New lung cancer treatment in updated NCCN guidelines

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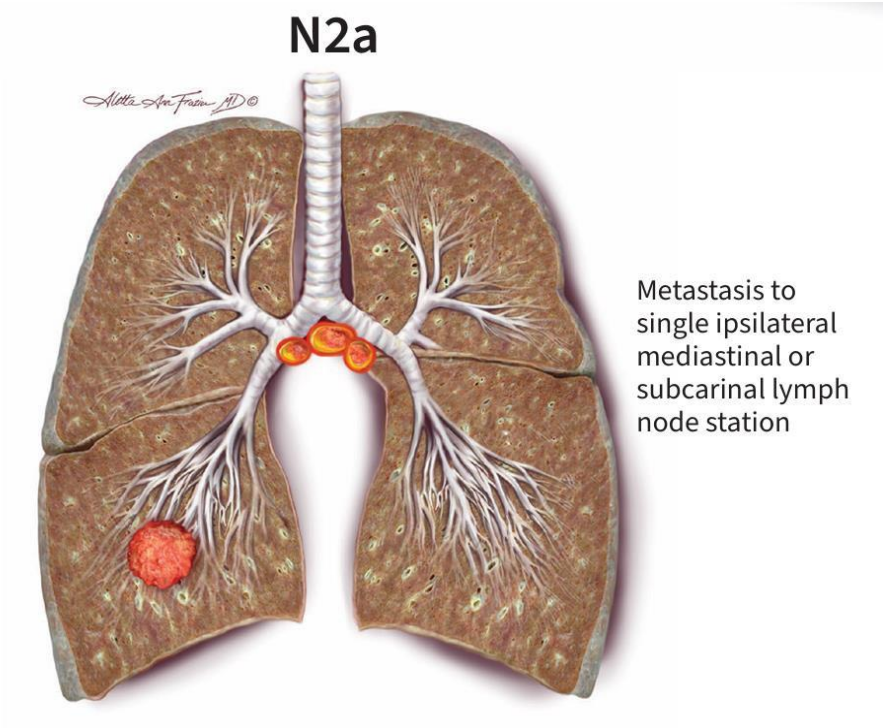
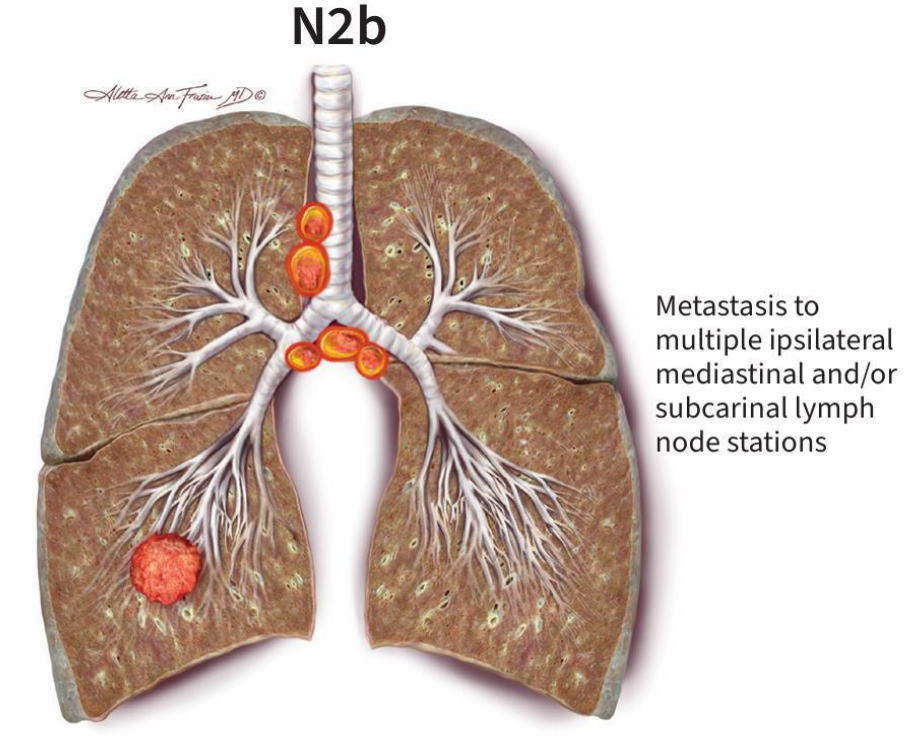
Changes of TNM Classification 9th edition

Subdivision of N2

N2a: single-station N2 involvement



N2b: multiple-station N2 involvement

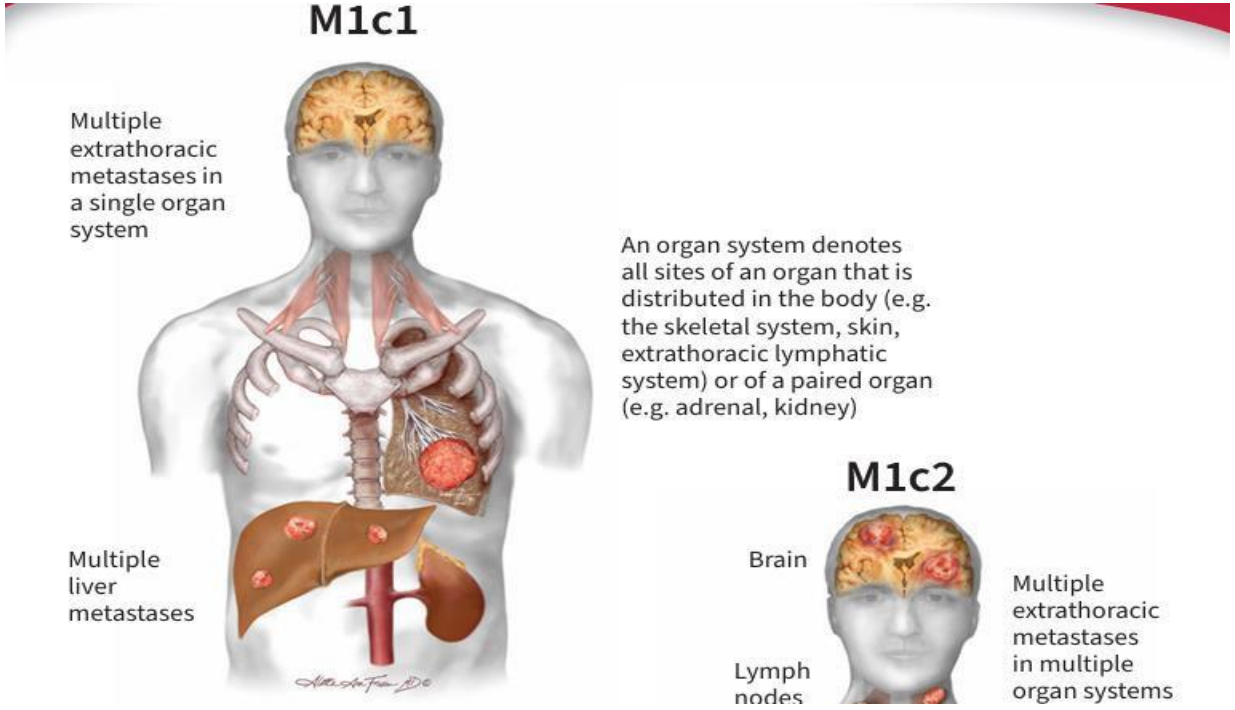


INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER Lung Cancer T Classifi cation–9th Edition

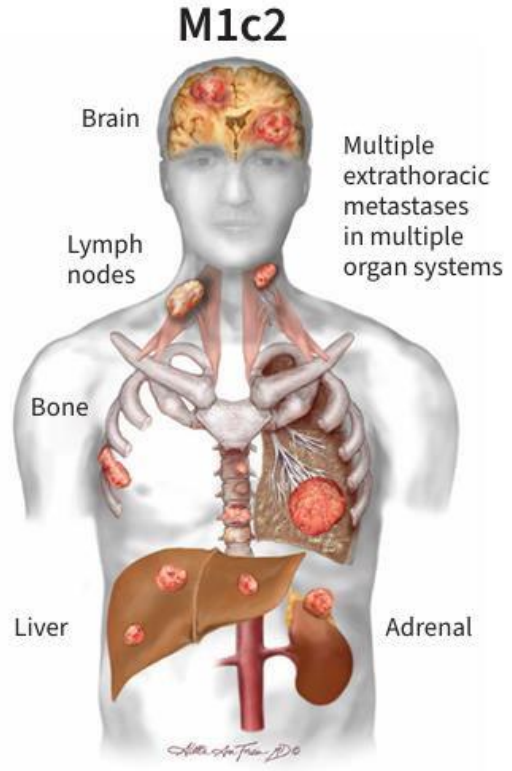
Changes of TNM Classification 9th edition

Subdivision of M1c

M1c1: multiple extrathoracic metastasis in single organ



M1c2: metastasis in multiple organ systems



Diagnosis of NSCLC

TABLE 1 Stages in lung cancer classification according to the 9th TNM (tumour–node–metastasis) edition *versus* the 8th TNM edition

T	Label	N0	N1	N2		N3
				N2a	N2b	
T1	T1a ⩽1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b >1 to ⩽2 cm	IA2	IIA	IIB	IIIA	IIIB
	T1c >2 to ⩽3 cm	IA3	IIA	IIB	IIIA	IIIB
T2	T2a >3 to ⩽4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b >4 to ⩽5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3	T3 >5 to ⩽7 cm	IIB	IIIA	IIIA	IIIB	IIIC
	T3 invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 satellite nodules	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4 >7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 ipsilateral nodules	IIIA	IIIA	IIIB	IIIB	IIIC

(IIB) (IIIA) (IIIB) (IIIA)

Changes showing comparison to the 8th TNM classification are flagged accordingly. Blue signifies downstaging either from stage IIIA to IIB, or from stage IIIB to IIIA. Red signifies upstaging from stage IIIA to IIIB. For the scope of this review, alterations in stage I and II, as well as stage IV disease (M descriptor), were disregarded.

Oke Dimas Asmara et al. *Breathe (Sheff).* 2024 Oct 1;20(3):240047.

Resectability of stage III NSCLC

Multidisciplinary Expert consensus document

TABLE 2 Consensus Summary of Surgical Resectability for Non-small Cell Lung Cancer

Variable	N0	N1	Nonbulky N2 Single	N2 I
T1/T2	Resectable	Resectable	Resectable	Pot re
T3	Resectable	Resectable	Resectable	Pot re
T3 (Pancoast)	Potentially resectable	Potentially resectable	Unresectable	Uni
T4 size	Potentially resectable	Potentially resectable	Unresectable	Uni
T4 satellite	Potentially resectable	Potentially resectable	Potentially resectable	Uni
T4 invasion	Potentially resectable	Potentially resectable	Unresectable	Uni

[a]This table represents a general recommendation f
may be considered after a multidisciplinary discus

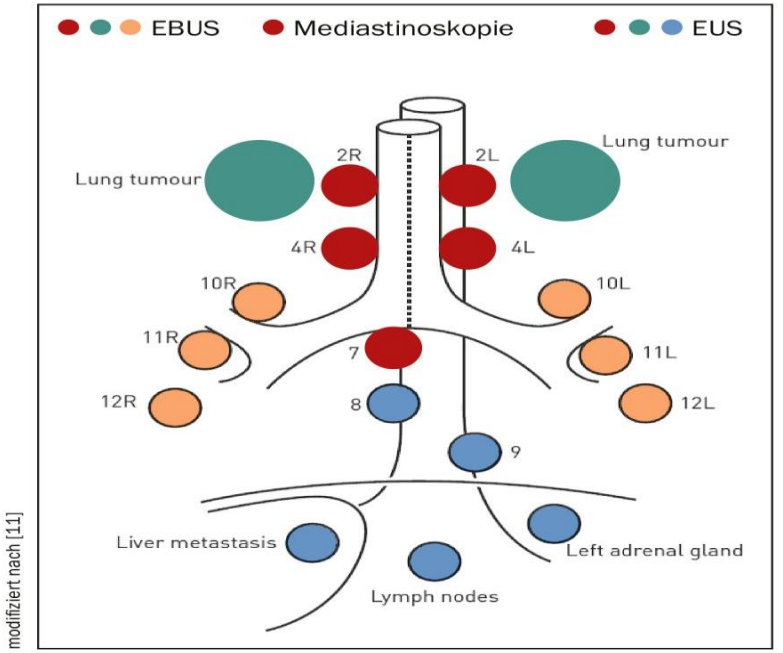
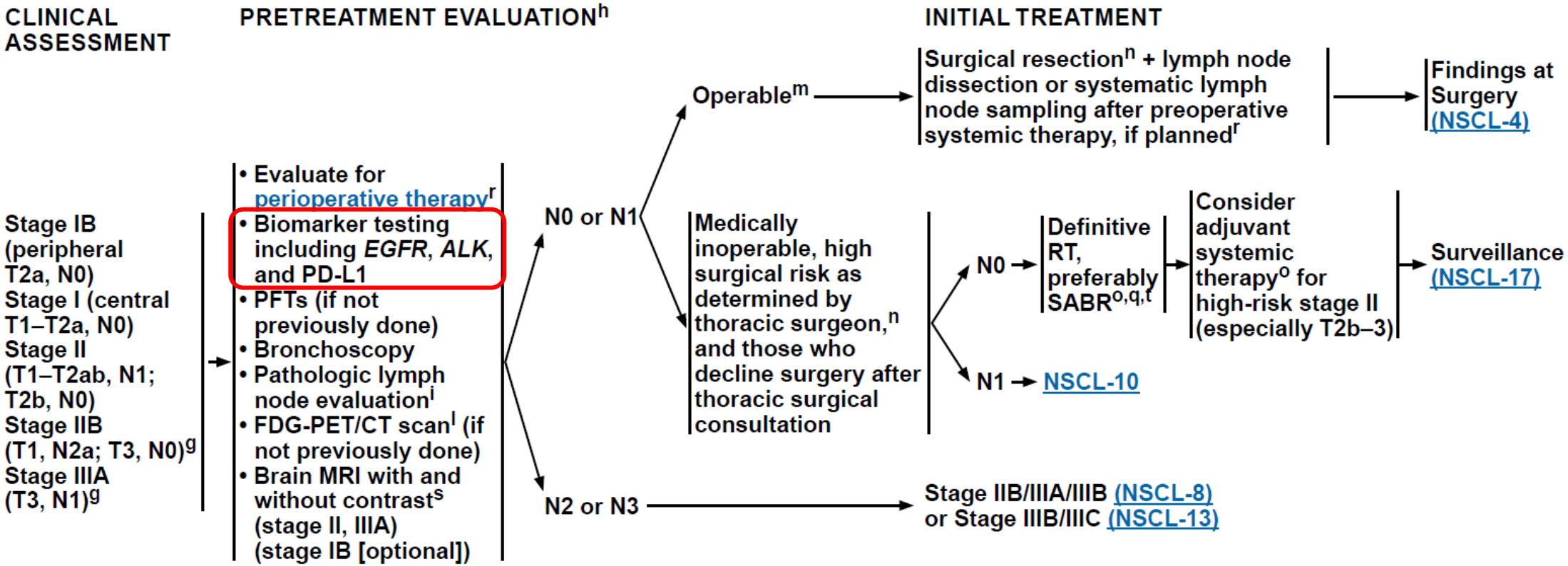


Abb. 3: Vereinfachte Darstellung der Lymphknotenkarte nach IASLC 2009. Die Reichweite der verschiedenen Methoden (Mediastinoskopie, EBUS, EUS) ist farbig dargestellt.

LN staging … Targeted vs. Systematic
Systematic EBUS & EUS and separate needle… according to LN stage

Samuel S Kim, et al. *Ann Thorac Surg.* 2025 Jan;119(1):16-33.

Diagnosis of NSCLC



NCCN Guideline (NSCLC). 2026. Version 3.

Contents

Perioperative Tx for NSCLC

PRINCIPLES OF PERIOPERATIVE SYSTEMIC THERAPY

PRINCIPLES OF PERIOPERATIVE SYSTEMIC THERAPY

Neoadjuvant Systemic Therapy in Patients Who Are Candidates for Immune Checkpoint Inhibitors

Patients with ≥4 cm or node-positive tumors should be evaluated for the following treatment options:

- Nivolumab and platinum-based doublet chemotherapy[1,2] with the option of continuing single-agent nivolumab as adjuvant treatment after surgery (for patients with no known *EGFR* mutations or *ALK* gene fusions) (category 1);[2] Other Adjuvant Systemic Therapy
  - Platinum-doublet chemotherapy options include:
    - Carboplatin/Paclitaxel (any histology)
    - Cisplatin/Docetaxel (any histology)
    - Cisplatin/Pemetrexed (nonsquamous)
    - Carboplatin/Pemetrexed (nonsquamous)
    - Cisplatin/Gemcitabine (squamous)
    - Carboplatin/Gemcitabine (squamous)
- Pembrolizumab and cisplatin-based doublet chemotherapy then continued as single-agent pembrolizumab as adjuvant treatment after surgery (category 1);[3] Other Adjuvant Systemic Therapy
  - Platinum-doublet chemotherapy options include:
    - Cisplatin/Pemetrexed (nonsquamous)
    - Cisplatin/Gemcitabine (squamous)
- Durvalumab and platinum-based doublet chemotherapy then continued as single-agent durvalumab as adjuvant treatment after surgery (for patients with no known *EGFR* mutations or *ALK* gene fusions) (category 1);[4] Other Adjuvant Systemic Therapy
  - Platinum-doublet chemotherapy options include:
    - Cisplatin/Pemetrexed (nonsquamous)
    - Carboplatin/Pemetrexed (nonsquamous)
    - Cisplatin/Gemcitabine (squamous)
    - Carboplatin/Gemcitabine (squamous)
    - Carboplatin/Paclitaxel (squamous)

NCCN Guideline (NSCLC). 2026. Version 3.

Neoadjuvant and Perioperative IO + CTx

TABLE 1. Neoadjuvant and Perioperative Phase III Trial Evaluating Chemoimmunotherapy Versus Chemotherapy

Study	Treatment	No.	Stage III, %	Percent With Surgery, %	pCR Rate (ICI arm), %	EFS, months (ICI arm)	EFS, HR (95% CI)	OS, HR (95% CI)
CheckMate-816	Neoadjuvant nivolumab	358	63	83	24	31.6	HR, 0.63 (97.38% CI, 0.43 to 0.91); $P = .005$	NA
KEYNOTE-671	Perioperative pembrolizumab	797	70	82	18	47.2	HR, 0.59 (95% CI, 0.48 to 0.72)	HR, 0.72 (95% CI, 0.56 to 0.93); $P = .0052$
CheckMate-77T	Perioperative nivolumab	461	64	77	25	40.1	HR, 0.59 (95% CI, 0.45 to 0.79)	HR, 0.72 (95% CI, 0.56 to 0.93); $P < .01$
AEGEAN	Perioperative durvalumab	802	71	81	17	NR	HR, 0.58 (95% CI, 0.53 to 0.88); $P = .004$	NR
NEOTORCH	Perioperative toripalimab	501	100	82	25	NR	HR, 0.40 (95% CI, 0.28 to 0.57); $P < .001$	HR, 0.62 (95% CI, 0.38 to 1.00); $P = .05$
RATIONALE 315	Perioperative tislelizumab	453	58	84	41	NR	HR, 0.56 (95% CI, 0.40 to 0.79); $P = .0003$	HR, 0.62 (95% CI, 0.39 to 0.98); $P = .019$

Abbreviations: EFS, event-free survival; HR, hazard ratio; ICI, immune checkpoint inhibitor; NA, non application; NR, not reported; OS, overall survival; pCR, pathologic complete response.

Opalikhin A et al. Am Soc Clin Oncol Educ Book. 2025 Jun;45(3):e481060.

2025 ASCO ANNUAL MEETING

Overall survival with neoadjuvant nivolumab + chemotherapy in patients with resectable NSCLC in CheckMate 816

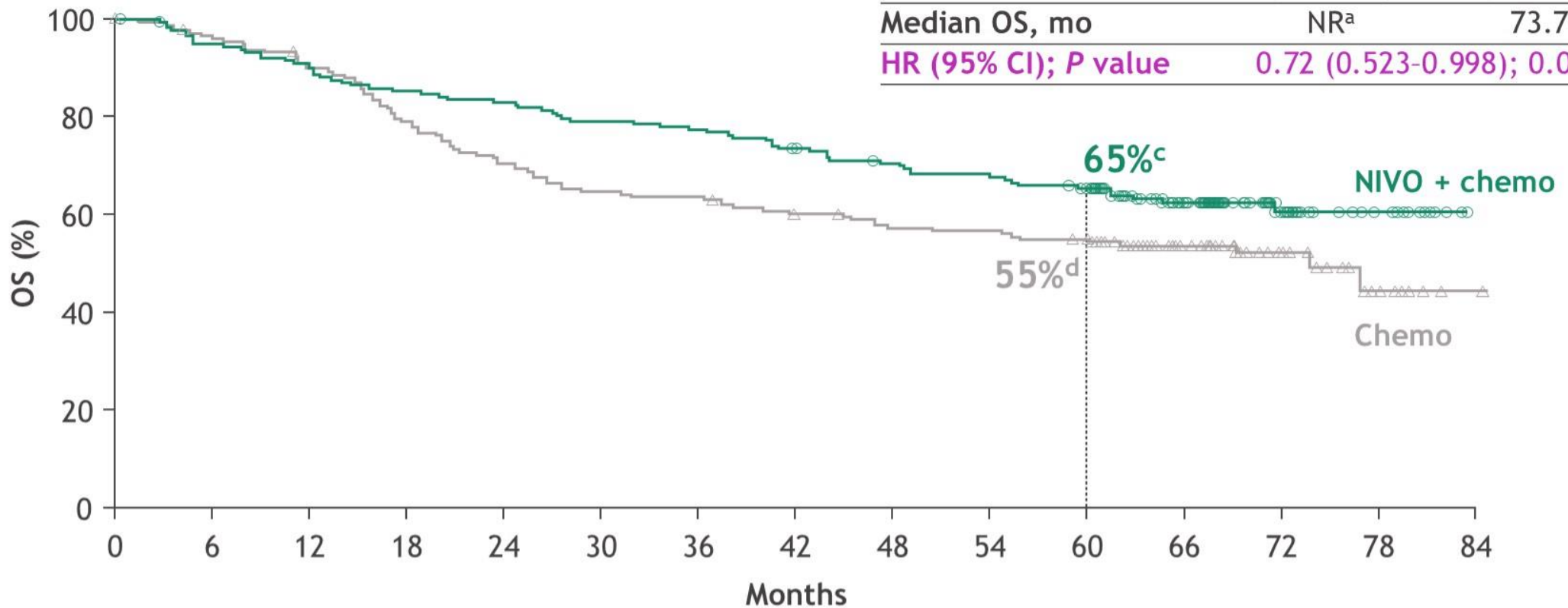
Patrick M. Forde,[1] Jonathan D. Spicer,[2] Mariano Provencio,[3] Tetsuya Mitsudomi,[4] Mark M. Awad,[5] Changli Wang,[6] Shun Lu,[7] Enriqueta Felip,[8] Stephen Broderick,[9] Scott J. Swanson,[10] Julie Brahmer,[9] Keith Kerr,[11] Tudor-Eliade Ciuleanu,[12] Fumihiro Tanaka,[13] Gene B. Saylors,[14] Ke-Neng Chen,[15] Lily Wang,[16] Quyen Duong,[16] Nicolas Girard[17]

[1]Trinity St. James's Cancer Institute, Trinity College Dublin, Dublin, Ireland; [2]McGill University Health Centre, Montreal, Quebec, Canada; [3]Hospital Universitario Puerta de Hierro, Madrid, Spain; [4]Kindai University Faculty of Medicine, Ohno-Higashi, Osaka-Sayama, Japan; [5]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [6]Tianjin Lung Cancer Center, Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; [7]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [8]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Universitat Autònoma de Barcelona, Barcelona, Spain; [9]The Bloomberg-Kimmel Institute for Cancer Immunotherapy, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medicine, Baltimore, MD, USA; [10]Brigham and Women's Hospital, Boston, MA, USA; [11]Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [12]Institutul Oncologic Prof Dr Ion Chiricuță and University of Medicine and Pharmacy Iuliu Hațieganu, Cluj-Napoca, Romania; [13]The University of Occupational and Environmental Health, Kitakyushu, Japan; [14]Charleston Oncology, Charleston, SC, USA; [15]State Key Laboratory of Molecular Oncology, Peking University Cancer Hospital & Institute, Beijing, China; [16]Bristol Myers Squibb, Princeton, NJ, USA; [17]Institut du Thorax Curie-Montsouris, Institut Curie, Paris, France

