 (27.5)	15 (16.5)	8 (8.8)	2 (2.2)	0 (0.0)	44 (39.6)	33 (29.7)	9 (8.1)	2 (1.8)	0 (0.0)
Anemia	28 (30.8)	15 (16.5)	9 (9.9)	4 (4.4)	0 (0.0)	42 (37.8)	18 (16.2)	17 (15.3)	7 (6.3)	0 (0.0)
Paronychia	24 (26.4)	13 (14.3)	11 (12.1)	0 (0.0)	0 (0.0)	42 (37.8)	24 (21.6)	17 (15.3)	1 (0.9)	0 (0.0)
Vomiting	26 (28.6)	16 (17.6)	10 (11.0)	0 (0.0)	0 (0.0)	41 (36.9)	29 (26.1)	11 (9.9)	1 (0.9)	0 (0.0)
Decreased appetite	39 (42.9)	26 (28.6)	13 (14.3)	0 (0.0)	0 (0.0)	34 (30.6)	19 (17.1)	11 (9.9)	4 (3.6)	0 (0.0)
Dry skin	18 (19.8)	12 (13.2)	6 (6.6)	0 (0.0)	0 (0.0)	27 (24.3)	24 (21.6)	3 (2.7)	0 (0.0)	0 (0.0)
Blood creatinine increased	25 (27.5)	19 (20.9)	5 (5.5)	1 (1.1)	0 (0.0)	25 (22.5)	22 (19.8)	3 (2.7)	0 (0.0)	0 (0.0)
Pruritus	23 (25.3)	20 (22.0)	2 (2.2)	1 (1.1)	0 (0.0)	25 (22.5)	18 (16.2)	6 (5.4)	1 (0.9)	0 (0.0)
Stomatitis	20 (22.0)	14 (15.4)	5 (5.5)	1 (1.1)	0 (0.0)	19 (17.1)	11 (9.9)	7 (6.3)	1 (0.9)	0 (0.0)
Lipase increased	21 (23.1)	11 (12.1)	8 (8.8)	1 (1.1)	1 (1.1)	16 (14.4)	7 (6.3)	5 (4.5)	3 (2.7)	1 (0.9)

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; TRAE, treatment-related adverse event.

Janne P, WCLC 2025 and Yang JCH, JCO 2025

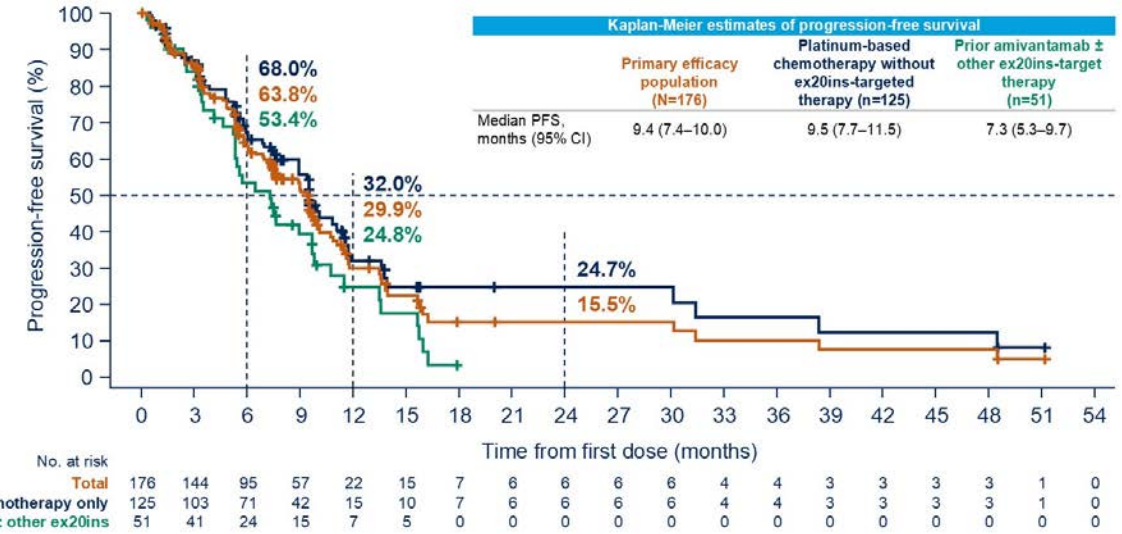
Zipalertinib Updates (ASCO 2025)

Best Tumor Response



	ORR, % (95% CI)
Prior platinum-based chemotherapy (n=125)	40 (31–49)
Prior amivantamab without other ex20ins (n=30)	30 (15–49)
Prior amivantamab and other ex20ins (n=21)	14 (3–36)
Primary efficacy population (N=176)	35 (28–43)

PFS (ICR)



Kaplan-Meier estimates of progression-free survival	Primary efficacy population (N=176)	Platinum-based chemotherapy without ex20ins-targeted therapy (n=125)	Prior amivantamab ± other ex20ins-target therapy (n=51)
Median PFS, months (95% CI)	9.4 (7.4–10.0)	9.5 (7.7–11.5)	7.3 (5.3–9.7)

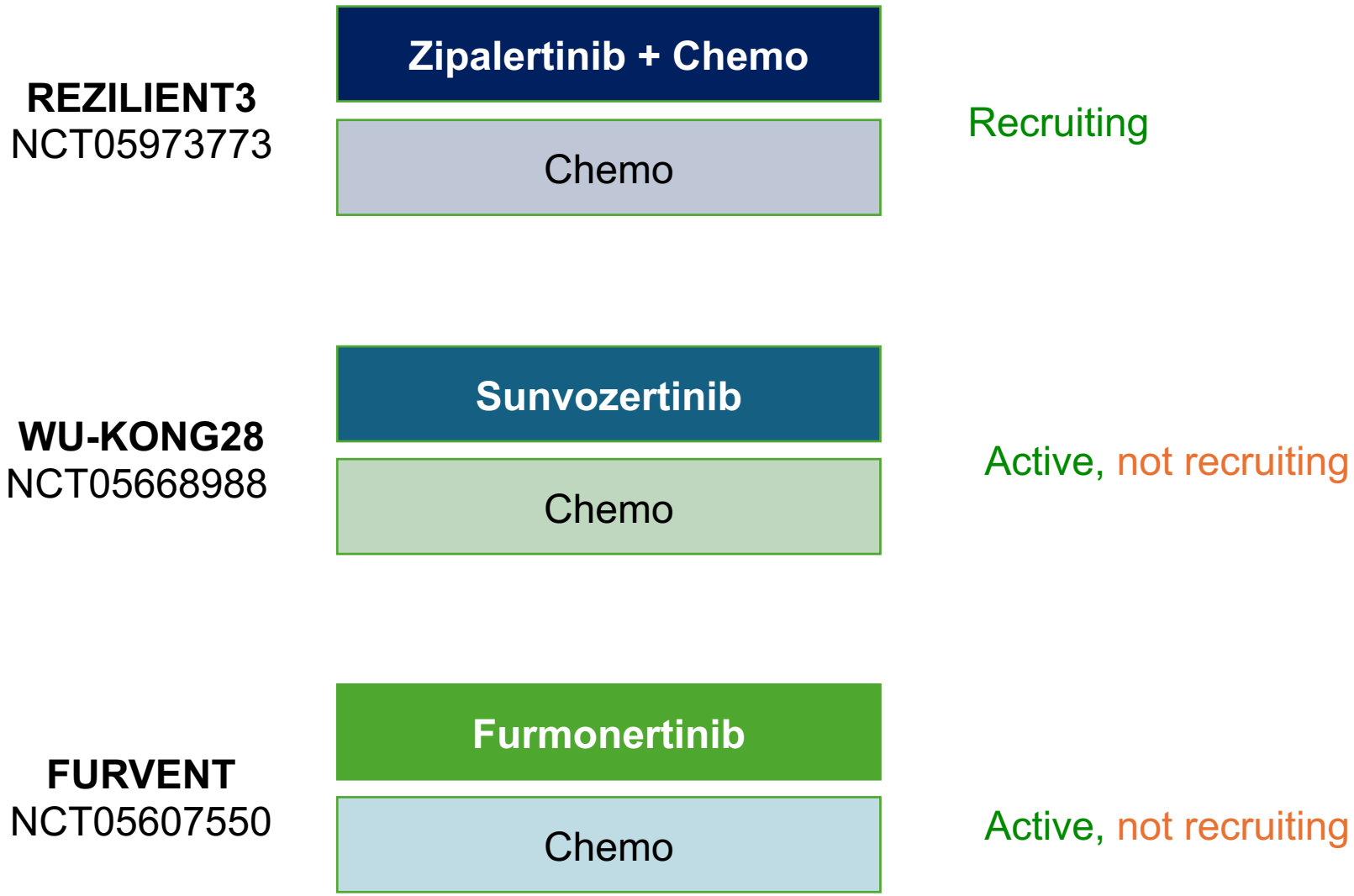
No. at risk																			
Total	176	144	95	57	22	15	7	6	6	6	6	4	4	3	3	3	3	1	0
Platinum-based chemotherapy only	125	103	71	42	15	10	7	6	6	6	6	4	4	3	3	3	3	1	0
Prior amivantamab ± other ex20ins	51	41	24	15	7	5	0	0	0	0	0	0	0	0	0	0	0	0	0

Treatment-Related AEs

Any-grade TRAEs reported in ≥10% of patients, No. (%)	Any grade	Grade 3
Paronychia	94 (38.5)	0
Rash	74 (30.3)	6 (2.5)
Dermatitis acneiform	60 (24.6)	1 (0.4)
Dry skin	60 (24.6)	0
Diarrhea	53 (21.7)	5 (2.0)
Stomatitis	49 (20.1)	4 (1.6)
Anemia	48 (19.7)	17 (7.0)
Pruritus	44 (18.0)	1 (0.4)
Nausea	35 (14.3)	2 (0.8)
Rash maculopapular	34 (13.9)	3 (1.2)
Fatigue	29 (11.9)	0

Yu HA, ASCO 2025 and Piotrowska Z, WCLC 2025

Ongoing First-Line EGFR Exon 20 TKI Trials

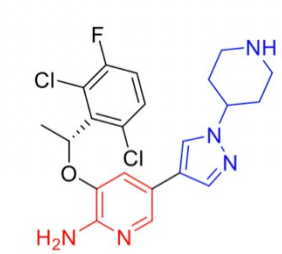


Slide courtesy of Z Piotrowska

ALK Inhibitors

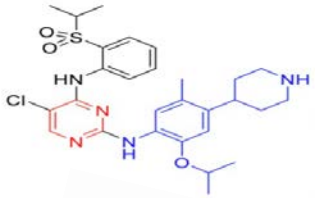
First-Generation

Crizotinib

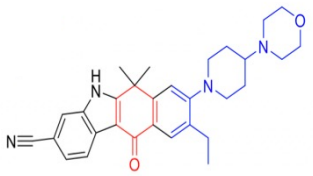


Second-Generation

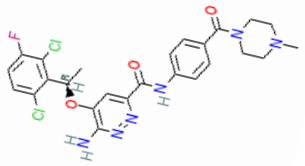
Ceritinib



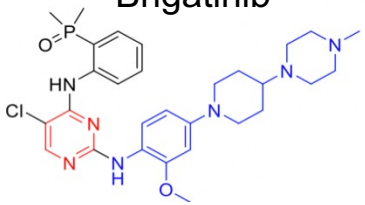
Alectinib



Ensartinib

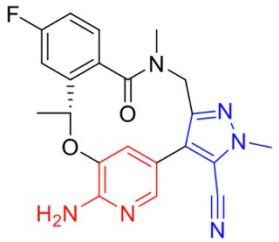


Brigatinib



Third-Generation

Lorlatinib



Potency

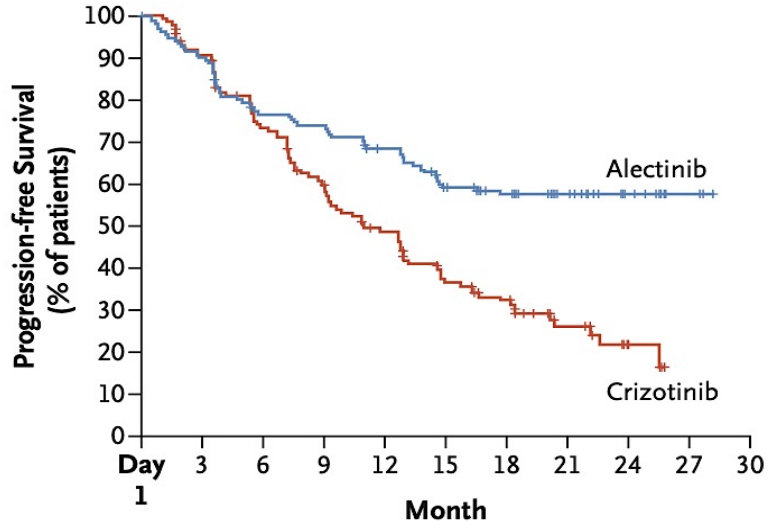
CNS Penetration

ALK Resistance Coverage

Global ALEX Study

Progression-Free Survival

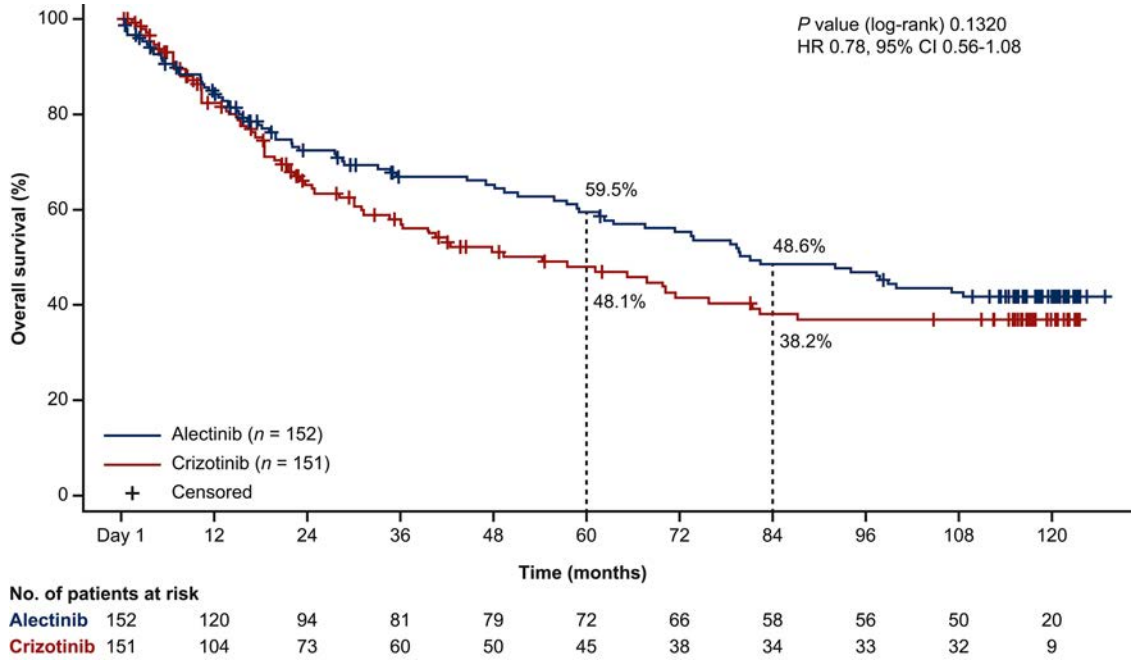
	Crizotinib	Alectinib
Median PFS (months) (95% CI)	11.1 (9.1-13.1)	NR (17.7-NR)
HR (95% CI)	0.47 (0.34-0.65)	
P-value	P <.0001	



No. at Risk

Alectinib	152	135	113	109	97	81	67	35	15	3
Crizotinib	151	132	104	84	65	46	35	16	5	

Overall Survival



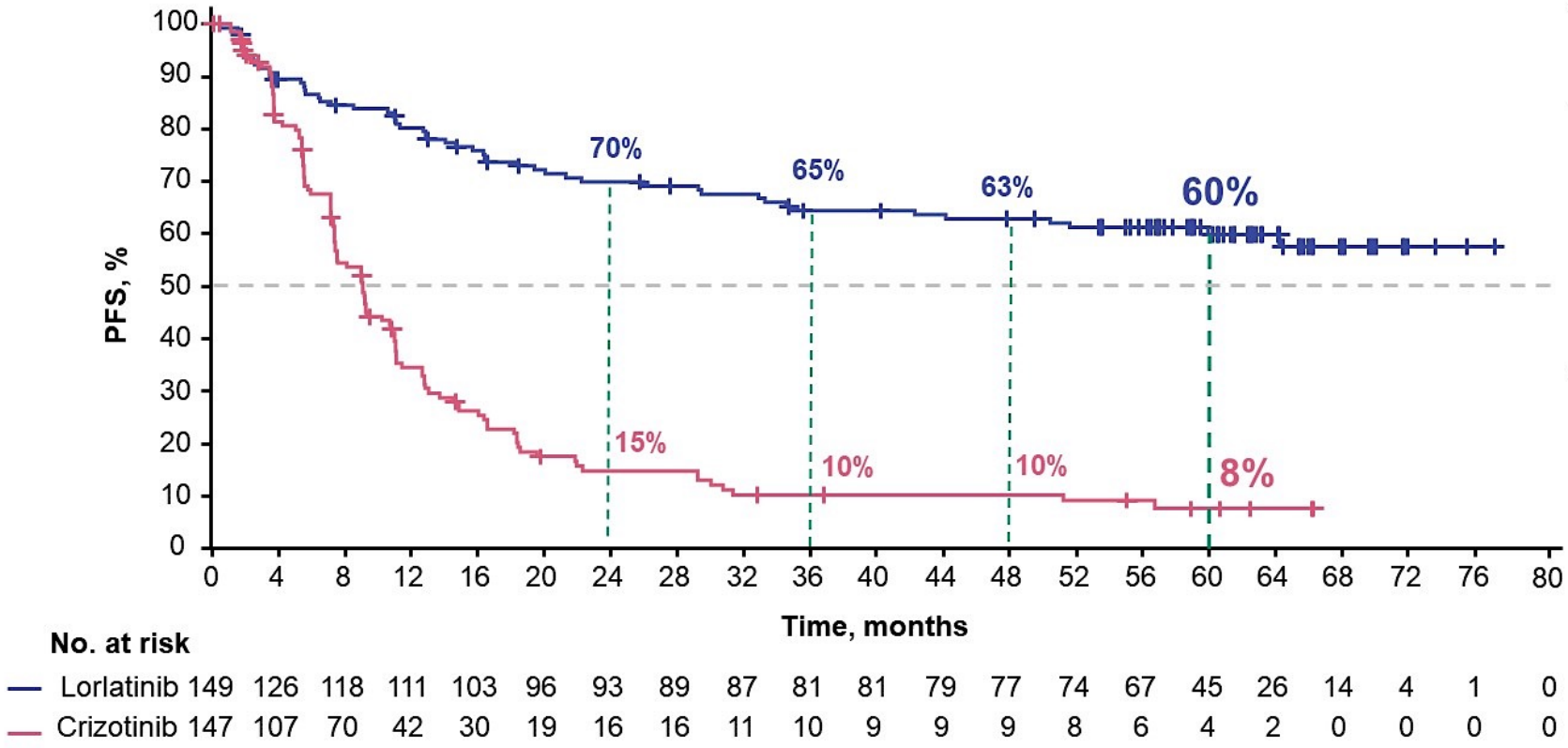
No. of patients at risk

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

	Alectinib (n=152)	Crizotinib (n=151)
Patients with event, n (%)	76 (**50.0**)	73 (**48.3**)
Median, months (95% CI)	**81.1** (62.3–NE)	**54.2** (34.6–75.6)
Stratified HR (95% CI)	**0.78** (0.56–1.08)	
p-value (stratified log-rank)	0.1320	

1. Peters S, et al. *N Engl J Med.* 2017;377:829-838. 2. Camidge DR, et al. *N Engl J Med.* 2018;379:2027-2039.
3. Mok T et al. ESMO 2025;Abstract LBA73. 4. Peters S et al. Ann Oncol. 2025

CROWN



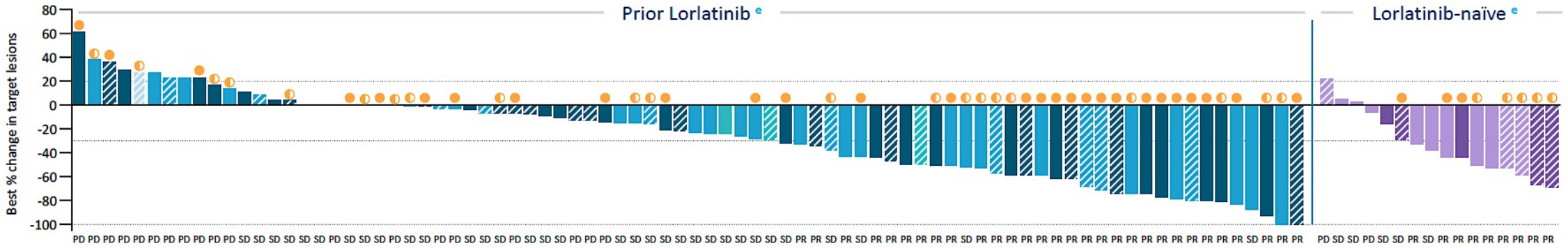
	Lorlatinib (n=149)	Crizotinib (n=147)
Events, n	55	115
PFS, median (95% CI), months	NR (64.3-NR)	9.1 (7.4-10.9)
HR (95% CI)	**0.19 (0.13-0.27)**	

At the time of this analysis, the required number of OS events for a protocol-specified second interim analysis **has not been reached**. OS follow up is ongoing

Solomon B, et al. ASCO 2024

Neladalkib (NVL-655)

RECIST 1.1 ORR, % (n/N) *All patients ± chemotherapy*	NSCLC Response-Evaluable (Any Prior ALK TKI, range 1 – 5)			Prior Lorlatinib (≥2 ALK TKIs)			Lorlatinib-naive (≥1 2G ± 1G)	
	All	Any ALK mutation [a]	G1202R [b]	All	Any ALK mutation	Compound ALK mutation [c]	All	Any ALK mutation
All Doses	**38%** (39/103)	**52%** (30/58)	**69%** (22/32) [d]	**35%** (30/85)	**47%** (23/49)	**54%** (15/28)	**53%** (9/17)	**88%** (7/8)
RP2D	**38%** (15/39)	**55%** (12/22)	**71%** (10/14)	**35%** (11/31)	**50%** (8/16)	**64%** (7/11)	**57%** (4/7)	**80%** (4/5)



Data cut-off: 15 June 2024. Response-evaluable patients with NSCLC. All responses were confirmed.

NSCLC, non-small cell lung cancer; **ORR**, objective response rate; **PD**, progressive disease; **PR**, partial response; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumours version 1.1; **RP2D**, Recommended Phase 2 dose (150 mg QD); **SD**, stable disease; **TKI**, tyrosine kinase inhibitor.

[a] Includes all patients with ≥1 identified ALK resistance mutation as per local or central testing of blood (ctDNA) or tissue. Responses observed in patients with ALK I1171N/S, V1180L, L1196Q, L1198F, D1203N, or E1210K mutations, including where multiple mutations co-occur, in addition to those with G1202R.

[b] Includes patients with G1202R single and compound (≥2) mutations.

[c] Cis-allelic configuration has not been confirmed for all patients with compound (≥2) ALK resistance mutations.

[d] **ORR = 67% (20/30) for G1202R patients with prior lorlatinib, and ORR= 100% (2/2) for lorlatinib-naïve G1202R patients.**

[e] Five response-evaluable patients (4 with no known ALK mutations and 1 with single ALK mutation) not shown due to incomplete or missing post-baseline tumor assessments in the setting of PD or symptomatic deterioration.

BARCELONA 2024 ESMO congress

KEY: PATIENT DETAILS

Lorlatinib Pre-treated:
- ≥ 3 prior ALK TKIs
- 2 prior, 2G + lorlatinib
- 2 prior, 1G + lorlatinib
- 1 prior (lorlatinib only)

Lorlatinib-naïve:
- ≥ 2 prior ALK TKIs
- 1 prior, alectinib

Patient treated at RP2D

ALK single resistance mutation

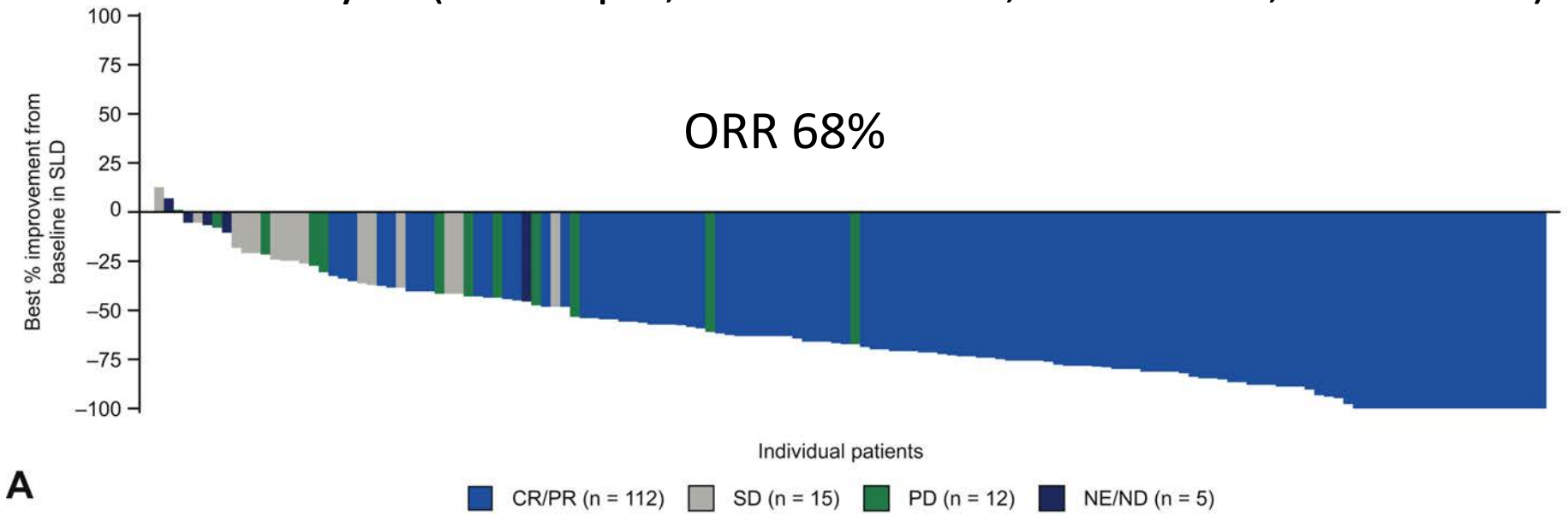
ALK compound (≥2) resistance mutation

Drilon A, et al. ESMO 2024

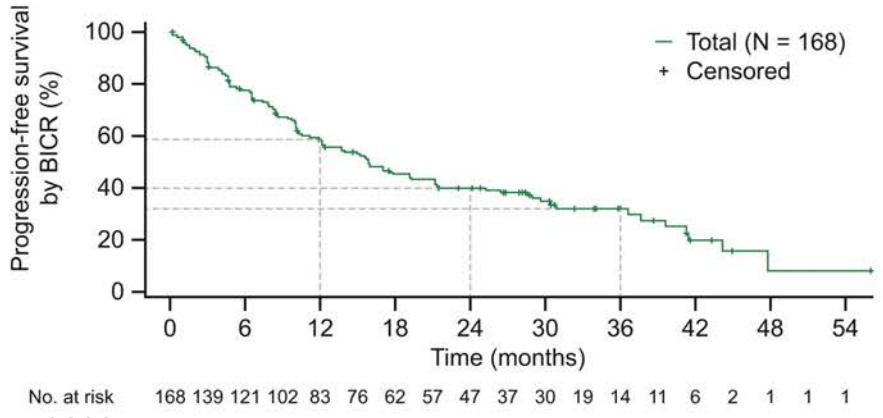
ROS1 Fusions: Entrectinib

Pooled Analysis (n=168 pts; ALKA-372-001, STARTRK-1, STARTRK-2)

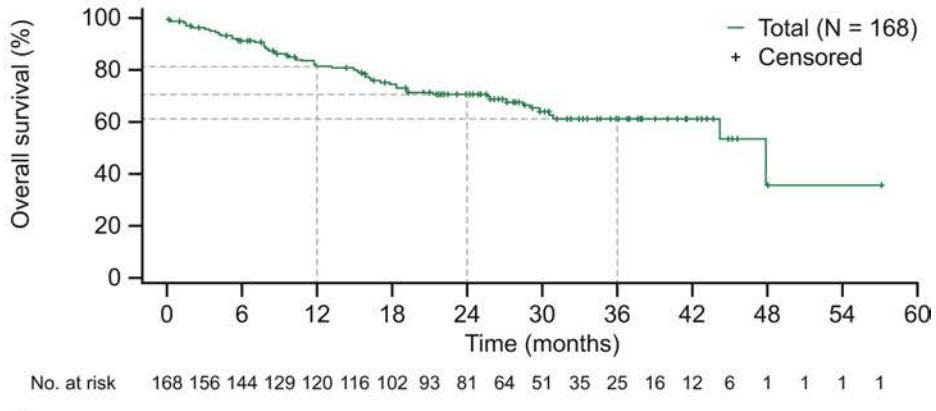
ORR 68%



mPFS 15.7 mo

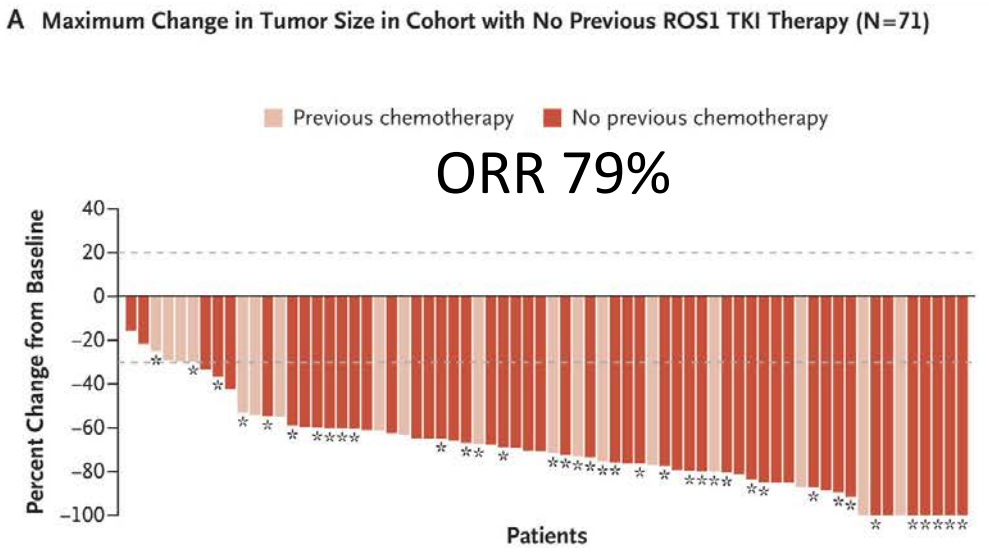


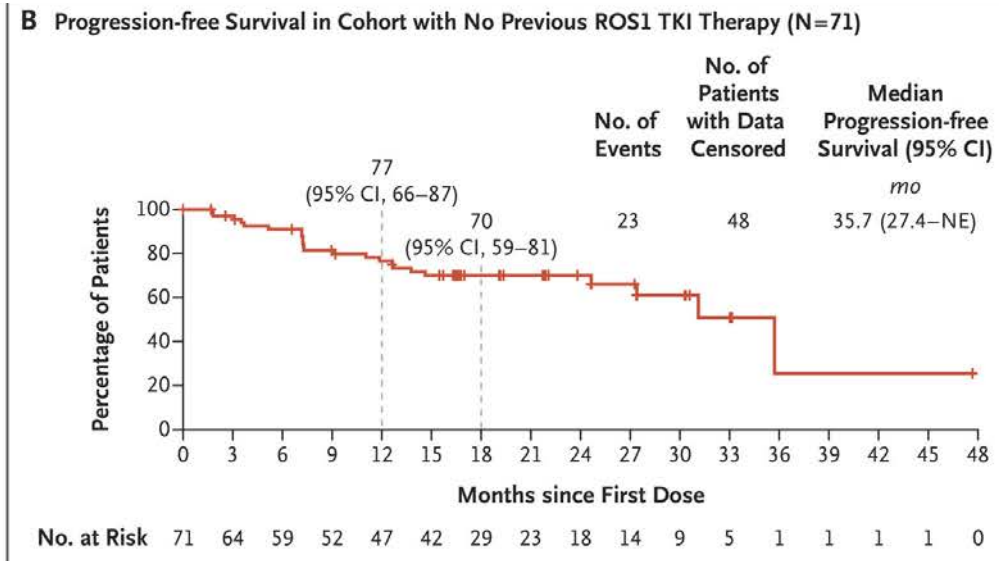
mOS 47.8 mo



Drilon A, et al. JTO CRR 2022

ROS1 Fusions: Repotrectinib





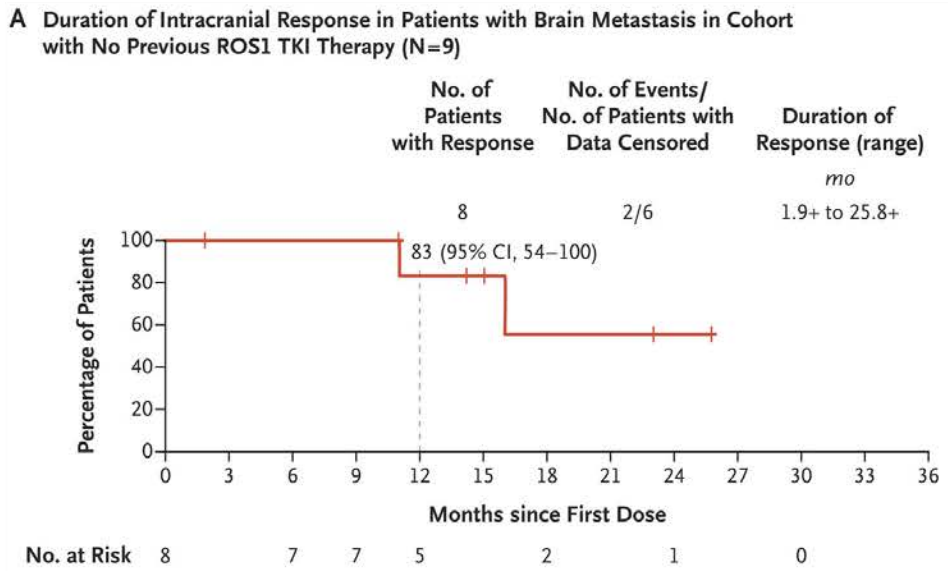
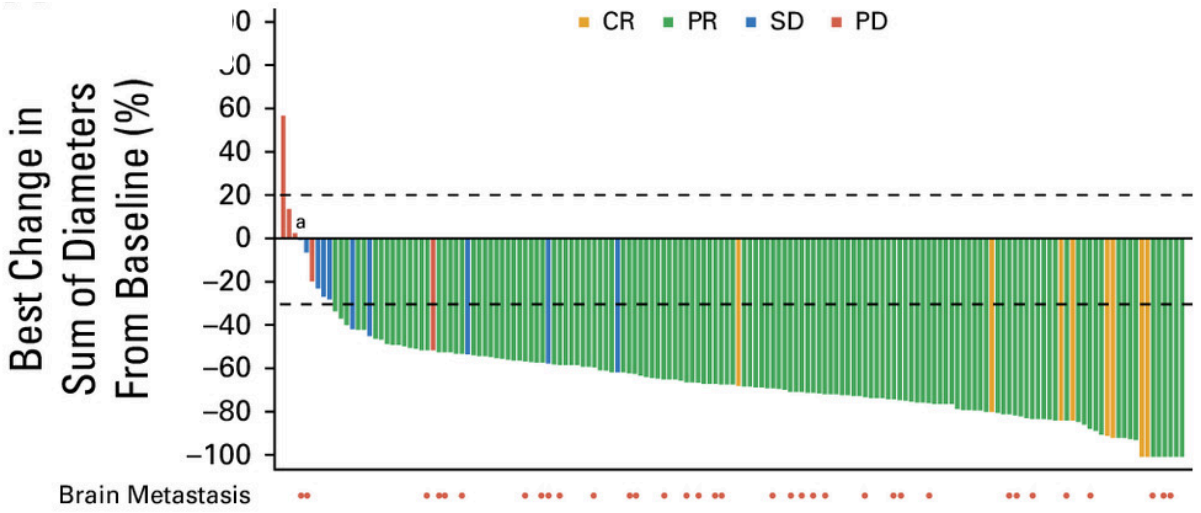