Abstract number LBA8000

Final analysis: OS with neoadjuvant NIVO + chemo vs chemo

	NIVO + chemo (n = 179)	Chemo (n = 179)
Median OS, mo	NR[a]	73.7[b]
HR (95% CI); *P* value	0.72 (0.523-0.998); 0.0479	



No. at risk														
NIVO + chemo	179	168	159	151	147	140	137	129	122	117	111	67	29	9	0
Chemo	179	170	159	139	124	114	112	104	98	97	91	58	29	6	1

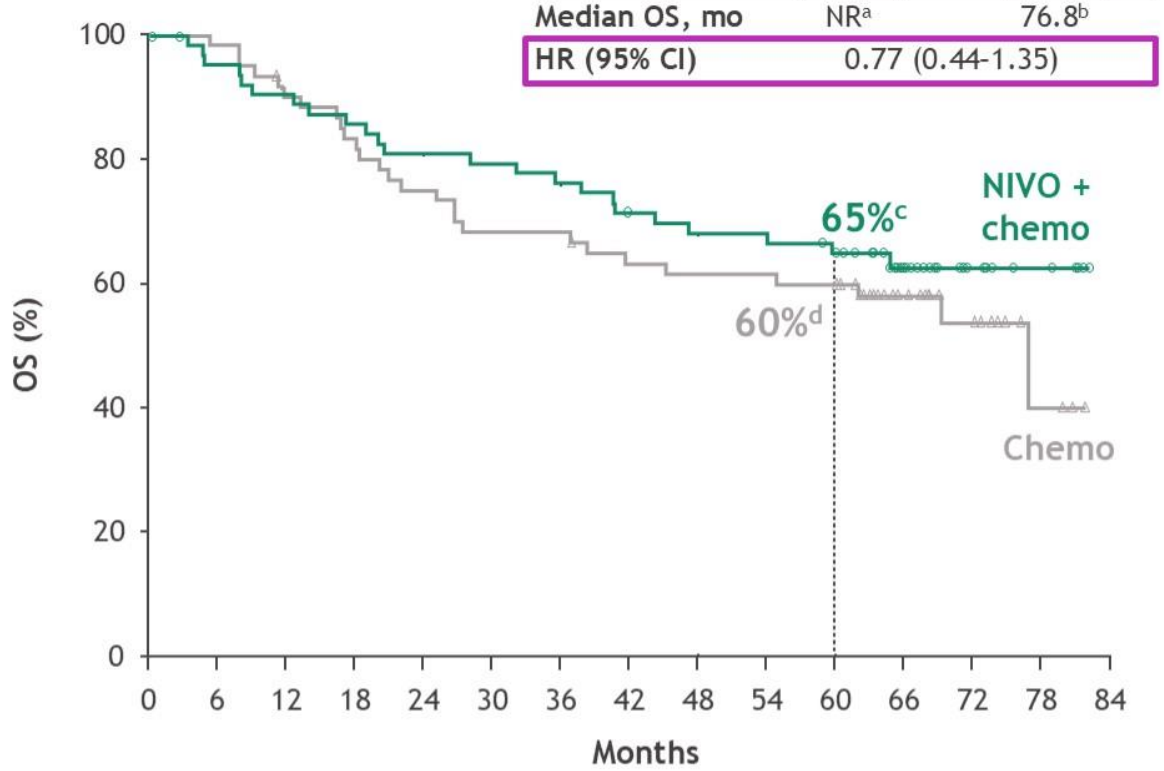
Minimum/median follow-up: 59.9/68.4 months.

[a-d]95% CI: [a]NR; [b]47.3-NR; [c]58-72; [d]47-62.

OS by baseline stage of disease

Stage IB-II

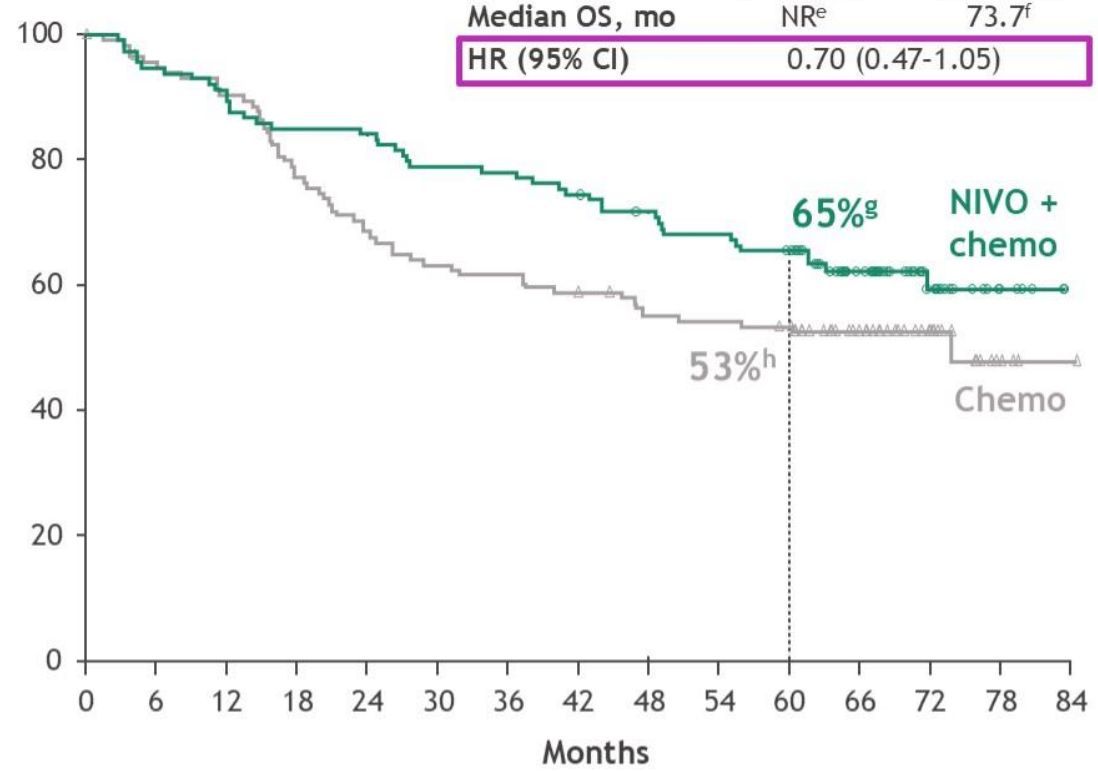
	NIVO + chemo (n = 65)	Chemo (n = 61)
Median OS, mo	NR[a]	76.8[b]
HR (95% CI)	0.77 (0.44-1.35)	



No. at risk															
NIVO + chemo	65	60	57	54	51	50	48	44	42	41	39	21	11	4	0
Chemo	61	60	54	50	45	41	41	37	36	36	34	20	12	3	0

Stage IIIA

	NIVO + chemo (n = 113)	Chemo (n = 116)
Median OS, mo	NR[e]	73.7[f]
HR (95% CI)	0.70 (0.47-1.05)	



113	107	101	96	95	89	88	84	79	75	71	46	18	5	0
116	108	103	88	78	72	70	66	61	60	57	38	17	3	1

Minimum/median follow-up: 59.9/68.4 months.

[a-h]95% CI: [a]64.7-NR; [b]41.6-NR; [c]52-75; [d]46-71; [e]71.6-NR; [f]39.8-NR; [g]56-73; [h]44-62.

2025 ASCO ANNUAL MEETING

Perioperative nivolumab vs placebo in patients with resectable NSCLC: updated survival and biomarker analyses from CheckMate 77T

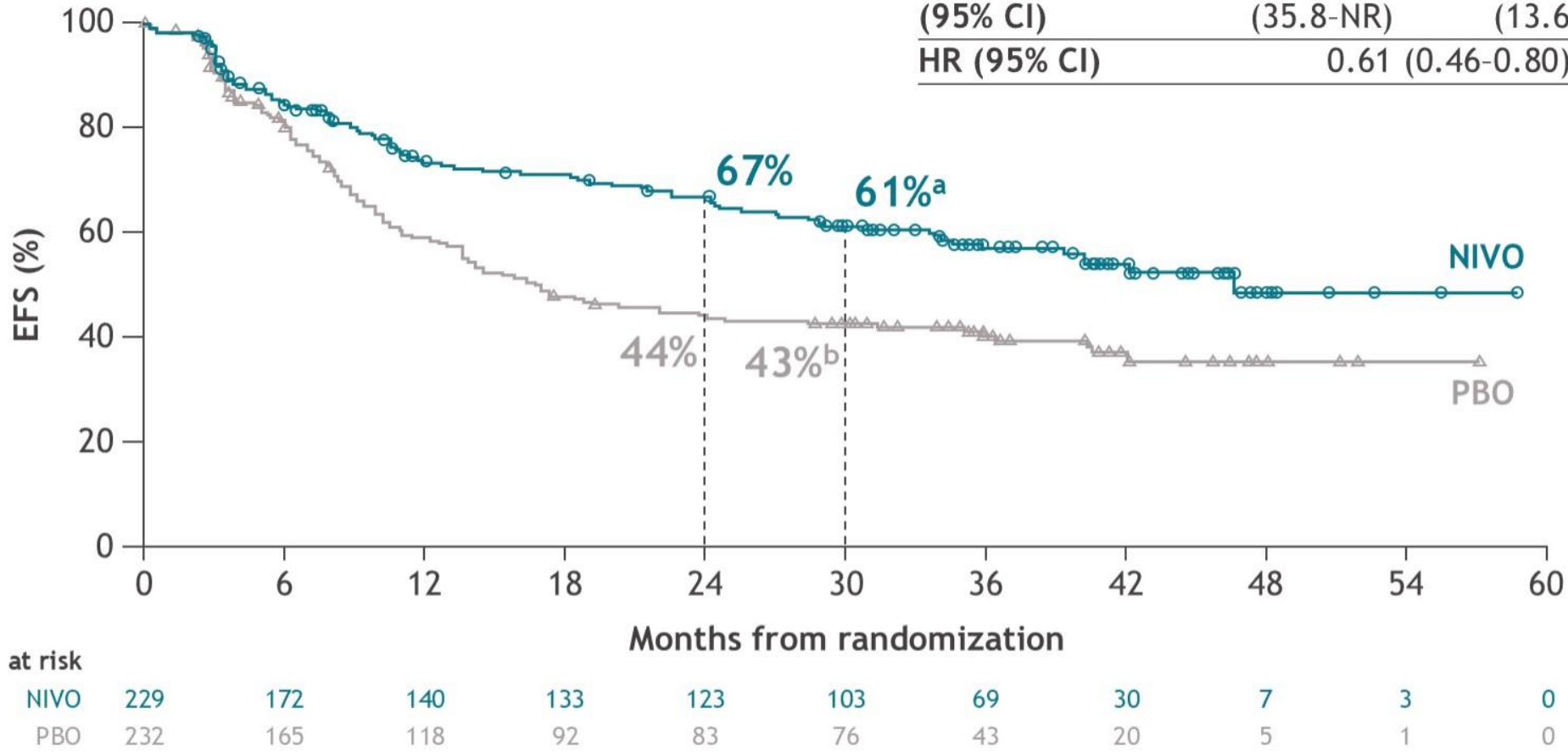
Tina Cascone,[1] Mark M. Awad,[2] Jonathan D. Spicer,[3] Jie He,[4] Shun Lu,[5] Fumihiro Tanaka,[6] Robin Cornelissen,[7] Lubos B. Petruzelka,[8] Hiroyuki Ito,[9] Ludmila de Oliveira Muniz Koch,[10] Lin Wu,[11] Sabine Bohnet,[12] Cinthya Coronado Erdmann,[13] Stephanie Meadows-Shropshire,[14] Jaclyn Neely,[14] Yu-Han Hung,[14] Padma Sathyanarayana,[14] Sumeena Bhatia,[14] **Mariano Provencio**[15]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]McGill University Health Centre, Montreal, Quebec, Canada; [4]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [5]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [6]University of Occupational and Environmental Health, Kitakyushu, Japan; [7]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [8]Charles University, Prague, Czech Republic; [9]Kanagawa Cancer Center, Yokohama, Japan; [10]Hospital Israelita Albert Einstein, Sao Paulo, Brazil; [11]Hunan Cancer Hospital, Changsha, China; [12]University Medical Center Schleswig-Holstein, Lubeck, Germany; [13]Bristol Myers Squibb, Boudry, Switzerland; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]Hospital Universitario Puerta de Hierro, Madrid, Spain

Abstract number LBA8010

EFS per BICR

	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)	



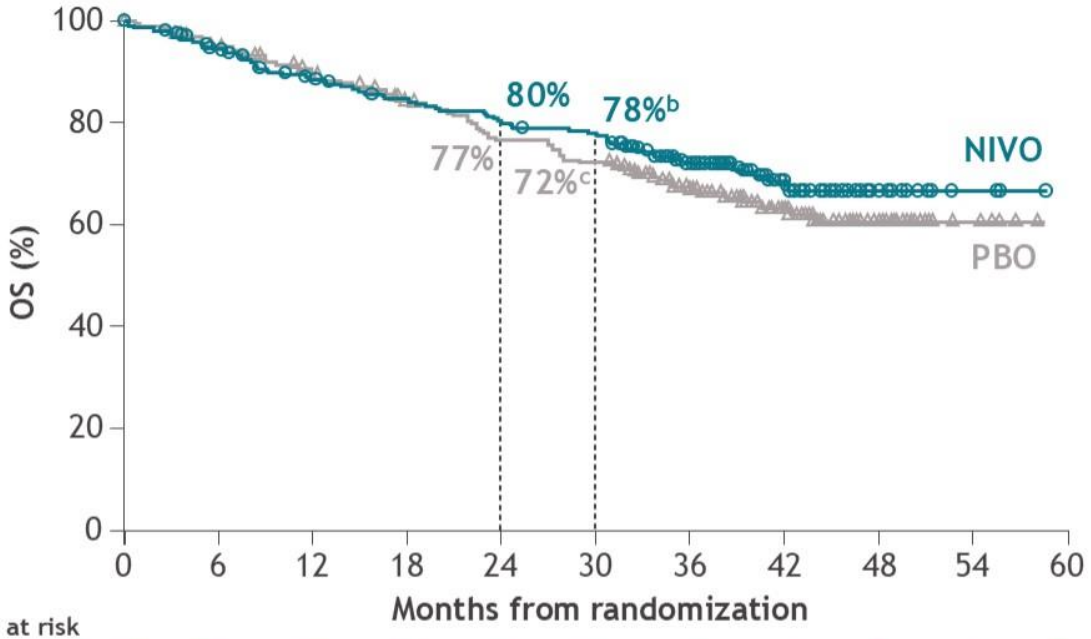
Database lock date: December 16, 2024; median follow-up (range): 41.0 months (31.3–59.8).

[a,b]95% CI: [a]54-68; [b]36-50.

OS and lung cancer-specific survival

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)	

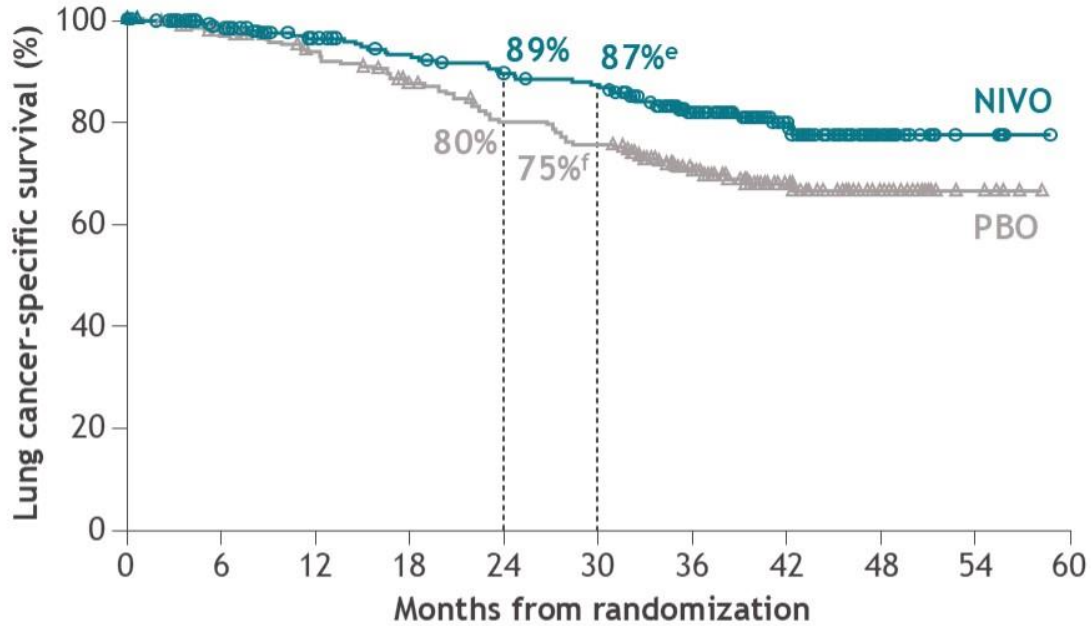


No. at risk

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

Lung cancer-specific survival[d]

	NIVO (n = 229)	PBO (n = 232)
Median lung cancer-specific survival, mo (95% CI)	NR (NR-NR)	NR (NR-NR)
HR (95% CI)	0.60 (0.40-0.89)	



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

Median follow-up (range): 41.0 months (31.3-59.8).

67 (29%) patients in the NIVO arm and 101 (44%) patients in the PBO arm received subsequent therapy of any type; 50 (22%) and 87 (38%) patients, respectively, received subsequent systemic therapy.

[a]HR (95% CI), 0.85 (0.61-1.18). Significance boundary for OS was not met at this interim analysis. [b,c]95% CI: [b]72-83; [c]66-78. [d]Exploratory analysis; events were deaths with noted reason of "disease" per investigator assessment. [e,f]95% CI: [e]82-91; [f]69-81.

Perioperative Pembrolizumab in Early-Stage Non–Small-Cell Lung Cancer (NSCLC): 5-Year Follow-Up From KEYNOTE-671

H. Wakelee,[1] J.D. Spicer,[2] S. Gao,[3] M. Liberman,[4] M. Tsuboi,[5] T. Kato,[6] K.-N. Chen,[7] C. Dooms,[8] M. Majem,[9] G.L. Martinengo,[10] O. Bylicki,[11] D. Rodríguez-Abreu,[12] B. Halmos,[13] D.R. Jones,[14] J.E. Chaft,[14] M. Reck,[15] E. Jensen,[16] S.M. Keller,[16] A. Samkari,[16] M.C. Garassino[17]

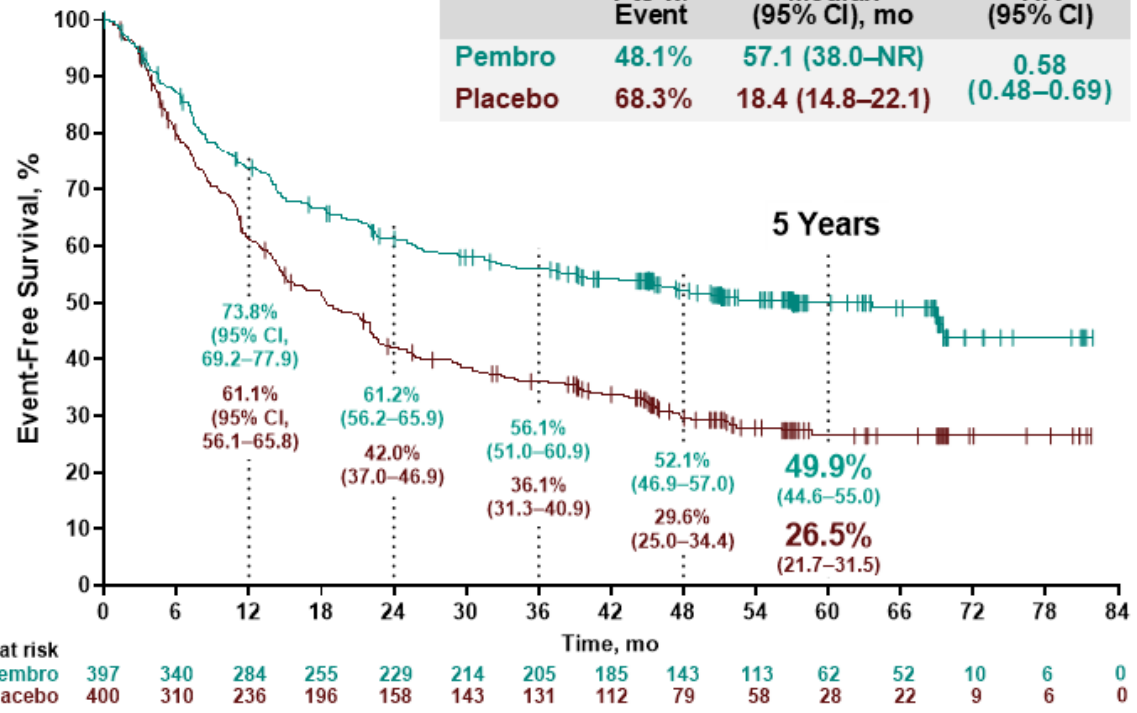
[1]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [2]McGill University Health Centre, Montreal, QC, Canada; [3]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [4]Centre Hospitalier de l'Université de Montréal (CHUM), University of Montreal, Montreal, QC, Canada; [5]National Cancer Center Hospital East, Kashiwa, Japan; [6]Kanagawa Cancer Center, Yokohama, Japan; [7]State Key Laboratory of Molecular Oncology, Peking University Cancer Hospital and Institute, Beijing, China; [8]University Hospitals Leuven, Leuven, Belgium; [9]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [10]Sanatorio Parque, Rosario, Argentina; [11]HIA Sainte-Anne, Toulon, France; [12]Hospital Universitario Insular de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; [13]Montefiore Medical Center–Albert Einstein College of Medicine, Bronx, New York, NY, USA; [14]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA; [15]LungenClinic Grosshansdorf, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany; [16]Merck & Co., Inc., Rahway, NJ, USA; [17]University of Chicago Medicine and Biological Sciences, Chicago, IL, USA

H Wakelee. ESMO 2025

5-Year Update of Event-Free Survival[a]

Overall Population

	Pts w/ Event	Median (95% CI), mo	HR (95% CI)
Pembro	48.1%	57.1 (38.0–NR)	0.58 (0.48–0.69)
Placebo	68.3%	18.4 (14.8–22.1)	



Key Subgroups

Subgroup	Events/participants Pembro	Events/participants Placebo	Hazard Ratio (95% CI)
Overall	191/397	273/400	0.58 (0.48–0.69)
Disease stage			
II	42/118	72/121	0.52 (0.35–0.76)
III	149/279	201/279	0.58 (0.47–0.72)
Nodal status			
N0	62/148	89/142	0.55 (0.40–0.77)
N1	31/82	48/73	0.48 (0.30–0.75)
N2	97/166	136/185	0.64 (0.49–0.83)
Histology			
Nonsquamous	114/226	147/227	0.66 (0.51–0.84)
Squamous	77/171	126/173	0.49 (0.37–0.65)
PD-L1 TPS			
≥50%	45/132	81/134	0.44 (0.31–0.64)
1%–49%	63/127	83/115	0.54 (0.39–0.75)
<1%	83/138	109/151	0.74 (0.55–0.98)

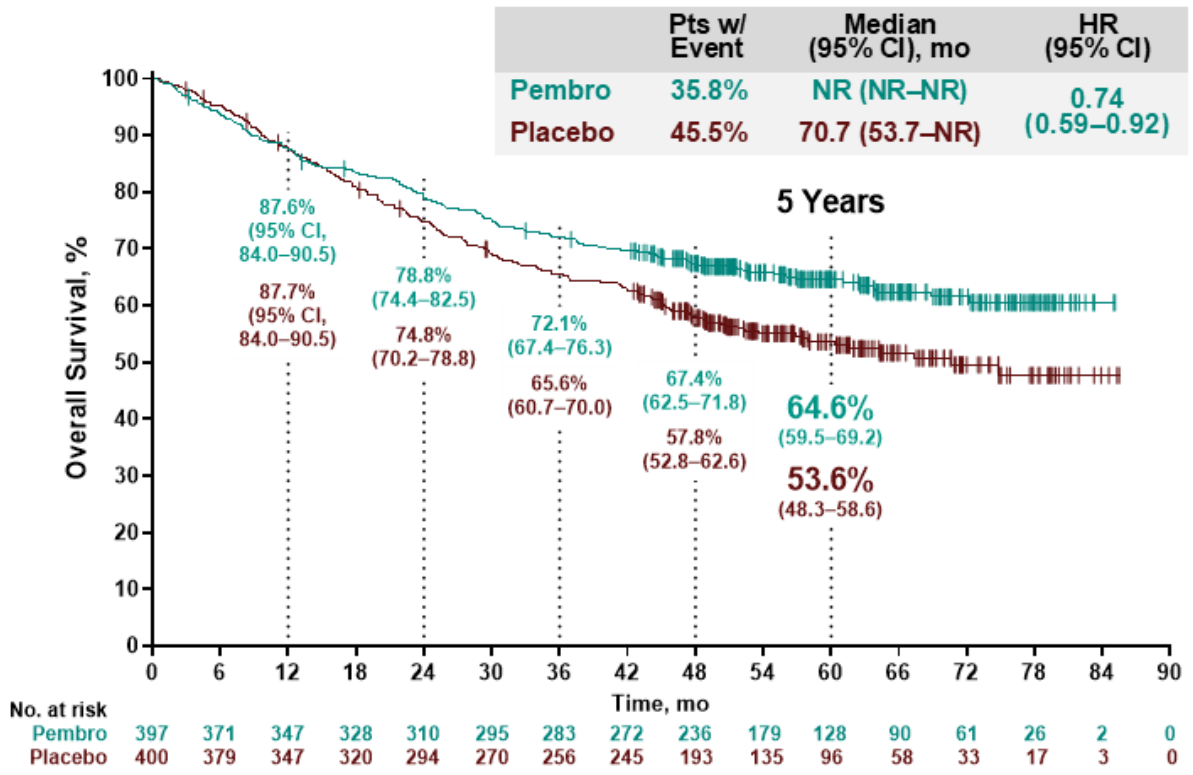
[a]Assessed per RECIST version 1.1 by investigator assessment.
Median time from randomization to data cutoff was 60.4 (range, 42.6–85.8) months.
Data cutoff date: July 3, 2025.

JBUH

H Wakelee. ESMO 2025

5-Year Update of Overall Survival

Overall Population



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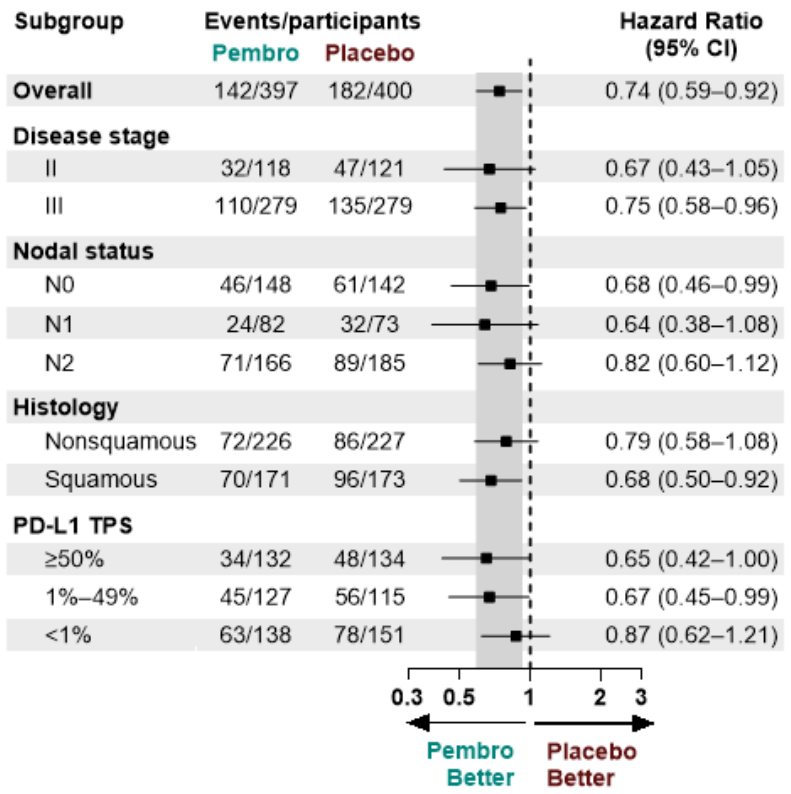
Key Subgroups



JBUH

Surgical outcomes following neoadjuvant treatment

Intervention group	N	Undergo Op. %(N)	Cancelled Op. %(N)	Reasons %(N)			
				Progression	A/E	Physician decision (Unfit)	Others
CheckMate816	179	83.2 (149)	15.6 (28)	6.7 (12)	1.1 (2)	2.2 (4)	5.6 (10)
KEYNOTE671	397	86.4 (342)	17.9 (71)	4.1 (16)	6.3 (25)	4 (16)	3.5 (14)
CheckMate77T	229	77.7 (178)	20.1 (46)	5.7 (13)	3.1 (7)	3.5 (8)	7.9 (18)
AEGEAN	400	81.0 (324)	19 (76)	6.8 (27)	1.8 (7)	4.3 (17)	3.4 (14)
NEOTORCH	202	82.2 (166)	17.8 (36)	2.5 (5)	3.0 (6)	3.5 (7)	8.9 (18)
RATIONALE315	226	84.0 (190)	15.9 (36)	2.6 (6)	2.6 (6)	1.3 (3)	9.3 (21)

Adjuvant Tx after resection

PRINCIPLES OF PERIOPERATIVE SYSTEMIC THERAPY[b]

Other Adjuvant Systemic Therapy

Targeted Therapy Options for Patients with Resected NSCLC

- Alectinib[15] (for patients with ≥4 cm or node-positive NSCLC stages IB–IIIA, IIIB [T2–T3, N2b; T4, N2], and positive for *ALK* gene fusions) (category 1).
- Osimertinib (for patients with NSCLC positive for *EGFR* exon 19 deletion or L858R mutation).
  - For patients with stage IB–IIIA, IIIB (T2–T3, N2b; T4, N2) NSCLC who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy (category 1)[16]
  - For patients who received previous neoadjuvant Osimertinib ± chemotherapy[5]

Immune Checkpoint Inhibitor Options for Patients with Resected NSCLC Tumors

- Atezolizumab[17] (for patients with ≥4 cm or node-positive NSCLC stages IB–IIIA, IIIB [T2–T3, N2b; T4, N2] who received previous adjuvant chemotherapy with NSCLC PD-L1 ≥1% and no known *EGFR* mutations or *ALK* gene fusions) (category 1).
- Pembrolizumab
  - For up to a year for patients with ≥4 cm or node-positive NSCLC stages IB–IIIA, IIIB (T2–T3, N2b; T4, N2) who received previous adjuvant chemotherapy and no known *EGFR* mutations or *ALK* gene fusions (category 1).[18] The benefit for patients with PD-L1 <1% is unclear.
  - For up to 39 weeks for patients who received previous neoadjuvant chemotherapy + Pembrolizumab (category 1).[3]
- Durvalumab[4] (for patients who received previous neoadjuvant chemotherapy + Durvalumab and no known *EGFR* mutations or *ALK* gene fusions) (category 1).
- Nivolumab[2] (for patients who received previous neoadjuvant chemotherapy + Nivolumab and no known *EGFR* mutations or *ALK* gene fusions) (category 1).

NCCN Guideline (NSCLC). 2026. Version 3.

BERLIN 2025 ESMO congress

Updated results from the phase III ALINA study of adjuvant alectinib vs chemotherapy in patients with early-stage *ALK*+ non-small cell lung cancer (NSCLC)

R. Dziadziuszko[1], B.J. Solomon[2], Y. Wu[3], J.S. Ahn[4], M. Nishio[5], D.H. Lee[6], J. Lee[7], W. Zhong[3], H. Horinouchi[8], W. Mao[9], M.J. Hochmair[10], F. de Marinis[11], M.R. Migliorino[12], I. Bondarenko[13], T. Xu[14], A. Cardona[15], A. Scalori[16], V. McNally[16], A.A. Higgerson[17], F. Barlesi[18]

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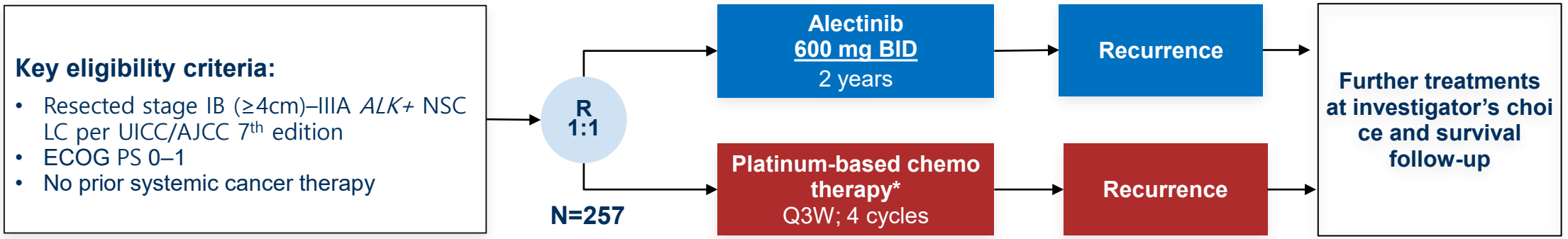
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

- **Alectinib**, an ALK inhibitor, is an approved **standard-of-care** for patients with **resected or advanced *ALK*+ NSCLC**[1–3]
  - Alectinib has **demonstrated efficacy and delayed disease progression in the CNS**[1–3]
  - Long-term data show alectinib is tolerable and has a manageable safety profile[1–3]
- **ALINA** is the only **positive phase III trial** of an ALK inhibitor in **resectable, stage IB–IIIA** (UICC/AJCC 7th edition), *ALK*+ NSCLC[2–4]
  - The primary analysis showed a **significant DFS benefit** with alectinib vs chemotherapy (**HR: 0.24**; 95% CI 0.13–0.43; p<0.0001)[2,3]

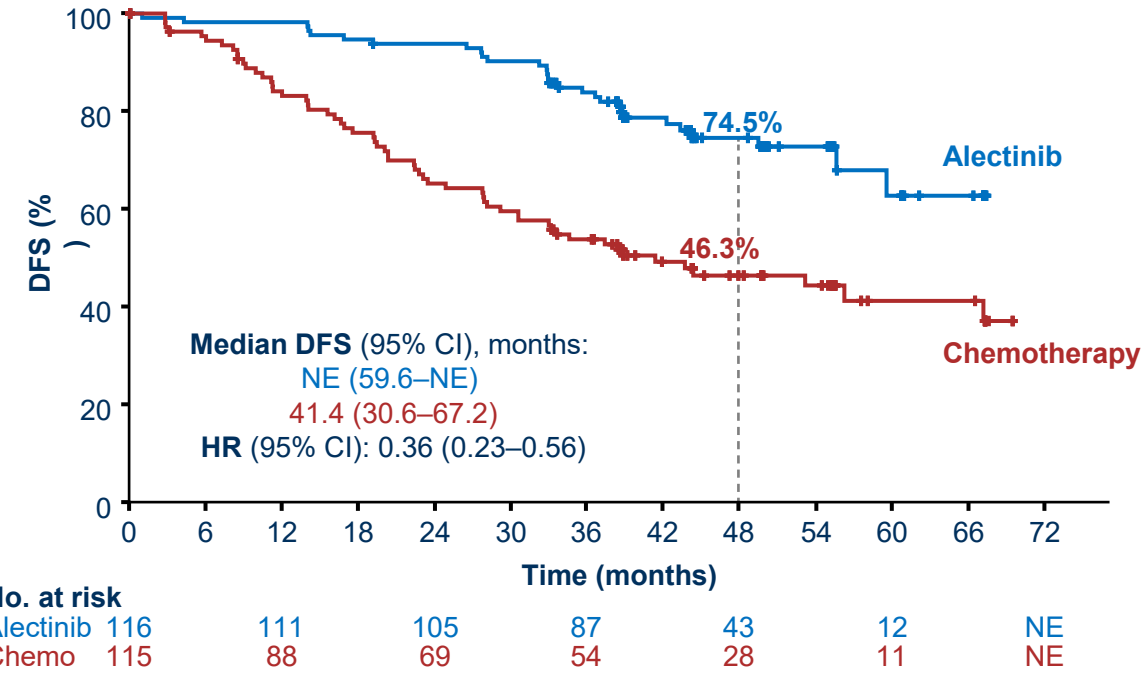


Here, we present updated data from the ALINA study with a median follow-up of 4 years
All patients in the alectinib arm had completed 2 years of treatment with ≥1 year of follow-up

NCT03456076. Crossover was not permitted prior to disease recurrence. *Cisplatin + pemetrexed, cisplatin + vinorelbine or cisplatin + gemcitabine; cisplatin could be switched to carboplatin in case of intolerability. †Stratification by patient race recorded in the interactive voice/web response system. 1. Alecensa Prescribing Information Genentech Inc. 2024; 2. Solomon et al. ESMO 2023 (LBA2); 3. Wu et al. N Engl J Med 2024; 4. Ahn et al. ESMO Asia 2023 (LBA1). *ALK*, anaplastic lymphoma kinase; AJCC, American Joint Committee on Cancer; BID, twice daily; CI, confidence interval; CNS, central nervous system; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; ITT, intention to treat; OS, overall survival; Q3W, every 3 weeks; R, randomisation; UICC, Union for International Cancer Control

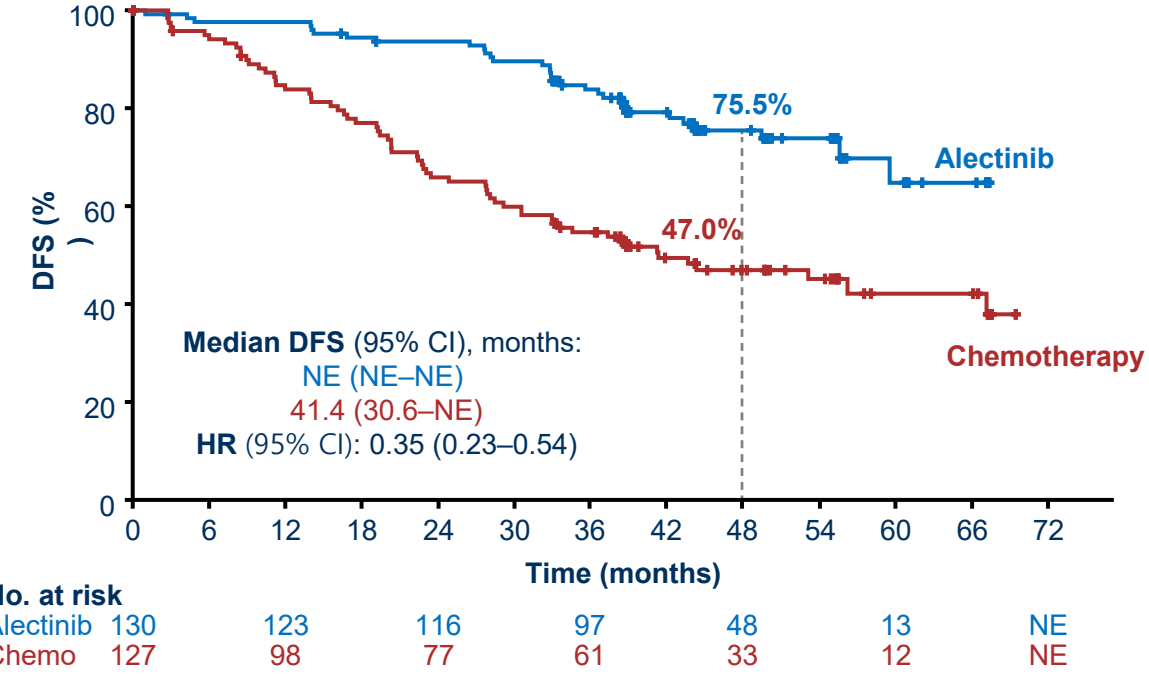
Prof. Rafal Dziadziuszko

DFS in stage II–IIIA*



No. at risk							
Alectinib	116	111	105	87	43	12	NE
Chemo	115	88	69	54	28	11	NE

DFS in stage IB–IIIA (ITT)*



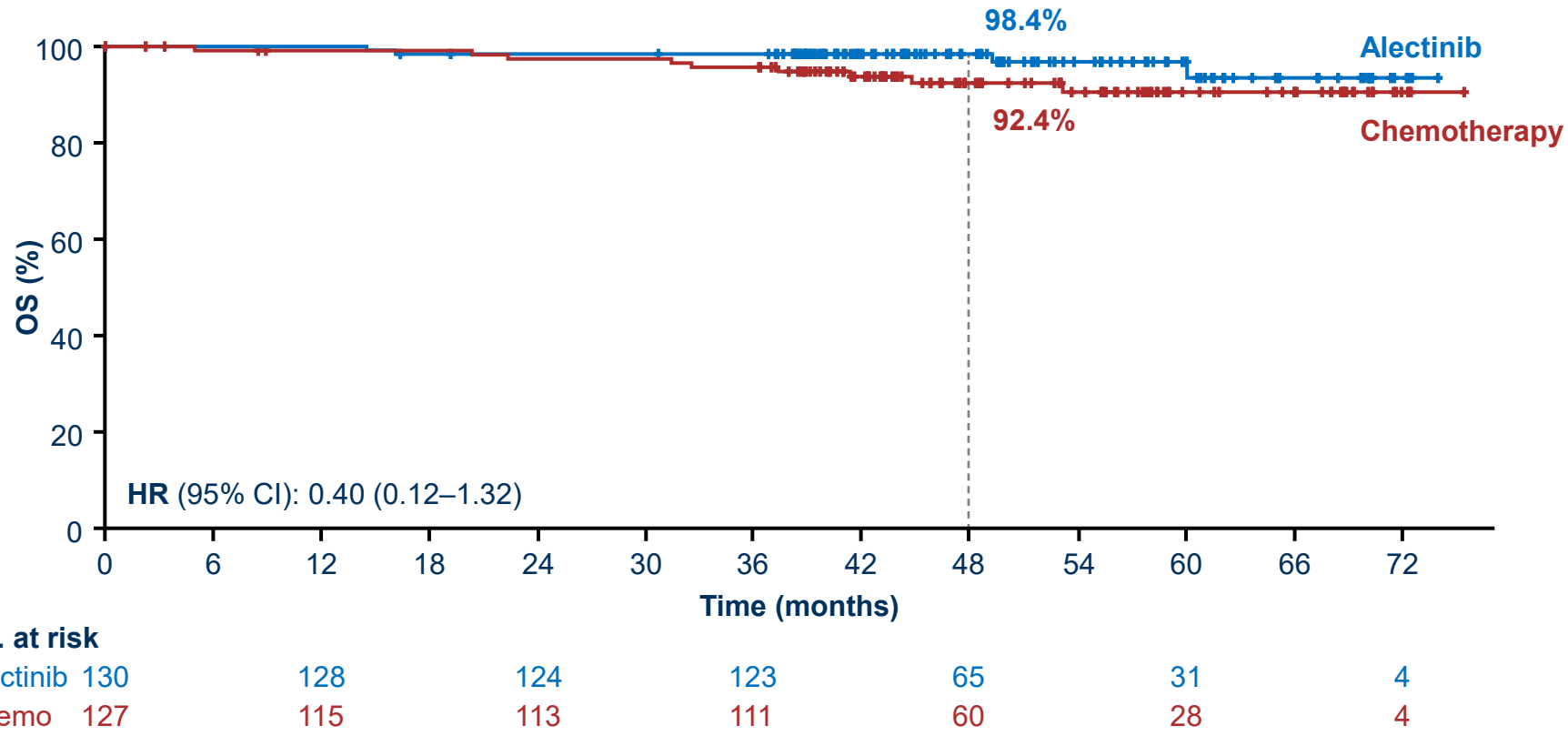
No. at risk							
Alectinib	130	123	116	97	48	13	NE
Chemo	127	98	77	61	33	12	NE

Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

DFS benefit was sustained with alectinib versus chemotherapy in the stage II–IIIA and stage IB-IIIA (ITT) populations

Data cut-off: 8 December 2024. DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurred first
*Per UICC/AJCC 7th edition. Chemo, chemotherapy; NE, not estimable

Prof. Rafal Dziadziuszko



Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

In the IB–IIIA* (ITT) population, there was a positive trend in OS with 4 years of median follow-up

Data cut-off: 8 December 2024. *Per UICC/AJCC 7th edition

Prof. Rafal Dziadziuszko

CCRTx for Un-resectable stage III NSCLC

CONCURRENT CHEMORADIATION REGIMENS

Concurrent Chemoradiation Regimens[a]

Preferred (nonsquamous)

- Carboplatin AUC 5 on Day 1, Pemetrexed 500 mg/m^2 on Day 1 every 21 days for 4 cycles; concurrent thoracic RT[1,b,c,d,e]
- Cisplatin 75 mg/m^2 on Day 1, Pemetrexed 500 mg/m^2 on Day 1 every 21 days for 3 cycles; concurrent thoracic RT[2,3,b,c,d,e,f]
- Carboplatin AUC 2; Paclitaxel 45–50 mg/m^2 weekly, concurrent thoracic RT[4,b,c,d,e,g]
- Cisplatin 50 mg/m^2 on Days 1, 8, 29, and 36; Etoposide 50 mg/m^2 Days 1–5 and 29–33; concurrent thoracic RT[5,6,b,c,d,e]

Preferred (squamous)

- Carboplatin AUC 2; Paclitaxel 45–50 mg/m^2 weekly, concurrent thoracic RT[6,b,c,d,e,g]
- Cisplatin 50 mg/m^2 on Days 1, 8, 29, and 36; Etoposide 50 mg/m^2 Days 1–5 and 29–33; concurrent thoracic RT[5,6,b,c,d,e]

Consolidation Therapy for Patients with Unresectable Stage II/III NSCLC, PS 0–1, and No Disease Progression After Definitive Concurrent Chemoradiation

- Durvalumab 10 mg/kg IV every 2 weeks or 1500 mg every 4 weeks for up to 12 months (patients with a body weight of ≥30 kg)[7,8,h,i] (category 1 for stage III; category 2A for stage II) (except tumors that are positive for *EGFR* exon 19 deletion or L858R mutation)
- Osimertinib 80 mg once daily until disease progression (category 1 for stage III; category 2A for stage II) if *EGFR* exon 19 deletion or L858R mutation[9,i]

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NCCN Guideline (NSCLC). 2026. Version 3.