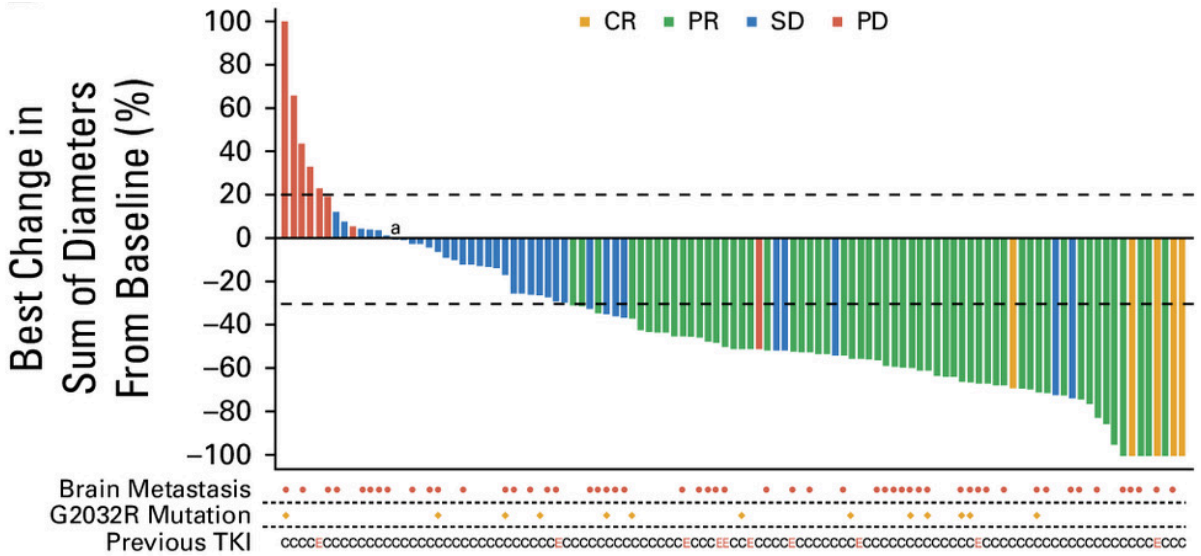
Table 3. Adverse Events in the 426 Patients Who Received the Phase 2 Dose of Repotrectinib.*

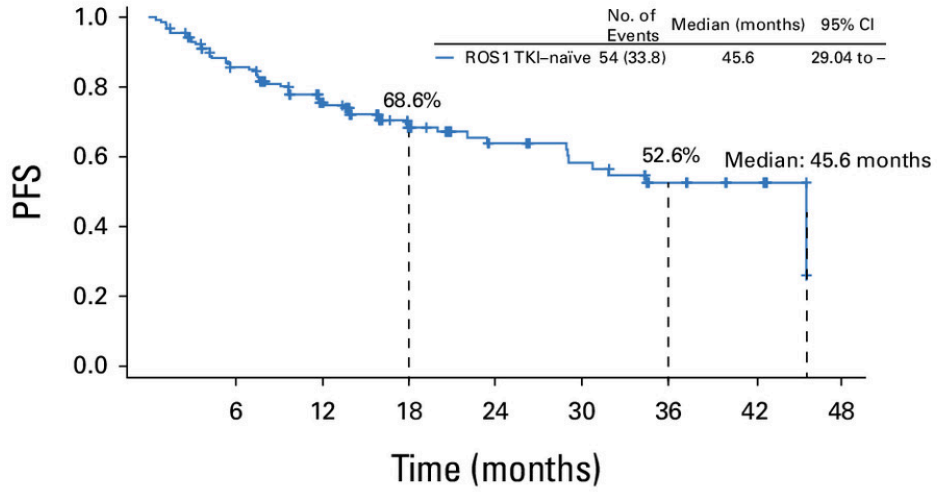
Event	During Treatment Period		Related to Treatment	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Any event	422 (99)	216 (51)	409 (96)	122 (29)
Event occurring in ≥15% of patients				
Dizziness	264 (62)	11 (3)	245 (58)	11 (3)
Dysgeusia	224 (53)	0	213 (50)	0
Constipation	162 (38)	1 (<1)	111 (26)	0
Anemia	160 (38)	33 (8)	111 (26)	16 (4)
Paresthesia	143 (34)	3 (1)	126 (30)	3 (1)
Dyspnea	117 (27)	27 (6)†	36 (8)	2 (<1)
Increased alanine aminotransferase level	99 (23)	8 (2)	76 (18)	6 (1)
Fatigue	95 (22)	4 (1)	70 (16)	3 (1)
Ataxia	90 (21)	1 (<1)	87 (20)	0
Increased aspartate aminotransferase level	89 (21)	9 (2)	75 (18)	6 (1)
Nausea	85 (20)	3 (1)	51 (12)	2 (<1)
Muscular weakness	85 (20)	8 (2)	59 (14)	6 (1)
Headache	79 (19)	0	42 (10)	0
Increased blood creatine kinase level	75 (18)	15 (4)	72 (17)	15 (4)
Weight increase	67 (16)	11 (3)	49 (12)	7 (2)
Memory impairment	65 (15)	1 (<1)	54 (13)	1 (<1)
Cough	64 (15)	1 (<1)	10 (2)	0

Drilon A, et al. NEJM 2024

Taletrectinib: TRUST I-II Pooled Analysis







Perol M, et al. JCO 2025

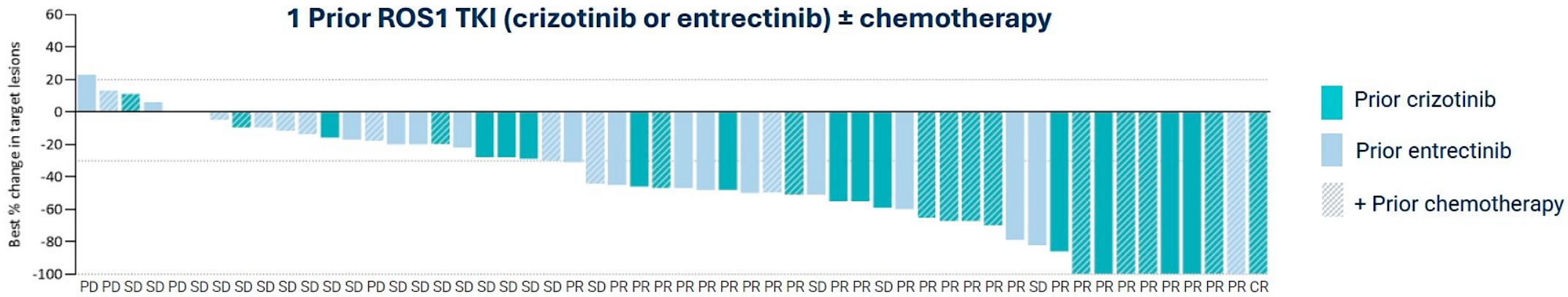
Phase I/II ARROS-1 Trial: Zidesamtinib for Advanced NSCLC with a ROS1 mutation — Responses in Patients Who Previously Received a TKI

Advanced *ROS1*+ NSCLC RECIST 1.1 by BICR	**Any prior ROS1 TKI (range 1 – 4) ± chemotherapy**	**1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy**
ORR, % (n/N) [95% CI]	**44%** (51/117) [34, 53]	**51%** (28/55) [a] [37, 65]
CR, % (n/N)	1% (1/117)	2% (1/55)

[a] Prior crizotinib only ± chemotherapy: ORR = 68% (19/28). Prior entrectinib only ± chemotherapy: ORR = 33% (9/27).

Responses were also observed in patients previously treated with:

- **≥2 prior ROS1 TKIs ± chemotherapy**: ORR = 38% (22/58; 95% CI: [26, 52])
- **Prior repotrectinib: ORR = 47% (8/17),** DOR range 3.5 to 17.2 months
- **Prior taletrectinib: ORR = 43% (3/7),** DOR range 5.2 to 7.0+ months

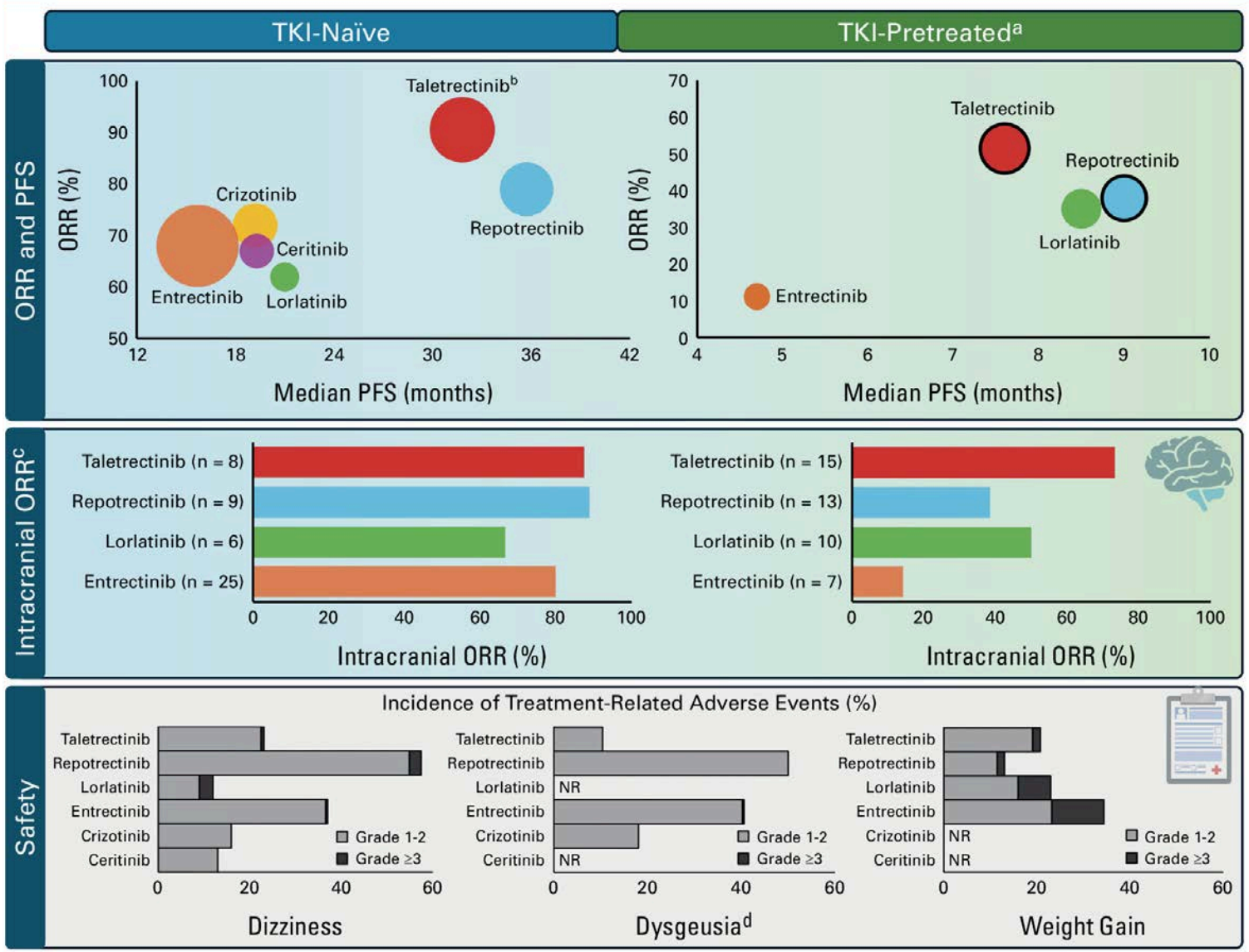


Data cut-off: March 21, 2025. CI, confidence interval; CR, complete response. PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SD, stable disease.

TKI = tyrosine kinase inhibitor; ORR = objective response rate

Drilon AE et al. WCLC 2025;Abstract PL02.15.

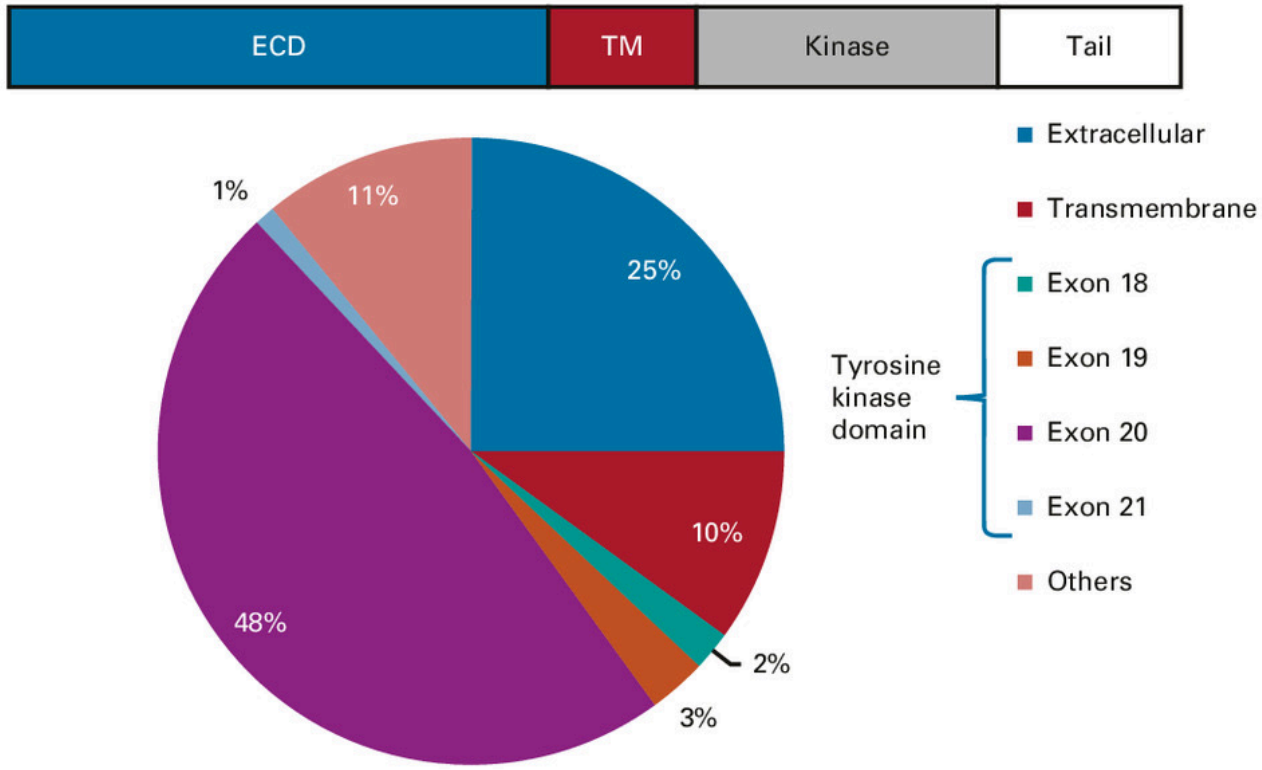
Summary of ROS1 Inhibitors



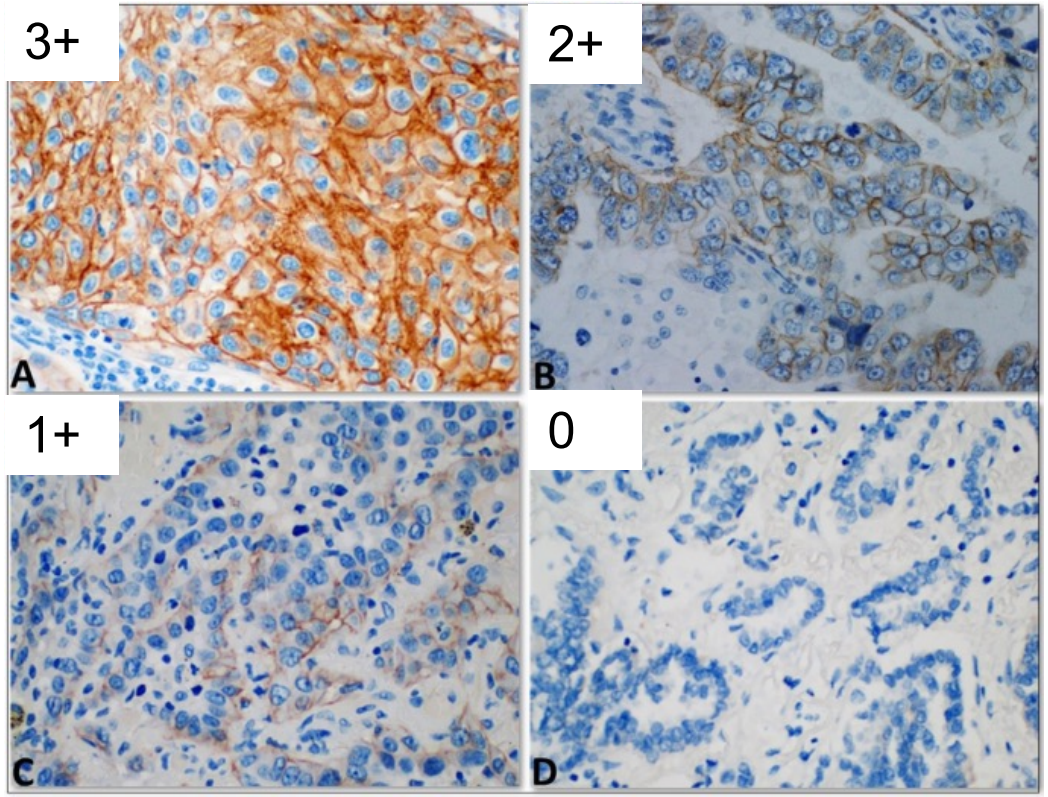
Waliany S, Lin JJ. JCO 2024

HER2 Alterations

HER2 Mutations

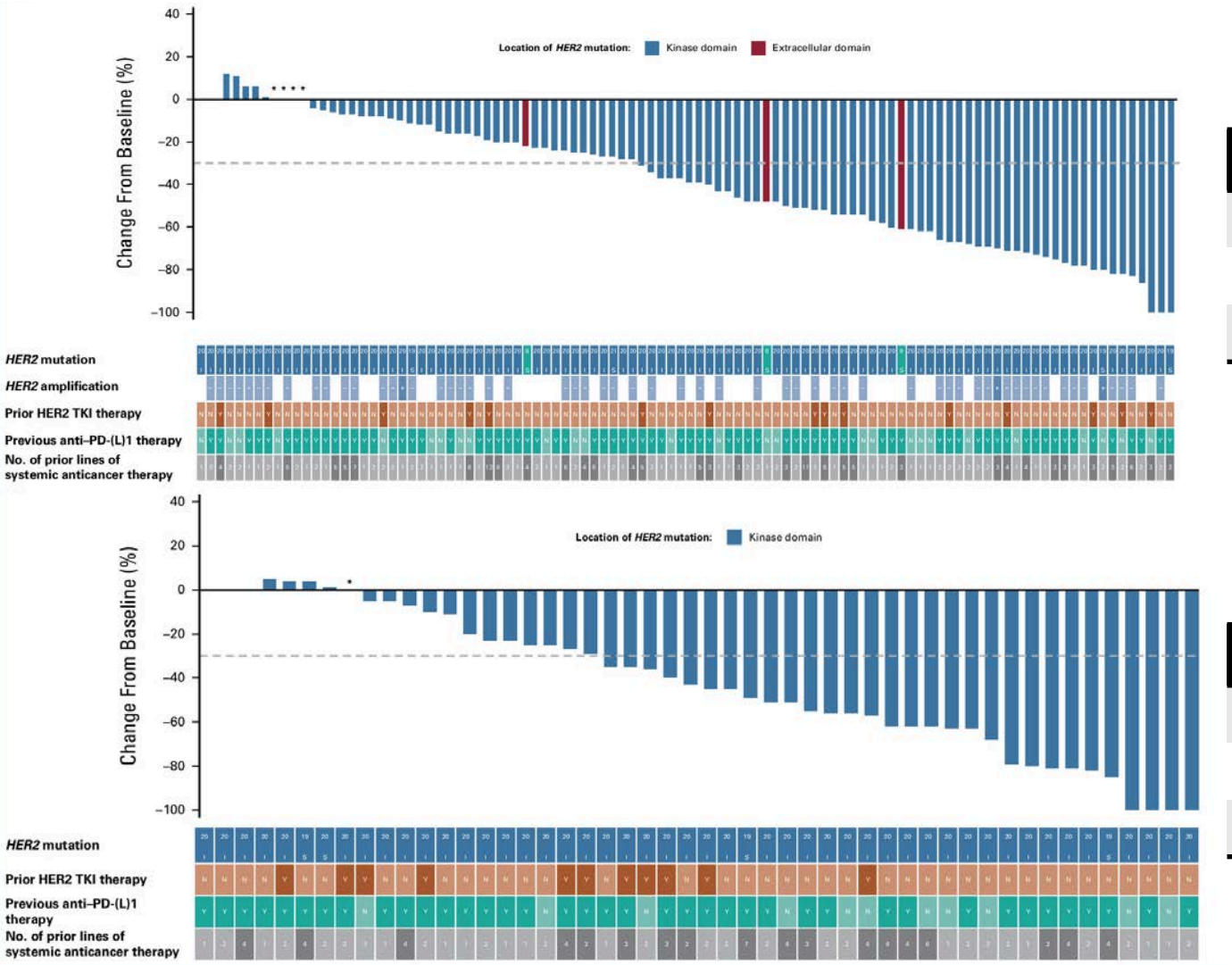


HER2 Expression



Cooper A, Gainor JF, J Clin Oncol 2022; Al Karsaneh OA, et al. Diag Path 2023

HER2 Mutations: T-DXd

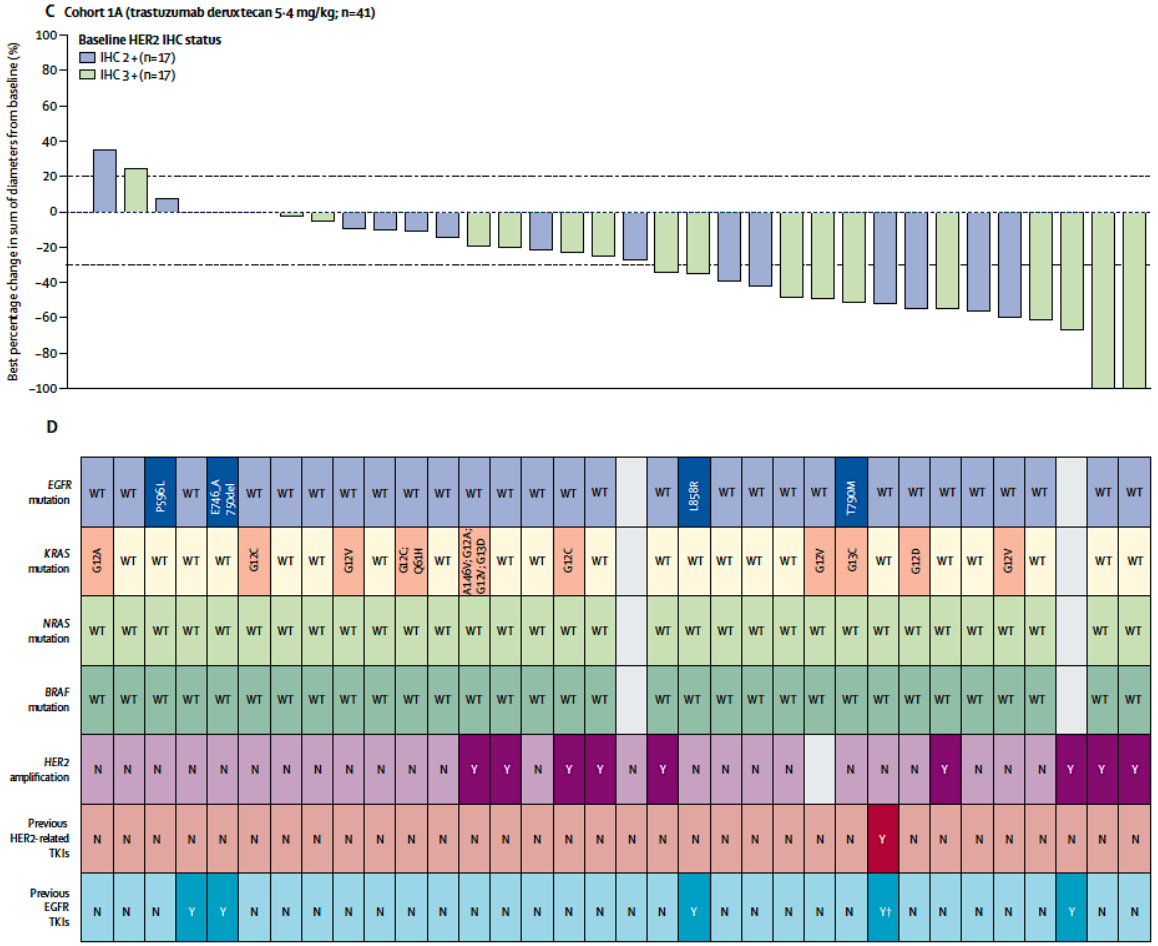


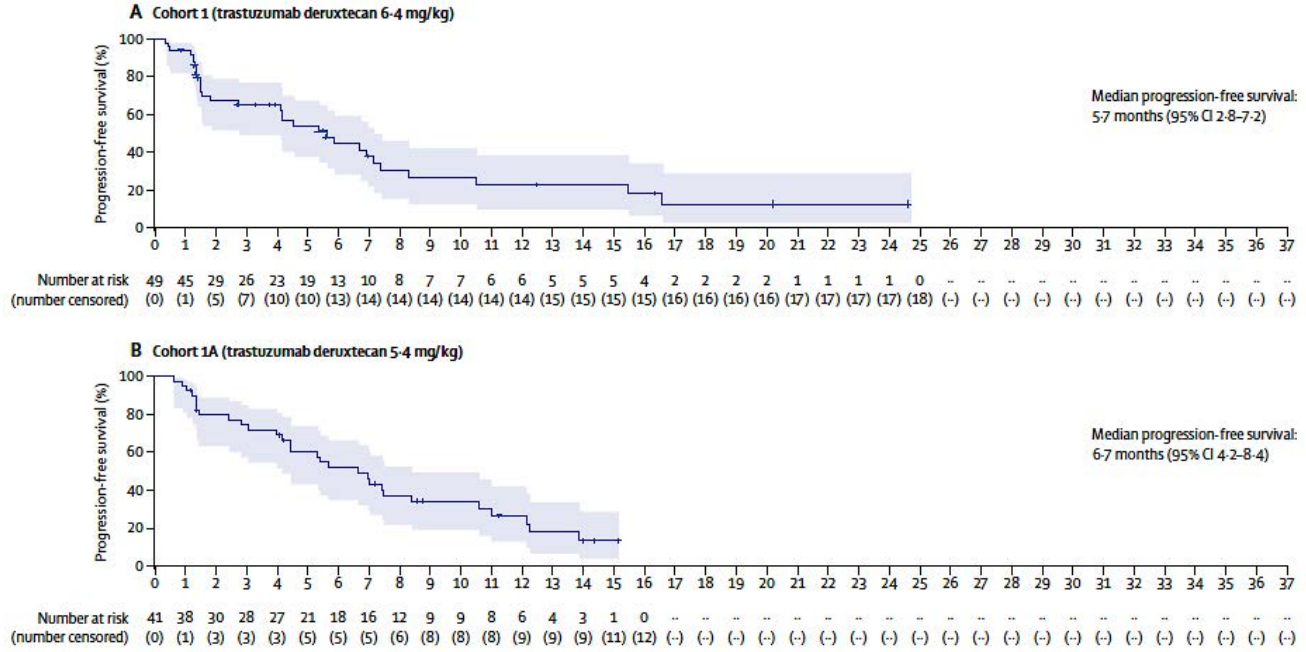
5.4 mg/kg Dose	
ORR	49%
mPFS	9.9 mo
DOR	16.8

6.4 mg/kg Dose	
ORR	56%
mPFS	15.4 mo
DOR	NE

Goto K, et al. J Clin Oncol 2023

HER2 Overexpression





HER2 IHC 3+
ORR 52.9%; mDOR 6.9 months

Smit E, et al. Lancet Oncol 2024

Zongertinib

Beamion LUNG-1 Study Design

Phase Ib (dose expansion): patients with advanced *HER2*-mutant NSCLC

In Phase Ia, the MTD was not reached at 360 mg QD
In Phase Ib, the selected dose after interim futility analysis was zongertinib 120 mg QD

Current analysis

Cohort 2 — Treatment-naïve patients with TKD mutations

Primary endpoint: Objective response by BICR (RECIST v1.1)

Secondary endpoints: DC, DoR, and PFS by BICR (RECIST v1.1)

Key inclusion criteria: aged ≥18 years, advanced/metastatic non-squamous *HER2*-mutant NSCLC (TKD mutation), ≥1 measurable non-CNS lesion (RECIST v1.1) and ECOG PS of 0/1. Patients with stable/asymptomatic brain metastases were eligible

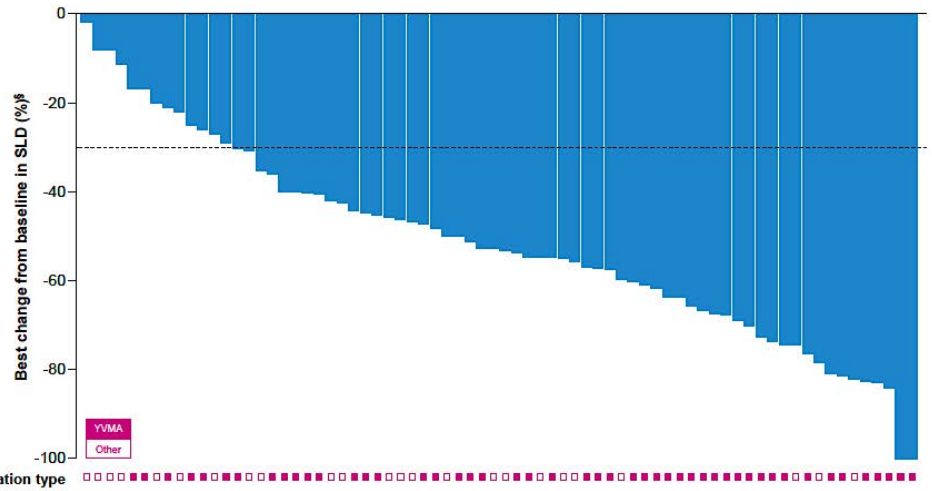
Here we present the efficacy and safety of zongertinib 120 mg given as a first-line therapy

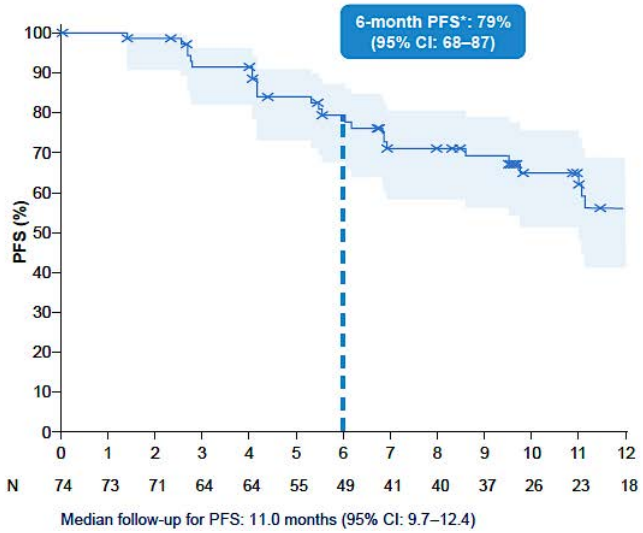
Additional cohorts not included in the current analysis

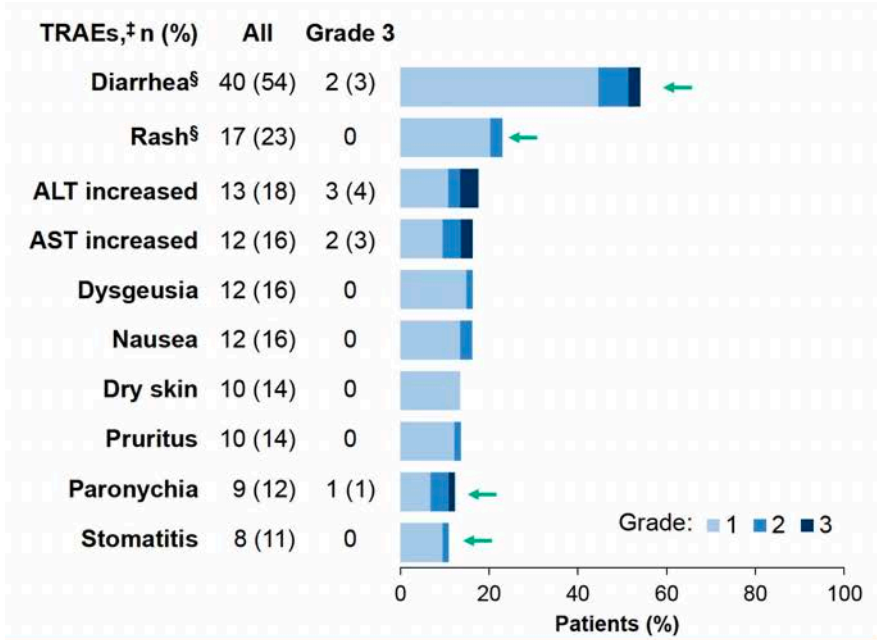
- Cohort 1 — Previously treated patients with TKD mutations
- Cohort 3 — Previously treated patients with non-TKD mutations
- Cohort 4 — Treatment-naïve or previously treated patients with TKD mutations and active brain metastases at baseline
- Cohort 5 — Patients previously treated with HER2-directed ADC and with TKD mutations

Zongertinib was recently approved in the United States (accelerated), China (conditional), and Japan for patients with previously treated advanced *HER2*-mutant NSCLC

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





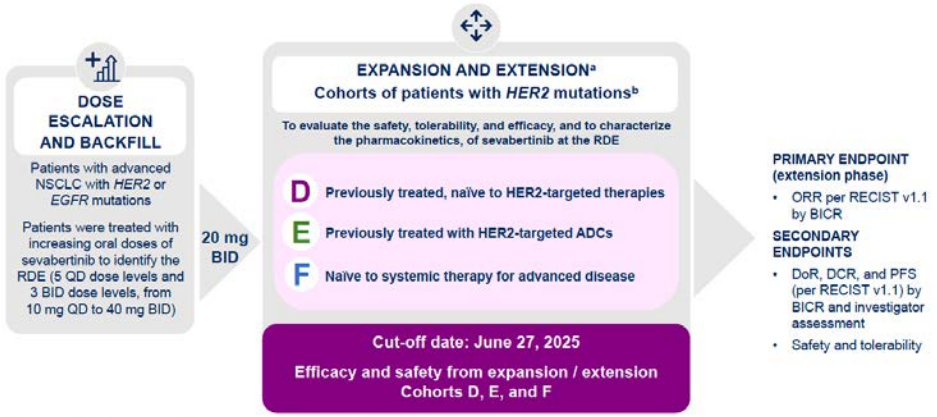


Popat S, et al. ESMO 2025; Abstract LBA74

Sevabertinib

Oral, reversible TKI that inhibits HER2, including secondary resistance mutations (C805S and gatekeeper mutations T798M/I)

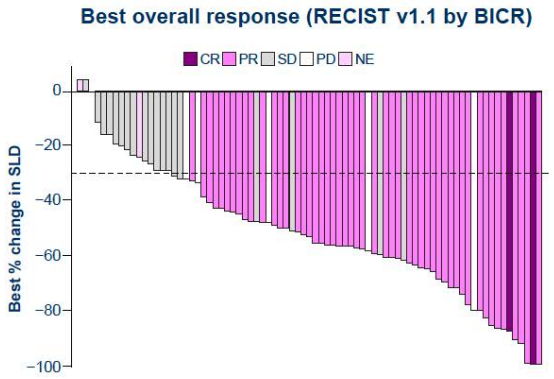
SOHO-01 study design (NCT05099172)



Cohort D (previously treated, *n*=81): Objective response (ORR) by BICR

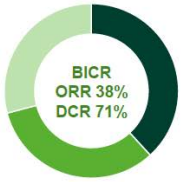
Median follow-up: 13.8 months (range 1-32)

n (%)	
CR	2 (2)
PR	50 (62)
SD	20 (25)
PD	6 (7)
Not evaluable[a]	3 (4)
ORR[b] [95% CI]	**52 (64)** [53, 75]

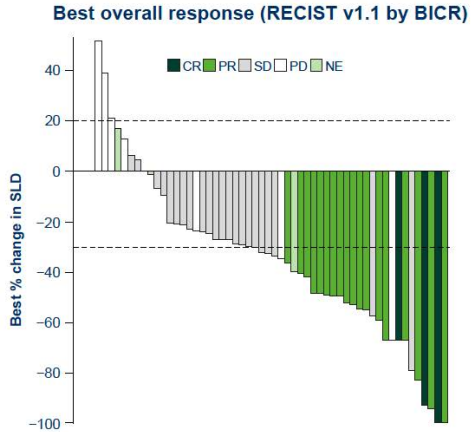


Cohort E (previous HER2 ADCs, *n*=55): Objective response by BICR

Median follow-up: 11.6 months (range 2-22)



n (%)	
CR	3 (5)
PR	18 (33)
SD	23 (42)
PD	7 (13)
Not evaluable[a]	4 (7)
ORR[b] [95% CI]	**21 (38)** [25, 52]
DCR[c] [95% CI]	**39 (71)** [57, 82]
DoR, median (months) [95% CI]	**8.5** [5.6, 16.4]
PFS, median (months) [95% CI]	**5.5** [4.3, 8.3]

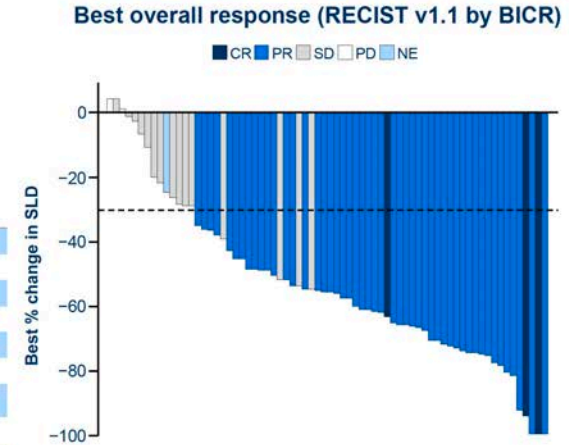


- Patients in Cohort E who had previously received trastuzumab deruxtecan achieved an ORR of 34% (14/41)

Cohort F (treatment-naïve, *n*=73): Objective response by BICR

Median follow-up: 9.9 months (range <1-15)

n (%)	
CR	3 (4)
PR	49 (67)
SD	16 (22)
PD	2 (3)
Not evaluable[a]	1 (1)
Not available[b]	2 (3)
ORR[c] [95% CI]	**52 (71)** [59, 81]
DCR[d] [95% CI]	**65 (89)** [80, 95]
DoR, median (months) [95% CI]	**11.0** [8.1, not estimable]
PFS, median (months) [95% CI]	Not estimable [9.6, not estimable]



Le X, et al. ESMO 2025; Abstract LBA75

Summary

- Treatment of oncogene-driven lung cancer continues to evolve rapidly
- Intensification strategies are now yielding OS benefits in EGFR-mutant NSCLC
- Bispecifics and ADCs are providing new therapeutic options in EGFR-mutant NSCLC
- Next-generation TKIs are demonstrating significant anti-tumor activity for patients with ALK, ROS1 and now HER2

Case Presentation: 65-year-old woman with ALK-mutant metastatic adenocarcinoma of the lung (PD-L1 TPS 70%)

Dr Zanetta Lamar (Naples, Florida)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

In general, what is your preferred first-line treatment for metastatic NSCLC with an ALK mutation?

What is your usual treatment approach for a patient with progressive disease after first-line alectinib and second-line lorlatinib?

What role, if any, do you see for new tyrosine kinase inhibitors, including neladalkib (NVL-655)?

Case Presentation: 84-year-old woman with EGFR exon 19-deleted adenocarcinoma of the lung with recurrence after 4 years of osimertinib

Dr Jennifer Yannucci (Savannah, Georgia)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How do you select first-line treatment for EGFR-mutant metastatic NSCLC, and what are the tolerability issues with the 3 major options?

How do you select second-line treatment for EGFR-mutant metastatic NSCLC, and how does that vary based on first-line treatment?

How might the availability of subcutaneous amivantamab affect your use of this agent?

QUESTIONS FOR THE FACULTY

What tolerability issues have you observed with datopotamab deruxtecan?

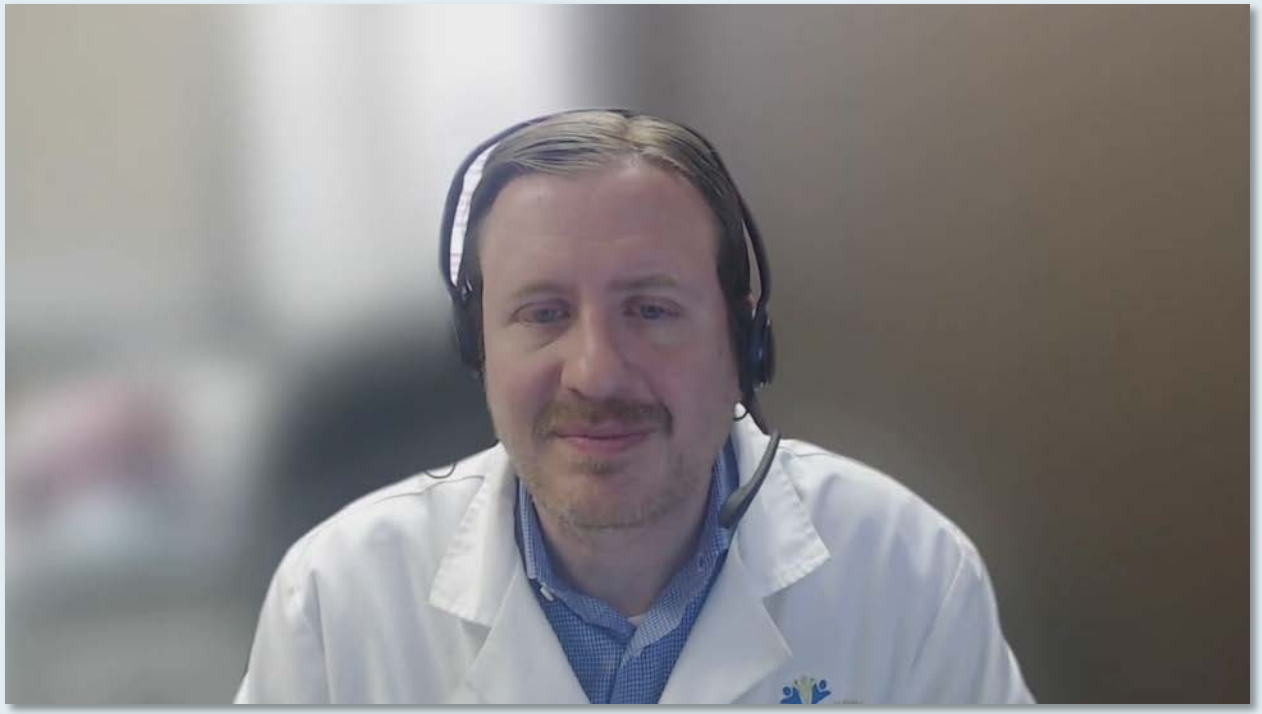
What strategies do you use to prevent the mucositis associated with the drug?

How problematic have you found the ocular toxicities?

QUESTIONS FOR THE FACULTY

What is your usual first-line therapy for EGFR exon 20-mutant NSCLC?

Case Presentation: 69-year-old woman with HER2-mutant metastatic adenocarcinoma of the lung



Dr Brian Mulherin (Indianapolis, Indiana)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How do you sequence trastuzumab deruxtecan and zongertinib for HER2-mutant NSCLC? What about for patients with HER2 overexpression?

How do zongertinib and sevabertinib compare in terms of efficacy? What about tolerability? What are the most common toxicities with these agents?

If sevabertinib were to become available, how do you think you would select between the 2 of them? Would you use them in sequence?

Case Presentation: 73-year-old man with locally recurrent squamous cell carcinoma of the lung and a MET exon 14 skipping mutation

Dr Sean Warsch (Asheville, North Carolina)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

In patients with locally advanced, unresectable NSCLC, for which actionable genomic alterations do you (or would you like to) recommend targeted treatment versus durvalumab consolidation after chemoradiation therapy?

How do you sequence targeted agents for patients with a MET exon 14 skipping mutation?

Case Presentation: 73-year-old woman with ROS1-mutant metastatic adenocarcinoma of the lung who responds to entrectinib and then to pembrolizumab/carboplatin/ pemetrexed administered upon disease progression

Dr Jennifer Yannucci (Savannah, Georgia)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

In general, how do you sequence the various available targeted agents for patients with ROS1-mutant lung cancer? Is there a role for immunotherapy in the care of these patients?

What role, if any, do you see for new tyrosine kinase inhibitors, including zidesamtinib? If zidesamtinib becomes available, where do you see it fitting into current algorithms?

Agenda

Module 1 — Lung Cancer: *Drs Gainor, Langer and Shields*

- **Targeted Therapy for Non-Small Cell Lung Cancer (NSCLC) —** *Dr Gainor*
- **Nontargeted Therapy for NSCLC; Small Cell Lung Cancer —** *Dr Langer*
- **Neoadjuvant, Perioperative and Adjuvant Anti-PD-1/PD-L1 Antibody-Based Approaches for Patients with Localized NSCLC —** *Dr Shields*

Penn Medicine
Abramson Cancer Center

Division of Hematology & Oncology

Headway in SCLC and Driver (-) mNSCLC

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November 08, 2025

Headway in SCLC and Driver (-) metastatic (m)NSCLC

mNSCLC: no targetable mutations or fusions

- Up-front therapy for higher risk populations of pts with Tx-naive mNSCLC and no targetable tumor mutations (eg, high-risk features such as KEAP1/STK11 mutations; Sq histology and PD-L1 < 1%, etc)
- IVONESCIMAB: Phase III trials (eg, HARMONi-2, HARMONi-6) in Tx-naïve mNSCLC

Limited SCLC

- LTS Durvalumab consolidation after chemoradiation in ADRIATIC

Extensive Stage:

- Long-term outcomes with durvalumab (CASPIAN) and atezolizumab (IMP133), as 1L Tx
- Phase III IMforte trial of maintenance lurbinectedin + atezolizumab vs atezo alone after first-line induction Tx with EP/Atezo
- Phase III DeLLphi-304 trial comparing tarlatamab to standard chemotherapy as 2L therapy for pts with progressive SCLC
- ADCs: Mechanism of antitumor activity of ifinatamab deruxtecan (I-DXd) and other ADCs; early-phase results and ongoing Phase III trials of I-DXd for patients with ES-SCLC

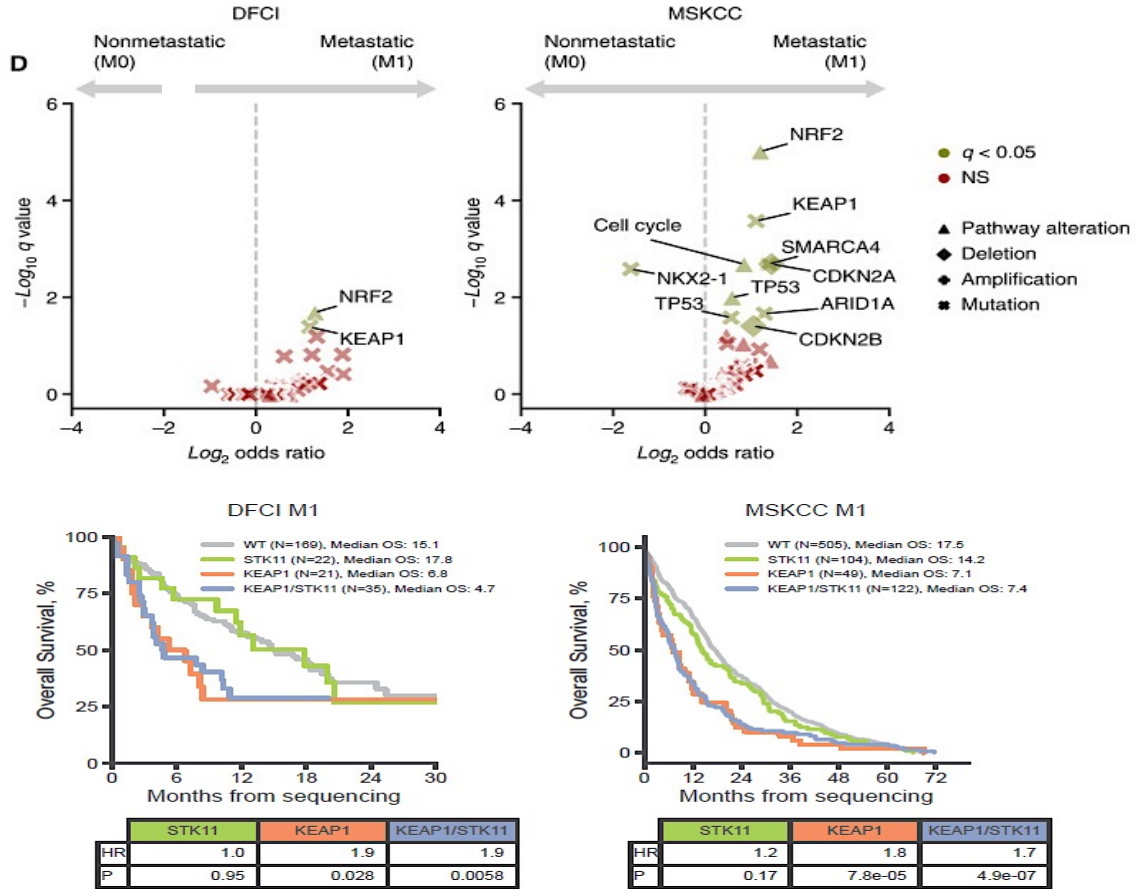
Langer's Current 1L Paradigm in wt NSCLC: November, 2025 (could change at any moment)

Tx Cohort	Non-Squamous	Squamous
PDL1 ≥ 50%	Pembro > Pem/Carbo/Pembro	Pembro > Taxane/Carbo/Pembro
PDL1 1-50%	Pem/Carbo/Pembro > Pembro	Taxane/Carbo/Pembro > Pembro
PDL1 < 1%	Pem/Carbo/Pembro	Taxane/Carbo/Pembro
PDL1 < 1% or TMB > 10	Pem/Carbo/Pembro vs Ipi/Nivo or 9LA* or Poseidon	Taxane/Carbo/Pembro vs Ipi/Nivo or 9LA* or Poseidon
TKI-Refractory	Pem/Carbo +/- Bev or Pac/Carbo/Bev/Atezo (IMP150)	
Tissue QNS	Pem/Carbo/Pembro	Taxane/Carbo/Pembro

*Ipilimumab/Nivolumab +/- 2 cycles of Histology-appropriate chemotherapy (9LA); could also consider Poseidon (Durvalumab/Tremelimumab/Carbo and either Taxane or Pem)

STK11/*KEAP1* Mutations Associated with Negative Prognostic Effects and Decreased Benefit to Anti-PD-L1

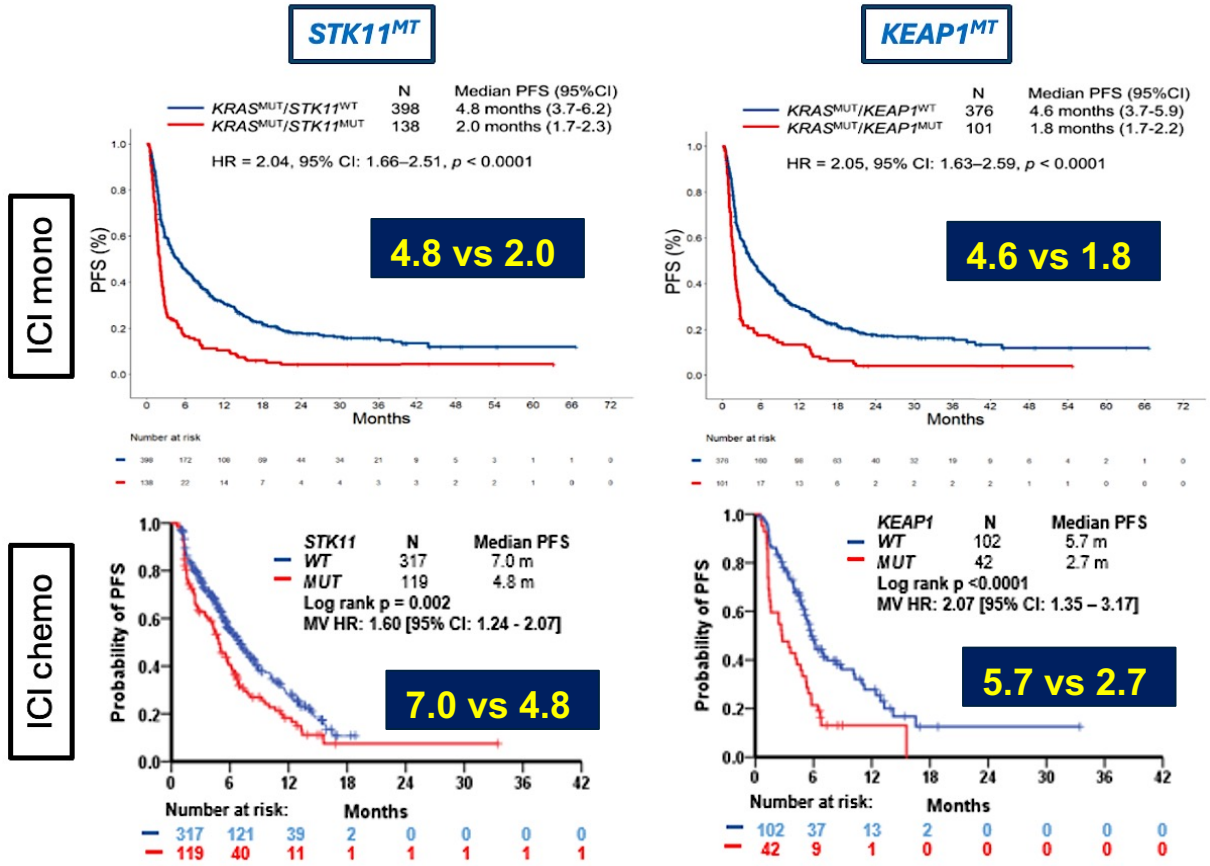
KEAP1 associated with metastasis and reduced OS



	STK11	KEAP1	KEAP1/STK11
HR	1.0	1.9	1.9
P	0.95	0.028	0.0058

	STK11	KEAP1	KEAP1/STK11
HR	1.2	1.8	1.7
P	0.17	7.8e-05	4.9e-07

KEAP1/*STK11* associated with reduced ICI outcomes



Boiarsky D, et al. *Ann Oncol*. 2023;34(7):589-604. Ricciuti B, et al. *J Thorac Oncol*. 2022;17(3):399-410. Skoulidis F, et al. Presented at: ASCO; 2019.

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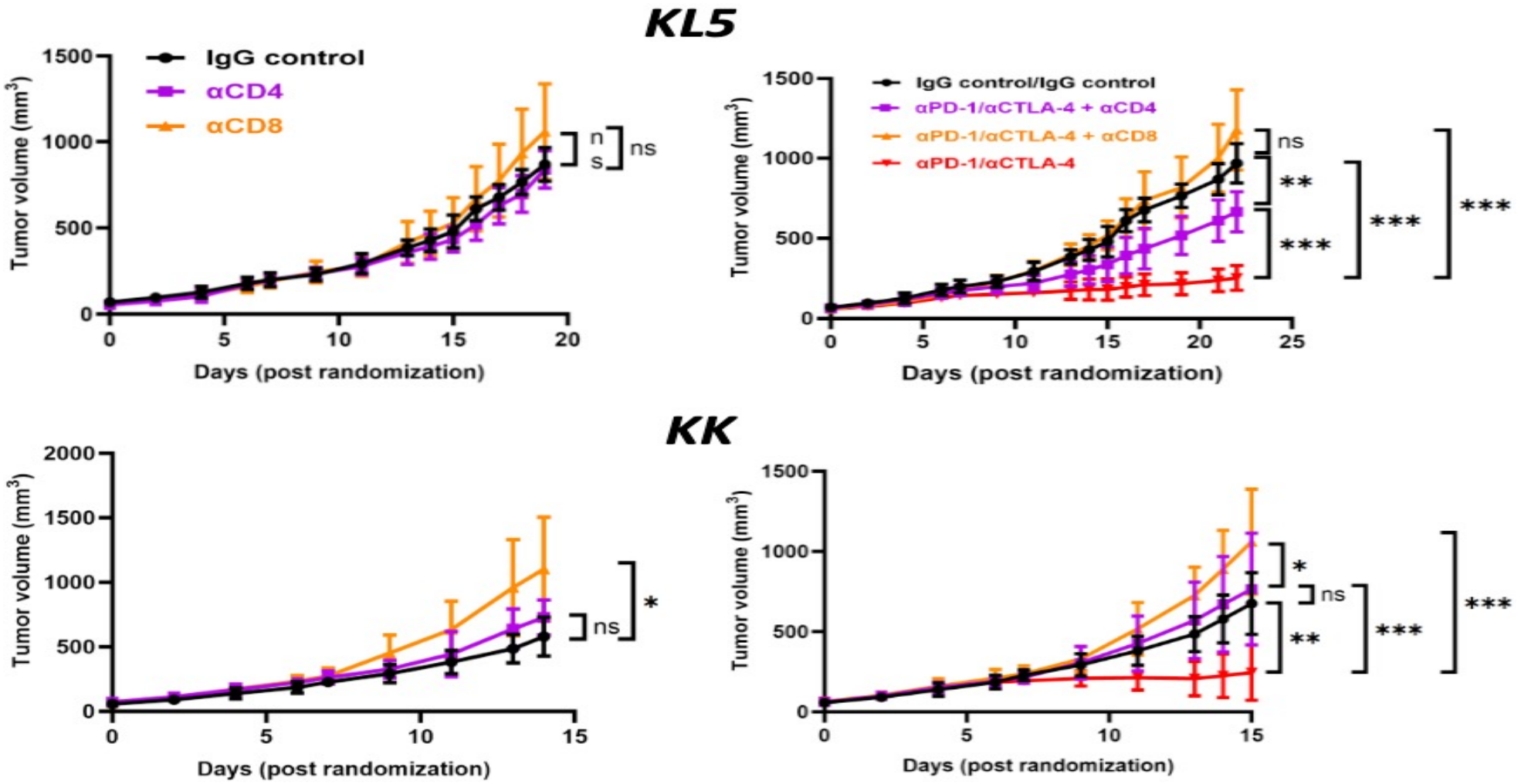
In Vivo Mouse Experiments Show Enhanced Anti-Tumor Effect from Adding CTLA-4 to PD-(L)1 inhibitors in *KEAP1*-Deficient Tumors



- *P<0.05; **P<0.01; ***P<0.001.

Skoulidis F, et al. *Nature*. 2024 .

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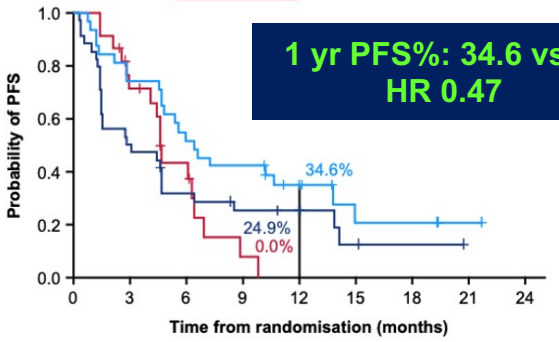
Potential Benefit from Addition of CTLA-4: POSEIDON
STK11 and KEAP1 mt (+) mNSCLC

PFS | **OS**

STK11 mutant

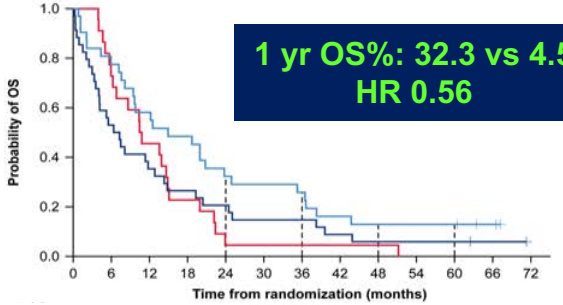
	T+D+CT	D+CT	CT
Events, n/N	22/31	27/34	17/22
mPFS, mo (95% CI)	6.4 (4.7–13.8)	2.9 (1.4–4.7)	4.6 (2.9–6.4)
HR* (95% CI)	0.47 (0.23–0.93)	1.02 (0.55–1.93)	–



1 yr PFS%: 34.6 vs 0; HR 0.47

***STK11*m**

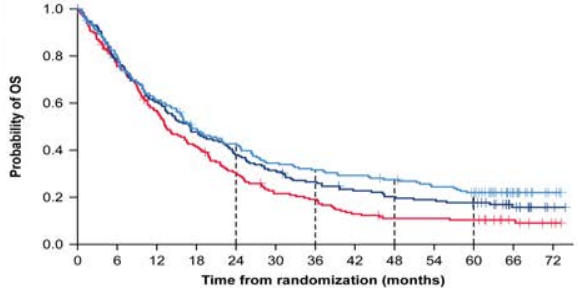
Nonsquamous *STK11* mutant	T+D+CT	D+CT	CT
Events/patients, n/N	27/31	32/34	22/22
mOS, months (95% CI)	15.0 (8.2–23.8)	6.9 (3.6–12.9)	10.7 (6.0–14.9)
HR (95% CI) vs CT	0.57 (0.32–1.04)	1.02 (0.59–1.80)	–
Landmark OS, % (95% CI)			
24 months	32.3 (16.9–48.6)	20.6 (9.1–35.3)	4.5 (0.3–18.9)
36 months	25.8 (12.2–41.8)	14.7 (5.4–28.5)	4.5 (0.3–18.9)
48 months	12.9 (4.1–27.0)	5.9 (1.1–17.2)	4.5 (0.3–18.9)
60 months	12.9 (4.1–27.0)	5.9 (1.1–17.2)	0 (NC)



1 yr OS%: 32.3 vs 4.5 HR 0.56

***STK11*wt**

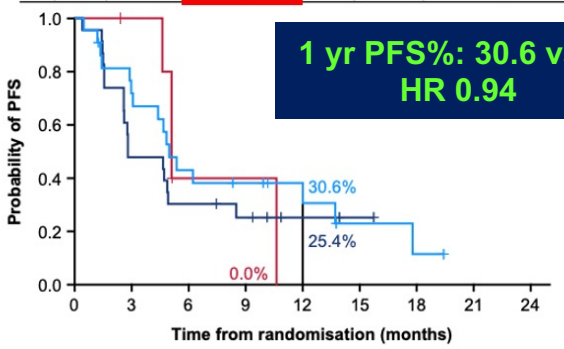
Nonsquamous *STK11* wild-type	T+D+CT	D+CT	CT
Events/patients, n/N	135/177	138/169	153/179
mOS, months (95% CI)	17.2 (14.9–22.1)	17.1 (13.3–22.3)	13.4 (11.5–16.8)
HR (95% CI) vs CT	0.71 (0.56–0.90)	0.79 (0.63–1.00)	–
Landmark OS, % (95% CI)			
24 months	42.7 (35.2–49.9)	38.1 (30.7–45.4)	30.1 (23.3–37.0)
36 months	31.6 (24.8–38.5)	26.5 (20.0–33.4)	19.1 (13.5–25.4)
48 months	27.5 (21.0–34.3)	20.2 (14.5–26.7)	11.0 (6.8–16.3)
60 months	22.0 (16.1–28.5)	17.7 (12.3–23.9)	10.4 (6.3–15.6)



KEAP1 mutant

PFS

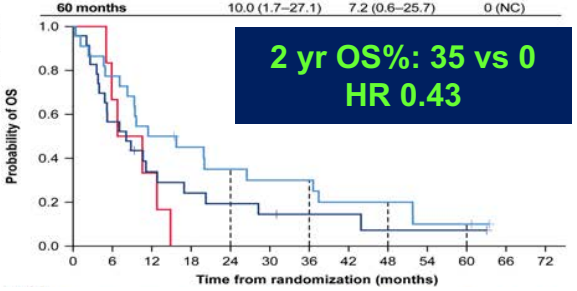
	T+D+CT	D+CT	CT
Events, n/N	16/22	17/23	4/6
mPFS, mo (95% CI)	5.0 (3.0–13.7)	2.8 (2.6–4.9)	5.1 (4.6–NE)
HR* (95% CI)	0.94 (0.33–3.35)	1.51 (0.55–5.25)	–



1 yr PFS%: 30.6 vs 0; HR 0.94

***KEAP1*m**

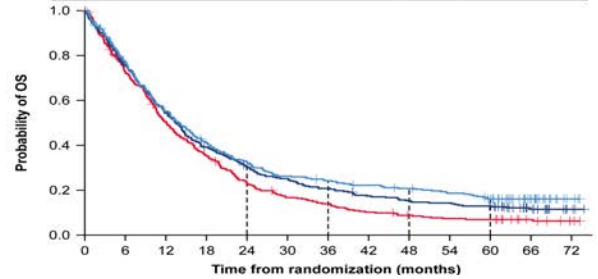
All patients *KEAP1* mutant	T+D+CT	D+CT	CT
Events/patients, n/N	19/22	20/23	6/6
mOS, months (95% CI)	13.7 (7.2–26.5)	8.1 (4.0–12.9)	8.7 (5.1–NE)
HR (95% CI) vs CT	0.43 (0.16–1.25)	0.77 (0.31–2.15)	–
Landmark OS, % (95% CI)			
24 months	35.0 (16.1–54.7)	19.3 (6.2–37.9)	0 (NC)
36 months	30.0 (12.5–49.8)	14.5 (3.7–32.3)	0 (NC)
48 months	20.0 (6.3–39.1)	7.2 (0.6–25.7)	0 (NC)
60 months	10.0 (1.7–27.1)	7.2 (0.6–25.7)	0 (NC)



2 yr OS%: 35 vs 0 HR 0.43

***KEAP1*wt**

All patients *KEAP1* wild-type	T+D+CT	D+CT	CT
Events/patients, n/N	249/303	266/307	281/312
mOS, months (95% CI)	14.0 (11.8–16.1)	13.5 (11.7–14.9)	12.1 (10.6–13.9)
HR (95% CI) vs CT	0.76 (0.64–0.90)	0.83 (0.70–0.98)	–
Landmark OS, % (95% CI)			
24 months	32.4 (27.1–37.7)	30.2 (25.2–35.5)	22.9 (18.3–27.7)
36 months	24.3 (19.6–29.3)	20.8 (16.4–25.6)	14.0 (10.4–18.2)
48 months	20.8 (16.4–25.6)	15.4 (11.6–19.7)	8.9 (6.0–12.4)
60 months	16.2 (12.2–20.6)	13.0 (9.5–17.1)	7.0 (4.4–10.3)

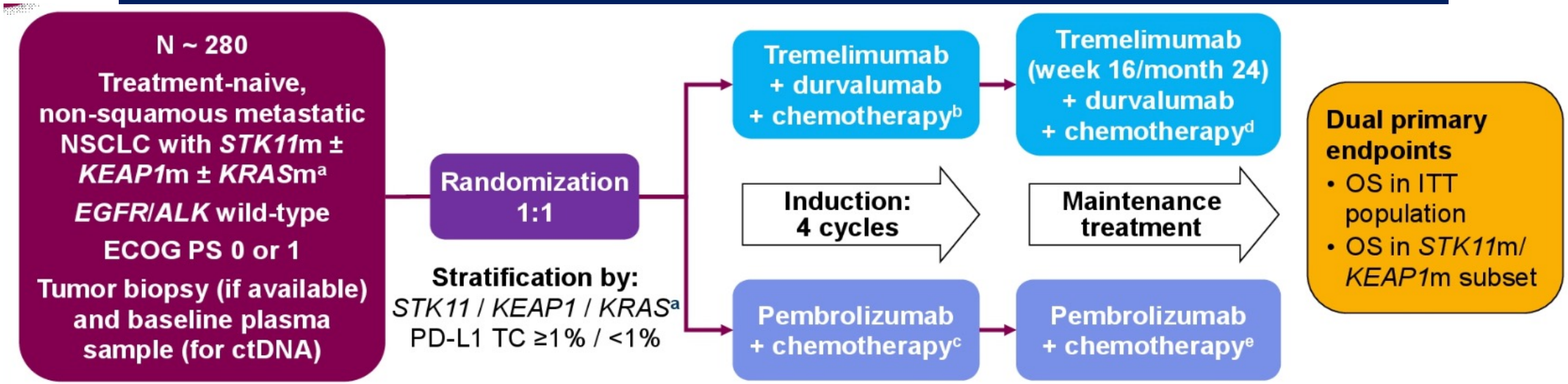


Peters S, et al. Presented at: WCLC; 2022. Peters S et al. J Thorac Oncol 2025

Penn Medicine Abramson Cancer Center

Ongoing Phase 3b TRITON Trial (NCT06008093) to Validate *STK11/KEAP1* as Biomarkers

TRITON : Phase 3b randomized, open-label, multicenter study POSEIDON vs KN189



[a]The proportion of participants with *KRAS* mutations alone (without *STK11* or *KEAP1* mutations) will be capped at 33% of the total sample size.
[b]Tremelimumab 75 mg Q3W + durvalumab 1500 mg Q3W + platinum (carboplatin AUC 5/6 or cisplatin 75 mg/m^2) + pemetrexed 500 mg/m^2 Q3W for up to 4 cycles.
[c]Pembrolizumab 200 mg Q3W + platinum (carboplatin AUC 5/6 or cisplatin 75 mg/m^2) + pemetrexed 500 mg/m^2 Q3W for up to 4 cycles.
[d]Tremelimumab 75 mg (a fifth dose given post-platinum at week 16, plus an optional dose at month 24 at the investigator's discretion) + durvalumab 1500 mg Q4W + pemetrexed 500 mg/m^2 Q4W until disease progression, unacceptable toxicity, or withdrawal of consent.
[e]Pembrolizumab 200 mg Q3W + pemetrexed 500 mg/m^2 Q3W until disease progression, unacceptable toxicity, or withdrawal of consent (and for pembrolizumab only, for up to 24 months).