2024 ASCO® ANNUAL MEETING

Osimertinib after definitive chemoradiotherapy in patients with unresectable stage III epidermal growth factor receptor-mutated (EGFRm) NSCLC: primary results of the Phase 3 LAURA study

Suresh S. Ramalingam,[1] Terufumi Kato, Xiaorong Dong, Myung-Ju Ahn, Le-Van Quang, Nopadol Soparattanapaisarn, Takako Inoue, Chih-Liang Wang, Meijuan Huang, James Chih-Hsin Yang, Manuel Cobo, Mustafa Özgüroğlu, Ignacio Casarini, Dang-Van Khiem, Virote Sriuranpong, Eduardo Cronemberger, Xiangning Huang, Toon van der Gronde, Dana Ghiorghiu, Shun Lu

[1]Emory University School of Medicine, Winship Cancer Institute, Atlanta, GA, USA

LAURA Phase 3 double-blind study design

Patients with locally advanced, unresectable stage III* EGFRm NSCLC with no progression during / following definitive CRT† treatment

Key inclusion criteria:
- ≥18 years (Japan: ≥20)
- WHO PS 0 / 1
- Confirmed locally advanced, unresectable stage III* NSCLC
- Ex19del / L858R‡
- Maximum interval between last dose of CRT and randomization: 6 weeks

Osimertinib 80 mg, once daily

Randomization 2:1 (N= 216)

Stratification by: Concurrent vs sequential CRT
Stage IIIA vs stage IIIB/IIIC
China vs non-China

Placebo, once daily

Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

Open-label osimertinib after BICR-confirmed progression offered to both treatment arms§

Tumor assessments:
- Chest CT / MRI and brain MRI
- At baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

Endpoints

- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Secondary endpoints included:** OS, CNS PFS, safety

*According to AJCC / UICC staging (8th edition);
†Concurrent or sequential CRT comprising ≥2 cycles of platinum-based chemotherapy (or 5 doses of weekly platinum-based chemotherapy) and a total dose of radiation of 60 Gy ±10%;
‡Central or FDA-approved local testing (from a CLIA-approved laboratory, or accredited local laboratory for sites outside of USA) based on tissue;
§If deriving clinical benefit (osimertinib arm); by the judgement of treating physician (placebo arm).

AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; CLIA, Clinical Laboratory Improvement Amendments; CNS; central nervous system; CRT, chemoradiotherapy; CT, computed tomography; EGFRm, epidermal growth factor receptor-mutated; Ex19del, exon 19 deletion; FDA, Food and Drug Administration; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; UICC, Union for International Cancer Control; WHO PS, World Health Organization performance status

LAURA statistical assumptions

- Planned sample size: ~200 patients randomized 2:1, osimertinib:placebo

Sequential multiple testing procedure

Primary analysis: PFS

Study designed with 90% power to detect a PFS HR of 0.53 at a 5% (2-sided) significance level (alpha); translating to improvement in median PFS from 8.0 to 15.0 months; primary analysis when approximately 120 BICR-confirmed progression events had occurred

If significant, recycle alpha

OS (interim and final analyses)*

Interim OS analysis at time of primary PFS analysis; final OS analysis at 60% maturity (approximately 120 deaths)

Non-statistically significant OS at interim analysis will not preclude further testing of OS

If significant, recycle alpha

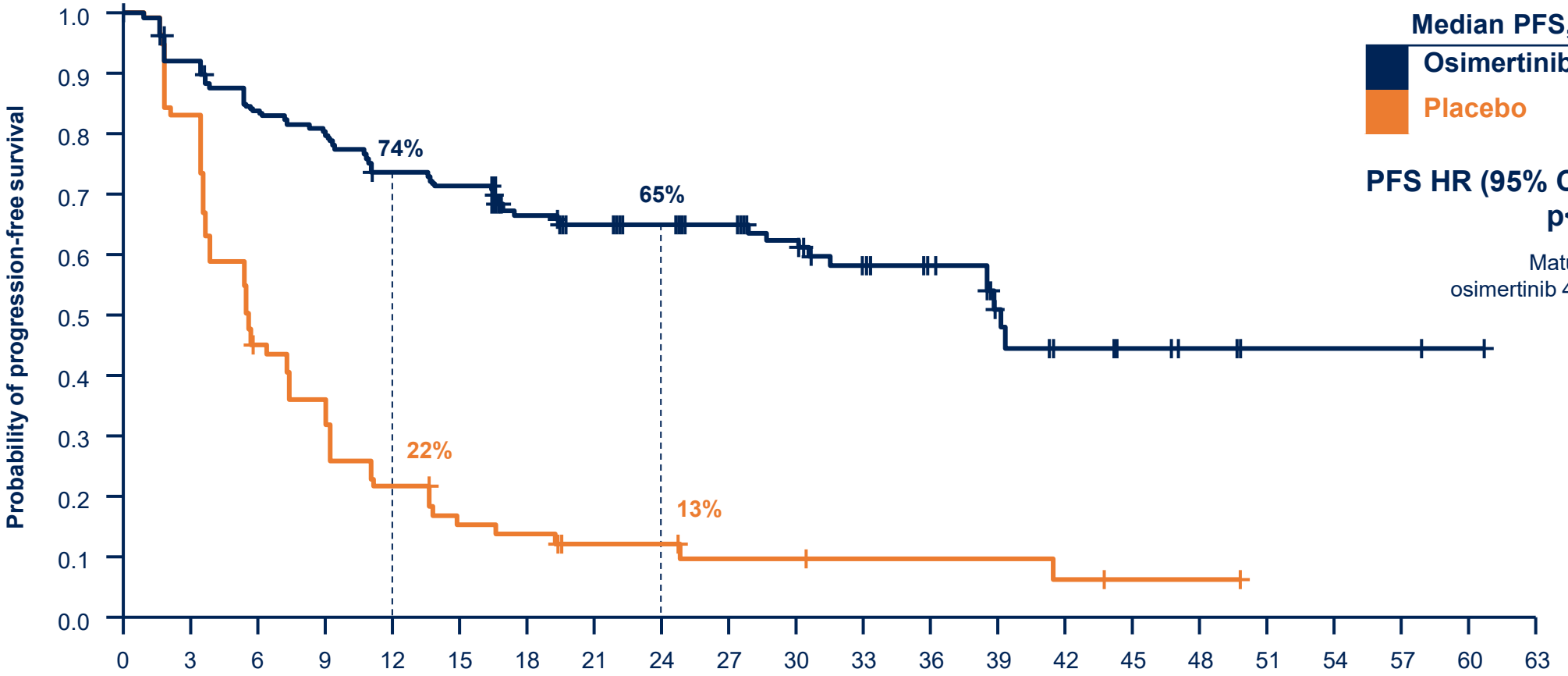
CNS PFS

Will be tested for significance if OS is statistically significant, either at interim or final analysis of OS

*Lan DeMets approach (that approximates the O'Brien and Fleming spending function) used to control the alpha level allocated to OS, where the alpha level applied at the interim depends upon the proportion of information available.

BICR, blinded independent central review; CNS; central nervous system; HR, hazard ratio; OS, overall survival; PFS, progression-free survival

Progression-free survival by BICR



Median PFS, months (95% CI)

Osimertinib	39.1 (31.5, NC)
Placebo	5.6 (3.7, 7.4)

PFS HR (95% CI): 0.16 (0.10, 0.24), p<0.001

Maturity 56%:
osimertinib 40%, placebo 86%

No. at risk

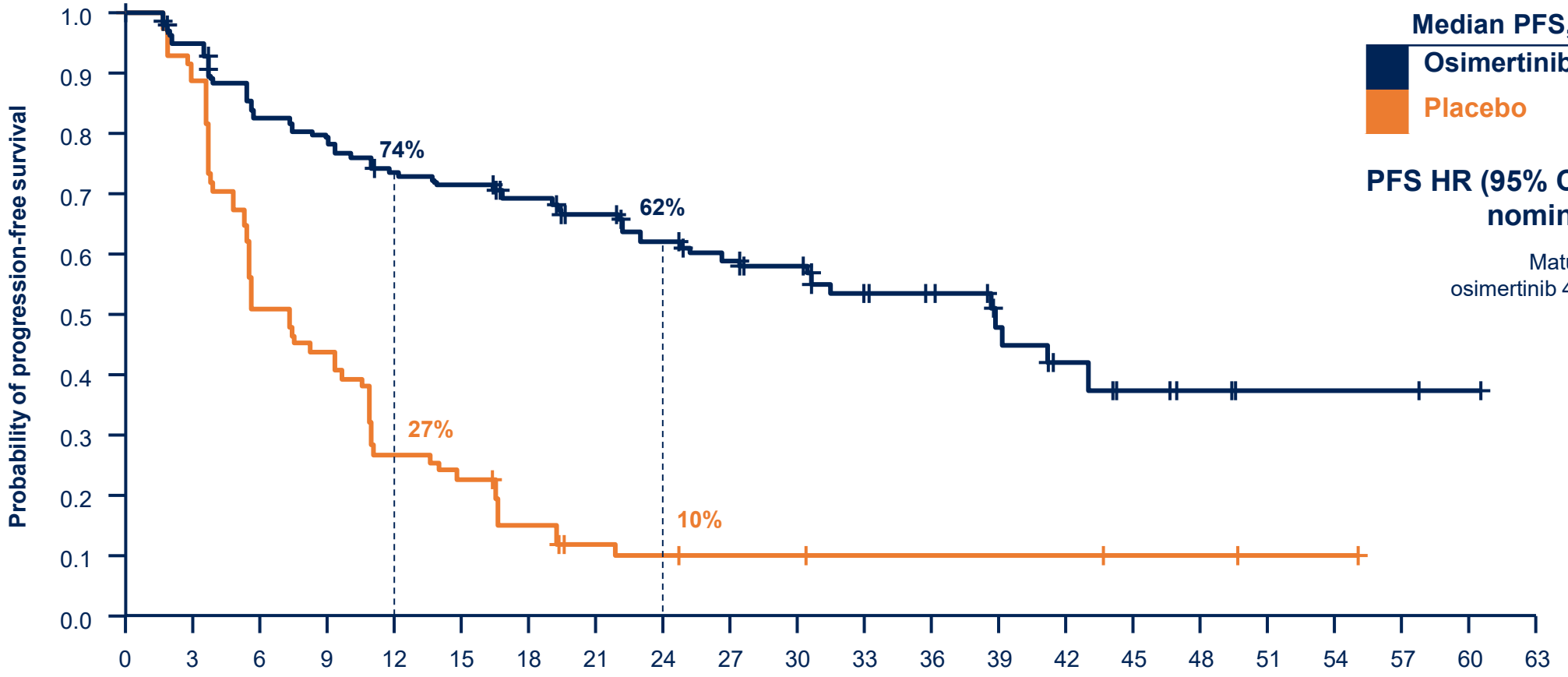
Osimertinib	143	127	1 14	109	99	96	83	76	69	61	49	37	28	16	9	6	4	2	2	2	1	0
Placebo	73	59	31	25	15	10	9	6	6	4	4	3	3	3	2	1	1	0	0	0	0	0

Data cut-off: January 5, 2024.

Tick marks indicate censored data. Median follow-up for PFS (all patients): osimertinib 22.0 months, placebo 5.6 months. Median follow-up for PFS (censored patients): osimertinib 27.7 months, placebo 19.5 months.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NC, not calculable; PFS, progression-free survival

Progression-free survival by investigator assessment



Median PFS, months (95% CI)

Osimertinib	38.9 (26.7, NC)
Placebo	7.3 (5.5, 10.3)

PFS HR (95% CI): 0.19 (0.12, 0.29), nominal p<0.001

Maturity 58%:
osimertinib 43%, placebo 86%

No. at risk																					
Osimertinib	143	131	112	108	99	96	87	78	67	56	45	35	26	16	9	6	4	2	2	2	1	0
Placebo	73	63	36	31	19	16	10	6	5	4	4	3	3	3	3	2	2	1	1	0	0	0

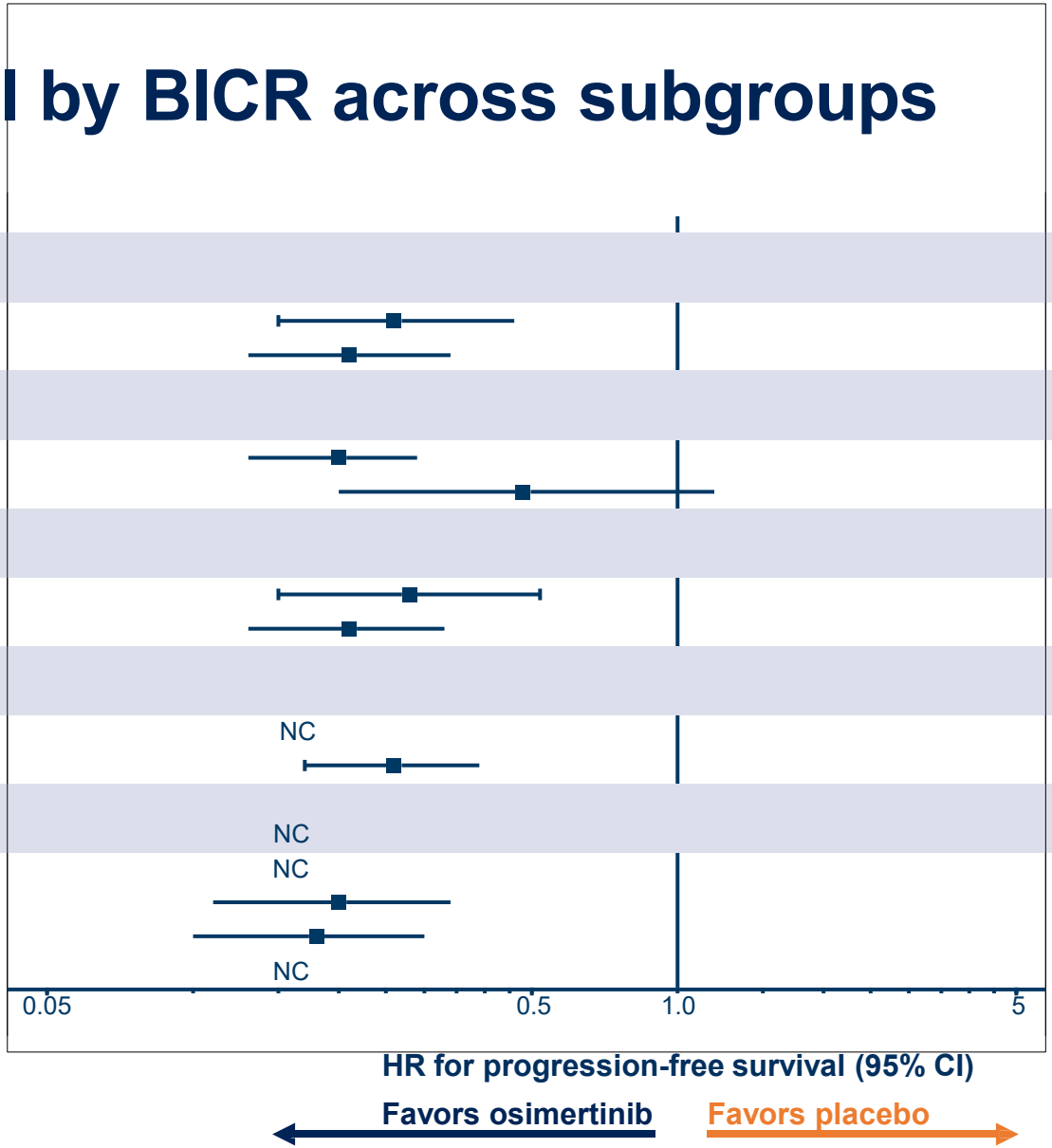
Tick marks indicate censored data. Median follow-up for PFS (all patients): osimertinib 22.2 months, placebo 5.7 months. Median follow-up for PFS (censored patients): osimertinib 27.6 months, placebo 22.1 months.

Data cut-off: January 5, 2024.

CI, confidence interval; HR, hazard ratio; NC, not calculable; PFS, progression-free survival

Progression-free survival by BICR across subgroups

Subgroup		No. of events / patients	HR	95% CI
Overall (N=216)	Stratified log-rank	120 / 216	0.16	0.10, 0.24
	Unadjusted Cox PH	120 / 216	0.23	0.16, 0.33
Sex	Male	50 / 84	0.26	0.15, 0.46
	Female	70 / 132	0.21	0.13, 0.34
Age	<65 years	67 / 120	0.16	0.10, 0.26
	≥65 years	53 / 96	0.33	0.19, 0.57
Race	Asian	98 / 178	0.20	0.13, 0.29
	Non-Asian	22 / 38	0.48	0.20, 1.19
Smoking history	Current / former (yes)	42 / 65	0.26	0.14, 0.48
	Never (no)	78 / 151	0.22	0.14, 0.34
Stage*	IIIA	42 / 76	0.28	0.15, 0.52
	IIIB / IIIC	78 / 140	0.21	0.13, 0.33
EGFR mutation†	Ex19del	65 / 117	0.17	0.10, 0.29
	L858R	55 / 98	0.32	0.19, 0.56
China cohort	Chinese	18 / 40	NC	NC, NC
	Non-Chinese	102 / 176	0.26	0.17, 0.39
Chemoradiotherapy	Concurrent	107 / 193	0.25	0.17, 0.36
	Sequential	13 / 23	NC	NC, NC
Response to prior CRT	Complete response	3 / 7	NC	NC, NC
	Partial response	53 / 94	0.20	0.11, 0.34
	Stable disease	58 / 98	0.18	0.10, 0.30
	Non-evaluable	6 / 17	NC	NC, NC

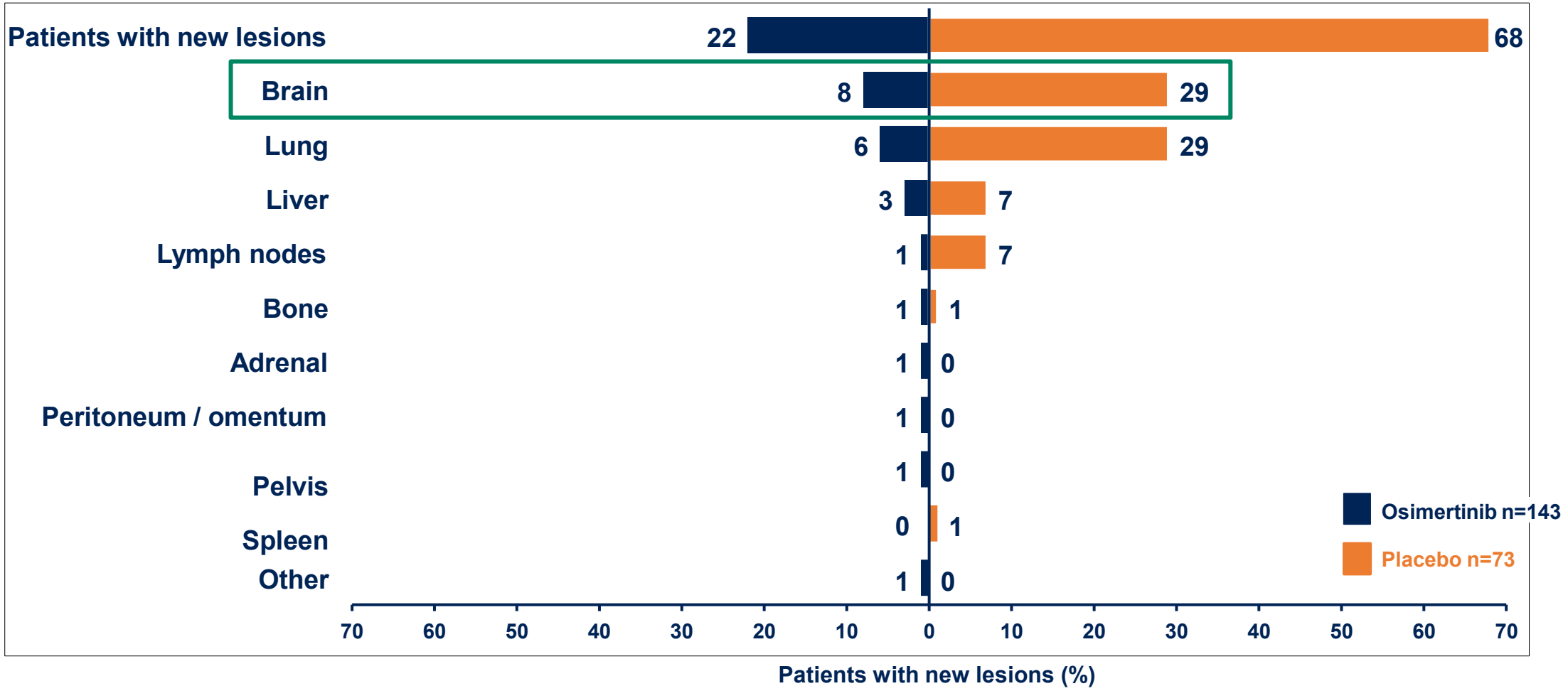


Data cut-off: January 5, 2024.

Note: HRs were calculated only for subgroups with >20 events across both arms to allow for meaningful analysis. Subgroup (not prespecified) of WHO PS: PS=0 HR 0.17 (95% CI 0.10, 0.28); PS=1 HR 0.34 (95% CI 0.20, 0.56);
*Stage prior to CRT by AJCC / UICC staging (8th edition);
†Central test of tumor tissue at screening, or local pre-existing test result; one patient in the osimertinib arm had missing EGFR mutation information.

AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; CI, confidence interval; CRT, chemoradiotherapy; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; HR, hazard ratio; NC, not calculable; PFS, progression-free survival; PH, proportional-hazards model; UICC, Union for International Cancer Control; WHO PS, World Health Organization performance status

Sites of new lesions by BICR



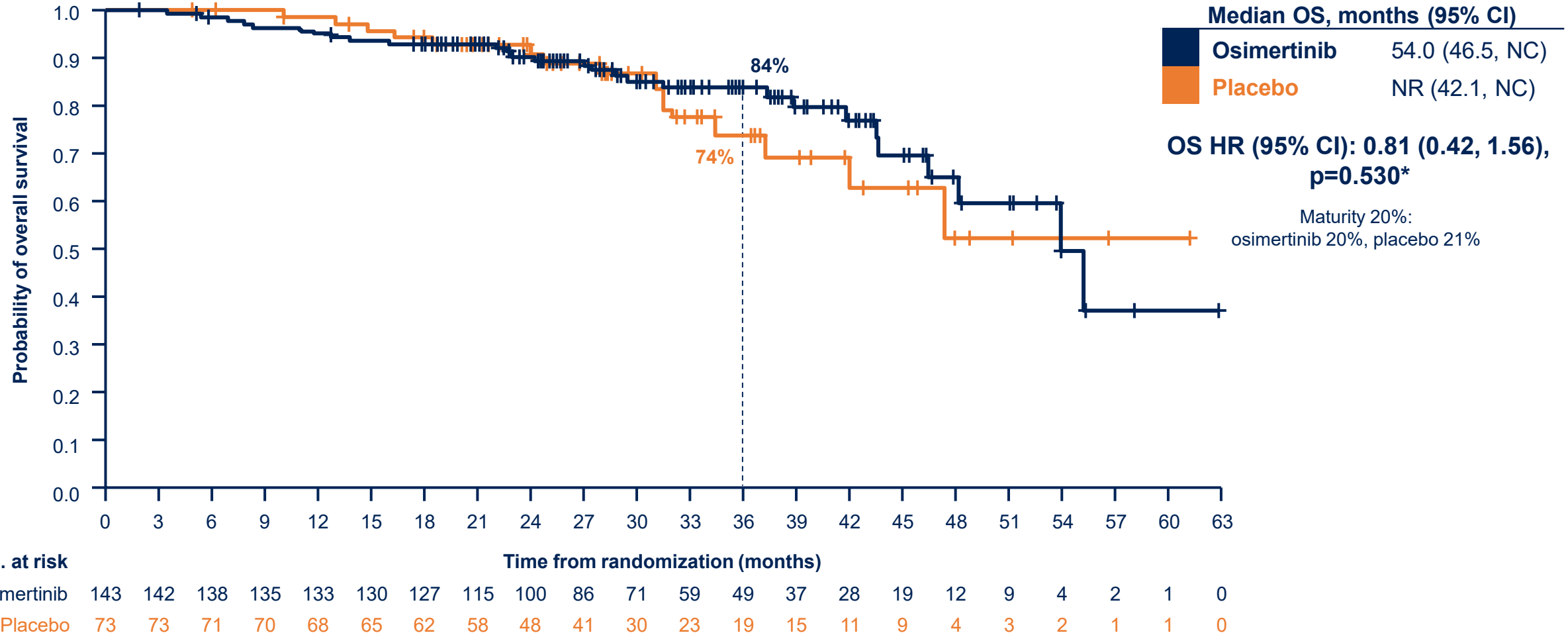
Data cut-off: January 5, 2024.

Percentages based on number of patients in each treatment arm. Patients can have more than one new lesion site. Based on BICR assessments according to RECIST v1.1 and includes all new lesions at any time (including those whose RECIST progression event had been censored).