Skoulidis F, et al. ASCO; 2024.

Penn Medicine
Abramson Cancer Center

Ivonescimab Versus Pembrolizumab for PD-L1–Positive NSCLC: A Subgroup Analysis of HARMONi-2 by Tumor Histology

Anwen Xiong,[1] Jianhua Chen,[2] Baogang Liu,[3] Hua Zhong,[4] Ying Cheng,[5] Hui Ge,[6] Qin Shi,[7] Bolin Chen,[2] Jinliang Wang,[8] Yanqiu Zhao,[9] Ligong Nie,[10] Xingya Li,[11] Yinghua Ji,[12] Xiaohong Ai,[13] Yu Lin,[14] Dingzhi Huang,[15] Jinlu Shan,[16] Wenting Li,[17] Michelle Xia,[17] Caicun Zhou[18]

[1]Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China; [2]Hunan Cancer Hospital, Changsha, China; [3]Harbin Medical University Cancer Hospital, Harbin, China; [4]Shanghai Chest Hospital, Shanghai, China; [5]Jilin Cancer Hospital, Changchun, China; [6]The Fourth Hospital of Hebei Medical University, Shijiazhuang, China; [7]Fuzhou Tuberculosis Prevention and Treatment Hospital, Fuzhou, China; [8]The Fifth Medical Center of the Chinese People's Liberation Army General Hospital, Beijing, China; [9]Henan Cancer Hospital, Zhongshan, China; [10]Peking University First Hospital, Beijing, China; [11]First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [12]The First Affiliated Hospital of Xinxiang, Xinxiang, China; [13]The First Affiliated Hospital of University of South China, Hengyang, China; [14]Fujian Cancer Hospital, Fuzhou, China; [15]Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [16]Daping Hospital, Army Medical University, Chongqing, China; [17]Akeso Biopharma, Inc, Zhongshan, China; [18]Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China

BACKGROUND

- A combination of platinum-based chemotherapy plus programmed cell death protein 1 (PD-1) and programmed cell death ligand 1 (PD-L1) is the most common treatment approach for patients with newly diagnosed Stage IV non-small cell lung cancer (NSCLC) regardless of tumor PD-L1 status[1]
- Ivonescimab is a first-in-class investigational bispecific antibody against PD-1 and vascular endothelial growth factor (VEGF; Figure 1)[2,3]
  - > By blocking both PD-1 and VEGF in the tumor microenvironment, ivonescimab has the potential to drive synergistic anti-tumor activity through higher binding affinity and increased activity of T cells
  - > In vitro studies have shown that the presence of VEGF increases PD-1 binding strength by more than 10-fold
- In Phase 3 studies, ivonescimab has yielded promising clinical outcomes in patients with advanced/metastatic NSCLC[4-6]

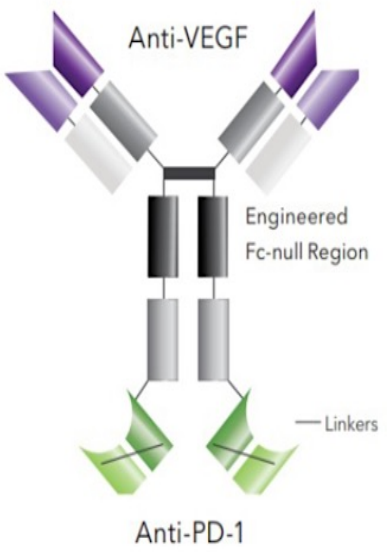


Figure 1. Ivonescimab PD-1/VEGF Bispecific Antibody. Anti-PD-1 scFv attaches to the C-terminus of each anti-VEGF-A antibody heavy chain. Ivonescimab has a heterotetrameric structure consisting of 2 heavy chains of the IgG1 subclass and 2 light chains of the kappa subclass, which are covalently linked through disulfide bonds.[2]

Fc, fragment crystallized; IgG1, immunoglobulin G1; PD-1, programmed cell death protein 1; scFv, single-chain variable fragment; VEGF, vascular endothelial growth factor.

Figure 1. Trial Design

Key Eligibility Criteria

- Age ≥18 years
- Advanced or metastatic (stage IIIB/C or stage IV) PD-L1–positive NSCLC[a]
- No previous systemic therapy for advanced disease
- ≥1 measurable lesion by RECIST v1.1
- ECOG PS score of 0 or 1
- No sensitizing *EGFR* mutations or *ALK* translocations

Randomization 1:1

Ivonescimab 20 mg/kg IV Q3W

Pembrolizumab 200 mg IV Q3W

Treatment until

- Intolerable toxicity

or

- Disease progression[b]

or

- 24 months of treatment

Safety and survival follow-up

Stratification Factors

- Disease stage (stage IIIB or IIIC vs stage IV)
- Histology (squamous vs non-squamous)
- PD-L1 TPS (1–49% vs ≥50%)

Study Endpoints

- Primary: PFS by IRRC per RECIST v1.1
- Key secondary: OS
- Other secondary: ORR, DCR, DOR, TTR by IRRC per RECIST v1.1, safety, PK, and immunogenicity
- Exploratory: HRQOL assessment

ALK, anaplastic lymphoma kinase; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, endothelial growth factor receptor; HRQOL, health-related quality of life; IRRC, independent radiology review committee; IV, intravenously; NSCLC, non–small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; TPS, tumor proportion score; TTR, time to response.

[a]Squamous or nonsquamous NSCLC subtype confirmed histologically or cytologically.

[b]Confirmed by masked IRRC.

Xiong A et al, WCLC 2025;Abstract P1.11.83

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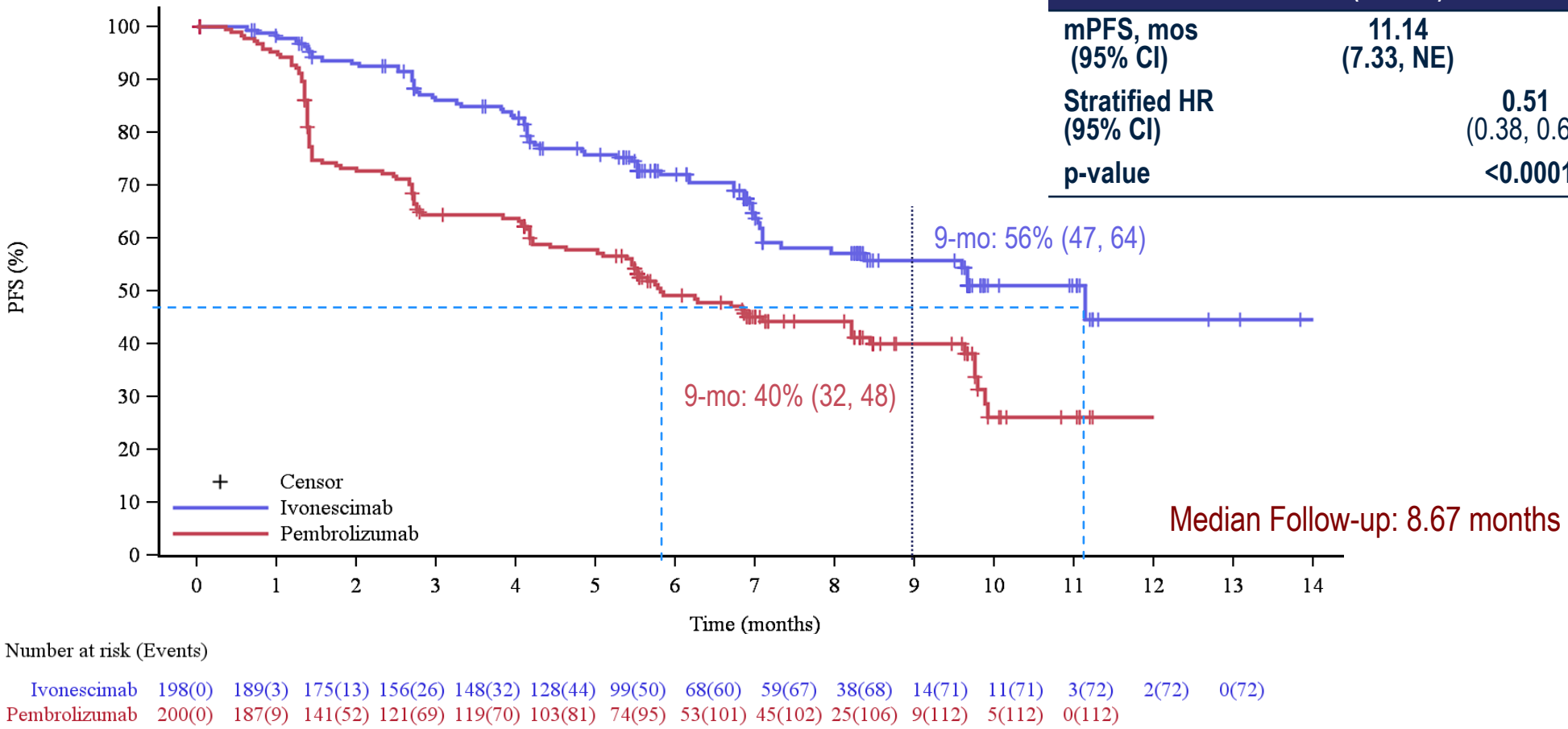
Primary endpoint: PFS per IRRC: HARMONI 2 – Pembro vs Ivonescimab

	Ivonescimab (n = 198)	Pembrolizumab (n = 200)
mPFS, mos (95% CI)	11.14 (7.33, NE)	5.82 (5.03, 8.21)
Stratified HR (95% CI)	0.51 (0.38, 0.69)	
p-value	<0.0001	



Ivonescimab demonstrated a statistically significant improvement in PFS vs. pembrolizumab with HR = 0.51, and a 5.3 months improvement in mPFS.

Abbreviations: mPFS, median progression-free survival; IRRC, independent radiology review committee; mo, month; NE, not estimable; HR: hazard ratio; CI, confidence interval.

Zhou, C et al, HARMONi2: WCLC 2024;Abstract PL02.04

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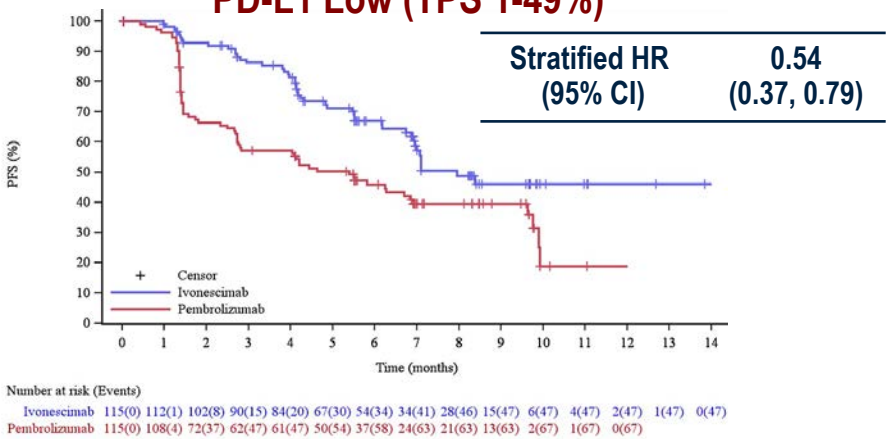
HARMONI-2: Key PFS Subgroup Analyses

Histology and PD-L1 status

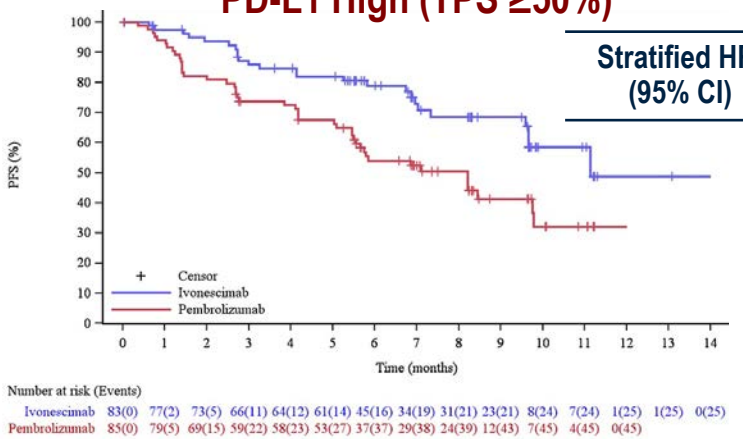
PD-L1 expression

PD-L1 Low (TPS 1-49%)



Stratified HR (95% CI): 0.54 (0.37, 0.79)

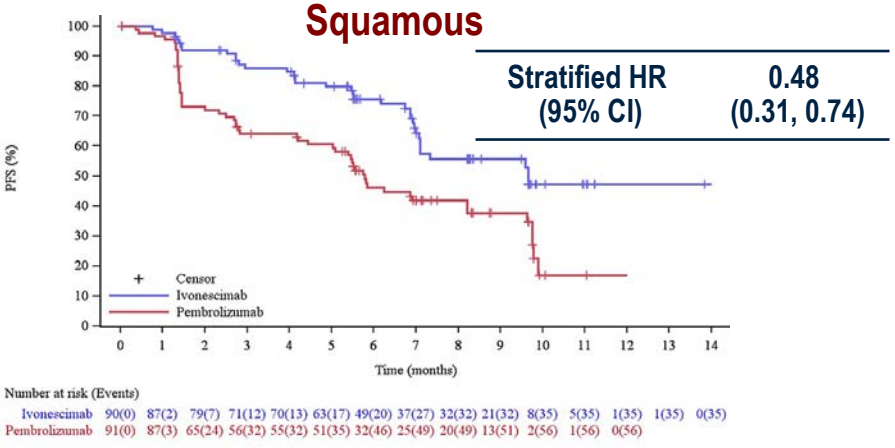
PD-L1 High (TPS ≥50%)



Stratified HR (95% CI): 0.46 (0.28, 0.75)

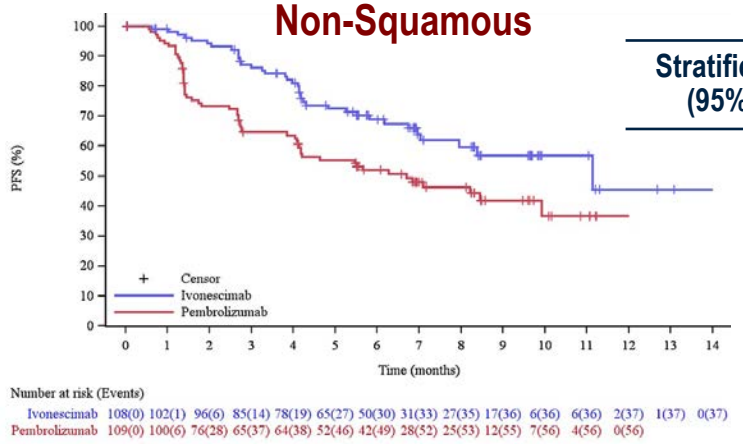
NSCLC Histology

Squamous



Stratified HR (95% CI): 0.48 (0.31, 0.74)

Non-Squamous



Stratified HR (95% CI): 0.54 (0.36, 0.82)

Ivonescimab showed meaningful improvement in PFS vs. pembrolizumab in patients with both low and high PD-L1, with squamous or non-squamous advanced NSCLC.

Abbreviations: PFS, progression-free survival; PD-L1, programmed death ligand 1; TPS, tumor proportion score; HR: hazard ratio; CI, confidence interval; NSCLC, non-small cell lung cancer.

Zhou, C et al, HARMONi2: WCLC 2024;Abstract PL02.04

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HARMONi-6: randomized, double-blind parallel-controlled phase III trial in Stage IIIB/IV sq NSCLC

Key Eligibility Criteria

- Pathologically confirmed sq-NSCLC
- Stage IIIB-IV
- No prior systemic therapy
- No EGFR mutations or ALK rearrangements
- ECOG PS 0 or 1

Stratification Factors:
- Stage: IIIB/IIIC vs. IV
- PD-L1 TPS: ≥1% vs. <1%

Data cutoff date: February 28, 2025

R 1: 1

N=532

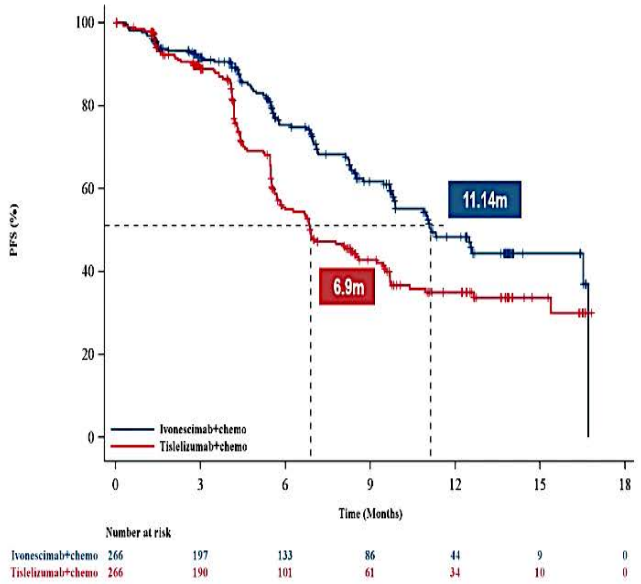
Ivonescimab (20 mg/kg, Q3W) + Carboplatin (AUC 5, Q3W) + Paclitaxel (175 mg/m², Q3W) up to 4 cycles → Ivonescimab (20 mg/kg, Q3W) up to 24 months or unacceptable toxicity

Tislelizumab (200 mg, Q3W) + Carboplatin (AUC 5, Q3W) + Paclitaxel (175 mg/m², Q3W) up to 4 cycles → Tislelizumab (200 mg, Q3W) up to 24 months or unacceptable toxicity

Endpoints:
- **Primary endpoint: PFS by IRRC per RECIST v1.1**
- Key secondary endpoint: OS
- Secondary endpoints: PFS by INV, ORR, DCR, DoR, TTR and safety

Primary endpoint: PFS by IRRC

Ivonescimab+chemo demonstrated a statistically significant improvement in PFS vs. tislelizumab+chemo with HR=0.60, representing a 4.2 months improvement in mPFS.



	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
mPFS, months (95% CI)	11.14 (9.86, NE)	6.90 (5.82, 8.57)
Stratified HR (95% CI)	0.60 (0.46, 0.78)	
p-value	<0.0001	

Median Follow-up: 10.28 months

Consistent PFS benefit by investigator-assessment: HR = 0.64 (95% CI: 0.50, 0.84)

Shun Lu, C et al, HARMONi6: ESMO 2025;Abstract LBA4

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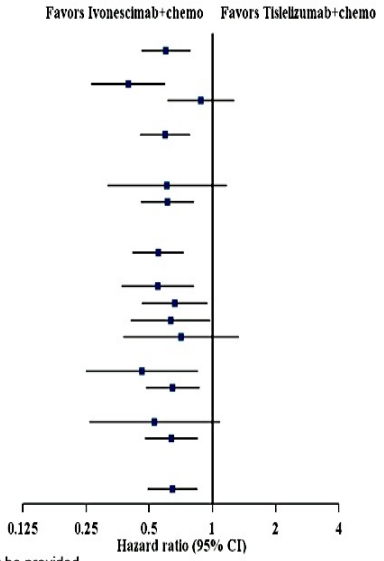
Subgroup Analysis of PFS by IRRC

- PFS benefit favored ivonescimab across all key subgroups.
- Observed important baseline imbalances in the older patient subgroup (Age ≥65), such as target lesion size, brain metastases. After adjusting for these covariates, the adjusted HR for Age ≥65 was 0.69.

Characteristic	Ivonescimab+chemo Events/Number of Subjects	Tislelizumab+chemo Events/Number of Subjects	Hazard ratio (95% CI)
Overall	94/266	127/266	0.60 (0.46, 0.78)
Age, years			
<65	37/135	69/139	0.40 (0.26, 0.59)
≥65	57/131	58/127	0.88 (0.61, 1.27)
Sex			
Male	90/256	118/238	0.59 (0.45, 0.78)
Female	4/10	9/28	
ECOG PS			
0	16/42	21/42	0.61 (0.32, 1.17)
1	78/224	106/222	0.61 (0.45, 0.82)
Disease Stage			
IIIB/IIIC	12/21	8/20	
IV	82/245	119/246	0.55 (0.41, 0.73)
PD-L1 TPS			
<1%	42/105	58/105	0.55 (0.37, 0.82)
≥1%	52/161	69/161	0.66 (0.46, 0.95)
1-49%	35/112	47/99	0.63 (0.41, 0.98)
≥50%	17/49	22/62	0.71 (0.37, 1.33)
≥3 metastases sites			
Yes	17/42	26/39	0.46 (0.25, 0.85)
No	77/224	101/227	0.64 (0.48, 0.87)
Liver metastases			
Yes	11/28	24/45	0.53 (0.26, 1.08)
No	83/238	103/221	0.64 (0.48, 0.85)
Brain metastases			
Yes	2/9	11/17	
No	92/257	116/249	0.64 (0.49, 0.85)



If the number of events at a level of a subgroup is less than 10, the median PFS and hazard ratio will not be provided.

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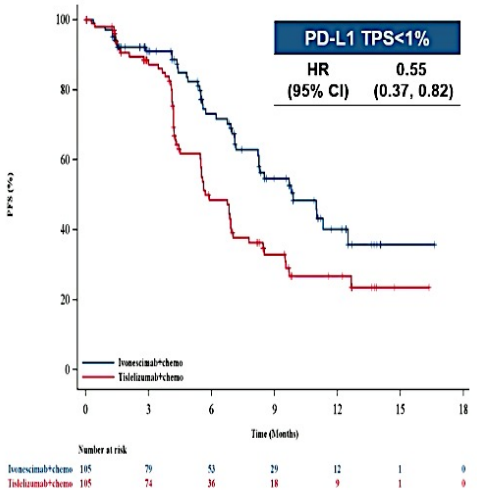
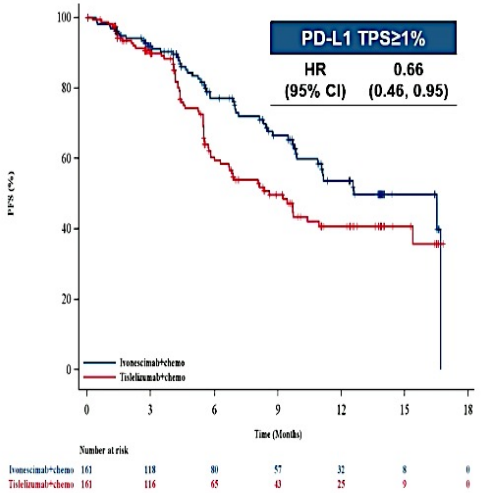
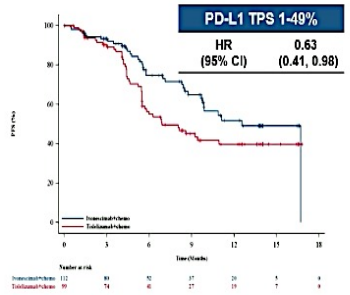
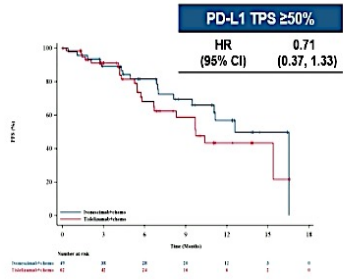
PFS in different PD-L1 expression Subgroups

Ivonescimab showed meaningful PFS improvement over tislelizumab regardless of PD-L1 expression.







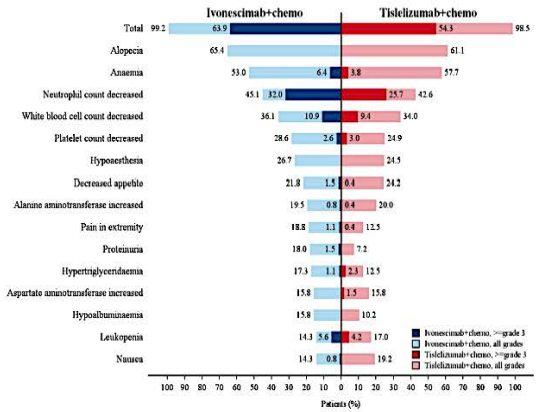


Safety Summary

Ivonescimab plus chemotherapy showed a manageable safety profile in sq-NSCLC.

	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=265)
TRAE	264 (99.2)	261 (98.5)
Grade ≥ 3 TRAE	170 (63.9)	144 (54.3)
Serious TRAE	86 (32.3)	80 (30.2)
Leading to ivonescimab or tislelizumab discontinuation	9 (3.4)	11 (4.2)
Leading to death	8 (3.0)	10 (3.8)

Most common TRAEs (incidence ≥15%)



Abbreviation: TRAE, treatment-related adverse events.

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Immune-Related and VEGF-Related AEs

Ivonescimab exhibited similar irAEs to tislelizumab.

Immune-related AEs	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=265)
Any grade	73 (27.4)	67 (25.3)
Grade ≥3 irAE	24 (9.0)	27 (10.2)
Serious irAE	23 (8.6)	26 (9.8)
Leading to ivonescimab or tislelizumab discontinuation	3 (1.1)	6 (2.3)
Leading to death	0	1 (0.4)

Possibly VEGF-related AEs occurred more frequently in the ivonescimab arm, most of which were grade 1-2.

Possibly VEGF-Related AEs#	Ivonescimab + chemo (N=266)		Tislelizumab + chemo (N=265)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any	123 (46.2)	20 (7.5)	60 (22.6)	6 (2.3)
Proteinuria	72 (27.1)	6 (2.3)	29 (10.9)	0
Haemorrhage	57 (21.4)	5 (1.9)	25 (9.4)	2 (0.8)
Hypertension	27 (10.2)	8 (3.0)	12 (4.5)	3 (1.1)
Arterial thromboembolism	3 (1.1)	3 (1.1)	0	0
Venous thromboembolism	2 (0.8)	0	3 (1.1)	1 (0.4)
Fistula	1 (0.4)	0	0	0

#AE terms were grouped terms.

Abbreviation: VEGF, vascular endothelial growth factor; AEs, adverse events; irAEs, immune-related adverse events.

Shun Lu

ADRIATIC Trial: LS-SCLC

ADRIATIC study design

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

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

N=730 (R‡)

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

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

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

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

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

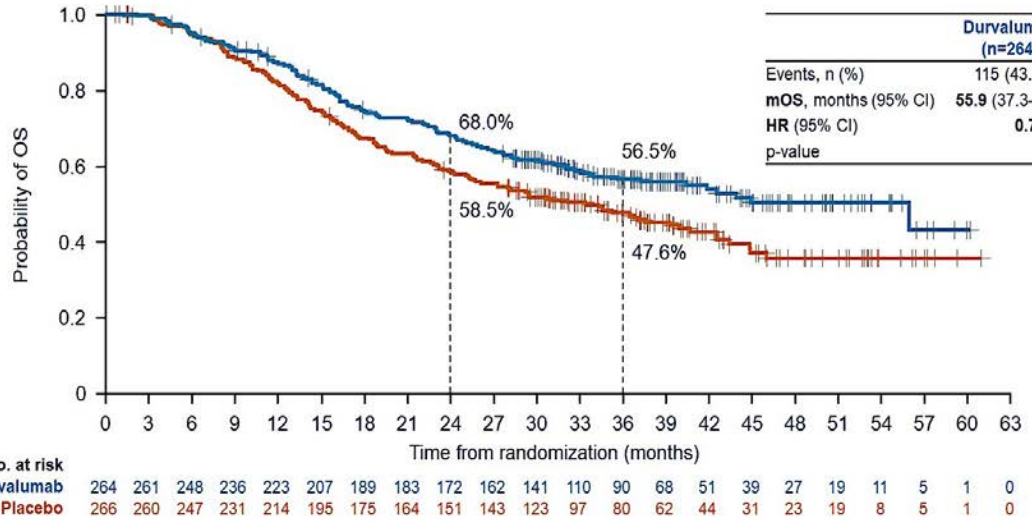
Dual primary endpoints:
- Durvalumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

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

Other secondary endpoints:
- OS/PFS landmarks
- Safety

Overall survival (dual primary endpoint)

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



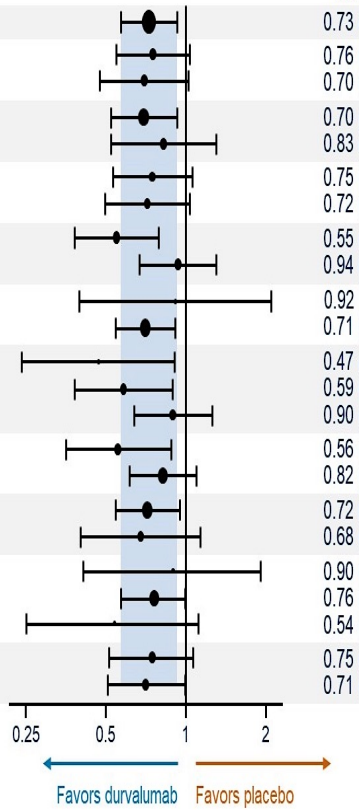
	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

No. at risk

Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

OS subgroup analysis

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



End of chemotherapy or radiotherapy, whichever was latest.
Intention-to-treat analysis stratified, subgroup analyses unstratified. Not all prespecified subgroups are included in the plot.