BICR, blinded independent central review

Interim analysis of overall survival

- In the placebo arm, 81% of patients with BICR-confirmed progression crossed over to osimertinib



Data cut-off: January 5, 2024.
Tick marks indicate censored data. *For statistical significance at this interim analysis, a p-value of <0.00036 was required;
Median follow-up for OS (all patients): osimertinib 29.5 months, placebo 28.1 months. Median follow-up for OS (censored patients): osimertinib 30.9 months, placebo 28.1 months.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NC, not calculable; NR, not reached; OS, overall survival

Conclusions

- In LAURA, osimertinib demonstrated a statistically significant and clinically meaningful improvement in PFS vs placebo by BICR in unresectable stage III EGFRm NSCLC following definitive chemoradiotherapy
  - **Median PFS** was **39.1 months** (95% CI 31.5, NC) with osimertinib, **5.6 months** (95% CI 3.7, 7.4) with placebo; **HR 0.16** (95% CI 0.10, 0.24), p<0.001
  - PFS benefit was consistent across subgroups
- Interim OS data showed a positive trend in favor of osimertinib, despite a high proportion of patients crossing over to osimertinib in the placebo arm (81%)
- Safety profile of osimertinib post-chemoradiotherapy was as expected and manageable
- EGFR mutation testing is critical in stage III disease to ensure optimal outcomes for patients with EGFRm NSCLC

Osimertinib will become the new standard of care for patients with unresectable st age III EGFRm NSCLC who have not progressed after definitive chemoradiotherapy

BICR, blinded independent central review; CI, confidence interval; EGFR, epidermal growth factor receptor; EGFRm, EGFR-mutated; HR, hazard ratio; NC, not calculable; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival

Data cut-off: January 5, 2024.

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Osimertinib after definitive chemoradiotherapy in patients with unresectable stage III EGFRm NSCLC: Updated overall survival analysis from the LAURA study

Suresh S. Ramalingam,[1] Mustafa Özgüroğlu,[2] Myung-Ju Ahn,[3] Xiaorong Dong,[4] James Chih-Hsin Yang,[5] Satoshi Oizumi,[6] Koichi Goto,[7] Manuel Cobo,[8] Sang-We Kim,[9] Te-Chun Hsia,[10] Jarin Chindaprasirt,[11] Fernanda Fujiki,[12] Natalia Valdiviezo,[13] Ignacio Casarini,[14] Terufumi Kato,[15] Xiangning Huang,[16] Azura Evans,[17] Ana Bolanos,[18] Shun Lu[19]

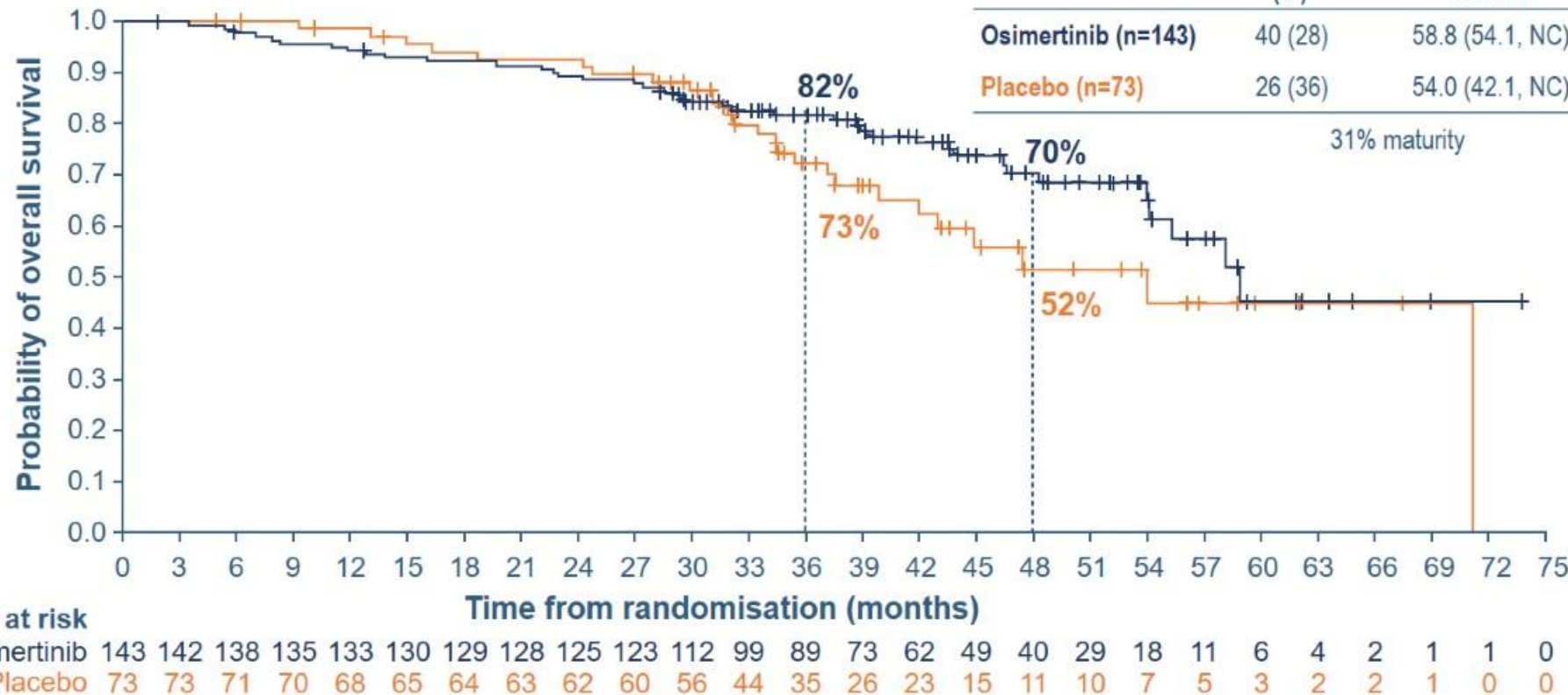
[1]Emory University School of Medicine, Winship Cancer Institute, Atlanta, GA, USA; [2]Clinical Trial Unit, Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Istanbul, Türkiye; [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [4]Cancer Center, Union Hospital and Huazhong University of Science and Technology, Wuhan, China; [5]National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei, Taiwan; [6]NHO Hokkaido Cancer Center, Sapporo, Japan; [7]National Cancer Center Hospital East, Kashiwa, Japan; [8]Hospitales Universitarios Regional y Virgen de la Victoria, IBIMA, Málaga, Spain; [9]Asan Medical Center, Seoul, Republic of Korea; [10]China Medical University Hospital, Taichung, Taiwan; [11]Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand; [12]ICESP – Instituto do Câncer do Estado de São Paulo, São Paulo, Brazil; [13]Instituto Nacional de Enfermedades Neoplasicas, Surquillo, Peru; [14]Hospital Bernardo Houssay, Mar del Plata, Buenos Aires, Argentina; [15]Kanagawa Cancer Center, Yokohama, Japan; [16]Late-stage Development, Oncology R&D, AstraZeneca, Cambridge, UK; [17]Late-stage Development, Oncology R&D, AstraZeneca, Macclesfield, UK; [18]Late-stage Development, Oncology R&D, AstraZeneca, Mississauga, ON, Canada; [19]Shanghai Chest Hospital and Shanghai Jiao Tong University, Shanghai, China

Final Publication Number: LBA4

Updated DCO

IMPROVED TREND TOWARDS OS BENEFIT SEEN WITH OSIMERTINIB AT UPDATED ANALYSIS

	No. of events (%)	Median (95% CI), months	HR (95% CI) Log-rank p-value
Osimertinib (n=143)	40 (28)	58.8 (54.1, NC)	0.67 (0.40, 1.14) p=0.140
Placebo (n=73)	26 (36)	54.0 (42.1, NC)	



- 55/69 (80%) patients who discontinued study treatment in the placebo group received subsequent treatment with a 3rd-gen EGFR-TKI*

Suresh S. Ramalingam

DCO: 29 November 2024.
Tick marks indicate censored data.
Median follow-up for OS (all patients): osimertinib 39.4 months, placebo 35.2 months. Median follow-up for OS (censored patients): osimertinib 42.6 months, placebo 37.5 months.
*Any-line.
CI, confidence interval; DCO, data cut-off; gen, generation; HR, hazard ratio; NC, not calculable; OS, overall survival

CONCLUSIONS

- The updated OS analysis from LAURA demonstrates an improved favourable trend for OS benefit with osimertinib over placebo
  - This was seen despite the high proportion of patients in the placebo group receiving subsequent treatment with a 3rd-generation EGFR-TKI post-treatment discontinuation (80%)

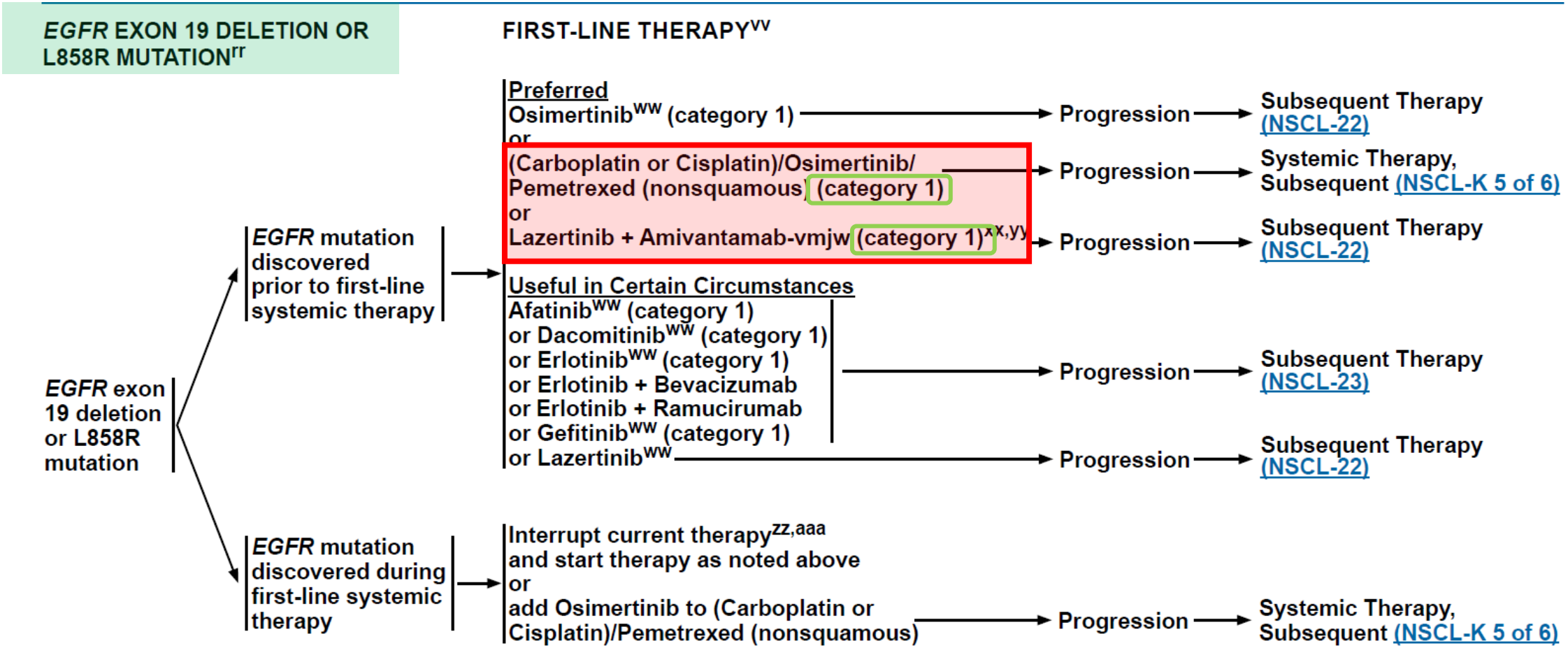
- Clinically meaningful improvements were observed with osimertinib over placebo in the post-progression outcomes TFST, PFS2 and TSST

Osimertinib after definitive chemoradiotherapy is the new standard of care for patients with unresectable stage III EGFRm NSCLC

Suresh S. Ramalingam

EGFRm, epidermal growth factor receptor-mutated; NSCLC, non-small cell lung cancer; OS, overall survival; PFS2, second progression-free survival; TFST, time to first subsequent treatment; TSST, time to second subsequent treatment

Treatments of advanced NSCLC



NCCN Guideline (NSCLC). 2026. Version 3.

MARIPOSA : Amivantamab + Lazertinib vs Osimertinib

MADRID 2023 ESMO congress

Serial brain MRIs were required for all patients

Key Eligible Criteria

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0 or 1

Strafication Factors

- EGFR mutation type (Ex 19del or L858R)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=1074)

- Amivantamab + Lazertinib (n=429; open-label)
- Osimertinib (n=429; blinded)
- Lazertinib (n=216; blinded)

Dosing (in 28-day cycles)

- Amivantamab: 1050mg (1400mg ≥if 80kg) weekly for the first 4 weeks, then every 2 weeks
- Lazertinib: 240mg daily
- Osimertinib: 80mg daily

Primary endpoint of progression-free survival (PFS) by BICR per RECIST v1.1:

Amivantamab+lazertinib *vs* osimertinib

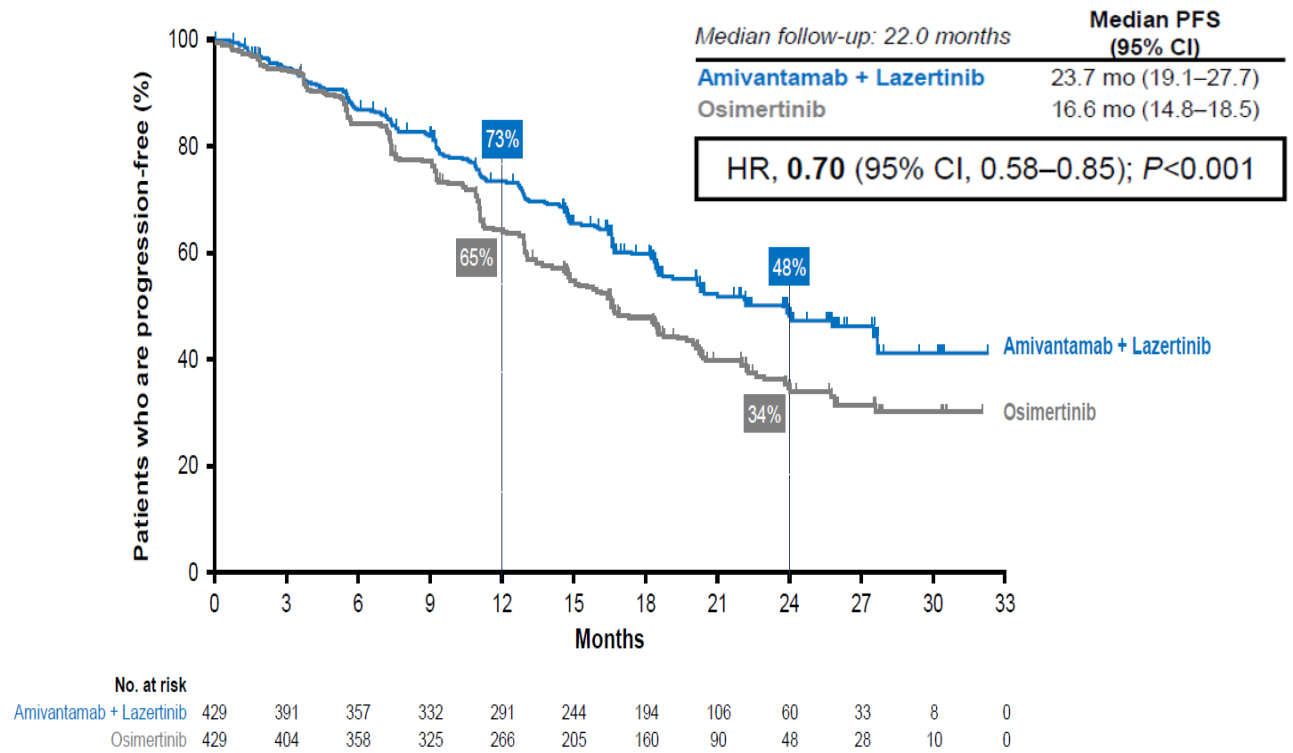
Secondary endpoints of Amivantamab+lazertinib *vs* osimertinib

- Overall survival (OS)
- Objective response rate (ORR)
- Duration of response (DoR)
- PFS after first subsequent therapy (PFS2)
- Symptomatic PFS
- Intracranial PFS
- Safety

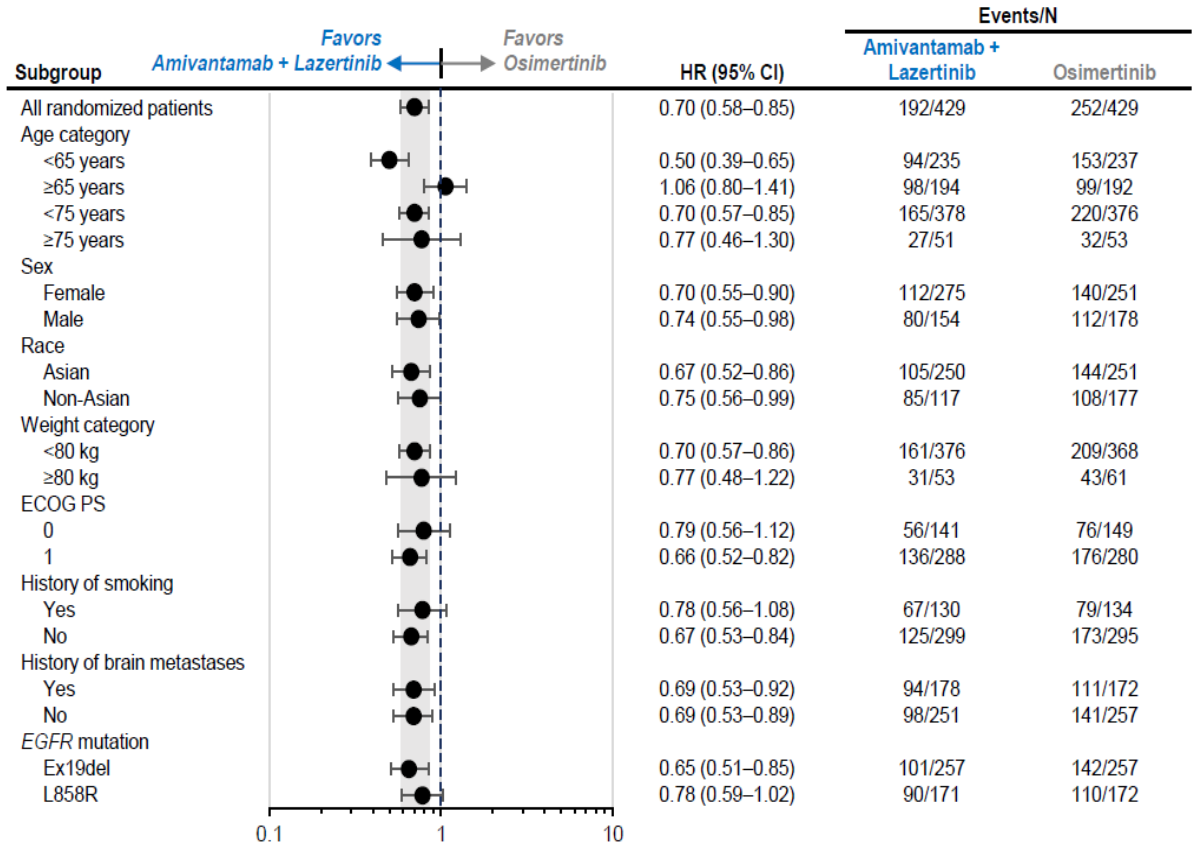
Cho BC, et al. Oral presentation at ESMO 2023 (Abstract LBA14)

MARIPOSA : PFS (by BICR)

Progression-free survival



PFS Benefit across Predefined Subgroups

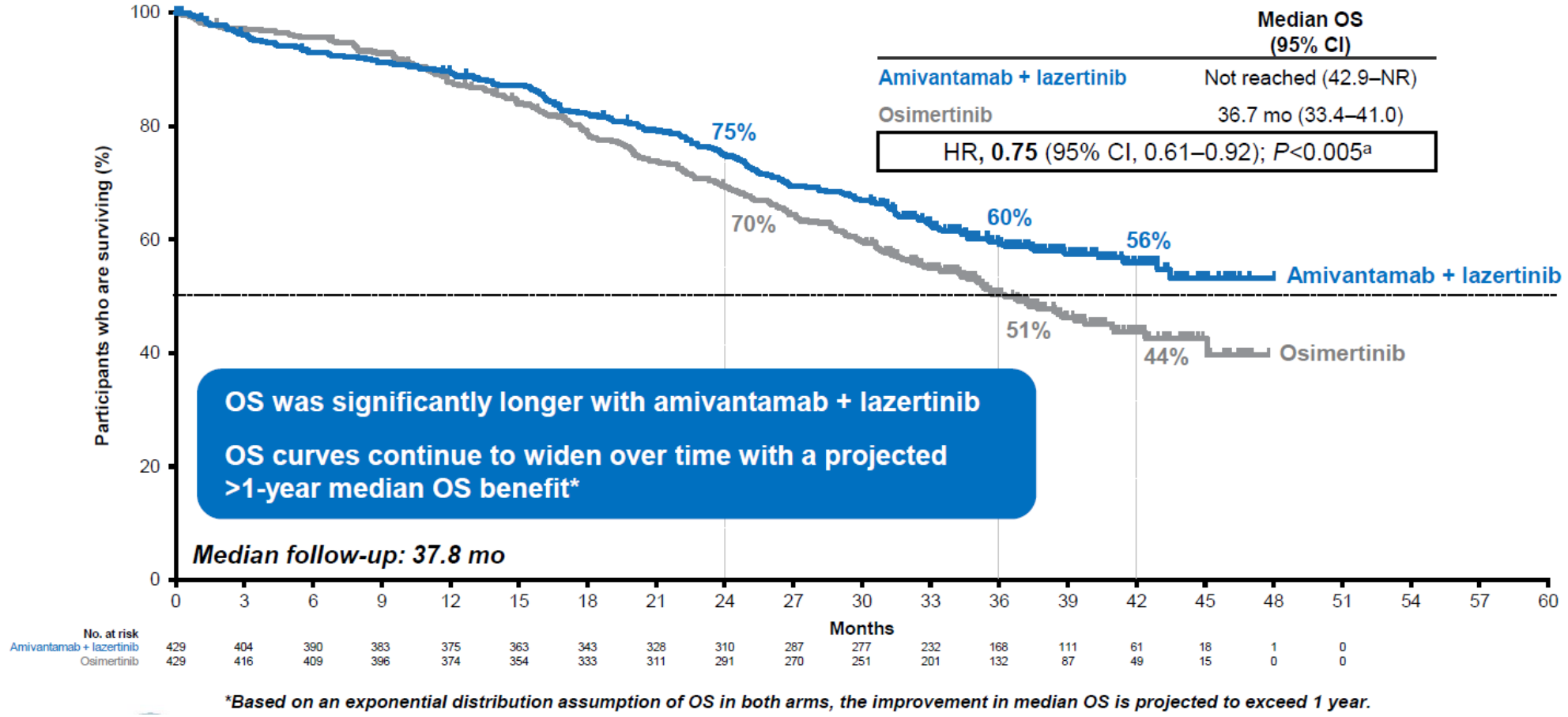


BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; mo, months; PFS, progression-free survival.