1.Spigel D, Cheng Y, Cho B, et al. ADRIATIC: durvalumab (D) as consolidation treatment (tx) for patients (pts) with limited-stage small-cell lung cancer (LS-SCLC). *J Clin Oncol* 42, 2024 (suppl 17; abstr LBA5) doi:10.1200/JCO.2024.42.17_suppl.LBA5 ASCO 2024

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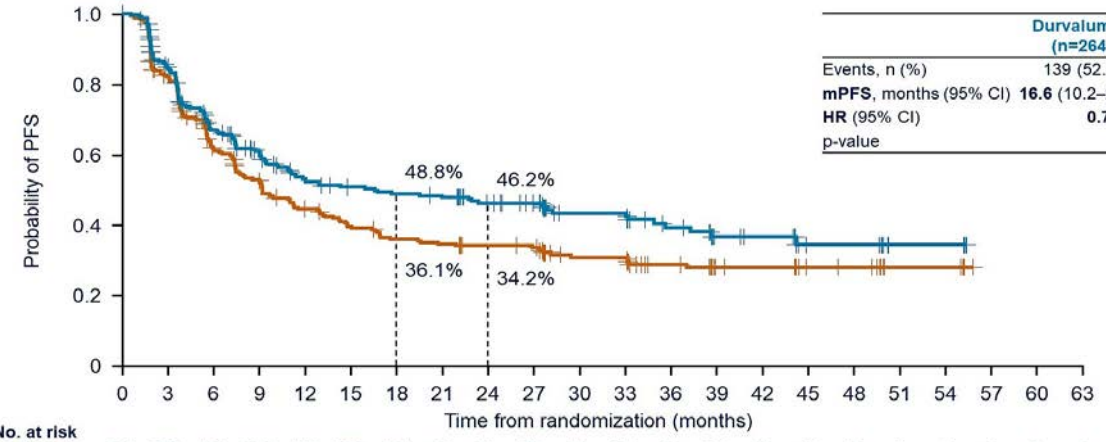
ADRIATIC Trial

Progression-free survival* (dual primary endpoint)

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

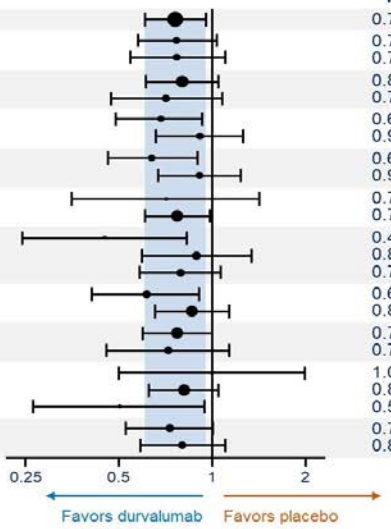


	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

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

PFS subgroup analysis

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

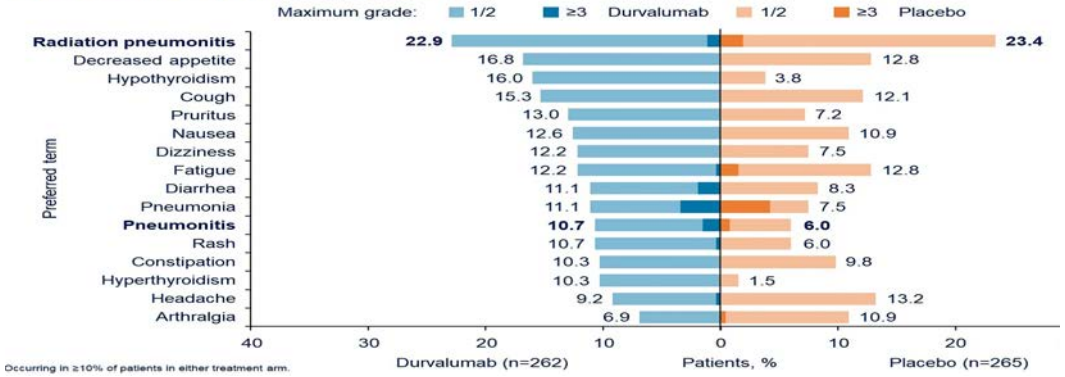


End of chemotherapy or radiotherapy, whichever was latest.
Intention-to-treat analysis stratified, subgroup analyses unstratified. Not all prespecified subgroups are included in the plot.

Exposure and safety summary

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

Most frequent AEs*



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

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

DR Spigel et al., ASCO 2024

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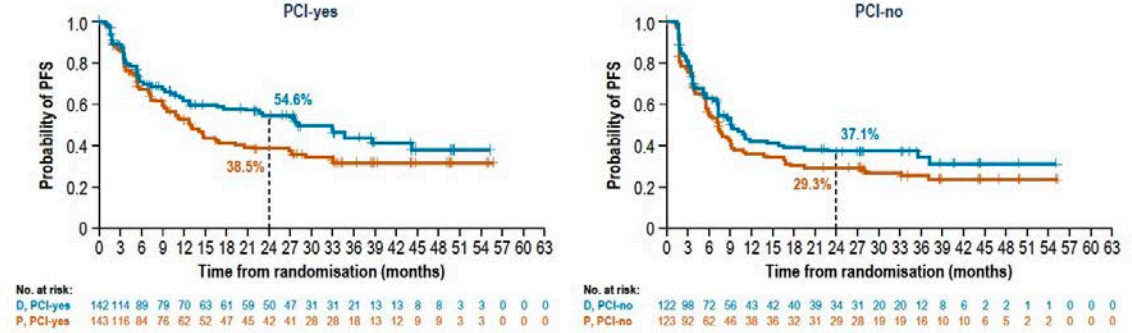
ADRIATIC Trial

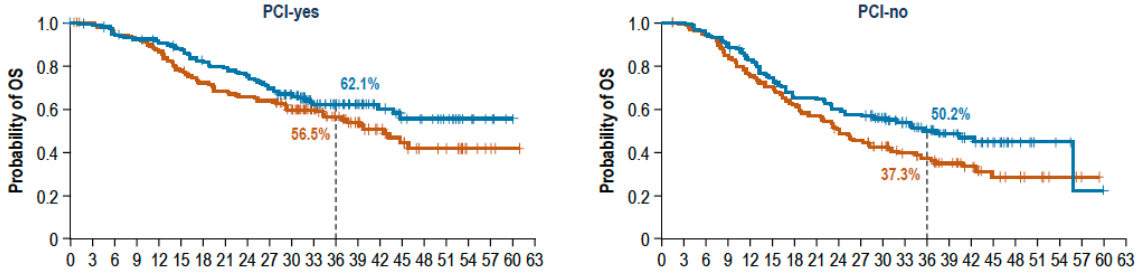
PCI-yes and PCI-no subgroups – PFS

	PCI-yes		PCI-no		ITT	
	D (n = 142)	P (n = 143)	D (n = 122)	P (n = 123)	D (n = 264)	P (n = 266)
Median PFS (95% CI), months	28.2 (16.8–44.2)	13.0 (9.2–17.0)	9.1 (7.3–14.3)	7.4 (5.7–9.2)	16.6 (10.2–28.2)	9.2 (7.4–12.9)
2-year PFS, %	54.6	38.5	37.1	29.3	46.2	34.2
HR (95% CI)	0.73 (0.52–1.00)*		0.80 (0.59–1.09)*		0.76 (0.61–0.95)†	
Multivariable HR (95% CI)	0.72 (0.52–0.99)‡		0.84 (0.61–1.15)‡		–	



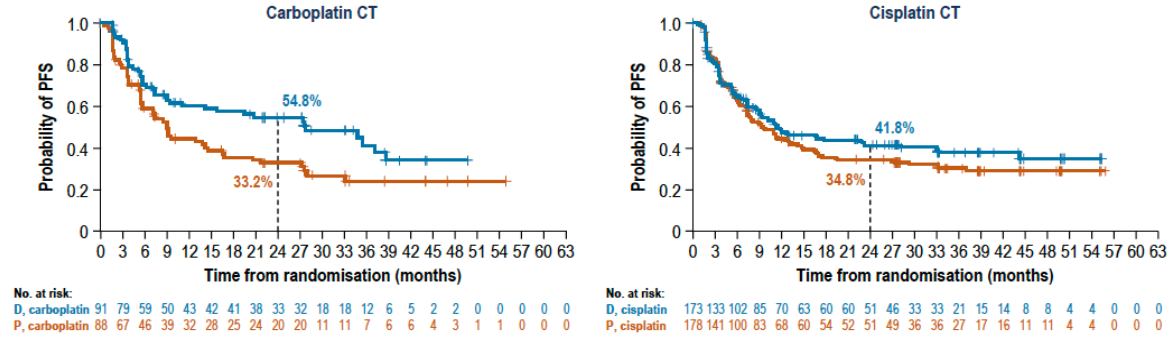
PCI-yes and PCI-no subgroups – OS

	PCI-yes		PCI-no		ITT	
	D (n = 142)	P (n = 143)	D (n = 122)	P (n = 123)	D (n = 264)	P (n = 266)
Median OS (95% CI), months	NR (43.9–NE)	42.5 (33.4–NE)	37.3 (24.3–NE)	24.1 (18.8–31.1)	55.9 (37.3–NE)	33.4 (25.5–39.9)
3-year OS, %	62.1	56.5	50.2	37.3	56.5	47.6
HR (95% CI)	0.75 (0.52–1.07)*		0.71 (0.51–0.99)*		0.73 (0.57–0.93)†	
Multivariable HR (95% CI)	0.72 (0.50–1.03)‡		0.73 (0.52–1.02)‡		–	



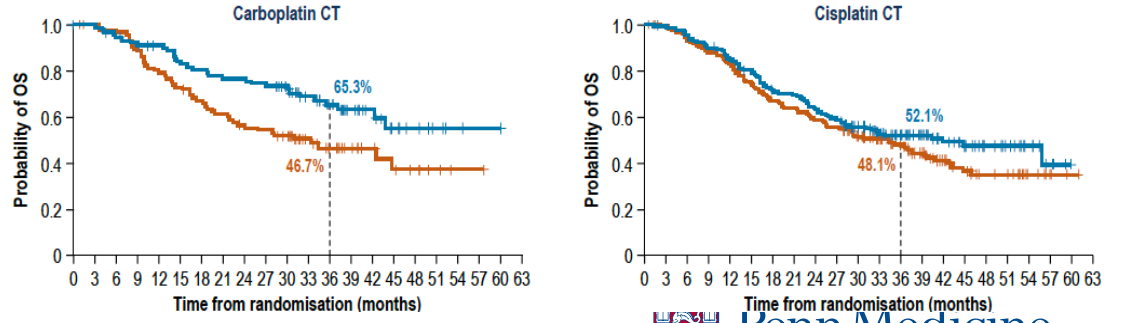
Carboplatin and cisplatin CT subgroups – PFS

	Carboplatin CT		Cisplatin CT		ITT	
	D (n = 91)	P (n = 88)	D (n = 173)	P (n = 178)	D (n = 264)	P (n = 266)
Median PFS (95% CI), months	27.9 (11.1–38.7)	9.2 (5.8–14.6)	11.4 (9.0–23.4)	9.7 (7.4–13.3)	16.6 (10.2–28.2)	9.2 (7.4–12.9)
2-year PFS, %	54.8	33.2	41.8	34.8	46.2	34.2
HR (95% CI)	0.61 (0.41–0.90)*		0.86 (0.65–1.13)*		0.76 (0.61–0.95)†	
Multivariable HR (95% CI)	0.60 (0.40–0.88)‡		0.89 (0.67–1.17)‡		–	



Carboplatin and cisplatin CT subgroups – OS

	Carboplatin CT		Cisplatin CT		ITT	
	D (n = 91)	P (n = 88)	D (n = 173)	P (n = 178)	D (n = 264)	P (n = 266)
Median OS (95% CI), months	NR (42.5–NE)	33.4 (21.7–NE)	41.9 (27.7–NE)	34.3 (25.4–40.7)	55.9 (37.3–NE)	33.4 (25.5–39.9)
3-year OS, %	65.3	46.7	52.1	48.1	56.5	47.6
HR (95% CI)	0.56 (0.35–0.89)*		0.82 (0.61–1.10)*		0.73 (0.57–0.93)†	
Multivariable HR (95% CI)	0.55 (0.35–0.87)‡		0.81 (0.60–1.08)‡		–	



S Senan et al., ESMO 2024;Abstract LBA81

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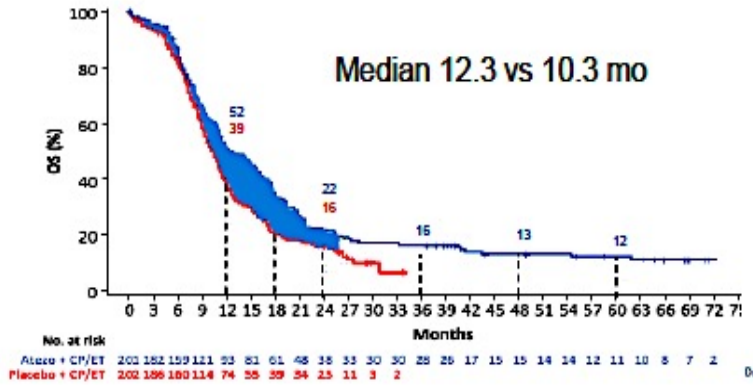
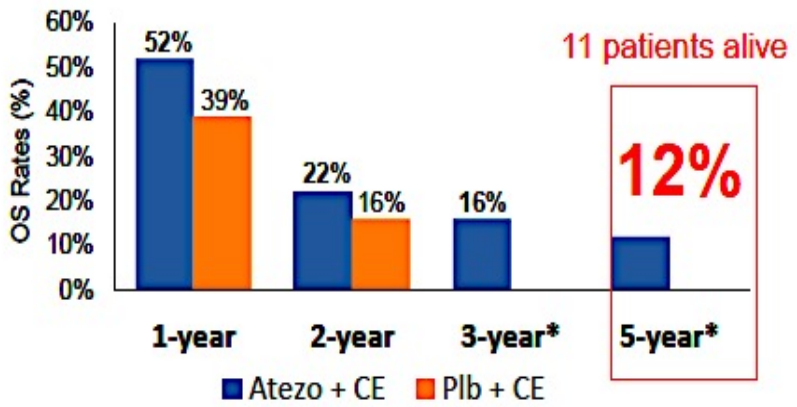
Pivotal Trials of ICIs in ES SCLC – Long term outcome

IMpower133 and IMbrella A

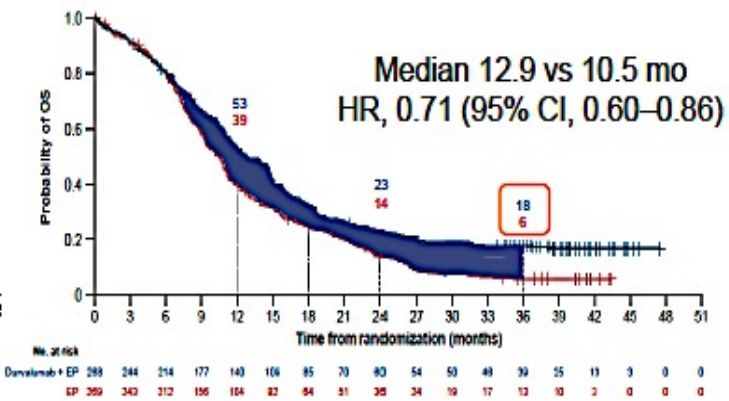
Atezolizumab + CP/ET vs CP/ET + Plb[1-2]

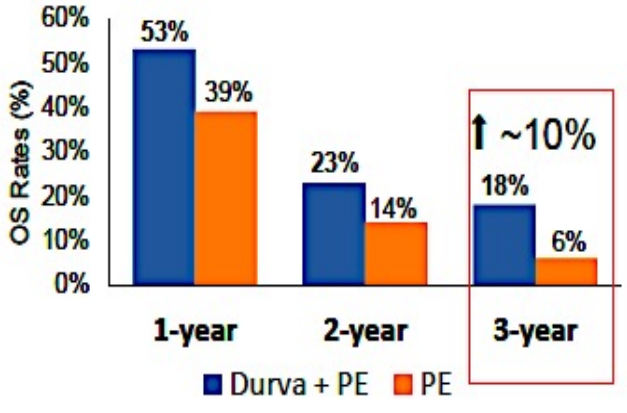




CASPIAN

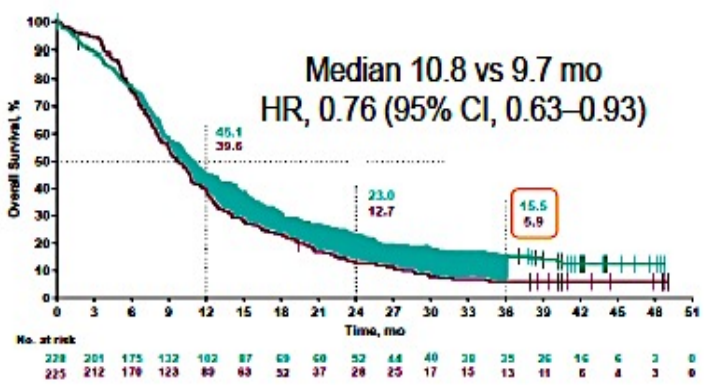
Durvalumab + P/ET vs P/ET[3-4]

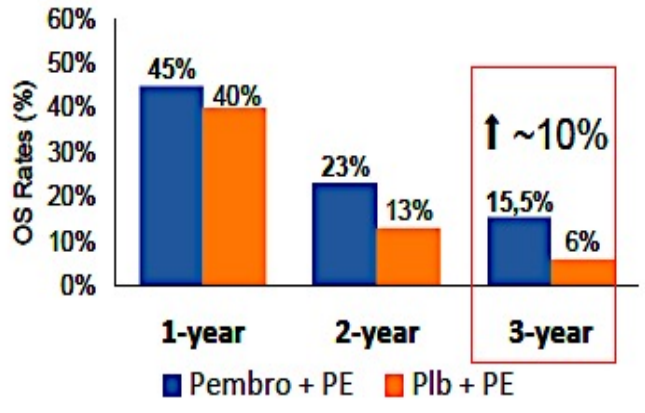




KEYNOTE-604

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

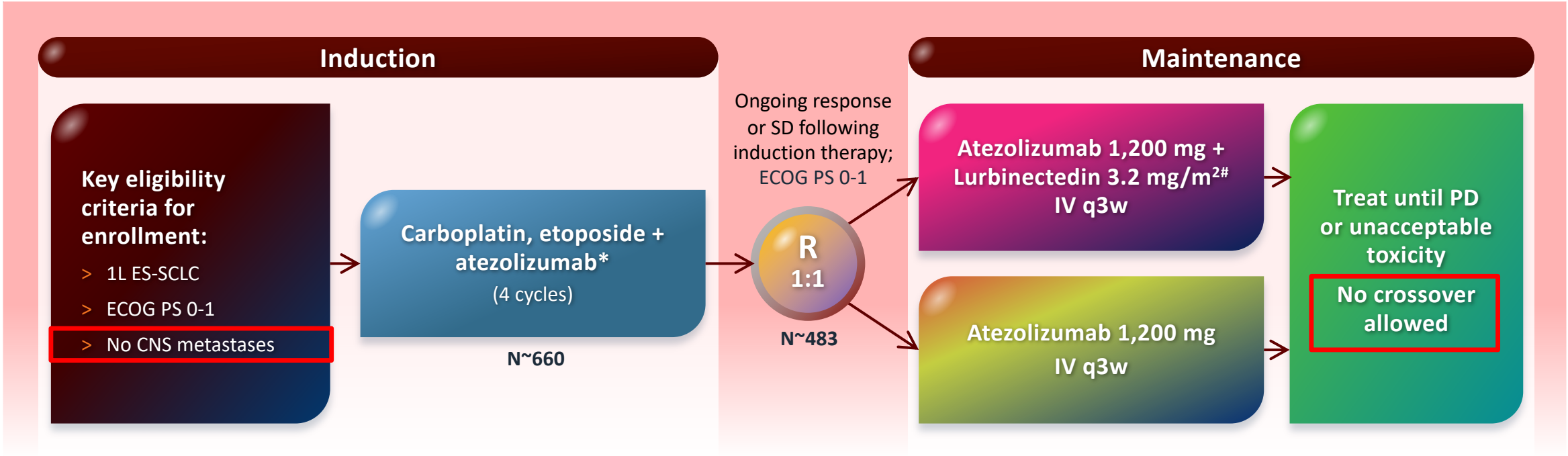




CP, carboplatin; ET, etoposide; P, platinum; Plb, placebo; NE, not estimable. * OS rates at 3-5 years were not estimable in the control arm as rollover to IMbrella A was not permitted.

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

IMforte Study Schema – Open Label Design



Stratification factors:

- ECOG PS 0 vs 1 *(at maintenance baseline)*
- LDH (≤ULN vs >ULN) *(at maintenance baseline)*
- Presence of liver mets *(at induction baseline)*
- Prior receipt of PCI

Primary endpoints:

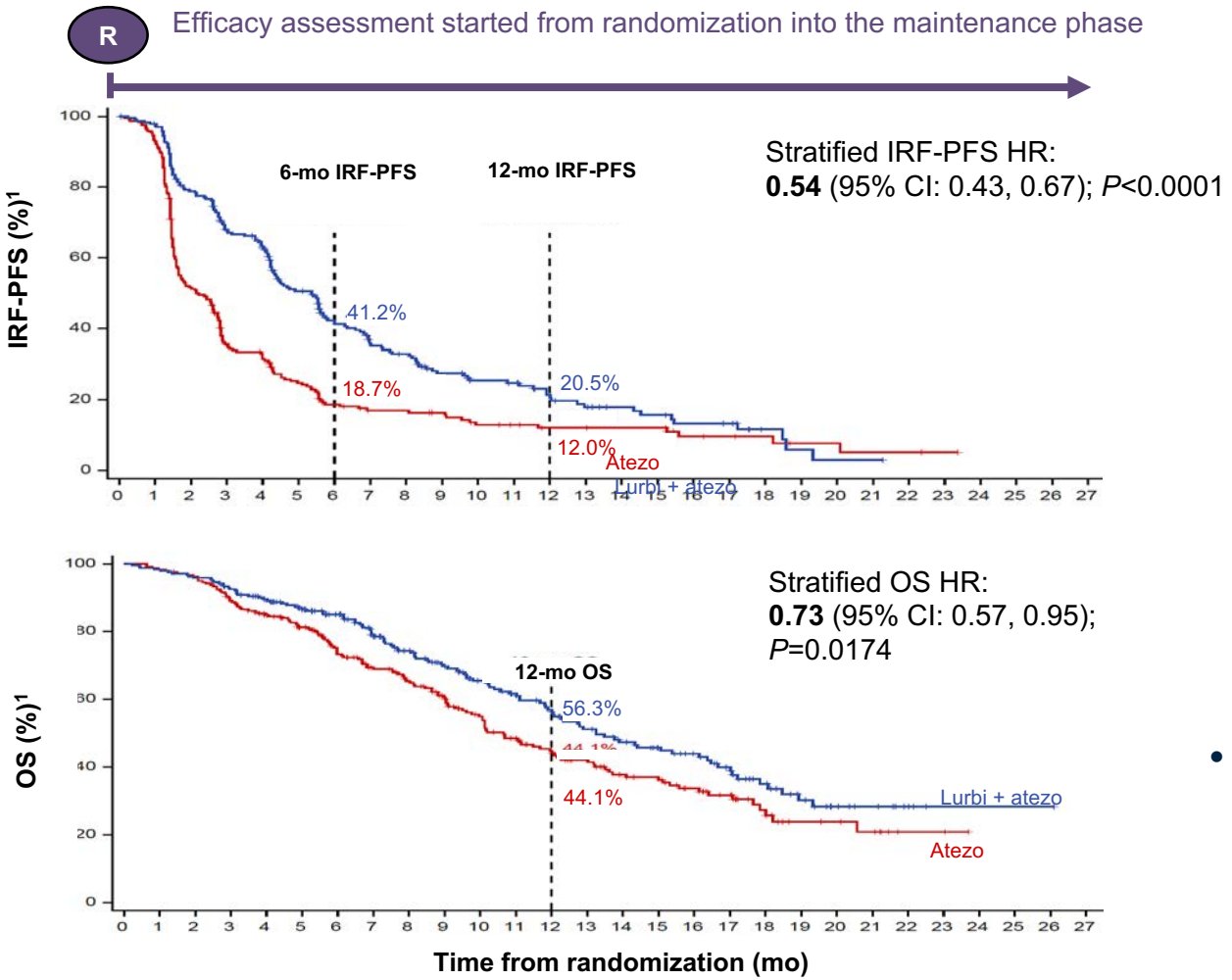
- IRF-assessed PFS and OS

Secondary endpoints:

- Inv-assessed PFS, ORR, DOR, landmark PFS & OS, safety

** PCI allowed following induction treatment and prior to start of maintenance therapy, 2 week window is required from last dose of radiotherapy to start of maintenance treatment;*
*# primary G-CSF prophylaxis and anti-emetic prophylaxis are mandatory; **DOR**, duration of response; **Inv**, investigator; **IRF**, independent review facility; **LDH**, lactate dehydrogenase; **ORR**, objective response rate; **OS**, overall survival; **PCI**, prophylactic cranial irradiation; **PD**, disease progression; **PFS**, progression-free survival; **SD**, stable disease*

Efficacy and safety summary during the maintenance phase



Patients with ≥1 AE, n (%)[1]	Lurbi + atezo (n=242)	Atezo (n=240)
Median treatment duration, mo	4.1 (lurbi)/ 4.2 (atezo)	2.1
All-cause AEs	235 (97.1)	194 (80.8)
Grade 3/4 AEs	92 (38.0)	53 (22.1)
Grade 5 AEs	12 (5.0)	6 (2.5)
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[a]	92 (38.0)	33 (13.8)
Lurbinectedin AESI[b,c]	93 (38.4)	62 (25.8)
Atezolizumab AESI[b,d]	76 (31.4)	54 (22.5)
Atezolizumab AESI requiring corticosteroids	40 (16.5)	18 (7.5)

- The safety profile of lurbi + atezo was predictable with an increased incidence of AEs, which were mostly low grade; rates of treatment discontinuation were low[1]

M Reck et al. WLCC 2025

Clinical cutoff: 29 July 2024; median safety follow-up: lurbi + atezo, 6.4 mo and atezo, 5.1 mo. One patient randomised to the atezo arm did not receive treatment and was not included in the safety analysis set. [a] Atezo dose modifications were not permitted. [b] 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. [c] Lurbi Grade 5 AESIs occurred in 7 patients (2.9%) in the lurbi + atezo arm and 4 patients (1.7%) in the atezo arm. [d] No atezo Grade 5 AESI occurred in either treatment arm. AE, adverse event; AESI, adverse event of special interest; HR, hazard ratio.

1. Paz-Ares L, et al. Lancet 2025;405:2129-2143.

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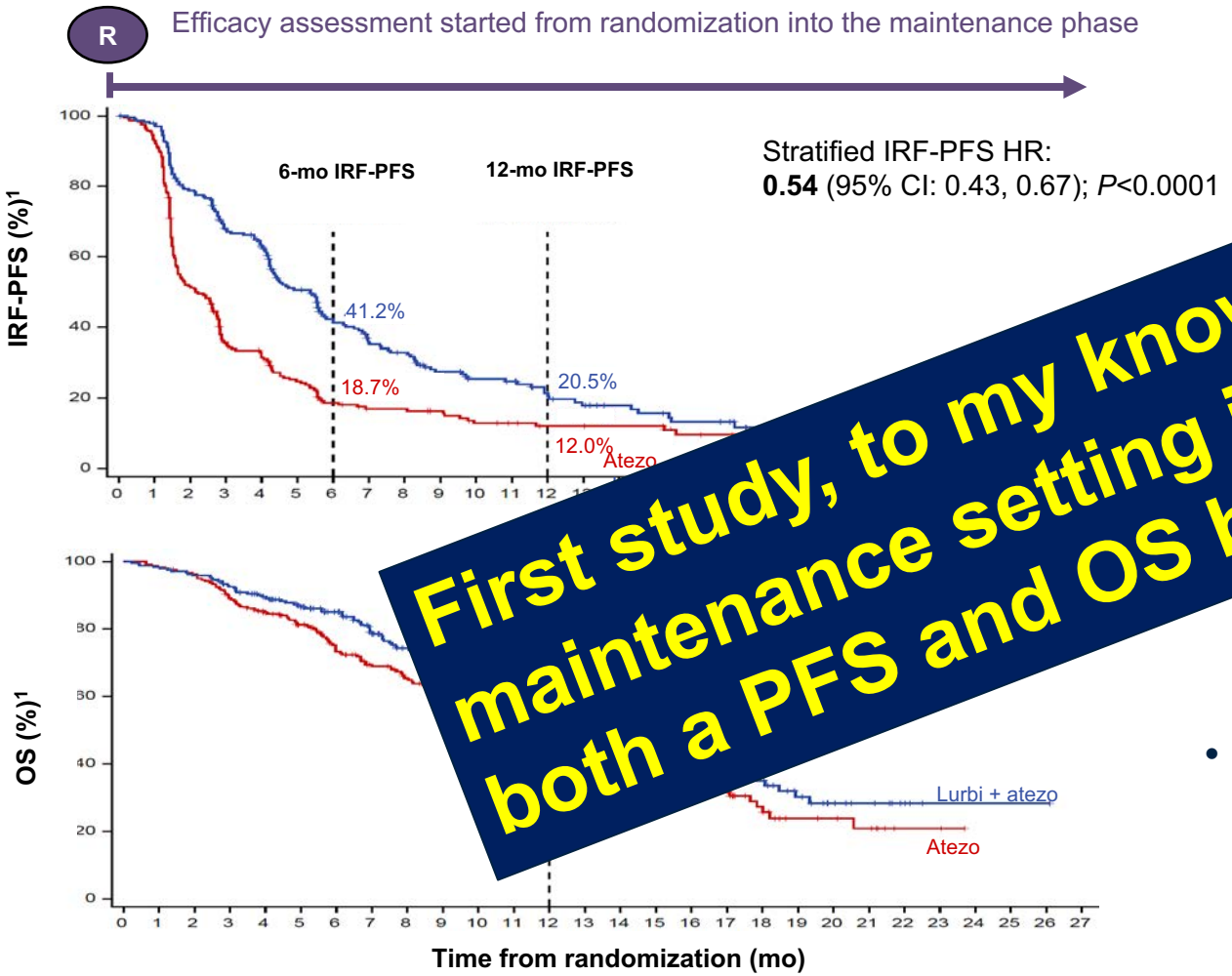
Efficacy and safety summary during the maintenance phase



First study, to my knowledge, in the maintenance setting in ES-SCLC, to show both a PFS and OS benefit

	bi + atezo =242)	Atezo (n=240)
Patients with ≥1 AE		
Media	lurbi)/ tezo)	2.1
	97.1)	194 (80.8)
	92 (38.0)	53 (22.1)
	12 (5.0)	6 (2.5)
	75 (31.0)	41 (17.1)
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1. Paz-Ares L, et al. Lancet 2025;405:2129-2143.

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FDA Approves Lurbinectedin in Combination with Atezolizumab or Atezolizumab and Hyaluronidase-Tqjs for Extensive-Stage Small Cell Lung Cancer

Press Release: October 2, 2025

"On October 2, 2025, the Food and Drug Administration approved lurbinectedin in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs for the maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin, and etoposide.

Efficacy was evaluated in IMforte (NCT05091567), a randomized, multicenter, open-label trial in patients receiving first-line treatment for ES-SCLC. In IMforte, 483 patients with ES-SCLC whose disease had not progressed after completion of four cycles of atezolizumab, carboplatin, and etoposide (induction treatment) were randomized (1:1) to receive either lurbinectedin in combination with atezolizumab administered intravenously (IV) or atezolizumab IV alone until disease progression or unacceptable toxicity."

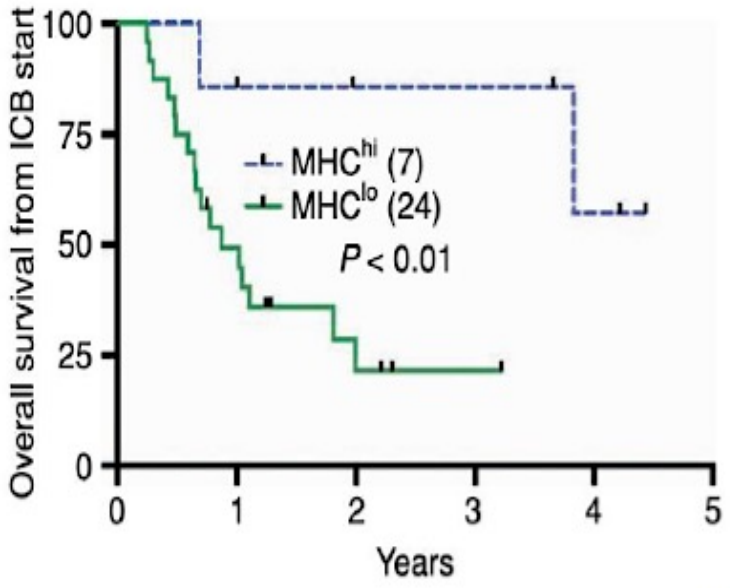
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lurbinectedin-combination-atezolizumab-or-atezolizumab-and-hyaluronidase-tqjs-extensive

RTP RESEARCH TO PRACTICE

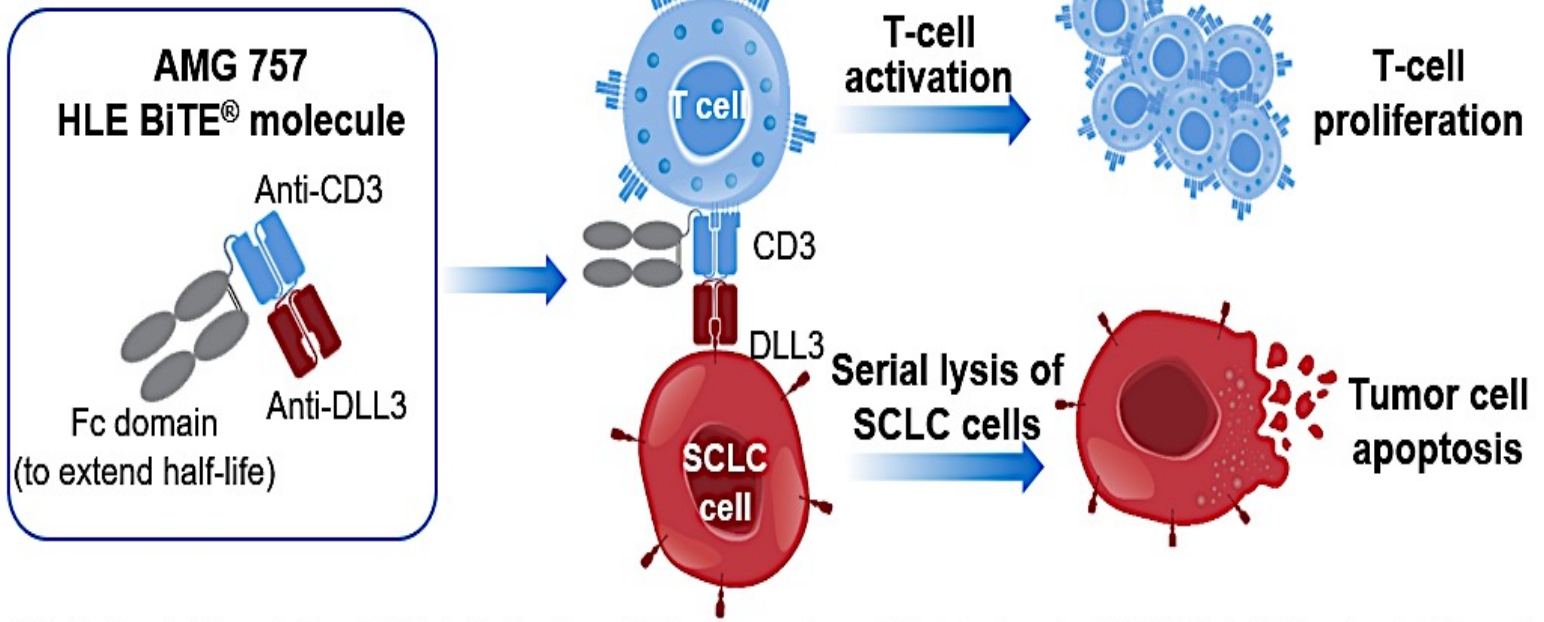
T Cell Engagers – Tarlatamab (AMG 757)
Overcoming lack of effective Ag presentation

Is downregulation of MHC-I a primary determinant of IO resistance in SCLC?