Cho BC, et al. *N Engl J Med* 2024;391(16):1486-1498

MARIPOSA : Overall Survival

elcc European Lung Cancer Congress 2025



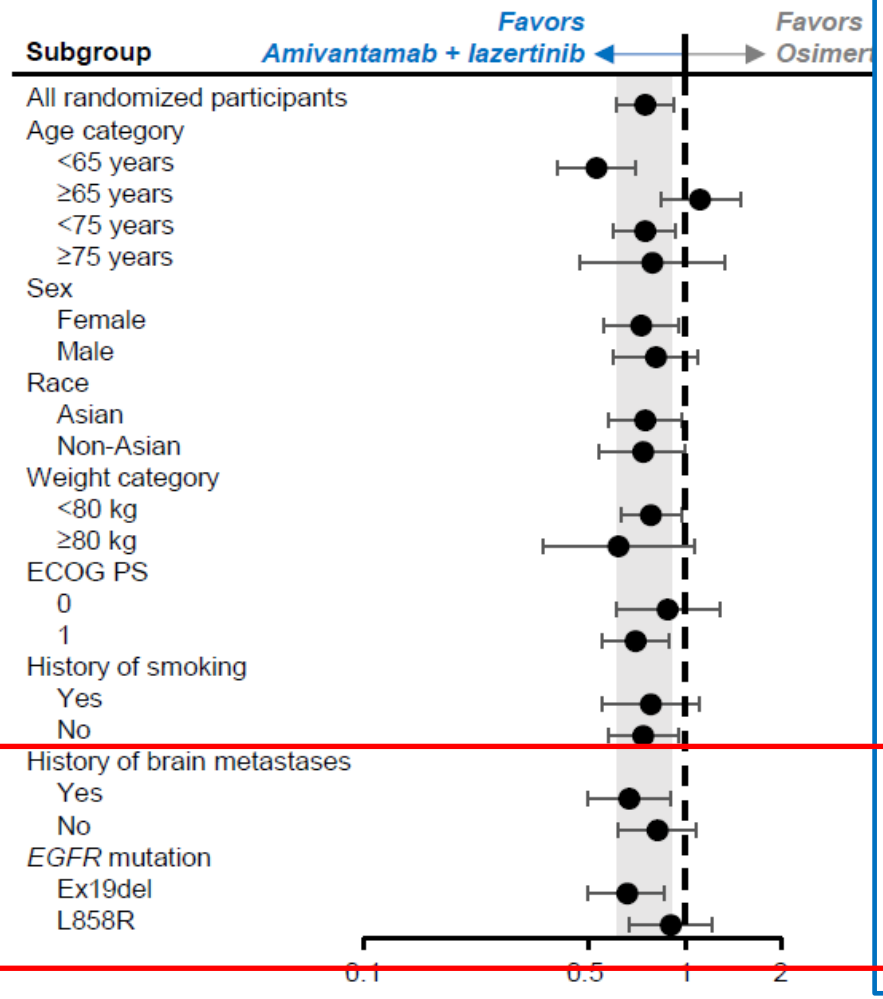
*Based on an exponential distribution assumption of OS in both arms, the improvement in median OS is projected to exceed 1 year.

Note: Last participant was enrolled in May 2022. Clinical cutoff date was December 4, 2024. In total, 390 deaths had occurred in the amivantamab + lazertinib (173 deaths) and osimertinib (217 deaths) arms.
a*P*-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model.

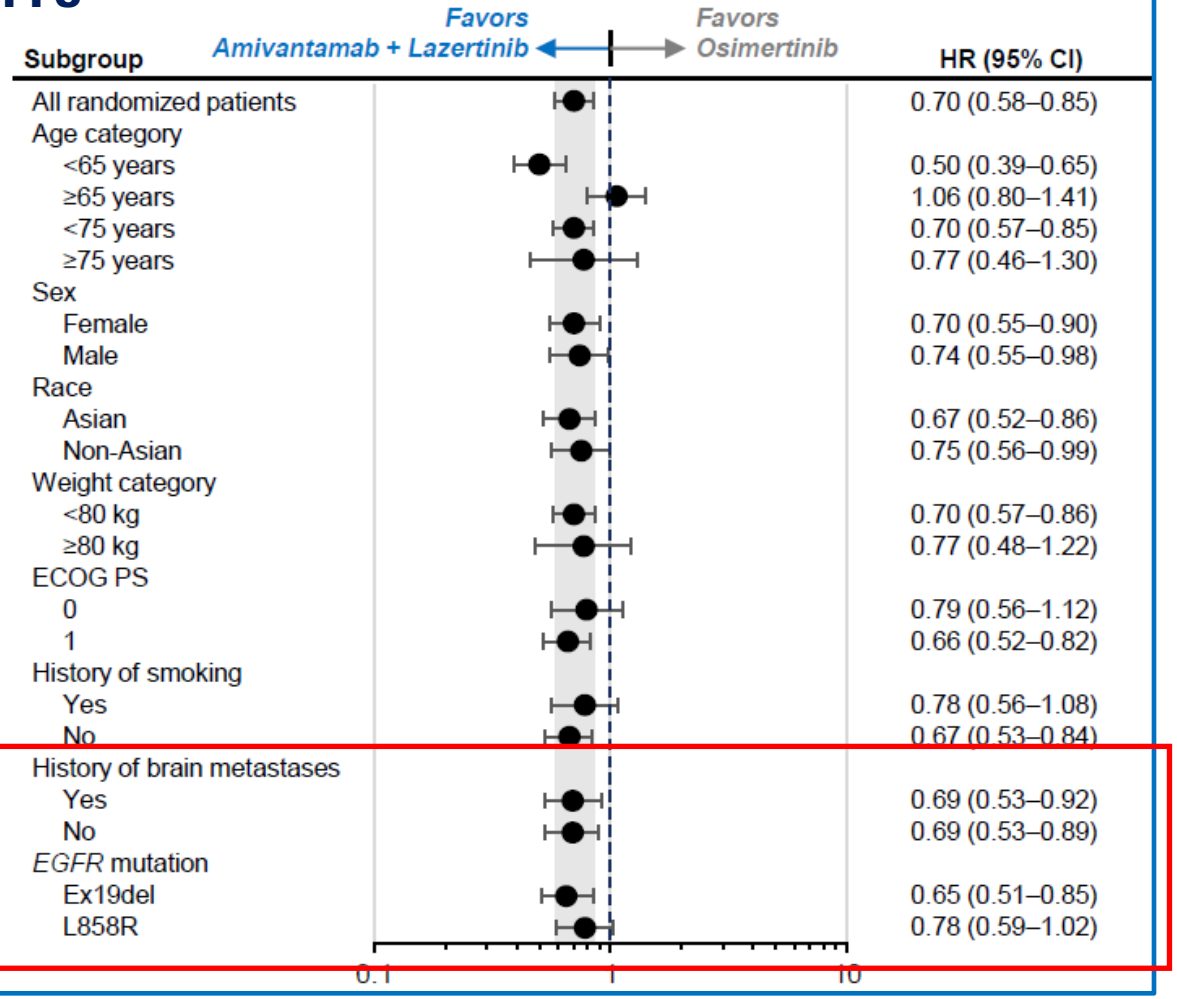
Yang JC, et al. *N Engl J Med.* Sep 6, 2025;

Yang JC, et al. ELCC 2025

MARIPOSA : Overall Survival in Predefined Subgroups



PFS



Yang JC, et al. ELCC 2025

Yang JC, et al. *N Engl J Med.* Sep 6, 2025;

FLAURA2 : Osimertinib + Chemotherapy vs Osimertinib

IASLC 2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

Safety run-in period (N=30)
Published in ESMO Open, 2021[1]

Patients with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:

- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC
- Stable CNS metastases were allowed*
- Brain scans at baseline (MRI / CT)

Stratification by:

- **Race** (Chinese Asian / non-Chinese Asian / non-Asian)
- **EGFRm** (local / central test)
- **WHO PS** (0 / 1)

Randomization 1:1 (N=557)

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles for platinum-based treatments)

Maintenance osimertinib 80 mg (QD) + pemetrexed (Q3W)†

Osimertinib 80 mg (QD)

Follow-up:

- RECIST 1.1 assessment at 6 and 12 weeks, then every 12 weeks until RECIST 1.1 defined radiological disease progression or other withdrawal criteria were met

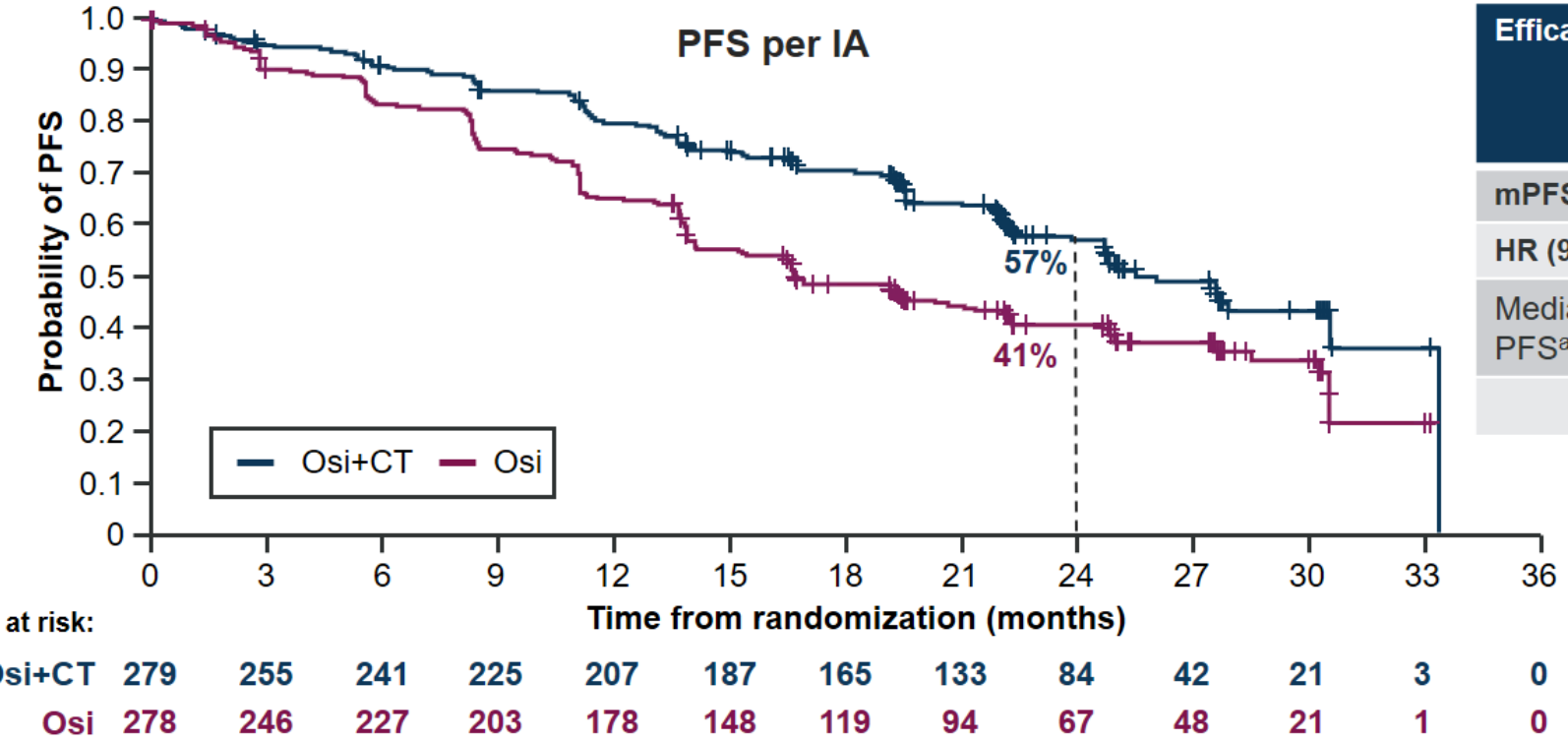
- **Primary endpoint:** PFS by investigator assessment per RECIST 1.1‡§
  - **Sensitivity analysis:** PFS by BICR assessment per RECIST 1.1
- **Secondary endpoints:** OS, ORR, DoR, DCR, HRQoL, safety (AEs by CTCAE v5) and PFS2‡

*Not requiring steroids for at least two weeks; †Pemetrexed maintenance continued until a discontinuation criterion was met; ‡Efficacy analyses in the full analysis set, defined as all patients randomized to study treatment regardless of the treatment actually received, and safety analyses in the safety analysis set, defined as all randomized patients who received ≥1 dose of study treatment – one patient who was randomized to osimertinib plus platinum-pemetrexed received only osimertinib and was therefore included in the osimertinib monotherapy safety analysis set; §The study provided 90% power to demonstrate a statistically significant difference in PFS assuming HR=0.68 at 5% two-sided significance level

AE, adverse event; AUC, area under curve; BICR, blinded independent central review; CNS, central nervous system; CT, computed tomography; CTCAE, Common Terminology Criteria for Adverse Events; DCR, disease control rate; DoR, duration of response; EGFRm, epidermal growth factor receptor-mutated; EGFR-TKI, EGFR-tyrosine kinase inhibitor; Ex19del, exon 19 deletion; HR, hazard ratio; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; QD, once-daily; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; WHO PS, World Health Organization performance status

Planchard D et al. *N Engl J Med.* 2023;389(21):1935-1948.

FLAURA2 : Investigator-Assessed PFS



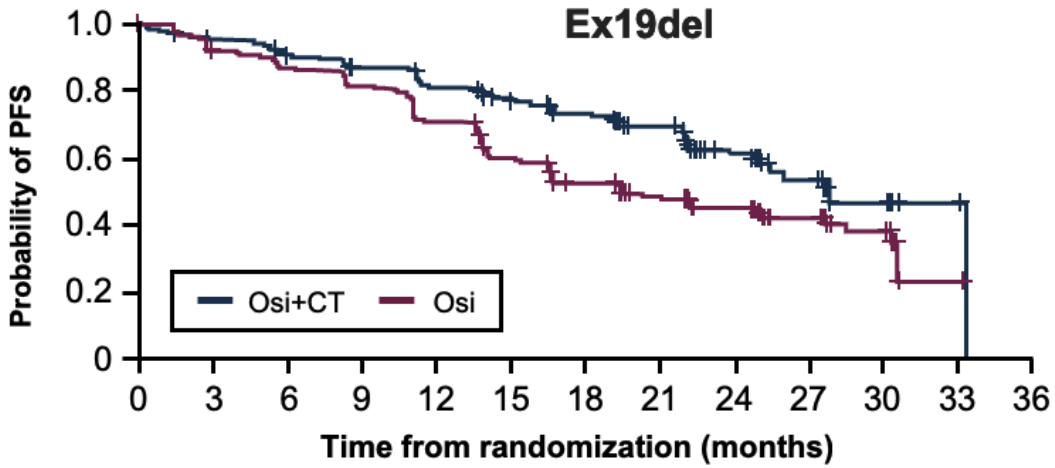
Efficacy	Osimertinib + platinum-pemetrexed[a] (n=279)	Osimertinib (n=278)
mPFS months (95% CI)	25.5 (24.7-NC)	16.7 (14.1-21.3)
HR (95% CI)[b]	0.62 (0.49-0.79); p<0.0001	
Median follow up for PFS[a], months (range)	19.5 (0–33.3)	16.5 (0–33.1)
Overall maturity: 51%		

DCO: April 03, 2023. **Note:** CT therapy includes cisplatin or carboplatin with pemetrexed. [a]In all patients.

CI = confidence interval; CT = chemotherapy; DCO = data cut-off; *EGFR*m = epidermal growth factor receptor mutation-positive; HR = hazard ration; mPFS = median progression-free survival; NC = not calculable.; NSCLC = non-small cell lung cancer; PFS = progression-free survival. NSQ=non squamous

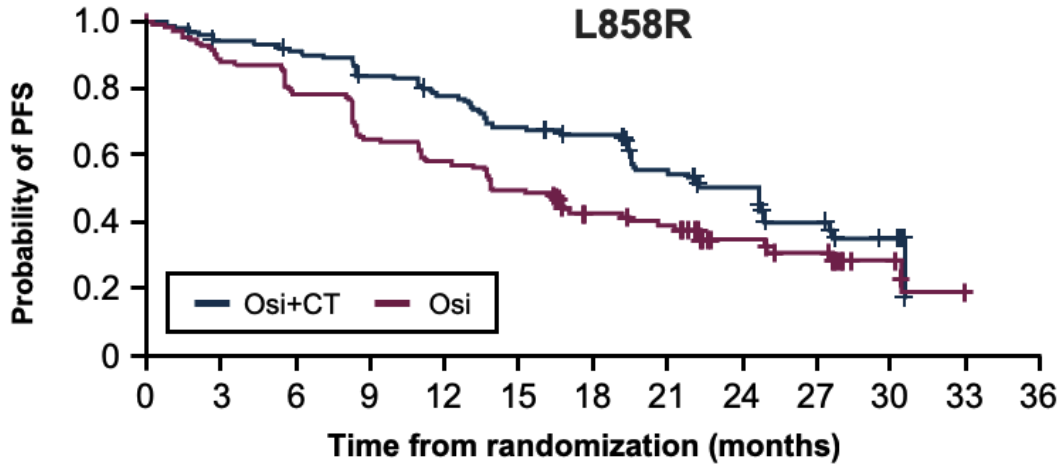
Planchard D et al. *N Engl J Med*. 2023;389(21):1935-1948.

FLAURA2 : PFS[a] Benefit according to EGFRm Type



No. at risk:

Osi+CT	172	159	150	142	131	120	103	86	53	23	9	3	0
Osi	169	152	144	135	117	96	79	63	48	33	16	1	0



No. at risk:

Osi+CT	106	95	91	83	76	67	62	47	31	19	12	0	0
Osi	107	92	82	68	61	52	40	31	19	15	5	0	0

Efficacy in Ex19del	Osimertinib + platinum-pemetrexed (n=172)	Osimertinib (n=169)
mPFS, months (95% CI)	27.9 (25.1-NC)	19.4 (16.5-27.6)
HR (95% CI)	0.60 (0.44-0.83)	

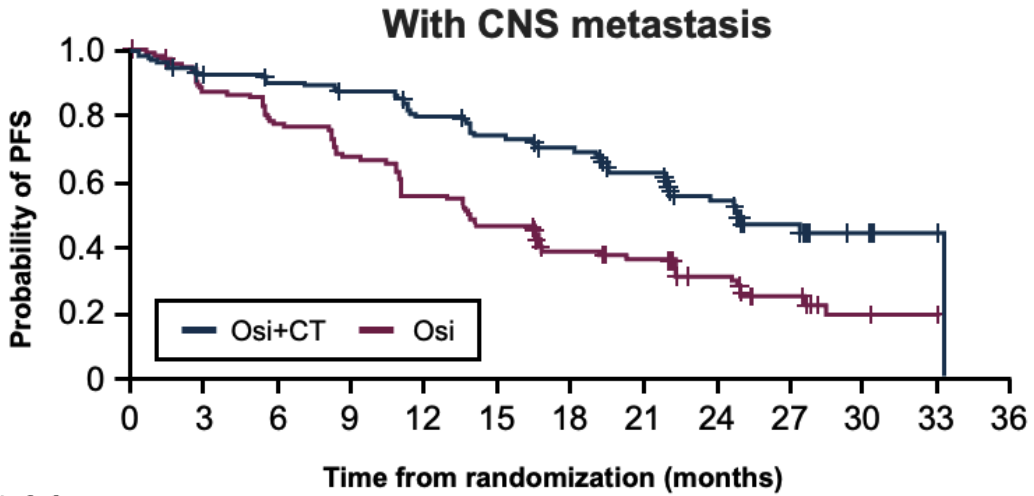
Efficacy in L858R	Osimertinib + platinum-pemetrexed (n=106)	Osimertinib (n=107)
mPFS, months (95% CI)	24.7 (19.5-27.4)	13.9 (11.1-19.4)
HR (95% CI)	0.63 (0.44-0.90)	

DCO: April 03, 2023. **Note:** CT includes cisplatin or carboplatin with pemetrexed. [a]Investigator assessed.

CI = confidence interval; CT = chemotherapy; DCO = data cut-off; *EGFR*m = epidermal growth factor receptor mutation-positive; Ex19del = exon 19 deletion; HR = hazard ratio; mPFS = median progression-free survival; NC = non calculable; PFS = progression-free survival.

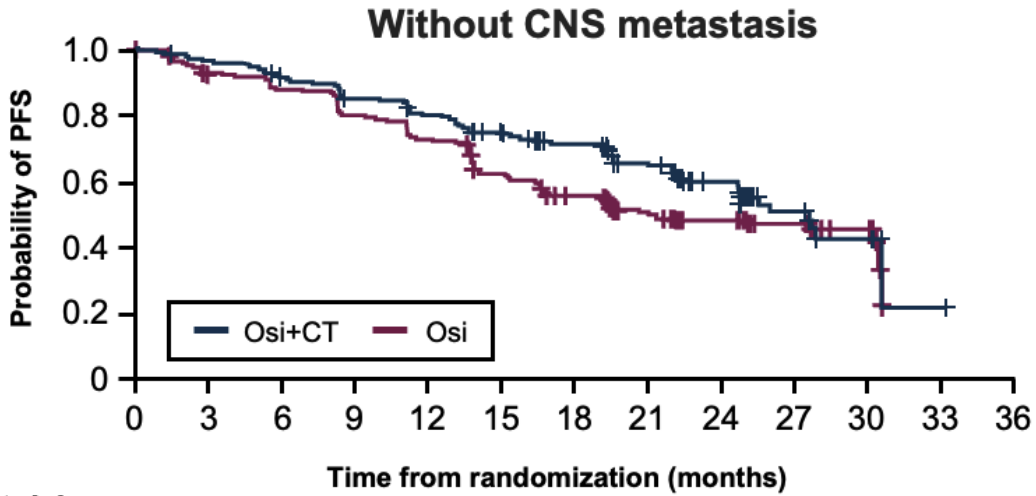
Planchard D et al. *N Engl J Med*. 2023;389(21):1935-1948.

FLAURA2 : PFS[a] Benefit according to CNS mets



No. at risk:

Osi+CT	116	101	98	93	84	77	70	58	34	19	8	2	0
Osi	110	95	74	73	60	50	37	32	21	13	5	1	0



No. at risk:

Osi+CT	163	153	143	132	123	110	95	75	50	23	13	1	0
Osi	168	151	143	130	118	98	82	62	46	35	16	0	0

Efficacy with CNS metastases	Osimertinib + platinum-pemetrexed (n=116)	Osimertinib (n=110)
mPFS, months (95% CI)	24.9 (22.0-NC)	13.8 (11.0-16.7)
HR (95% CI)	0.47 (0.33-0.66)	

Efficacy without CNS metastases	Osimertinib + platinum-pemetrexed (n=163)	Osimertinib (n=168)
mPFS, months (95% CI)	27.6 (24.7-NC)	21.0 (16.7-30.5)
HR (95% CI)	0.75 (0.55-1.03)	

DCO: April 03, 2023. **Note:** CT include cisplatin or carboplatin with pemetrexed. [a]Investigator assessed.

CI = confidence interval; CNS = central nervous system; CT = chemotherapy; DCO = data cut-off; HR = hazard ratio; NC = non calculable; PFS = progression-free survival

Planchard D et al. *N Engl J Med*. 2023;389(21):1935-1948.

IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

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First-line Osimertinib + Chemotherapy Versus Osimertinib Monotherapy in EGFRm Advanced NSCLC: FLAURA2 Final Overall Survival

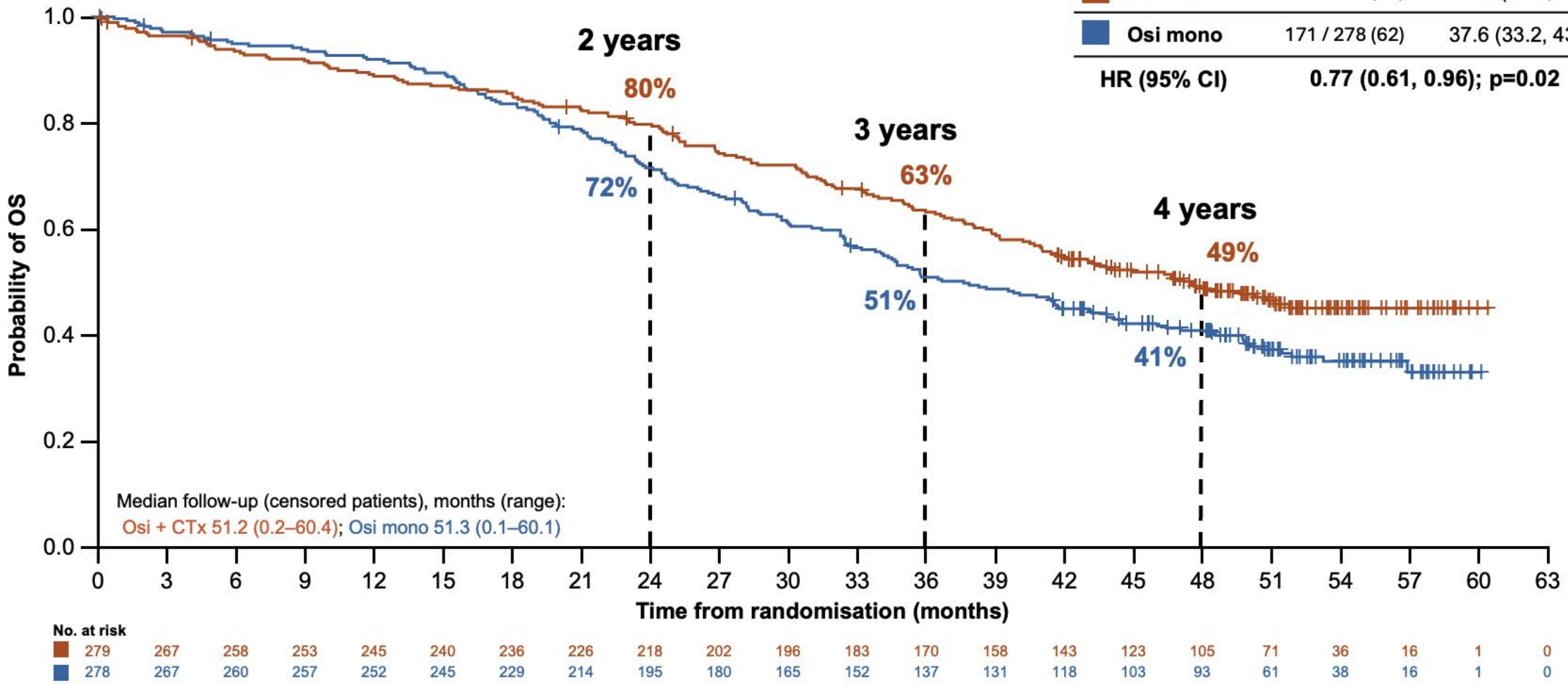
David Planchard,[1] Pasi A. Jänne, Kunihiko Kobayashi, James Chih-Hsin Yang, Ying Liu, Natalia Valdiviezo, Tae Min Kim, Liyan Jiang, Hiroshi Kagamu, Noriko Yanagitani, Jialei Wang, Bivas Biswas, Artem Poltoratskiy, Yeni Neron, Carlos Rojas, Leona Koubkova, Carles Escriu, Doreen Ezeife, Karen Barrett, Muna Albayaty, Haiyi Jiang, Chee K. Lee

[1]Department of Medical Oncology, Institut Gustave Roussy, Thoracic Unit, Villejuif, France and Faculty of Medicine, Université Paris-Saclay, Paris, France

FLAURA2: Overall survival

Median OS with osi + CTx was 47.5 months

	No. events / no. patients (%)	Median OS, months (95% CI)
Osi + CTx	144 / 279 (52)	47.5 (41.0, NC)
Osi mono	171 / 278 (62)	37.6 (33.2, 43.2)
HR (95% CI)	0.77 (0.61, 0.96); p=0.02	

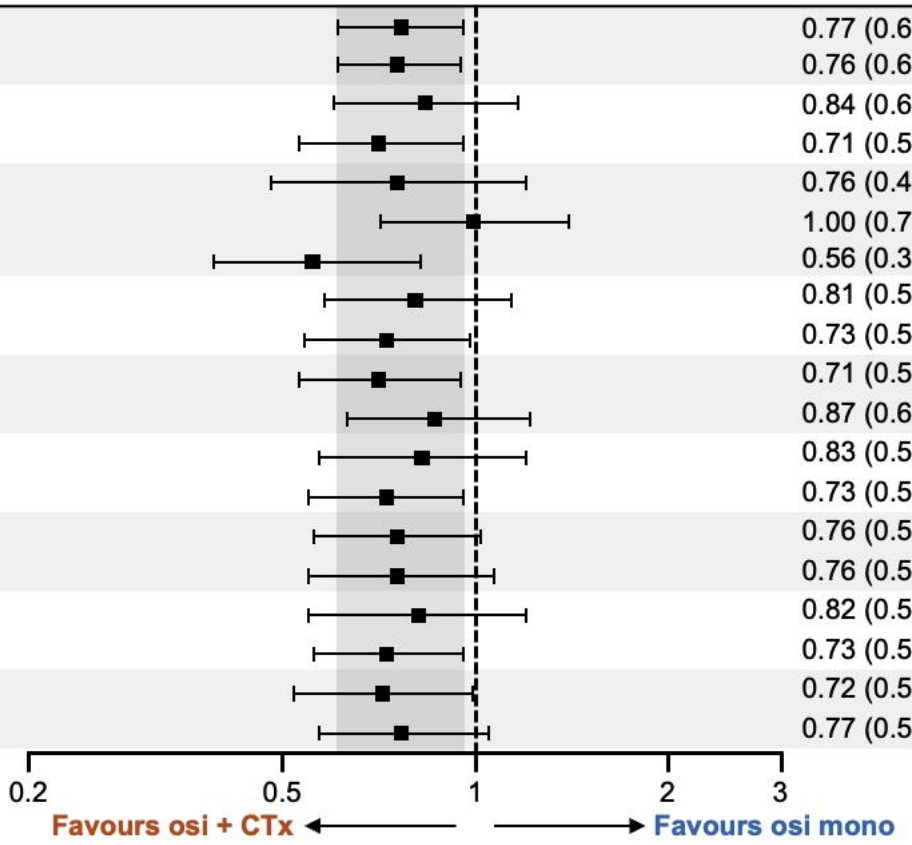


D. Planchard. First-line Osimertinib + Chemotherapy Versus Osimertinib Monotherapy in EGFRm Advanced NSCLC: FLAURA2 Final Overall Survival

Data cut-off: 12 June 2025.
Tick marks indicate censored data. A two-sided P value of <0.04953 was considered to indicate statistical significance at this final OS analysis.
CI, confidence interval; CTx, chemotherapy; HR, hazard ratio; mono, monotherapy; NC, not calculable; osi, osimertinib; RECIST, Response Evaluation Criteria in Solid Tumors

Overall survival across subgroups

Subgroup*		Osi + CTx (Events / patients)	Osi mono (Events / patients)	HR (95% CI)
All patients	Stratified log-rank	144 / 279	171 / 278	0.77 (0.61, 0.96)
	Unadjusted Cox PH	144 / 279	171 / 278	0.76 (0.61, 0.95)
Sex	Male	65 / 106	72 / 109	0.84 (0.60, 1.17)
	Female	79 / 173	99 / 169	0.71 (0.53, 0.96)
Race†	Asian Chinese	34 / 71	39 / 69	0.76 (0.48, 1.20)
	Asian non-Chinese	65 / 107	66 / 107	1.00 (0.71, 1.40)
	Non-Asian	45 / 101	66 / 102	0.56 (0.39, 0.82)
EGFR mutation test method	Central	65 / 121	73 / 119	0.81 (0.58, 1.14)
	Local	79 / 158	98 / 159	0.73 (0.54, 0.98)
Age at screening	<65 years	80 / 174	95 / 166	0.71 (0.53, 0.95)
	≥65 years	64 / 105	76 / 112	0.87 (0.63, 1.22)
Smoking history	Yes	52 / 91	60 / 97	0.83 (0.57, 1.20)
	No	92 / 188	111 / 181	0.73 (0.55, 0.96)
EGFR mutation type‡	Ex19del	78 / 172	95 / 169	0.76 (0.56, 1.02)
	L858R	66 / 106	74 / 107	0.76 (0.55, 1.07)
WHO PS	0	47 / 101	55 / 102	0.82 (0.55, 1.20)
	1	97 / 178	116 / 176	0.73 (0.56. 0.96)
CNS status at baseline	Yes	71 / 116	79 / 110	0.72 (0.52, 0.99)
	No	73 / 163	92 / 168	0.77 (0.57, 1.05)



OS benefit was consistent across predefined subgroups

Data cut-off: 12 June 2025.

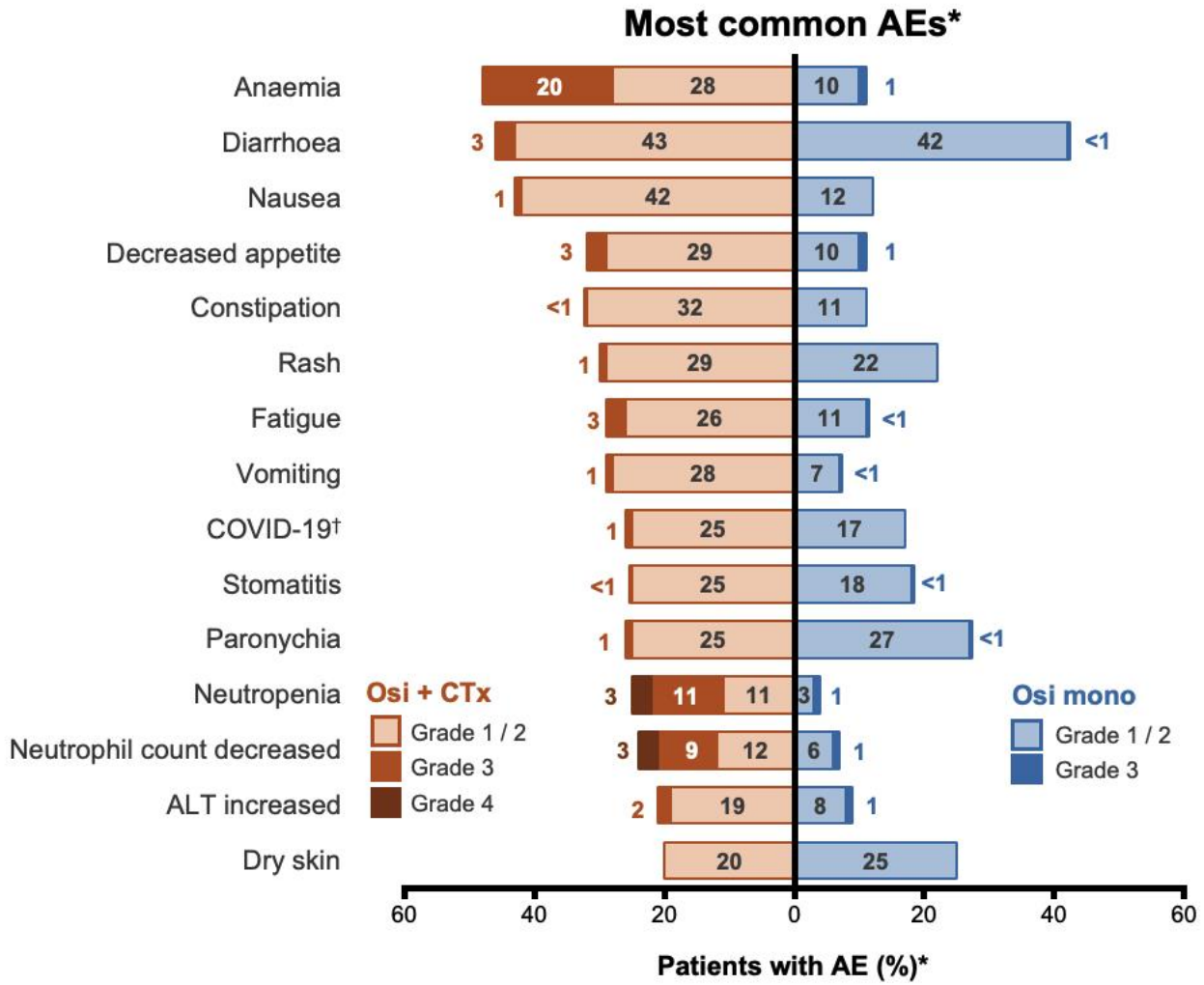
*Two additional subgroups performed to fulfil regulatory requirements for diagnostics are not included: EGFR mutations by central cobas® tissue test and EGFR mutations by central cobas® ctDNA test; †Race was reported by the patient; ‡For EGFR mutation type, patients with both Ex19del and L858R were included in the Ex19del group.
CI, confidence interval; CNS, central nervous system; CTx, chemotherapy; EGFR, epidermal growth factor receptor; Ex19del, Exon 19 deletion; HR, hazard ratio; mono, monotherapy; OS, overall survival; osi, osimertinib; PH, proportional hazard; WHO PS, World Health Organization performance status

Safety

Since the primary analysis[1] (>2 years additional follow-up):

- No new safety signals observed
- AEs leading to discontinuation of osi remained low
- No new treatment-related deaths observed with osi + CTx (vs 1 with osi mono)

AE summary	Osi + CTx (n=276)	Osi mono (n=275)
AE any cause, n (%)		
Any grade	276 (100)	269 (98)
Grade ≥3	193 (70)	94 (34)
Serious	126 (46)	75 (27)
Outcome of death	22 (8)	10 (4)
Considered possibly related to treatment	5 (2)	2 (1)
Leading to discontinuation of osi	34 (12)	20 (7)
Leading to discontinuation of pemetrexed	137 (50)	NA
Leading to discontinuation of platinum	46 (17)	NA



D. Planchard. First-line Osimertinib + Chemotherapy Versus Osimertinib Monotherapy in EGFRm Advanced NSCLC: FLAURA2 Final Overall Survival

Data cut-off: 12 June 2025.
1. Planchard D, et al. N Engl J Med 2023;389:1935–1948; 2. Planchard et al. ESMO Open 2021;6:100271.
*Reported in ≥20% of patients in either treatment arm; †One Grade 5 AE of COVID-19 was reported in the osimertinib plus platinum-pemetrexed arm.
AE, adverse event; ALT, alanine aminotransferase; CTx, chemotherapy; mono, monotherapy; NA, not applicable; osi, osimertinib

Conclusions

- **First-line osi + CTx demonstrated a statistically significant and clinically meaningful improvement in OS versus osi mono**
  - **OS HR: 0.77**; 95% CI (0.61, 0.96); **p=0.02**
  - **Median OS** with osi + CTx was **47.5 months** – longest reported in a global phase III study showing OS benefit in this population[1]
  - Observed OS benefit was **consistent** across pre-defined subgroups

- Osi + CTx arm had a long CTx-free period – median treatment duration was 30.5 months for osi and 8.3 months for pemetrexed

- In both arms, **CTx was the most common first subsequent treatment**
  - CTx rechallenge, primarily with platinum doublet, was the most common treatment after osi + CTx
  - OS benefit with osi + CTx was seen despite SoC CTx being the most common treatment after osi mono

- With 2 years additional follow up since the primary analysis, the **safety profiles remained as expected and manageable**

These compelling OS results from FLAURA2 confirm osimertinib-plus-chemotherapy as a first-line standard-of-care treatment in EGFRm advanced NSCLC

1. Ramalingam et al. N Engl J Med 2020;382:41–50.
Note: A two-sided P value of <0.04953 was considered to indicate statistical significance at this final OS analysis.
CTx, chemotherapy; EGFRm, epidermal growth factor receptor-mutated; mono, monotherapy; NSCLC, non-small cell lung cancer; OS, overall survival; osi, osimertinib; SoC, standard of care

What is the tradeoff with upfront combination therapy ?

	Osimertinib	Osimertinib-Pemetrexed-Platinum	Amivantamab-Lazertinib
Study	FLAURA	FLAURA2	MARIPOSA
Efficacy	PFS 18.9 m OS 38.6 m vs 31.8 m	PFS 25.5 m OS 47.5 m vs 37.6 m (HR 0.77)	PFS 23.7 m OS NR vs 36.7 m (HR 0.75)
Side effects (all grades)	Diarrhea 42% Rash 22% Paronychia 27% Neutropenia 4% Anemia 11%	Diarrhea 46% Rash 30% Paronychia 26% Neutropenia 25% Anemia 48% Creatinine increase 14%	Diarrhea 32% Rash 64% Paronychia 69% Infusion related reaction 65% Peripheral edema 38% Venous thromboembolism 40% Anemia 27%
Schedule	Daily oral tablet Visit every 2-3 months	Daily oral tablet, Iv infusion once every 3 weeks	Daily oral tablet, Iv infusion once per week for first 4weeks; once every 2 weeks thereafter
Finance	$	$$	$$$$

*Data are not from head-to-head trials and should not be directly compared.
Daniel Tan WCLC 2025

Ramalingam SS, *N Engl J Med.* 2020;382(1):41-50; Planchard WCLC 2025
Yang JC, et al. *N Engl J Med.* Sep 6, 2025

Target therapy for advanced or metastatic dz

PRINCIPLES OF BIOMARKER-DIRECTED THERAPY FOR ADVANCED OR METASTATIC DISEASE

Order does not imply preference. This is a listing for references.

***EGFR* Exon 19 Deletion or L858R Mutation**
- First-line therapy
  - Afatinib[1]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6]
  - (Carboplatin or Cisplatin)/ Osimertinib/Pemetrexed (nonsquamous)[7]
  - Erlotinib + Ramucirumab[8]
  - Erlotinib + Bevacizumab (nonsquamous)[9]
  - Lazertinib + Amivantamab-vmjw[10]
  - Lazertinib[10]
- Subsequent therapy
  - Osimertinib[11]
  - Carboplatin/Pemetrexed + Amivantamab-vmjw (nonsquamous)[12]
  - Datopotamab deruxtecan-dlnk (nonsquamous)[13]
  - Lazertinib + Amivantamab-vmjw[14,15]

***EGFR* S768I, L861Q, and/or G719X Mutations**
- First-line therapy
  - Afatinib[1,16]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6,17]

***EGFR* S768I, L861Q, and/or G719X Mutations** (continued)
- Subsequent therapy
  - Osimertinib[11]
  - Datopotamab deruxtecan-dlnk (nonsquamous)[13]

  - Ceritinib[26]
  - Crizotinib[23,27]
  - Ensartinib[28]
  - Lorlatinib[29]

***ALK* Gene Fusion** (continued)
- Subsequent therapy
  - Alectinib[30,31]
  - Brigatinib[32]
  - Ceritinib[33]
  - Ensartinib[34]
  - Dabrafenib/Trametinib[43,44]
  - Binimetinib/Encorafenib[42]

***NTRK1/2/3* Gene Fusion**
- First-line/Subsequent therapy
  - Larotrectinib[45]
  - Entrectinib[46]
  - Repotrectinib[47]

***MET* Exon 14 Skipping Mutation**[a]
- First-line therapy/Subsequent therapy
  - Capmatinib[48]
  - Crizotinib[49]
  - Tepotinib[50]

***RET* Gene Fusion**
- First-line therapy
  - Selpercatinib[51]
  - Pralsetinib[52]
- Subsequent therapy
  - Cabozantinib[53,54]

***ERBB2 (HER2)* Mutation**[a]
- Subsequent therapy
  - Fam-trastuzumab deruxtecan-nxki[55]
  - Ado-trastuzumab emtansine[56]
  - Zongertinib[57]
  - Sevabertinib[58]

***NRG1* Gene Fusion**
- Subsequent therapy
  - Zenocutuzumab-zbco[59]

HER2-positive IHC 3+
- Subsequent therapy
  - Fam-trastuzumab deruxtecan-nxki[60]

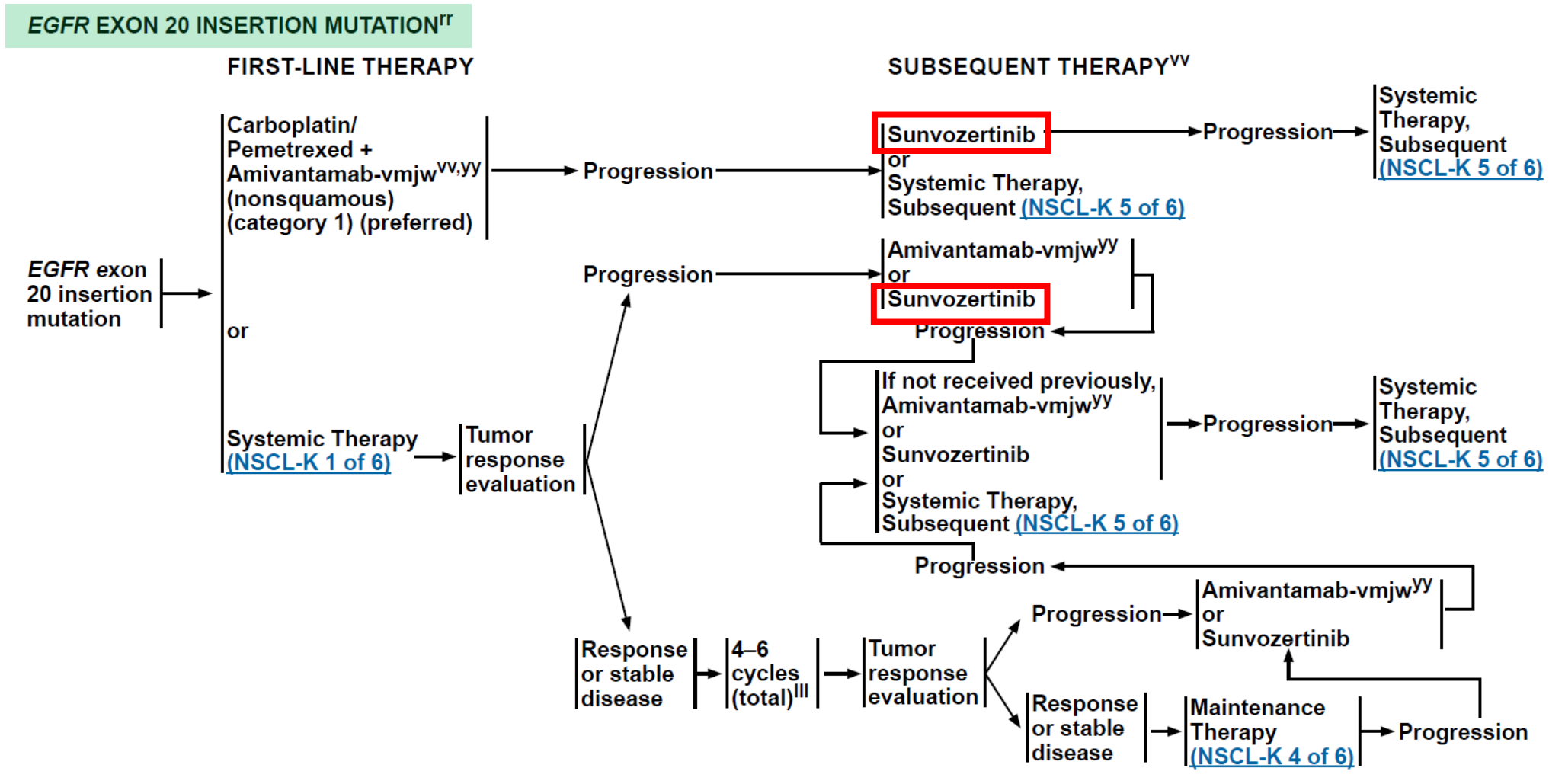
HGFR (*MET*) (≥50% IHC 3+ and *EGFR* wild-type)
- Subsequent therapy
  - Telisotuzumab vedotin-tllv (nonsquamous)[61]

[a] For agents with a similar mechanism of action, it is not recommended to switch between these drugs at the time of progression.

References

NCCN Guideline (NSCLC). 2026. Version 3.

NCCN Guidelines (NSCLC) ver3. 2026



NCCN Guideline (NSCLC). 2026. Version 3.