SCLC patients treated with immune checkpoint blockade



AMG 757 engages endogenous T cells and SCLC cells

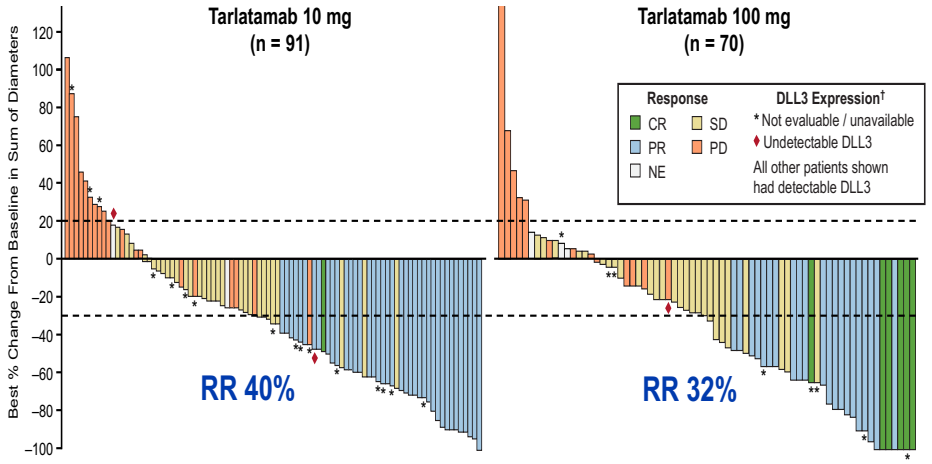


CD, cluster of differentiation; DLL3, delta-like ligand 3; Fc, fragment crystallizable domain; HLE BiTE, half-life extended bispecific T-cell engager; SCLC, small cell lung cancer.

BiTE molecules engage a pt's own T cells to attack and eradicate cancer cells[1–3]

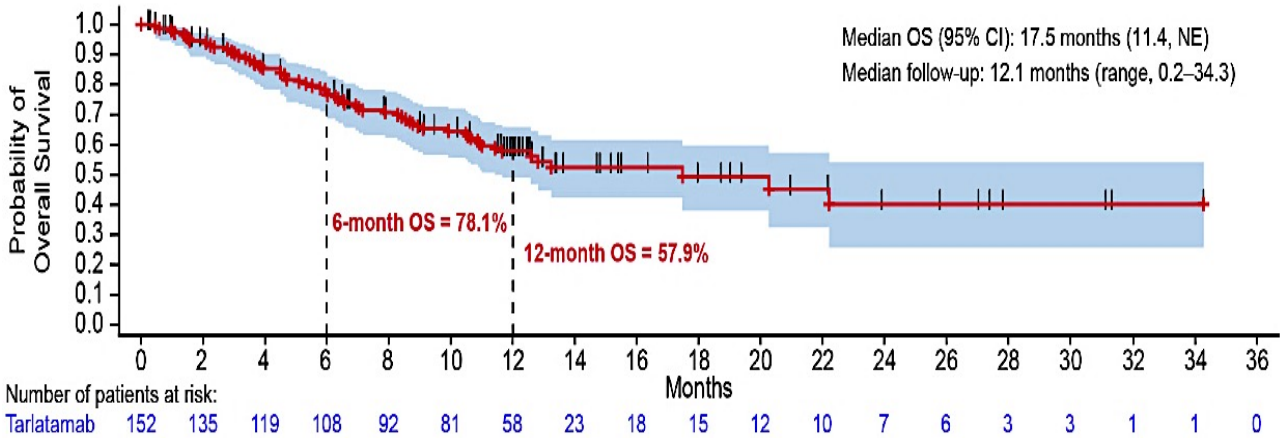
1.Stieglmaier J, et al. *Expert Opin Biol Ther*. 2015;15:1093-1099. 2. Einsele H, et al. *Cancer.* 2020;126:3192-3201. 3. Bargou R, et al. *Science.* 2008;321:974-977. 4. Mahadevan et al. Cancer Discov. 2021. 5. Blackhall F et al. ELCC 2021;Abstract 48MO

Tarlatamab: DeLLphi-300 & -301 Trials in pretreated SCLC pts



Responses were observed regardless of DLL3 expression, as well as in patients without evaluable tumor tissue

Shown are 91 of 100 patients (tarlatamab 10 mg) and 70 of 88 patients (tarlatamab 100 mg) who had available post-baseline measurements of target lesions.
†DLL3 expression was assessed by immunohistochemistry of tumor tissue samples.
CR, complete response; DLL3, delta-like ligand 3; NE, not evaluable; PD, progressive disease, PR, partial response; SD, stable disease.



Most Common TEAEs in ≥ 20% of Patients, n (%)	Part 1 + 2 Tarlatamab 10 mg (n = 99)	Part 1 Tarlatamab 100 mg (n = 87)	Part 3 Tarlatamab 10 mg (n = 34)
CRS	**49 (49)**	**53 (61)**	**19 (56)**
Grade 1–2	**49 (49)**	**48 (55)**	**18 (53)**
≥ Grade 3	**0**	**5 (6)**	**1 (3)**
Decreased appetite	25 (25)	38 (44)	13 (38)
Pyrexia	38 (38)	29 (33)	8 (24)
Constipation	28 (28)	22 (25)	8 (24)
Anemia	26 (26)	22 (25)	9 (26)
Asthenia	20 (20)	21 (24)	10 (29)
Dysgeusia	**24 (24)**	**12 (14)**	**14 (41)**
Fatigue	21 (21)	17 (20)	9 (26)

Paz-Ares et al. ESMO 2023 & NEJM 2023; HD Hummel et al., ELCC 2024

DeLLphi-304 trial

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)

R
1:1
(N = 509)

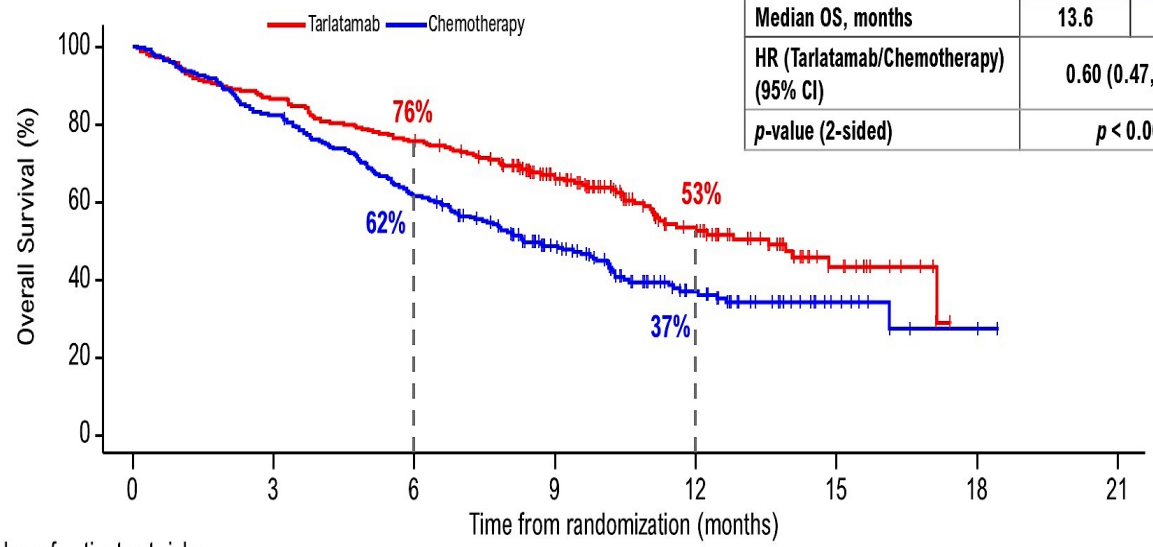
- Tarlatamab (n = 254)
- Chemotherapy* (n = 255)

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

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

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

C Rudin et al ASCO & NEJM 2025

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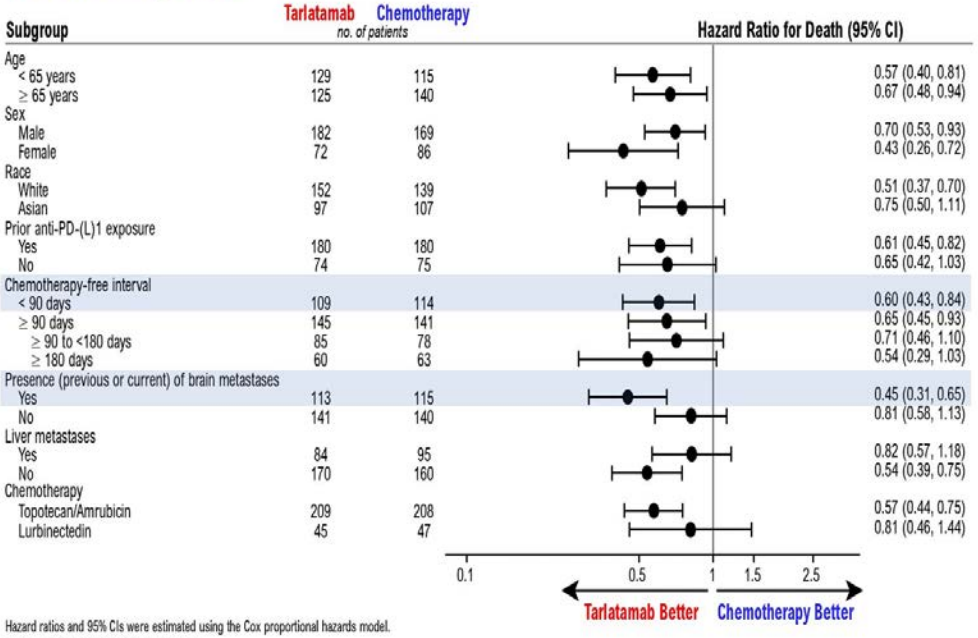
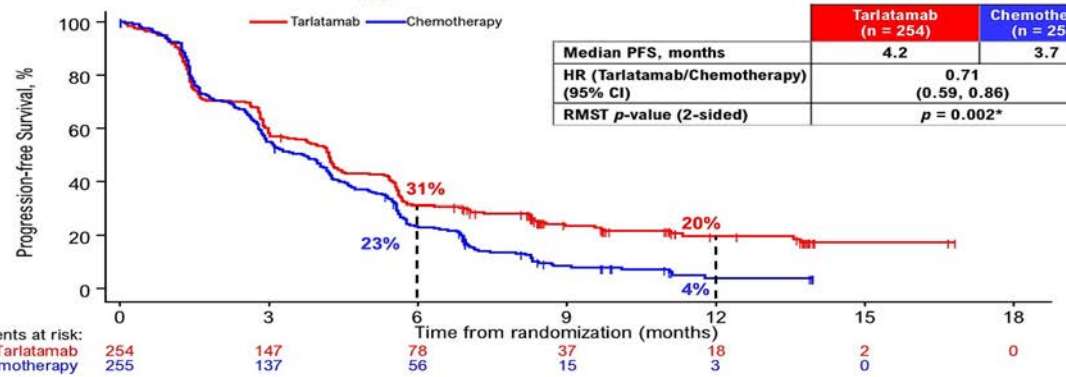
Survival benefit with tarlatamab was consistent across prespecified patient subgroups



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



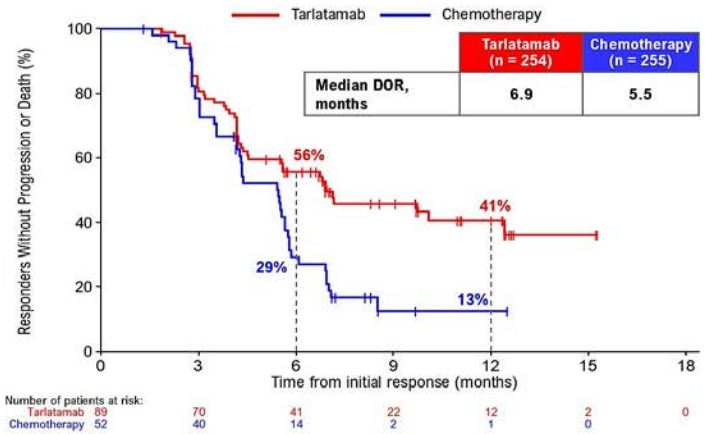
	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median PFS, months	4.2	3.7
HR (Tarlatamab/Chemotherapy) (95% CI)	0.71 (0.59, 0.86)	
RMST *p*-value (2-sided)	*p* = 0.002*	

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.

Tarlatamab was associated with more frequent and more durable responses

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

Duration of response



	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median DOR, months	6.9	5.5

*Assessment of disease response was based on RECIST 1.1 guidelines. Confirmation of complete response and partial response was required no fewer than 4 weeks after initial documentation of complete response or partial response. †Investigator-assessed response in the intention-to-treat analysis set; ‡Odds ratios and *p* value not shown as the difference in ORR between the 2 arms was not formally tested. §Percentage of total number of responders.
DOR, duration of response; **RECIST,** Response Evaluation Criteria in Solid Tumors.

C Rudin et al. ASCO 2025;Abstract LBA8008

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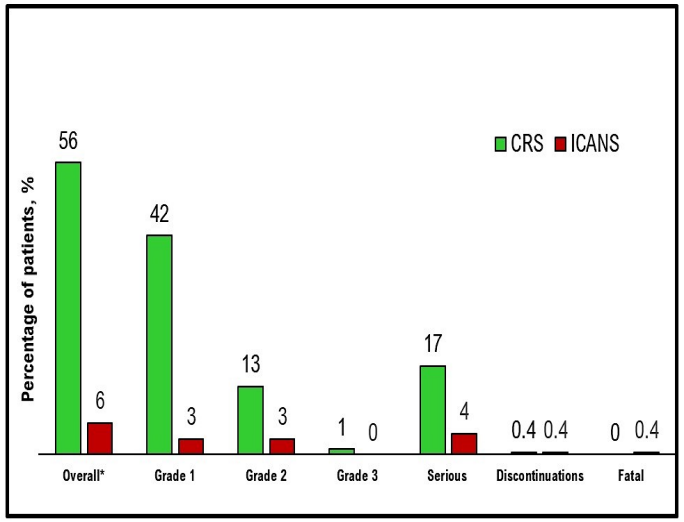
Toxicity Profile – DeLLphi-304

	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)

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

C Rudin et al. ASCO 2025;Abstract LBA8008

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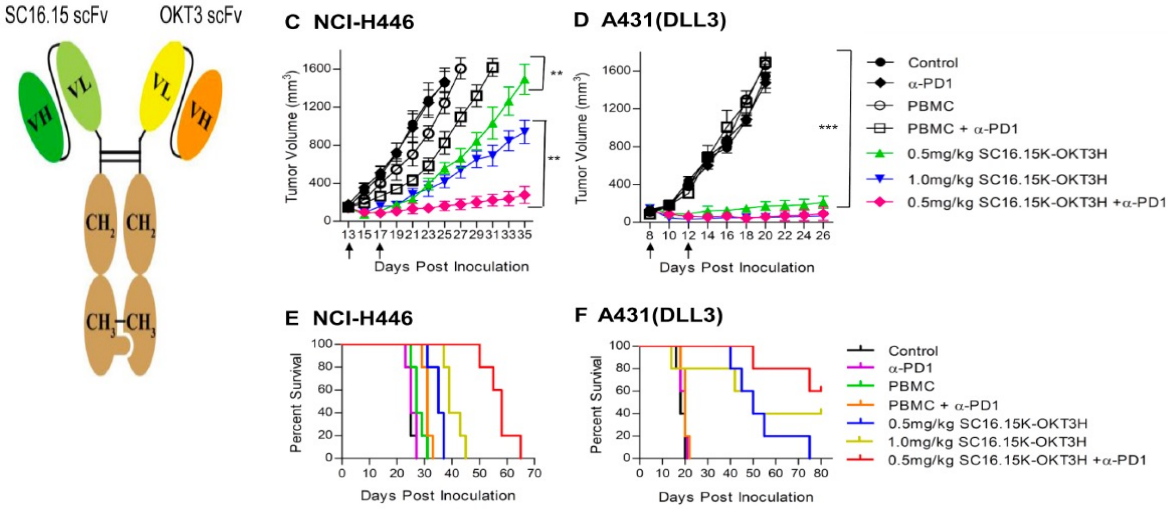
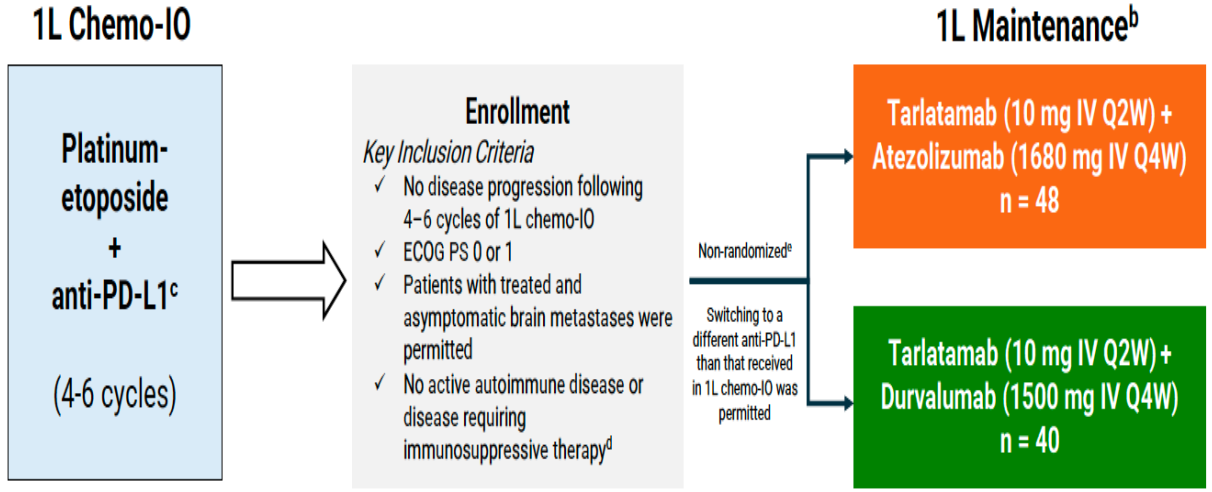
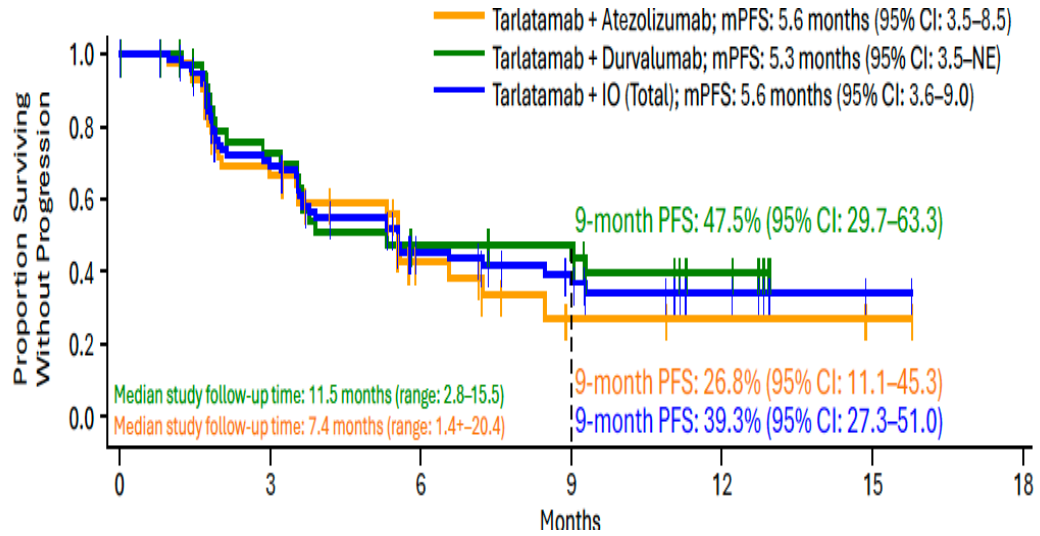
DLL3 TCE + PD-1 inhibition → DeLLphi-303 Trial



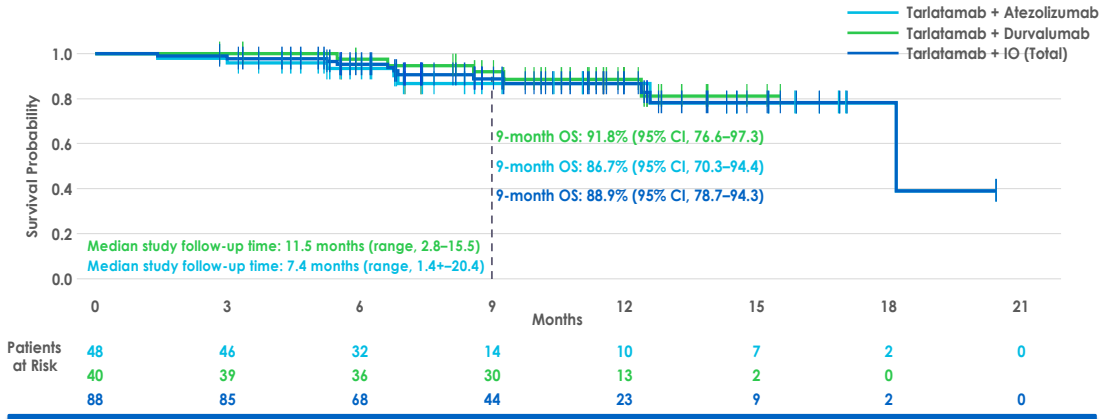




X Chen et al., JITC 2022

OS, Beginning From 1L Maintenance

303



Tarlatamab with a PD-L1 inhibitor as 1LM showed a 9-month OS* of 89%

SMC Lau et al., WLCC 2024

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ADCs in SCLC

Target	Payload/MOA	Agent	DAR	SCLC Activity RR, DOR
TROP2	SN-38; topo I inhibitor	Sacituzumab govitecan	~7-8	N 43; ORR 41,9%; PFS 4,4mo; OS 13,6 mo
TROP2	Rezetecan; topo I inhibitor	Tizetatug Rezetecan SHR-A1921	4	N 17; ORR 33,4%
SEZ6	Topo I inhibitor	ABBV-706	6	N 23; ORR 61%
SEZ6	Calicheamicin; induces DS breaks	ABBV-011	~2	N 450; ORR 25%; PFS 3,5 mo
EGFR/HER3	Ed-04; topo I inhibitor	Izabren	8	N 58; ORR 48,1%; PFS 4,1mo; OS 12,2 mo

Owonikoko et al. ASCO 2024; Dowlati et al., JTO 2024; Wang et al., WLCC 2024; Morgensztern et al. CCR 2024; Chandana et al. WLCC 2024; Huang et al., ASCO 2025

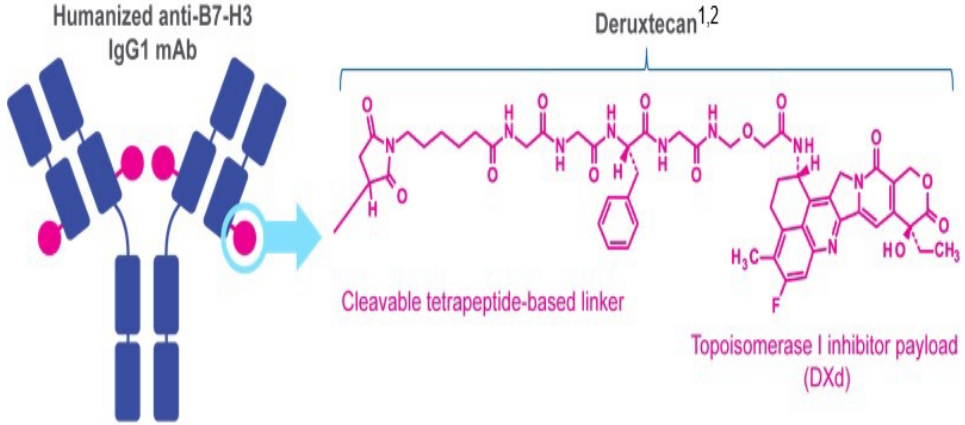
ADCs in SCLC

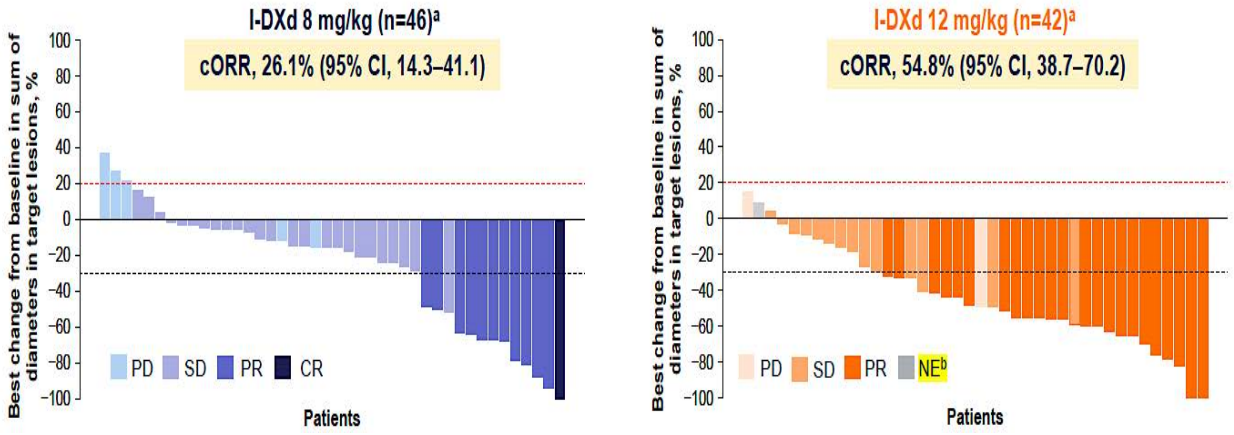
Target	Payload/MOA	Agent	DAR	SCLC Activity RR, DOR
DLL3	C24; Topo I inhibitor	ZL1310	8	N 42; ORR 42%
DLL3	Topo I inhibitor	IBI3009	8	Ongoing; NCT 06613009
B7-H3	Deruxtecan; topo I inhibitor	Ifinatamab deruxtecan	~4	N 48; ORR 54 %; PFS 5.5 mo
B7-H3	HS-9365 (Topo I inhibitor))	HS-20093	4	N 22; 61.3%; PFS 7.3 mo
B7-H3	Topo I inhibitor	YL201	8	N 72; 63,9%; PFS 6.3 mo
B7-H3	Super TopoI	MHB088C	4	N 93; RR43%; PFS 5.3 mo
B7-H3	Topo I Inhibitor	DB-1311/BNT324	~6	N 73; RR 56.2%; PFS 5.3 mo

Patel et al., ASCO 2025; Rudin et al., WLCC 2024; Wang et al., WLCC 2024; Ma et al., Nat Med 2025; Zhou et al. ASCO 2025

IDEATE Lung 01 Phase II trial

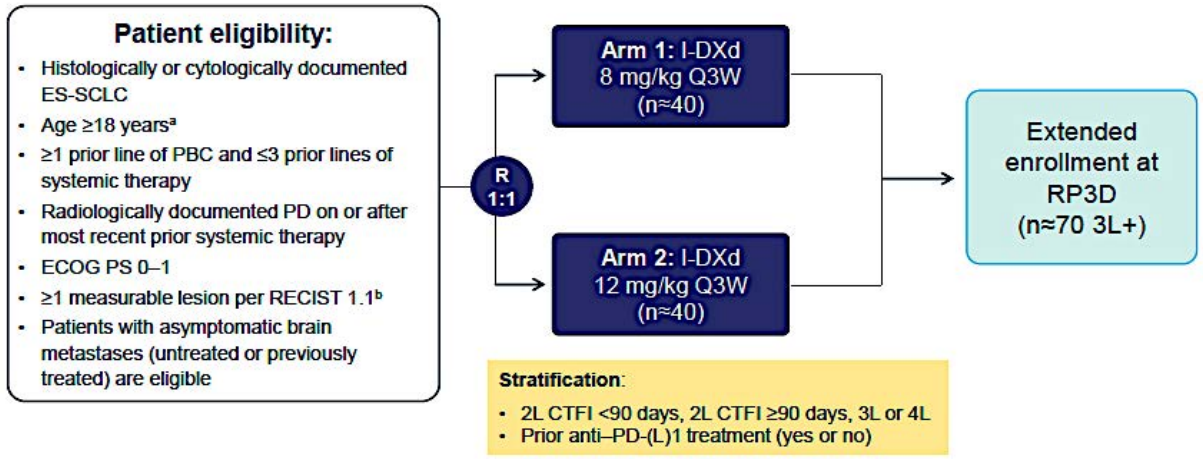
Ifinatamab Deruxtecan (DS 7300) – SCLC

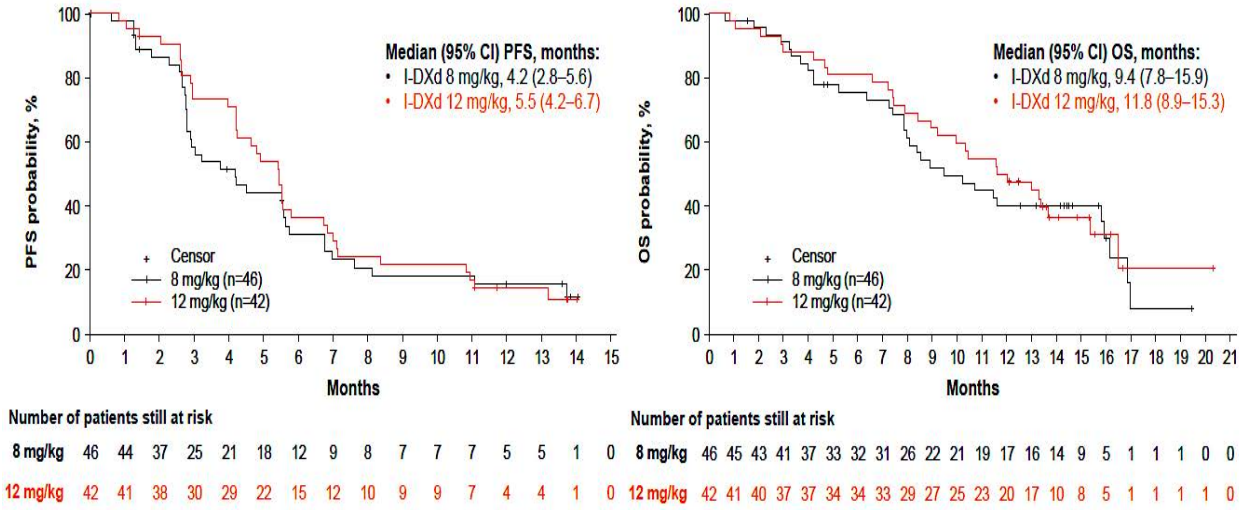




Peressini et al. Clin Cancer Res 2024

Phase 2 IDeate-Lung01 study (NCT05280470)



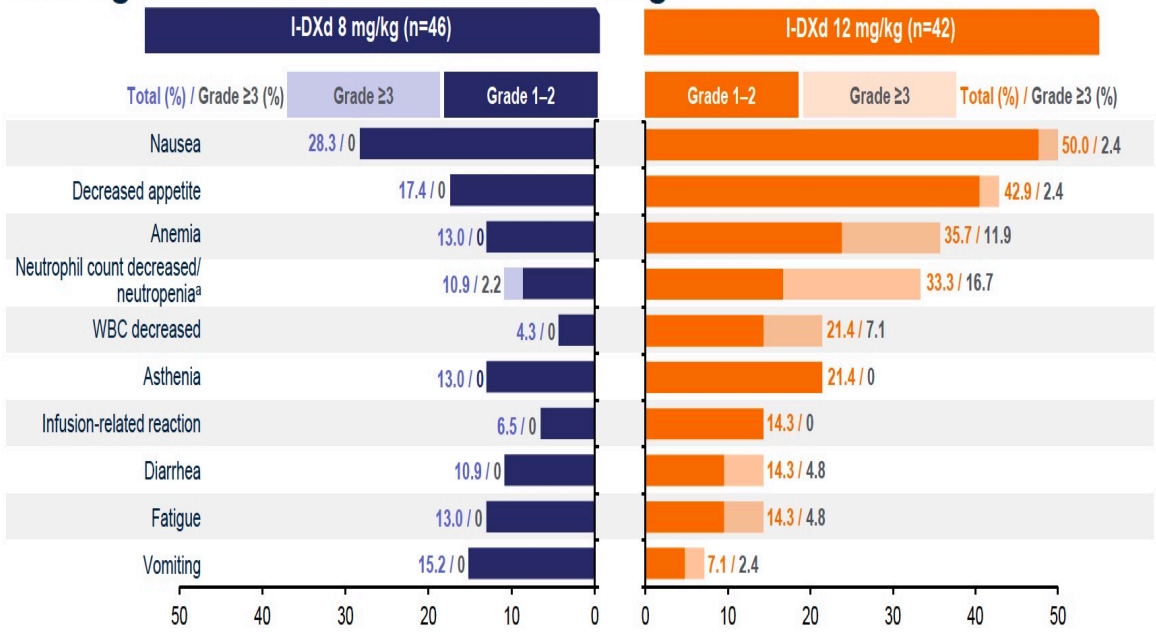


Rudin et al. WLCC 2024

IDEATE Lung 01 Phase II trial - Safety

	I-DXd 8 mg/kg n=46	I-DXd 12 mg/kg n=42
Median treatment duration, months (range)	3.5 (0.03–13.9)	4.7 (0.03–15.2)
Median cycles, n (range)	6.0 (1.0–21.0)	7.5 (1.0–23.0)
Any TEAE, n (%)	44 (95.7)	41 (97.6)
TEAE with CTCAE Grade ≥3, n (%)	20 (43.5)	21 (50.0)
TEAE associated with drug discontinuation, n (%)	3 (6.5)	7 (16.7)[a]
TEAE associated with dose delay, n (%)	10 (21.7)	15 (35.7)
TEAE associated with dose reduction, n (%)	4 (8.7)	6 (14.3)
TEAE associated with an outcome of death, n (%)	3 (6.5)	6 (14.3)

The most common treatment-related TEAEs (≥10% total population) were gastrointestinal and hematologic



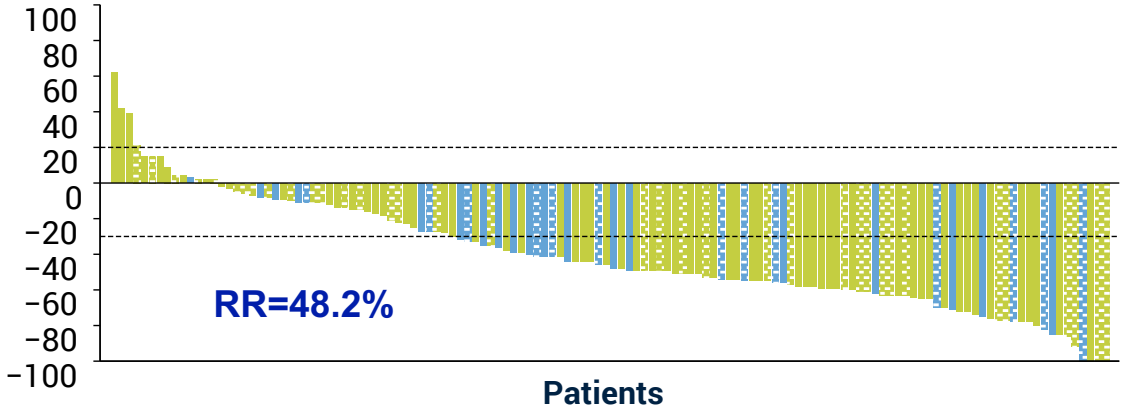
ILD/pneumonitis adjudicated as treatment-related was reported in:

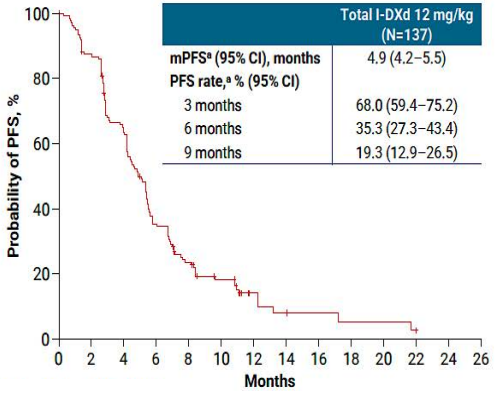
- Four (8.7%) patients in the 8-mg/kg cohort (Grade 2, n=3; Grade 5, n=1)
- Five (11.9%) patients in the 12-mg/kg cohort (Grade, 1 n=1; Grade 2, n=3; Grade 3, n=1)
- No ILD events were pending adjudication at the time of data cutoff

Rudin et al. WLCC 2024

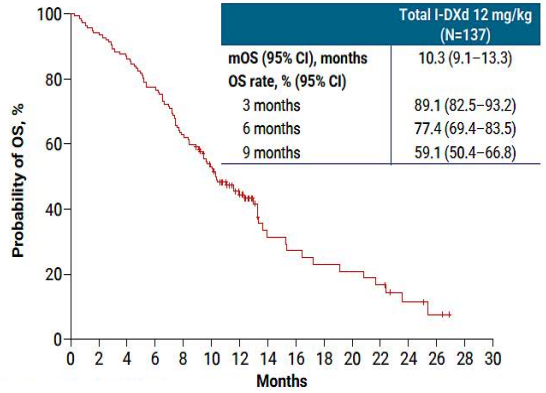
B7-H3 Antibody Drug Conjugates show strong activity in Relapsed Small Cell Lung Cancer

Ifinatamab Deruxtecan (I-DXd)





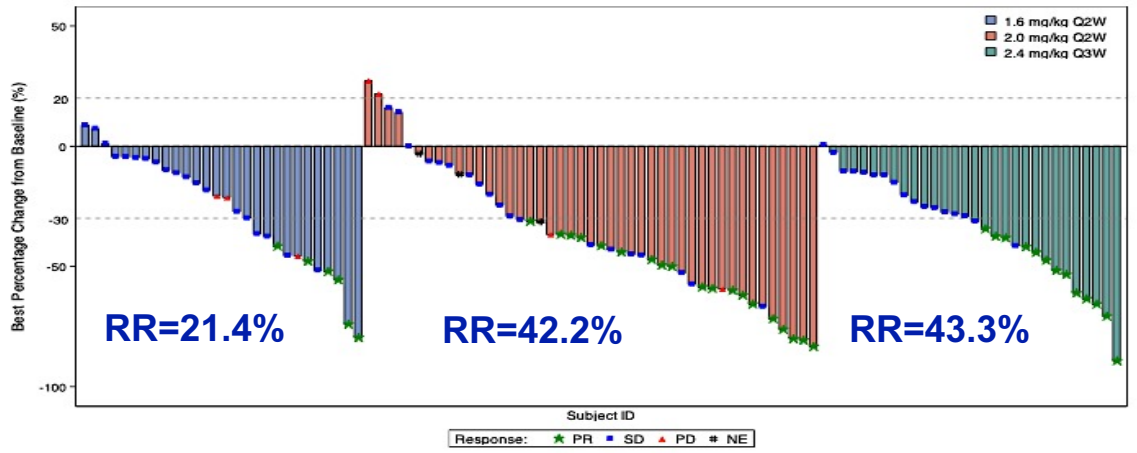
	Total I-DXd 12 mg/kg (N=137)
mPFS[a] (95% CI), months	4.9 (4.2–5.5)
PFS rate,[a] % (95% CI)	
3 months	68.0 (59.4–75.2)
6 months	35.3 (27.3–43.4)
9 months	19.3 (12.9–26.5)

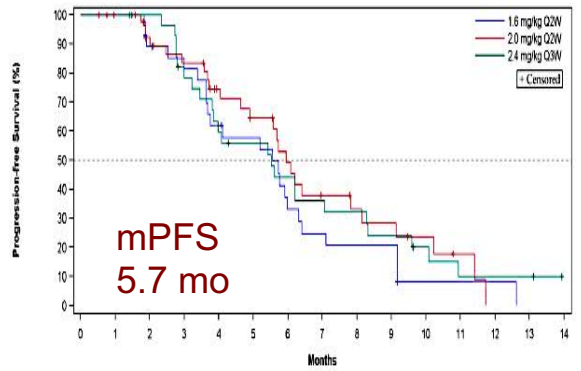


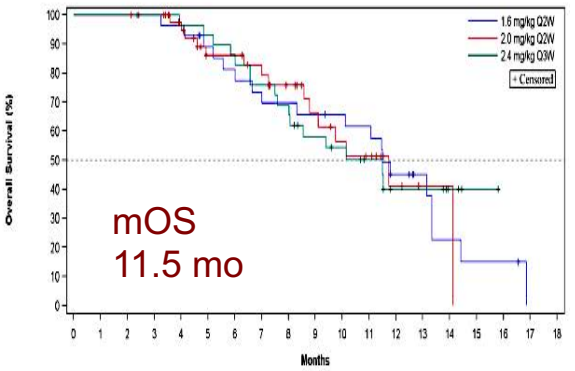
	Total I-DXd 12 mg/kg (N=137)
mOS (95% CI), months	10.3 (9.1–13.3)
OS rate, % (95% CI)	
3 months	89.1 (82.5–93.2)
6 months	77.4 (69.4–83.5)
9 months	59.1 (50.4–66.8)

MJ Ahn et al., WCLC 2025

QLC5508 (MHB088C) - B7-H3







C Zhou et al., WCLC 2025

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Conclusions and Challenges in SCLC

- In limited stage SCLC, Consolidation with Durvalumab for up to 2 yrs is the SOC with ~ 10-12% absolute improvement in long term OS
- The addition of CPIs to standard EP chemo in Ext stage SCLC has led to 5 yr OS rates ≥ 10%
- Lurbinectedin combined with atezolizumab in the maintenance setting in ES-SCLC has led to statistically significant and clinically meaningful improvements in PFS and OS, albeit heightened toxicity
- Tarlatamab is the New SOC in 2L SCLC dramatically displacing lurbinectedin and topotecan based on unprecedented RR%, PFS and OS advantages
- Role of ADCs will be determined in the next 12-24 mos
- We lack clear biomarkers and reproducible targets

Agenda

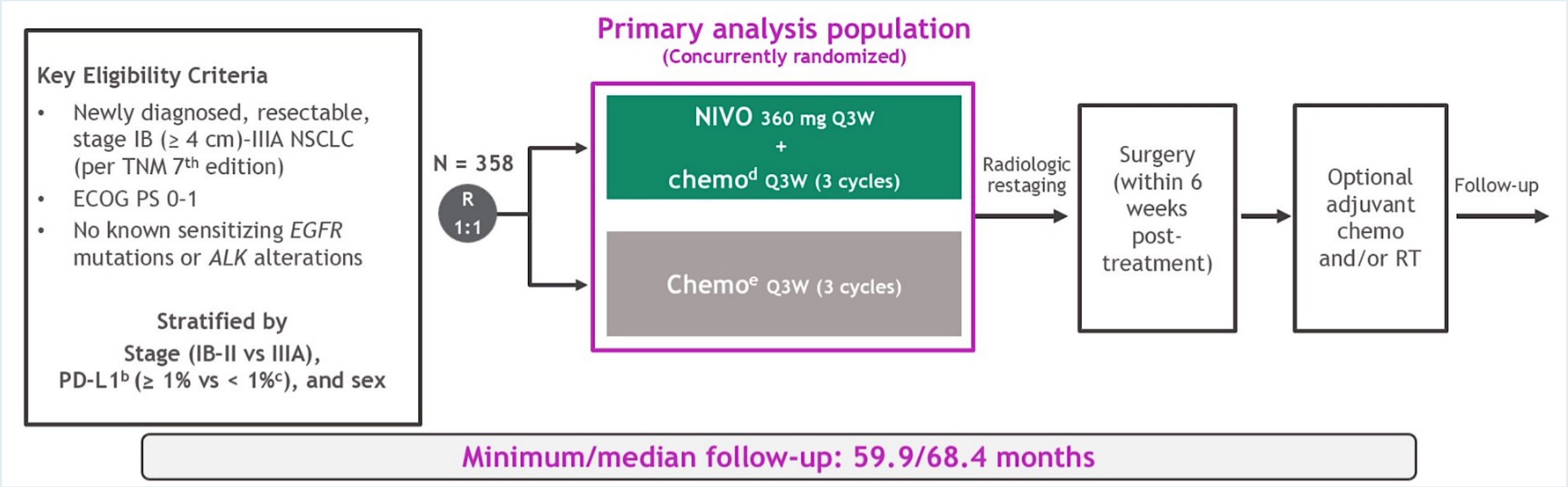
Module 1 — Lung Cancer: *Drs Gainor, Langer and Shields*

- **Targeted Therapy for Non-Small Cell Lung Cancer (NSCLC) —** *Dr Gainor*
- **Nontargeted Therapy for NSCLC; Small Cell Lung Cancer —** *Dr Langer*
- **Neoadjuvant, Perioperative and Adjuvant Anti-PD-1/PD-L1 Antibody-Based Approaches for Patients with Localized NSCLC —** *Dr Shields*

Neoadjuvant, Perioperative and Adjuvant Anti-PD-1/PD-L1 Antibody-Based Approaches for Patients with Localized NSCLC

Misty Dawn Shields, MD, PhD
Assistant Professor of Clinical Medicine
Indiana University School of Medicine
Adjunct Assistant Professor of Medical and Molecular Genetics
Associate Member, Experimental and Developmental Therapeutics
Department of Medicine, Division of Hematology/Oncology, Thoracic Oncology
Indiana University Melvin and Bren Simon Comprehensive Cancer Center
Indianapolis, Indiana

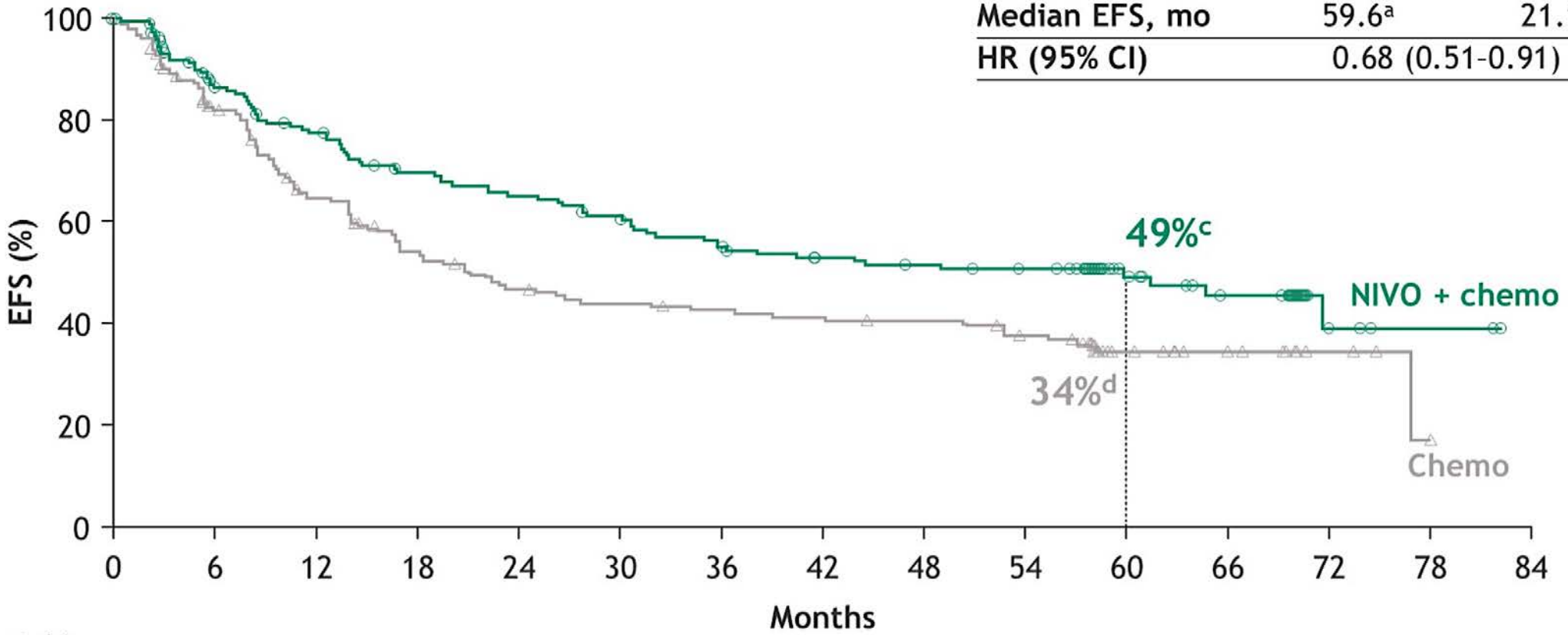
CheckMate 816 Study Design



Forde P et al. ASCO 2025;Abstract LBA8000.

CheckMate 816: Event-Free Survival (EFS) Outcomes

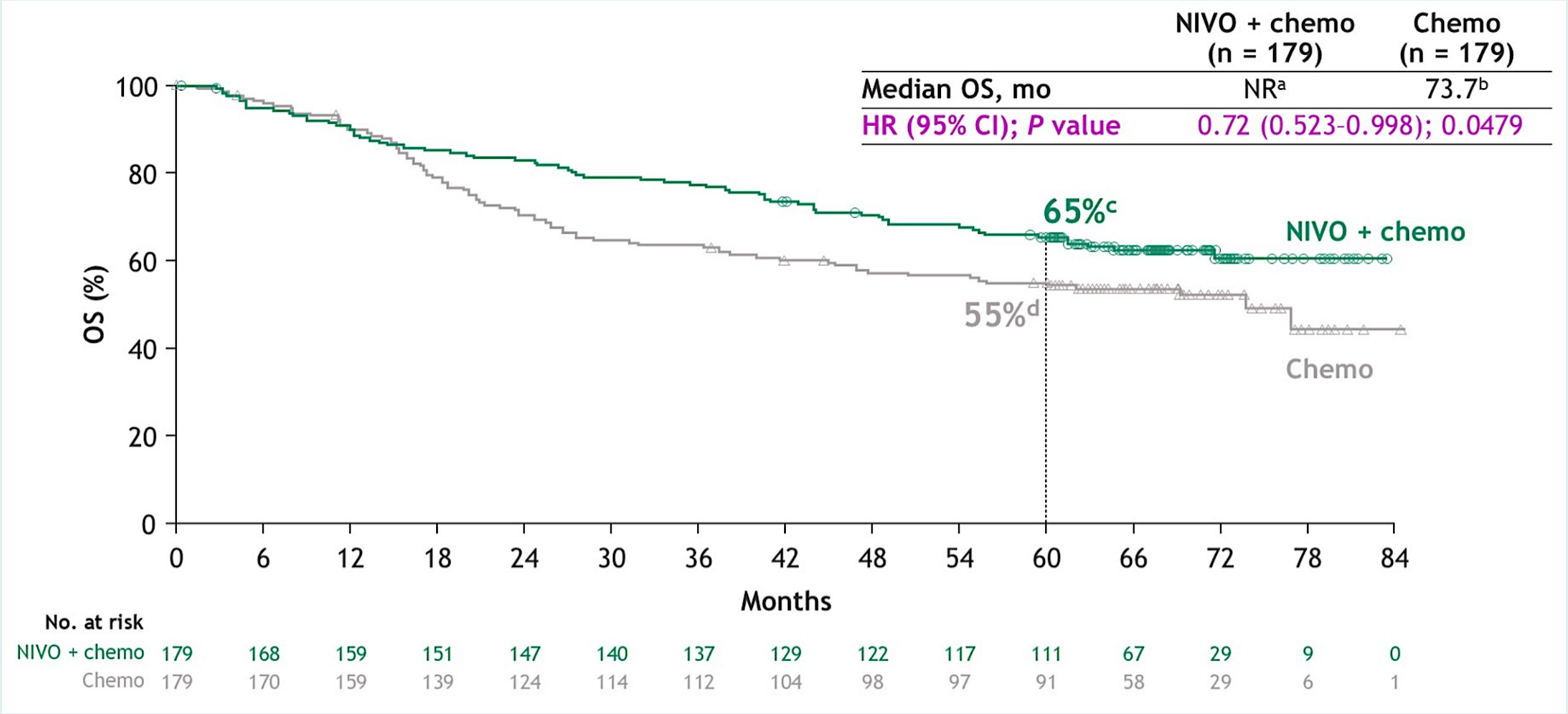
	NIVO + chemo (n = 179)	Chemo (n = 179)
Median EFS, mo	59.6[a]	21.1[b]
HR (95% CI)	0.68 (0.51-0.91)	



No. at risk														
NIVO + chemo	179	137	121	106	99	92	82	74	71	68	31	23	5	3	0
Chemo	179	132	100	81	69	64	61	59	57	51	25	17	4	0	0

Forde P et al. ASCO 2025;Abstract LBA8000.

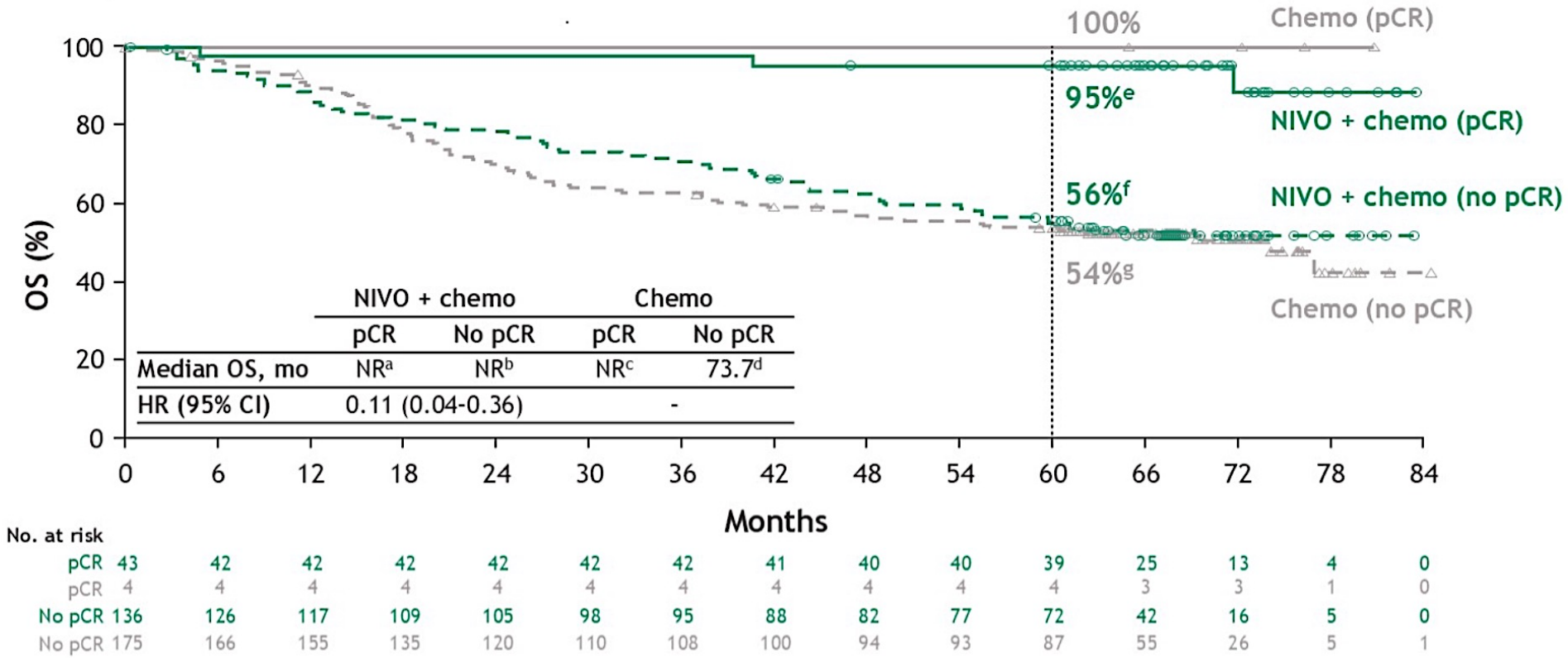
CheckMate 816: Final Overall Survival (OS)



Forde P et al. ASCO 2025;Abstract LBA8000.

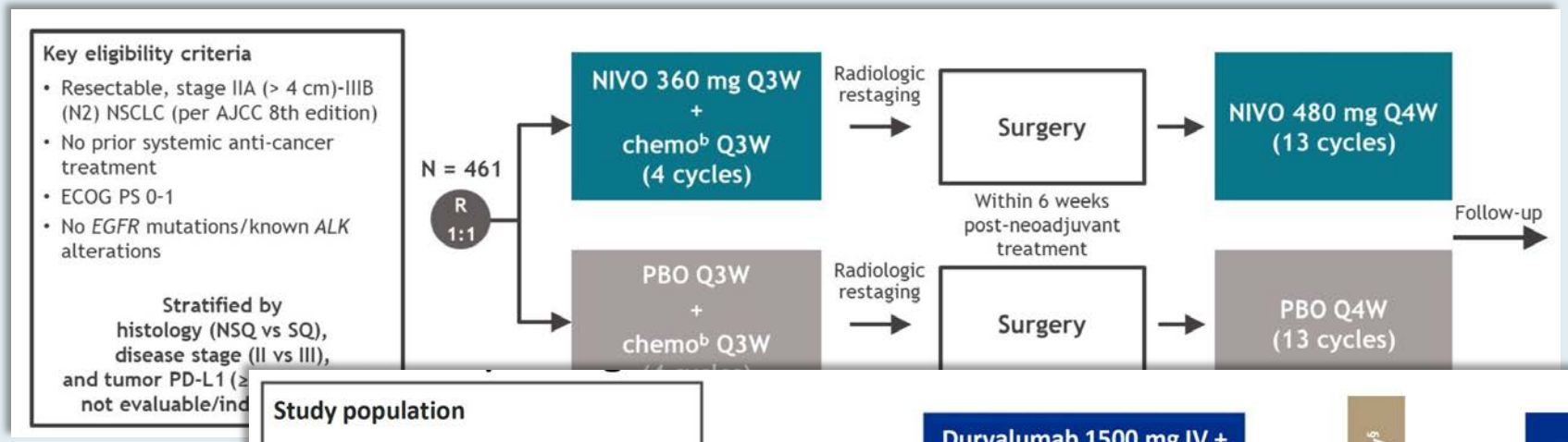
CheckMate 816: OS by Pathologic Complete Response (pCR) Status

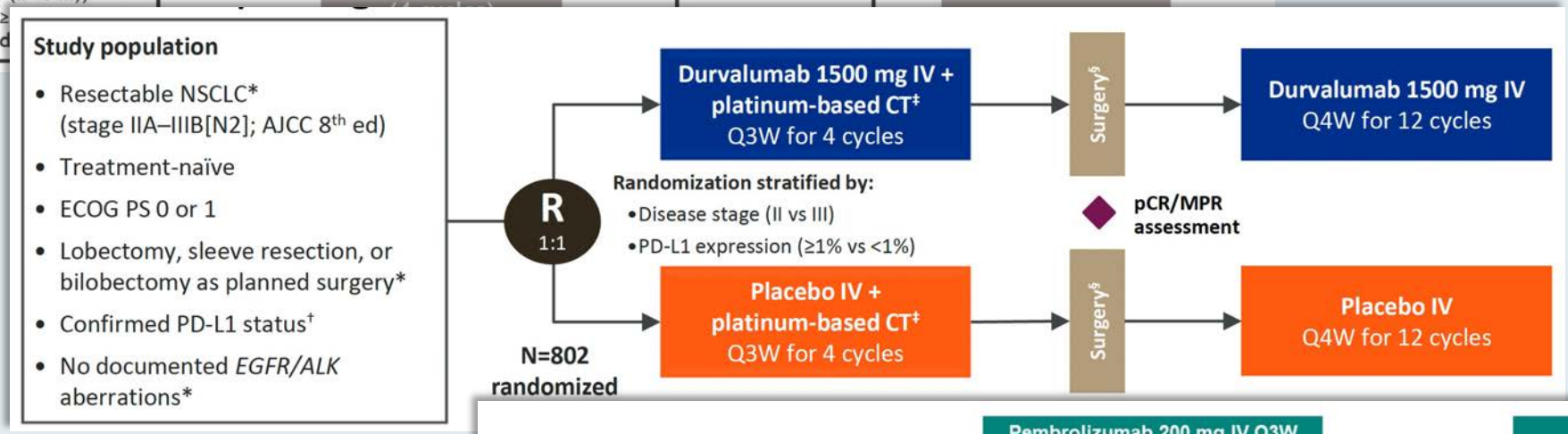
- Among concurrently randomized patients, 43/179 (24%) patients in the NIVO + chemo arm and 4/179 (2%) patients in the chemo arm had pCR[1]

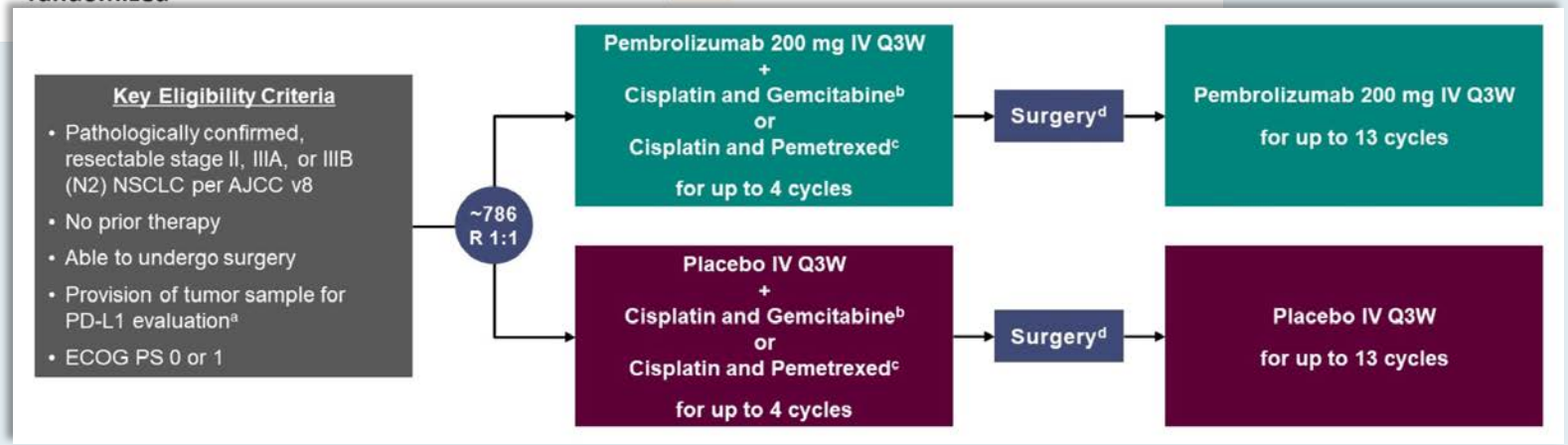


Forde P et al. ASCO 2025;Abstract LBA8000.

CheckMate 77T, AEGEAN and KEYNOTE-671 Trials







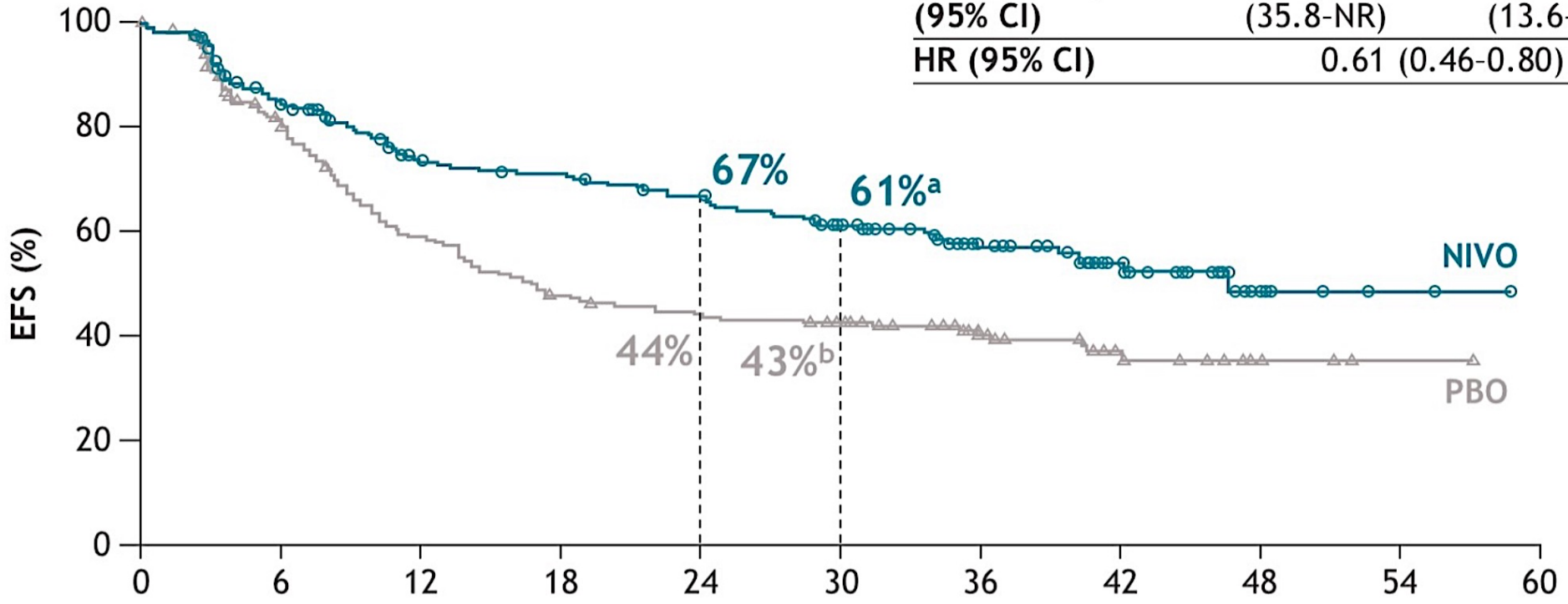
NSQ = nonsquamous; SQ = squamous;
PBO = placebo; CT = chemotherapy

Cascone T et al. ASCO 2025;Abstract LBA8010.
Heymach J et al. WCLC 2024;Abstract OA13.03.
Wakelee H et al. ESMO 2025;Abstract LBA67.

RTP RESEARCH TO PRACTICE

CheckMate 77T: EFS per Blinded Independent Central Review

	NIVO (n = 229)	PBO (n = 232)
Median EFS, mo (95% CI)	46.6 (35.8-NR)	16.9 (13.6-28.2)
HR (95% CI)	0.61 (0.46-0.80)	



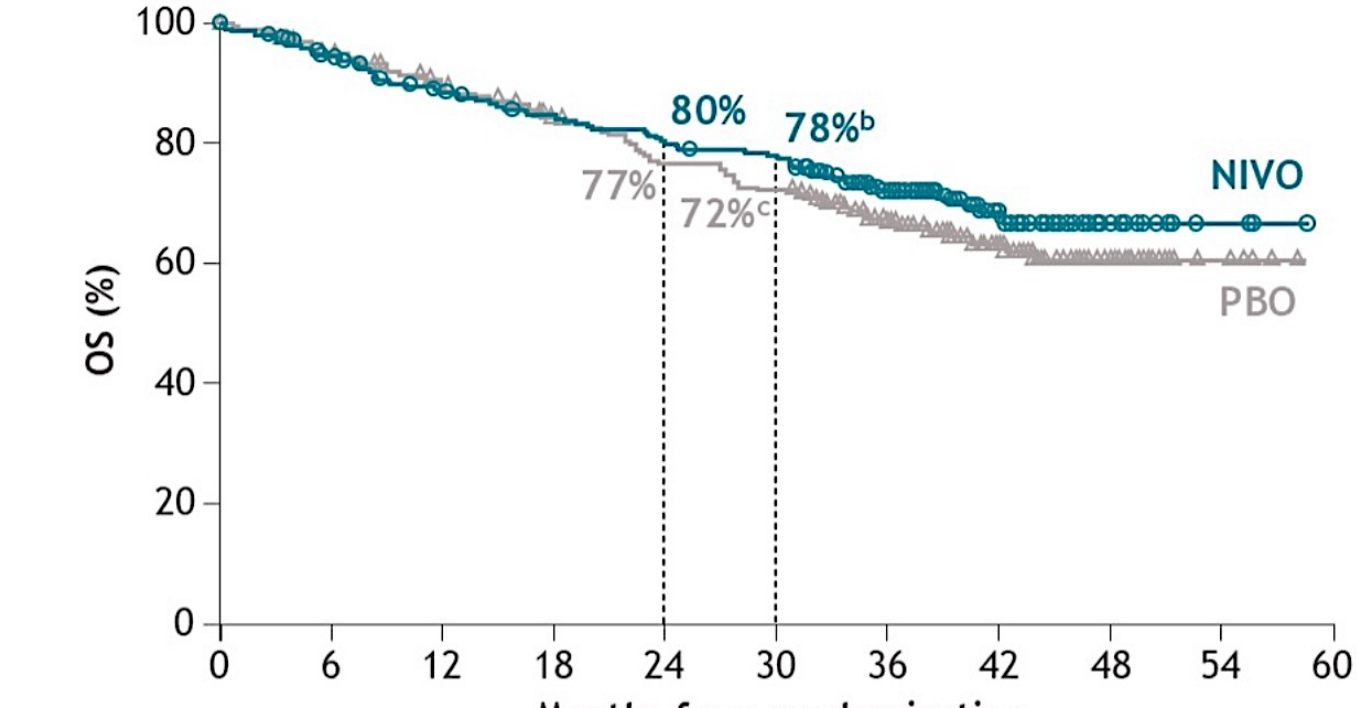
No. at risk

NIVO	229	172	140	133	123	103	69	30	7	3	0
PBO	232	165	118	92	83	76	43	20	5	1	0

Cascone T et al. ASCO 2025;Abstract LBA8010.

CheckMate 77T: OS

	NIVO (n = 229)	PBO (n = 232)
Median OS, mo (95% CI)	NR (NR-NR)	NR (NR-NR)
HR (97.63% CI)[a]	0.85 (0.58-1.25)	



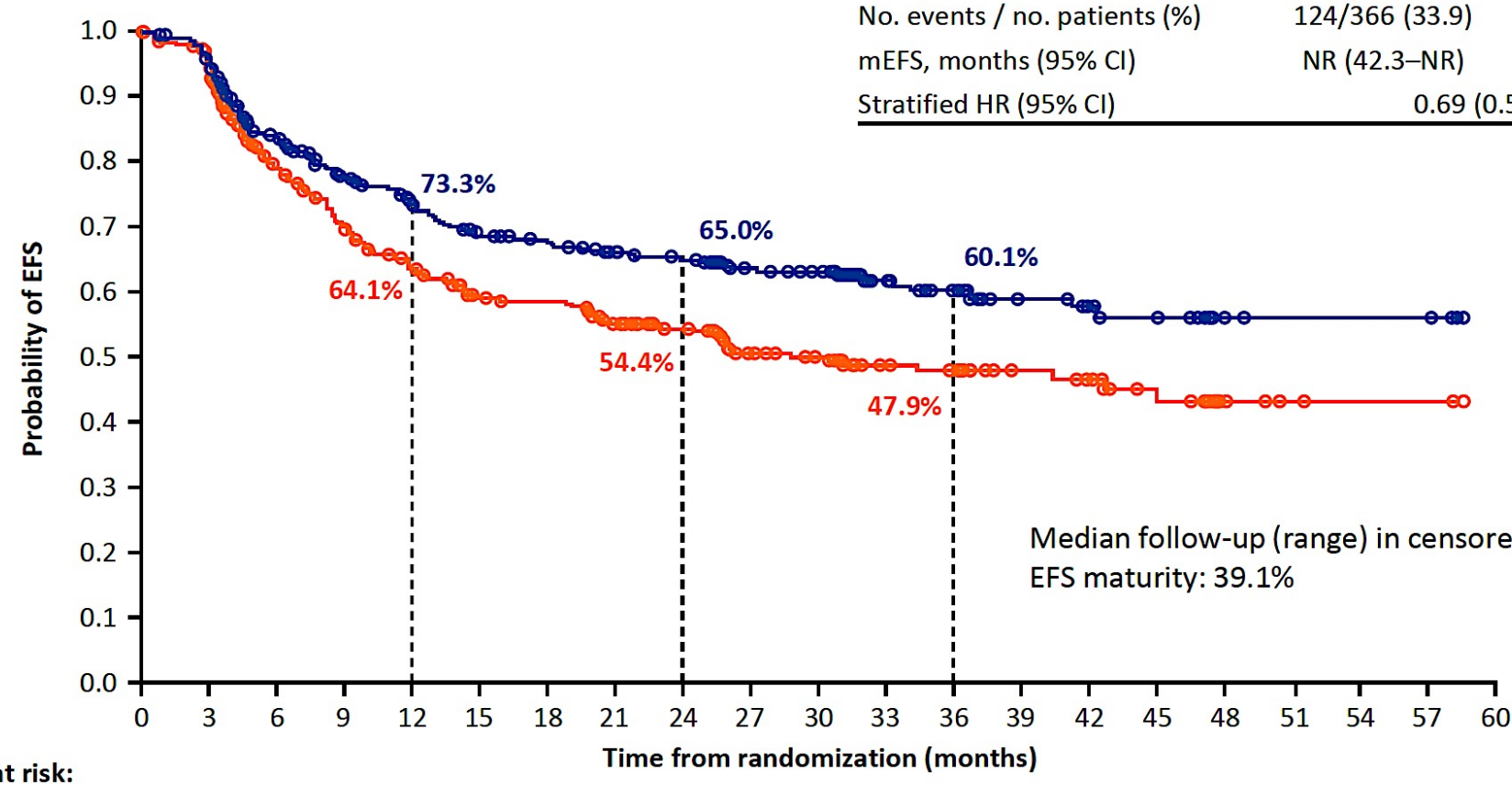
No. at risk

NIVO	229	206	187	176	166	161	114	66	23	6	0
PBO	232	216	197	178	161	152	103	52	20	7	0

Cascone T et al. ASCO 2025;Abstract LBA8010.

AEGEAN: EFS Outcomes

	D arm	PBO arm
No. events / no. patients (%)	124/366 (33.9)	165/374 (44.1)
mEFS, months (95% CI)	NR (42.3–NR)	30.0 (20.6–NR)
Stratified HR (95% CI)	0.69 (0.55–0.88)	



Median follow-up (range) in censored patients: 25.9 (0.0–58.6) months
EFS maturity: 39.1%

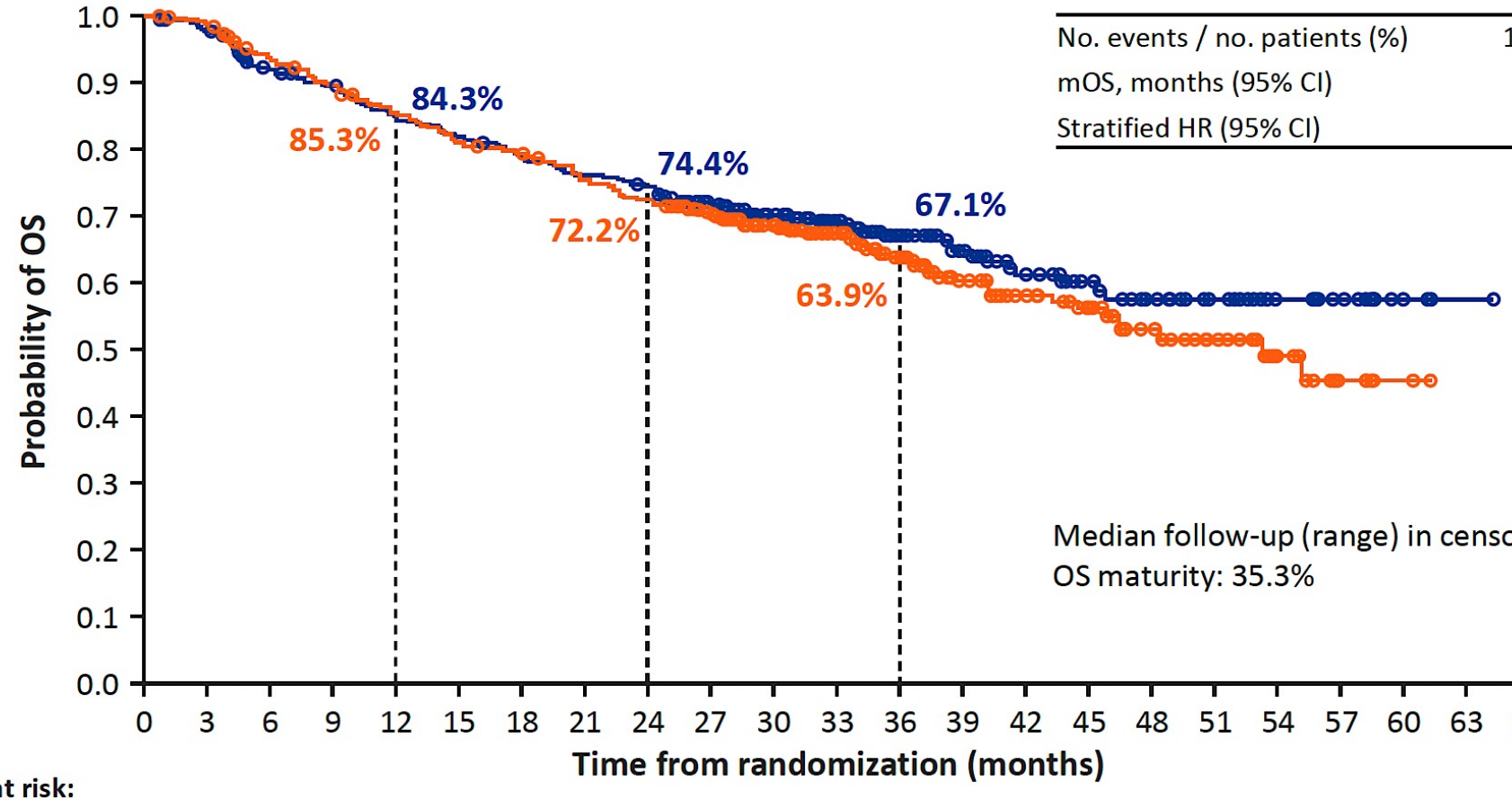
No. at risk:

D arm	366	337	276	240	219	201	194	179	172	128	121	76	67	48	36	29	6	4	4	4	0
PBO arm	374	338	261	225	201	176	172	151	142	93	83	57	53	36	32	25	8	3	2	2	0

mEFS = median event-free survival

Heymach J et al. WCLC 2024;Abstract OA13.03.

AEGEAN: OS Outcomes



	D arm	PBO arm
No. events / no. patients (%)	121/366 (33.1)	140/374 (37.4)
mOS, months (95% CI)	NR (NR–NR)	53.2 (44.3–NR)
Stratified HR (95% CI)	0.89 (0.70–1.14)	

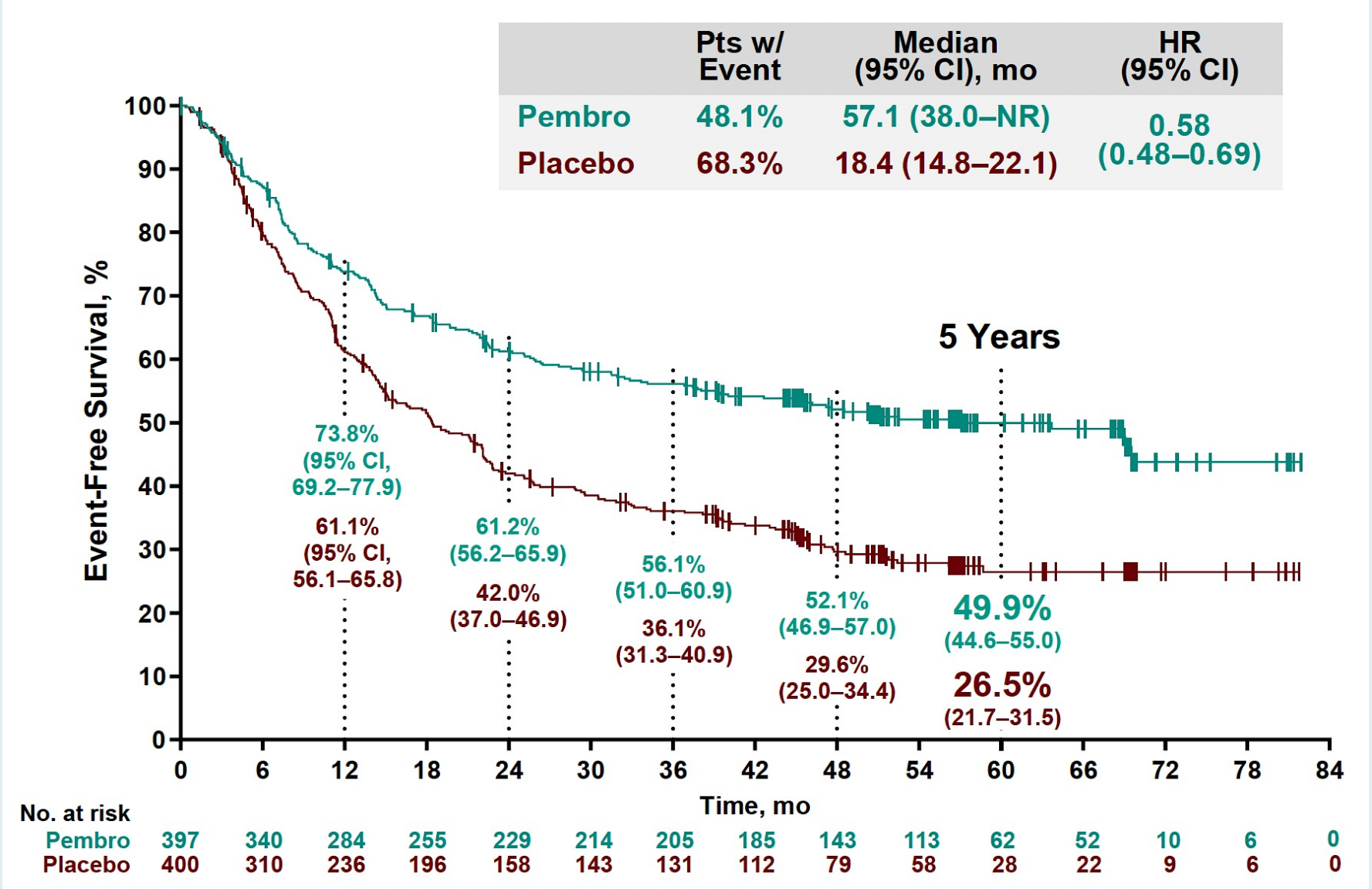
Median follow-up (range) in censored patients: 33.6 (0.7–64.3) months
OS maturity: 35.3%

No. at risk:

D arm	366	356	327	316	297	288	277	267	260	227	182	141	104	80	62	50	39	29	16	12	3	1	0
PBO arm	374	367	342	327	309	292	287	270	259	230	183	149	116	87	68	58	41	28	16	7	2	0	0

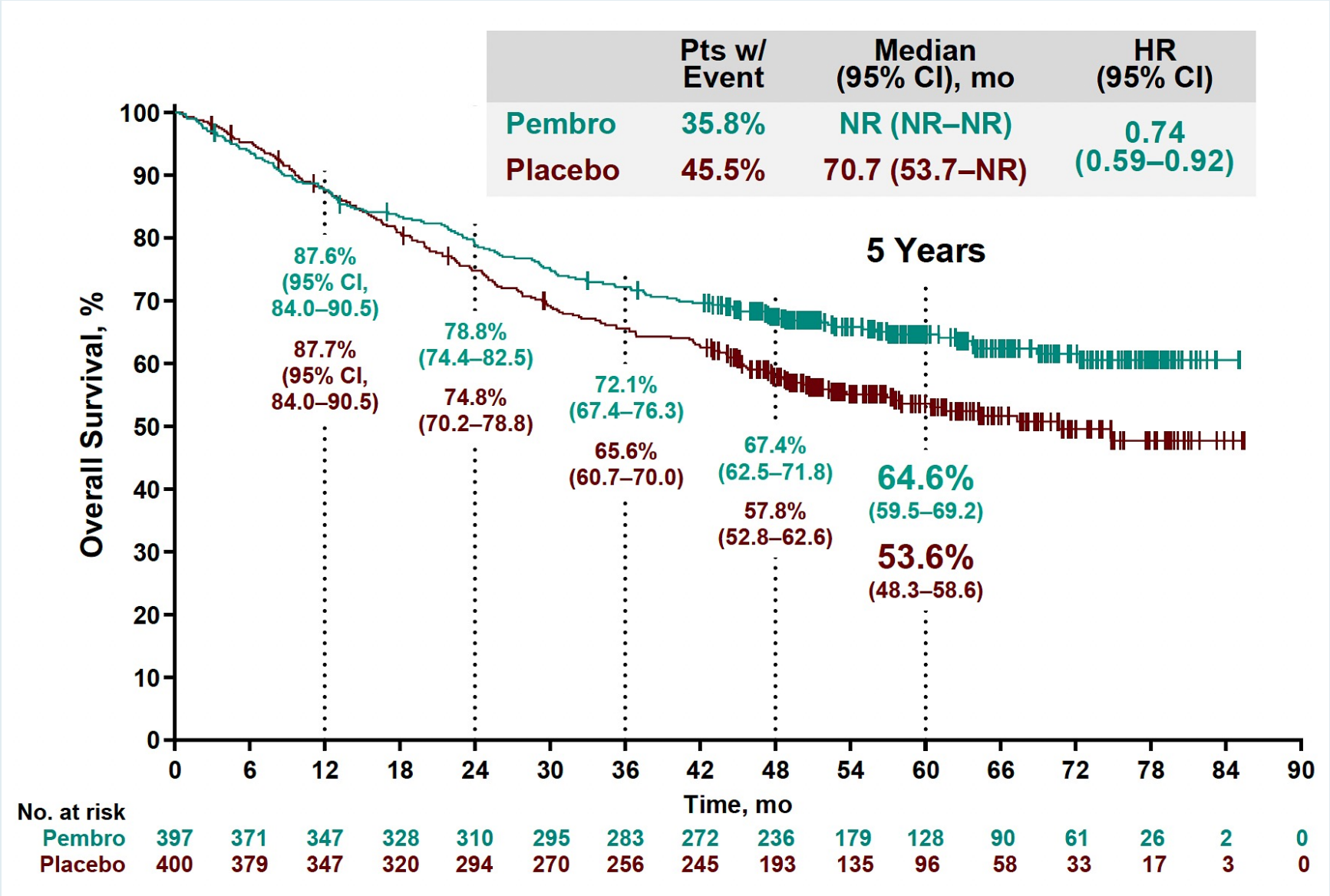
Heymach J et al. WCLC 2024;Abstract OA13.03.

KEYNOTE-671: EFS Outcomes



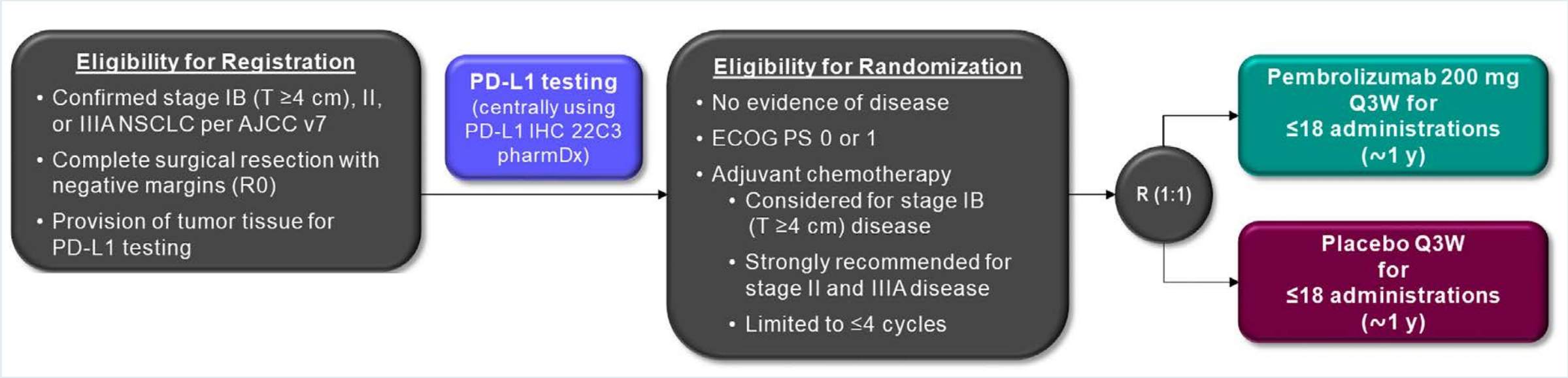
Wakelee H et al. ESMO 2025;Abstract LBA67.

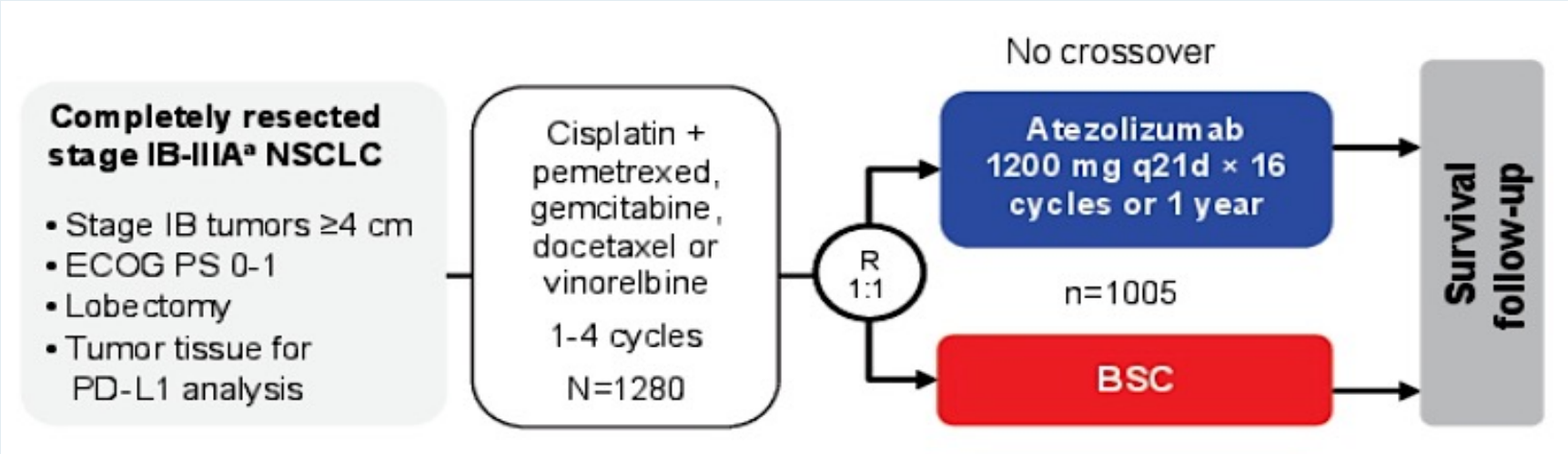
KEYNOTE-671: OS Outcomes



Wakelee H et al. ESMO 2025;Abstract LBA67.

KEYNOTE-091 and IMpower010 Trials

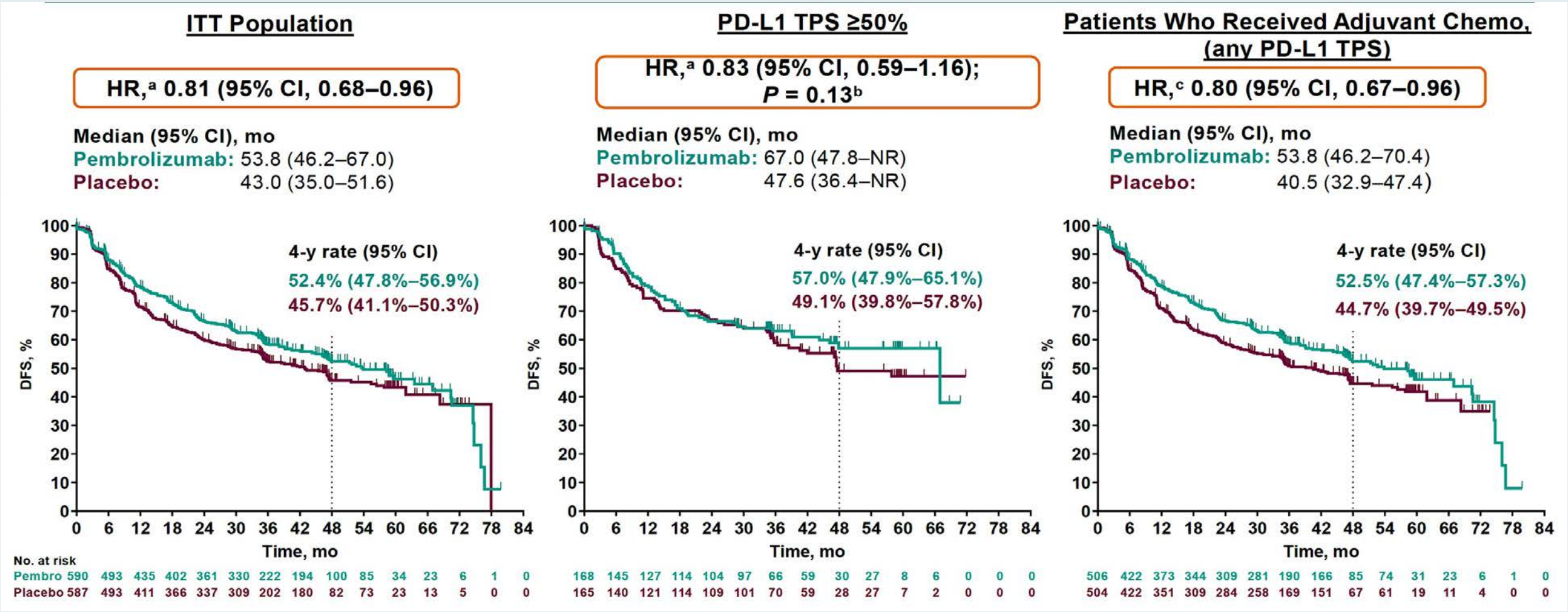




IHC = immunohistochemistry; BSC = best supportive care

Besse B et al. ESMO IO 2023;Abstract 120MO. Wakelee H et al. ASCO 2024;Abstract LBA8035.

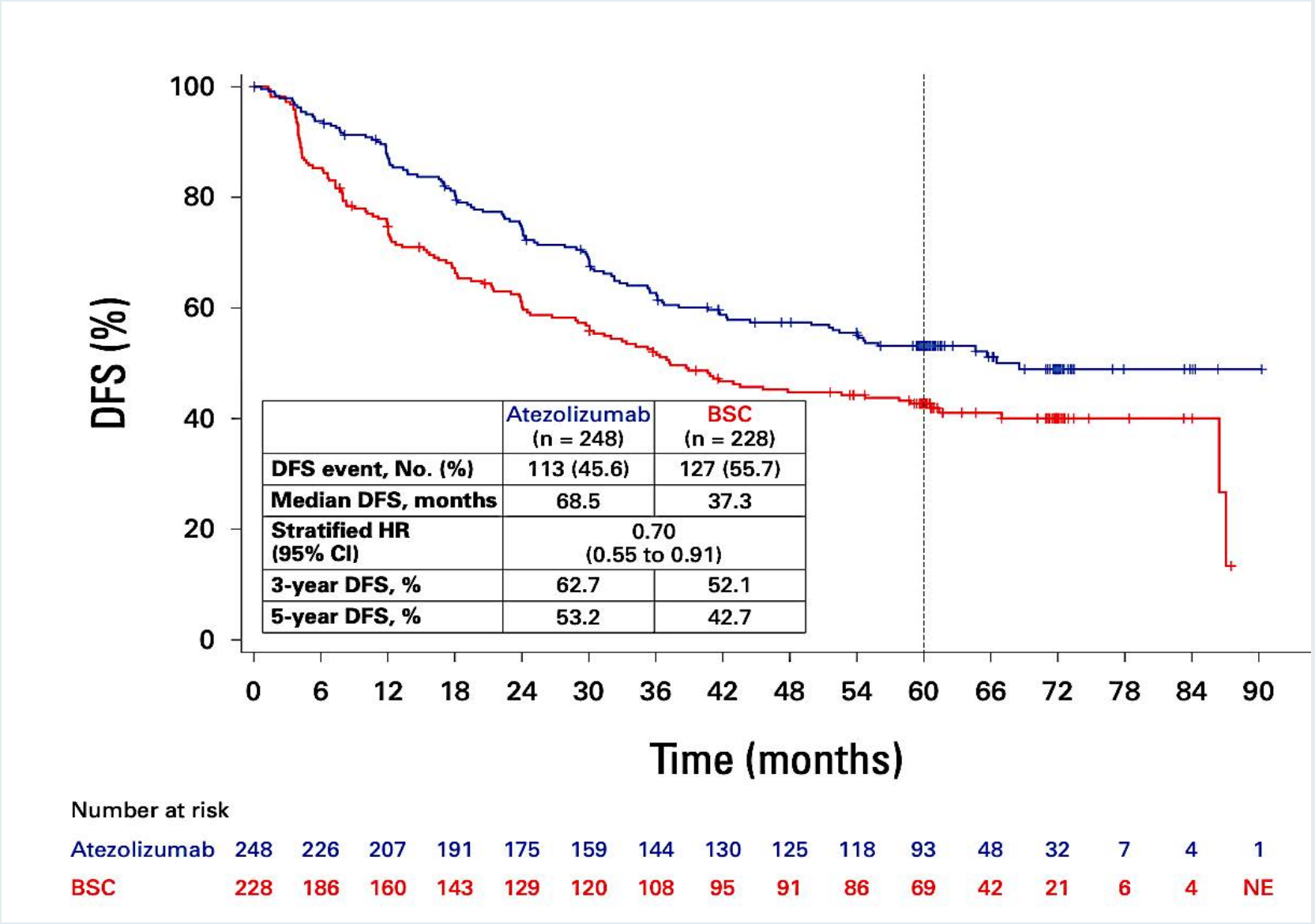
KEYNOTE-091: Disease-Free Survival (DFS) Outcomes



ITT = intention-to-treat population; TPS = tumor proportion score

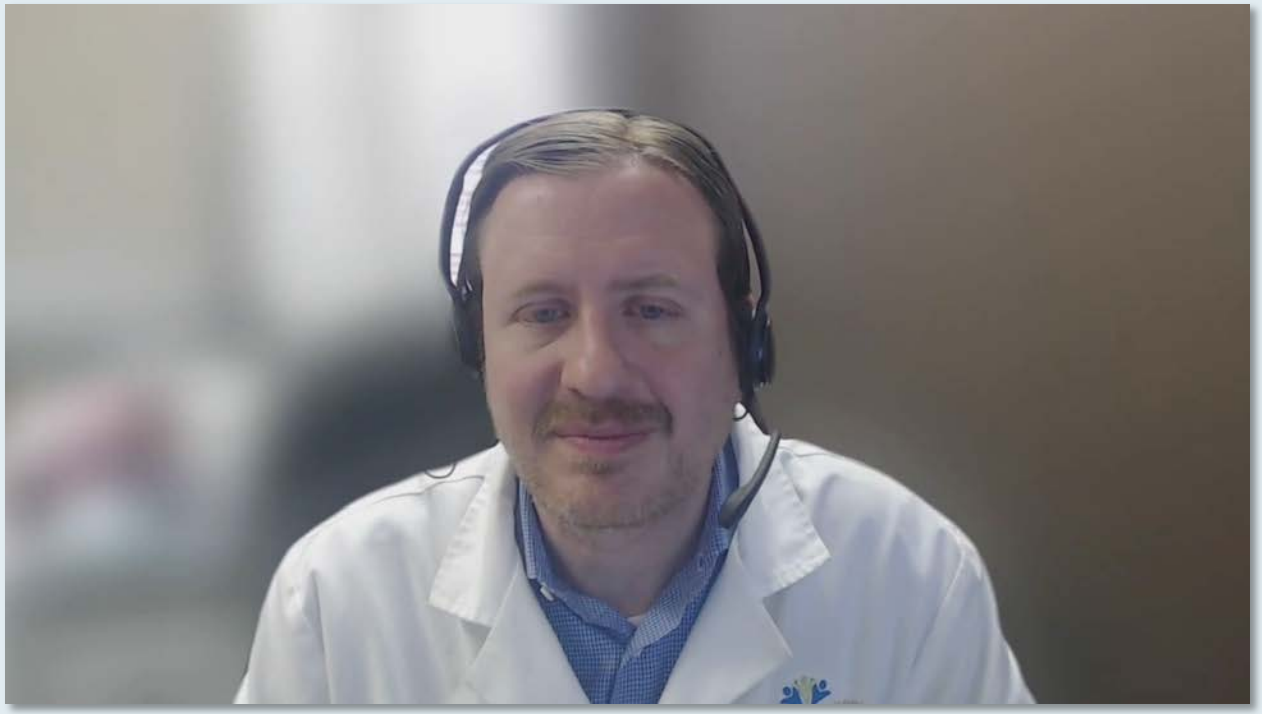
Besse B et al. ESMO IO 2023;Abstract 120MO.

IMpower010: DFS Outcomes — Stage II-IIIA, PD-L1 ≥1%



Wakelee H et al. ASCO 2024;Abstract LBA8035. Felip E et al. *J Clin Oncol* 2025;43(21):2343-49.

Case Presentation: 64-year-old man with localized adenocarcinoma of the lung who receives neoadjuvant cisplatin/pemetrexed/pembrolizumab and achieves a pCR



Dr Brian Mulherin (Indianapolis, Indiana)

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QUESTIONS FOR THE FACULTY

How do you generally approach neoadjuvant chemoimmunotherapy for localized NSCLC?

Do all patients receive postoperative immunotherapy?

Do you use cell-free DNA in this situation, and if so, how?

Case Presentation: 60-year-old man with metastatic mixed adenosquamous NSCLC (PD-L1 TPS 50%)

Dr Sunil Babu (Fort Wayne, Indiana)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

In general, how do you approach first-line therapy for patients with PD-L1-negative disease?

How, if at all, does the presence of STK11 or KEAP1 mutations affect your choice of first-line treatment? Should community-based oncologists be factoring these into their decision-making?

Do you ever start first-line immunotherapy and add chemotherapy later?

Case Presentation: 59-year-old man diagnosed with ES-SCLC who receives carboplatin/etoposide/durvalumab

Dr Sean Warsch (Asheville, North Carolina)

RTP RESEARCH TO PRACTICE

QUESTIONS FOR THE FACULTY

How do you approach maintenance lurbinectedin? Would you be comfortable administering it with durvalumab for a patient such as this one, who already started on that agent?

In what situations do you use tarlatamab? Are there preexisting conditions that are relative or absolute contraindications to its use?

Based on available data, would you like to have access to ifinatamab deruxtecan? If so, where would you envision using it opposite other available options? What are the side effects of this agent?

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We are taking a lunch break!

The program will resume at 12:30 PM CT

Up Next …

Dr Kerry A Rogers discusses the management of chronic lymphocytic leukemia

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