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A Multinational Phase 2 Randomized Pivotal Study of Sunvozertinib in Pretreated NSCLC with EGFR Exon 20 Insertion Mutations

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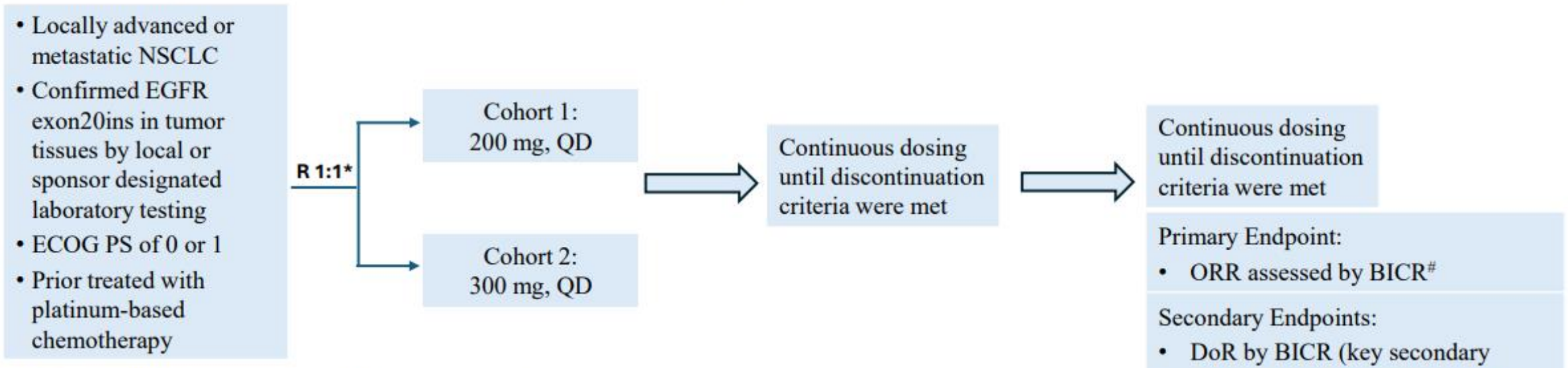
Introduction and Study Design

- Sunvozertinib (DZD9008) is a rationally designed, potent, selective and irreversible EGFR inhibitor targeting EGFR exon 20 insertion mutations (exon20ins).
- WU-KONG1 Part B (WU-KONG1B, NCT03974022) is a multinational phase 2 dose randomized pivotal study of sunvozertinib in platinum pretreated NSCLC with EGFR exon20ins. Sunvozertinib was approved by US FDA under accelerated approval, supported by WU-KONG1B study.
- Here we report the latest results of WU-KONG1B study in dose randomization cohorts.

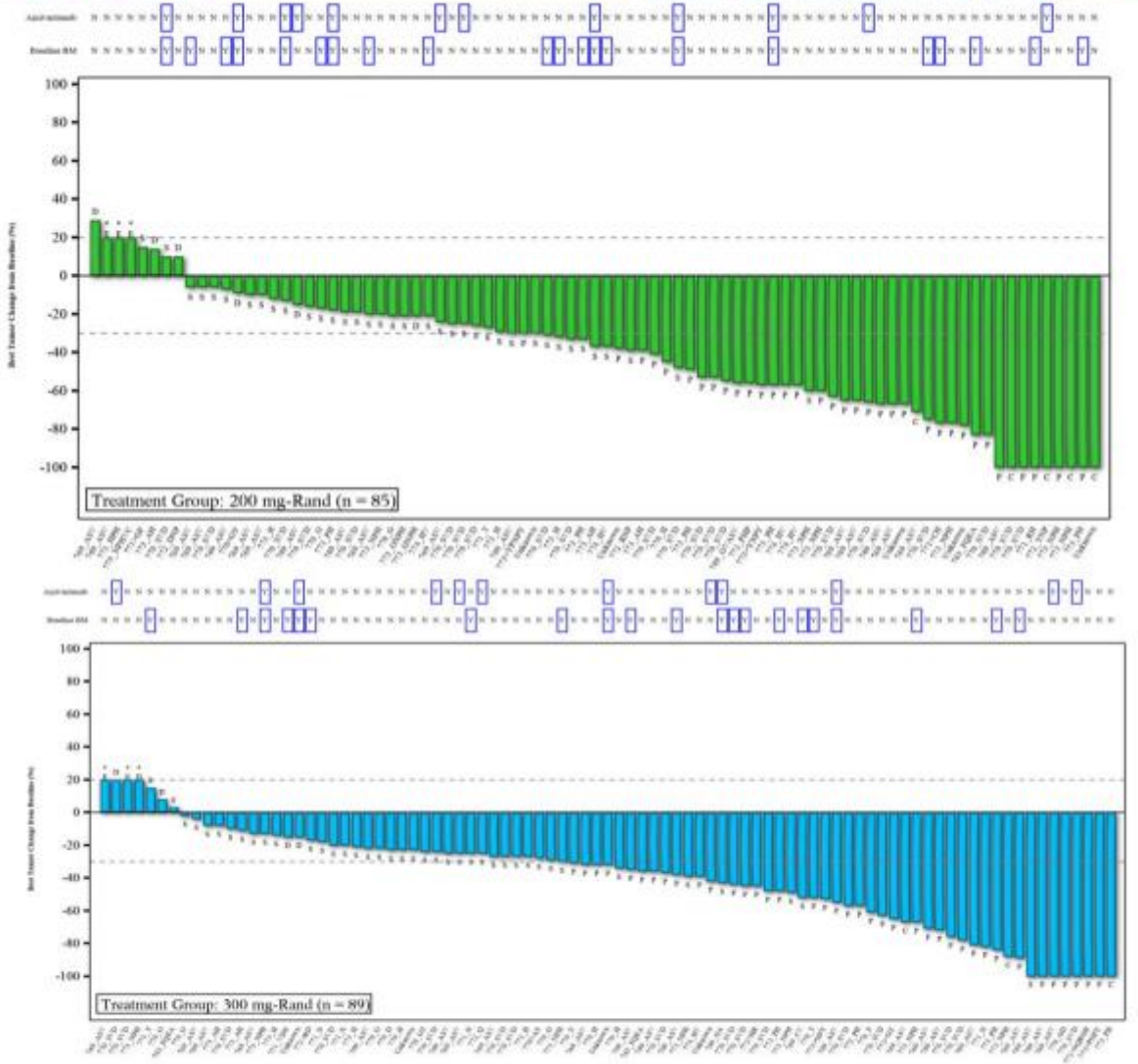


*Randomization ratio 1:1, and stratified by 1) baseline brain metastasis; 2) number of prior treatment regimens.
#According to RECIST 1.1. Tumor assessment every 6 weeks from C1D1 until progression.
ORR: objective response rate; DoR: duration of response; BICR: Blinded Independent Central Review; QD: once daily.

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 *.

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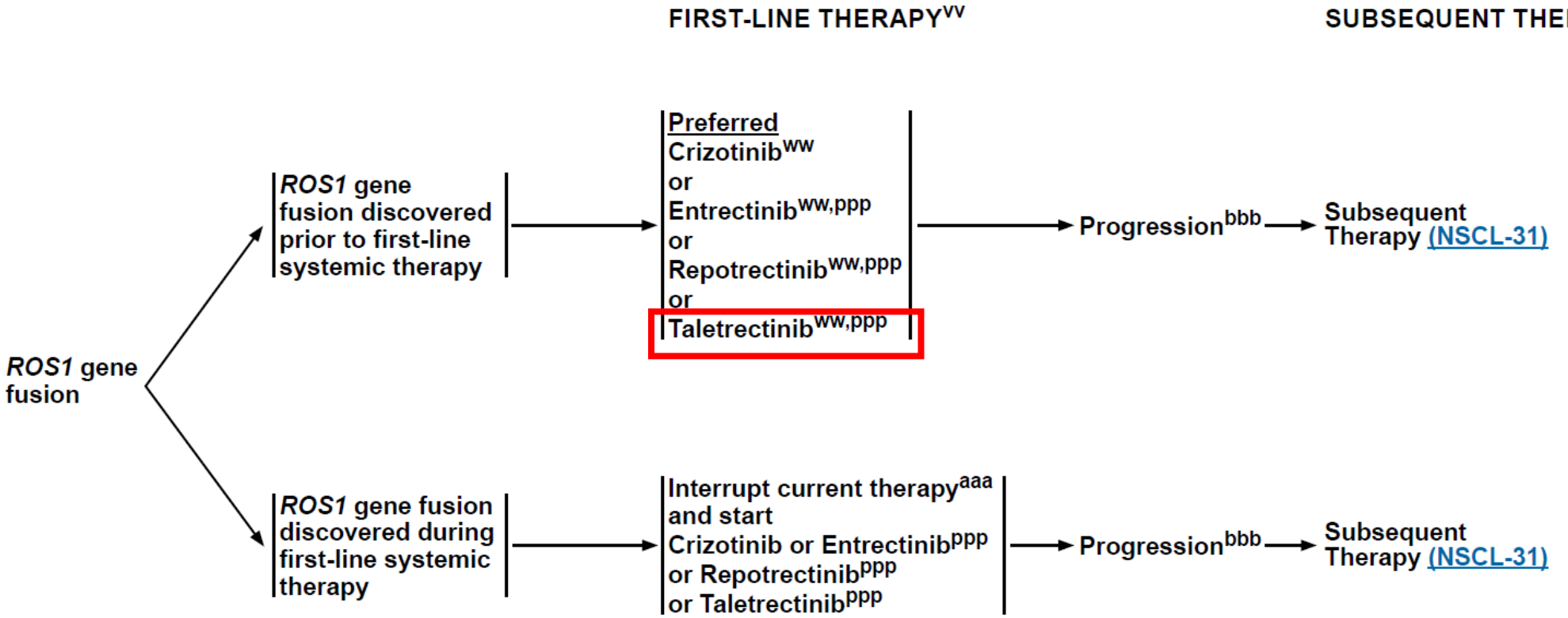
ROS1 GENE FUSION[rr]



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Updated Efficacy and Safety of Taletrectinib in Patients With ROS1+ Non-Small Cell Lung Cancer: The Global TRUST-II Study

Geoffrey Liu,[1] Chang-Min Choi,[2] Shunichi Sugawara,[3] Noriko Yanagitani,[4] Filippo De Braud,[5] Jorge Nieva,[6] Misako Nagasaka,[7] Caicun Zhou,[8] Enriqueta Felip,[9] Xianyu Zhang,[10] Wei Wang,[10] Nathan A. Pennell,[11] Maurice Pérol,[12] Lyudmila Bazhenova[13]

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TRUST-II[a]: Phase 2 Trial of Taletrectinib in ROS1+ NSCLC

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC with ROS1 fusion
- Age ≥18 years[b]
- ECOG PS 0–1

Cohort 1
TKI-naïve[c]

Cohort 2
TKI-pretreated[c]

Taletrectinib
600 mg QD

Endpoints

Primary:
- IRC-assessed **cORR** per RECIST v1.1

Secondary:
- DOR
- TTR
- OS
- IC-ORR[d]
- PFS
- Safety[e]

Additional 5 month follow-up To > 20 months

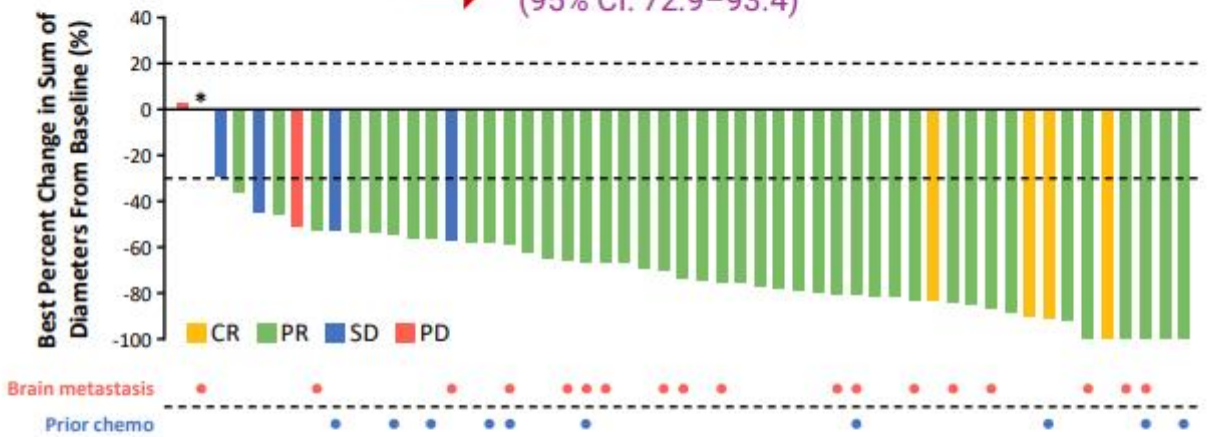
Baseline Characteristics	TKI-naïve (n=55)[c]	TKI-pretreated (n=50)[c]	Safety Population (N=171)[e]
Median age, years (range)	57.0 (27–83)	55.5 (27–79)	57.0 (27–83)
Female, n (%)	31 (56.4)	27 (54.0)	96 (56.1)
Never smoker, n (%)	28 (50.9)	30 (60.0)	95 (55.6)
Region: Asia / non-Asia, n (%)	**34 (61.8) / 21 (38.2)**	**22 (44.0) / 28 (56.0)**	**74 (43.3) / 97 (56.7)**
ECOG PS: 0 / 1, n (%)	22 (40.0) / 33 (60.0)	24 (48.0) / 26 (52.0)	70 (40.9) / 101 (59.1)
Stage IV disease, n (%)	49 (89.1)	49 (98.0)	162 (94.7)
Prior chemotherapy, n (%)	**11 (20.0)**	**19 (38.0)**	67 (39.2)
Brain metastases at baseline,[d] n (%)	**19 (34.5)**	**28 (56.0)**	78 (45.6)
Prior crizotinib / entrectinib, n (%)	-	**40 (80.0) / 10 (20.0)**	86 (50.3) / 29 (17.0)

Data cutoff: October 28, 2024. c, confirmed; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, intracranial; IRC, independent review committee; (m)RECIST v1.1, (modified) Response Evaluation Criteria In Solid Tumors version 1.1; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily; TKI, tyrosine kinase inhibitor; TTR, time to response.
[a]NCT04919811. [b]Or ≥20 years, as required by local regulations. [c]Registrational cohorts are shown. [d]Assessed by IRC per mRECIST v1.1. [e]Safety population includes all patients who received ≥1 dose of taletrectinib 600 mg.

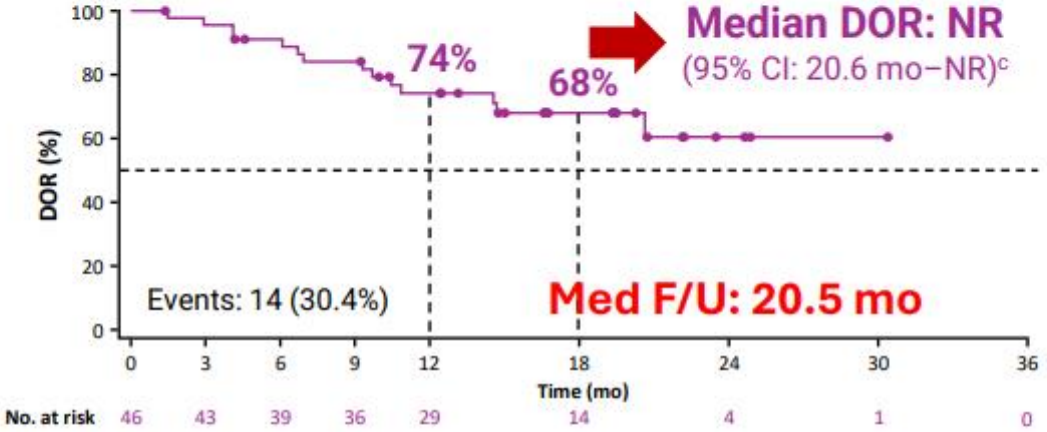
Taletrectinib: Efficacy Outcomes in TKI-naïve ROS1+ NSCLC

TKI-naïve (n=54)[a,b]
Median follow-up: 20.5 mo (range: 8.3–34.5)

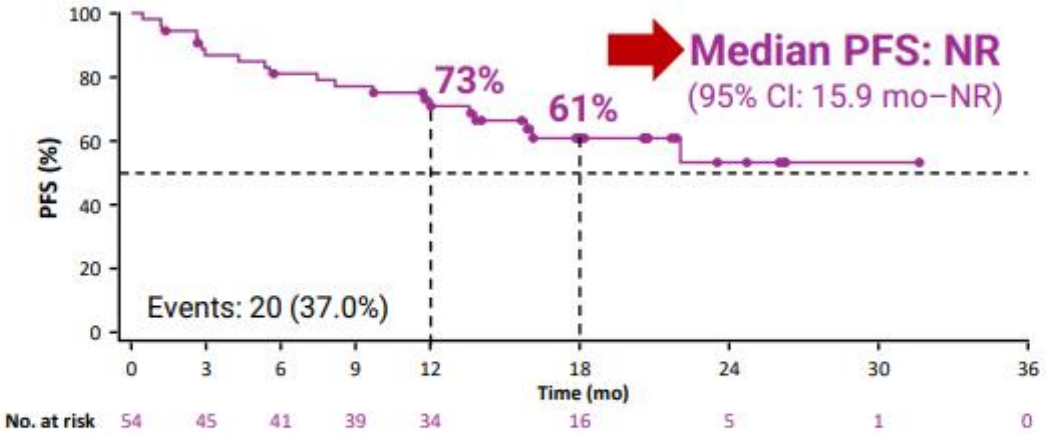
cORR: 85.2%
(95% CI: 72.9–93.4)



Median DOR: NR
(95% CI: 20.6 mo–NR)[c]



Median PFS: NR
(95% CI: 15.9 mo–NR)



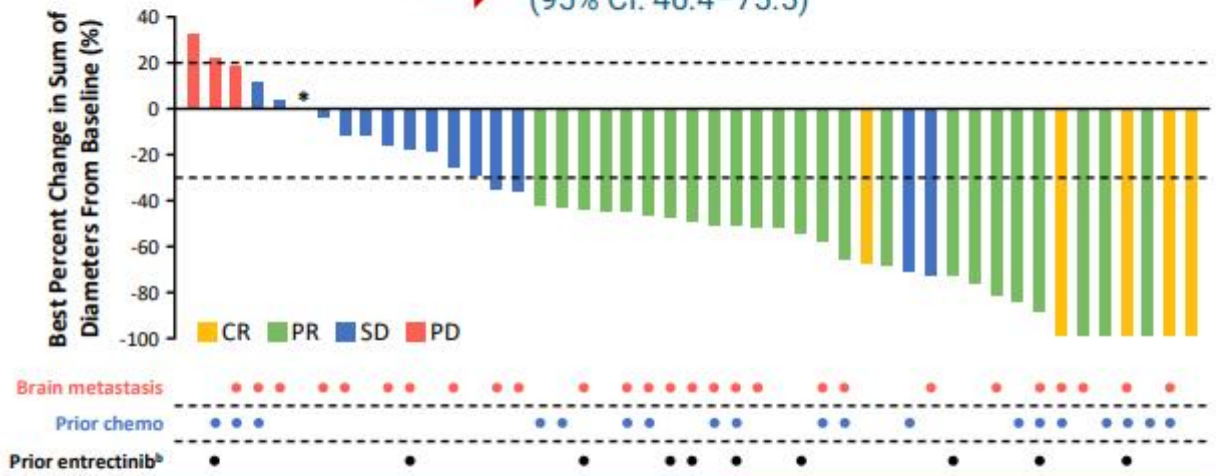
Efficacy	TKI-naïve (n=54)
cORR: prior chemo, yes / no, n/N (%)	9/10 (90.0) / 37/44 (84.1)
Median TTR,[c] mo (95% CI)	1.4 (1.3–1.4)
IC efficacy	**(n=9)[d]**
IC-ORR, % (95% CI)	66.7 (29.9–92.5)

Data cutoff: October 28, 2024. BOR, best overall response; CI, confidence interval; CR, complete response; mo, months; NE, not evaluable; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Response evaluable population includes patients with ≥1 measurable lesion at baseline who received ≥1 dose of taletrectinib. [b]One patient with cBOR of NE is not shown in the waterfall plot. [c]TTR and DOR reported in responders only.
[d]Patients with ≥1 measurable brain metastasis at baseline. *One patient with cBOR of SD had a best percent change of 0%.

Taletrectinib: Efficacy Outcomes in TKI-pretreated ROS1+ NSCLC

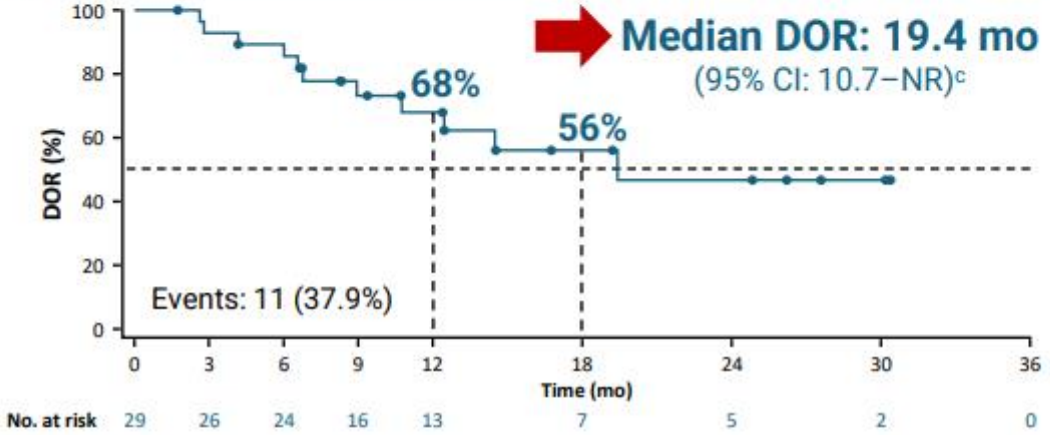
TKI-pretreated (n=47)[a]
Median follow-up: 20.4 mo (range: 8.6–34.5)

cORR: 61.7%
(95% CI: 46.4–75.5)

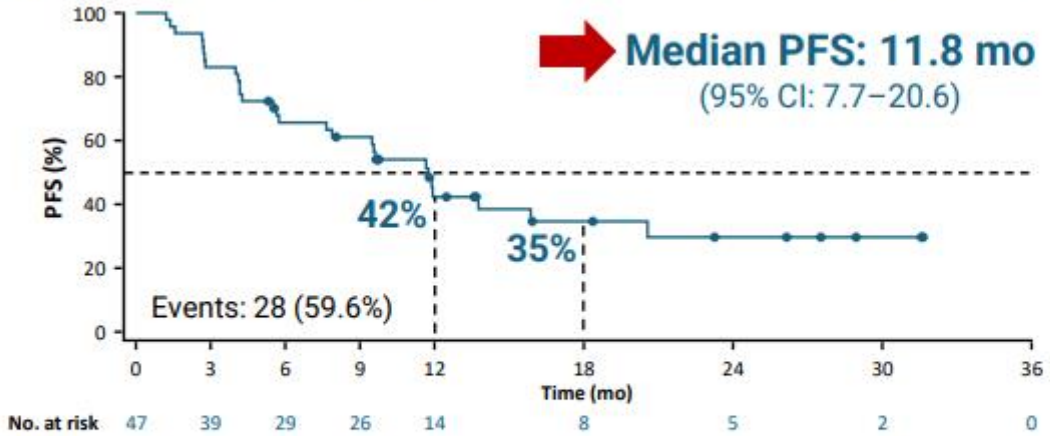


Efficacy	TKI-pretreated (n=47)
cORR: prior chemo, yes / no, n/N (%)	15/19 (78.9) / 14/28 (50.0)
Median TTR,[c] mo (95% CI)	1.4 (1.4–1.6)
IC efficacy	**(n=16)[d]**
IC-ORR, % (95% CI)	56.3 (29.9–80.3)

Median DOR: 19.4 mo
(95% CI: 10.7–NR)[c]



Median PFS: 11.8 mo
(95% CI: 7.7–20.6)



Data cutoff: October 28, 2024. [a]Response evaluable population includes patients with ≥1 measurable lesion at baseline who received ≥1 dose of taletrectinib. [b]All other patients received prior crizotinib. [c]TTR and DOR reported in responders only. [d]Patients with ≥1 measurable brain metastasis at baseline. *One patient with cBOR of SD had a best percent change of 0%.

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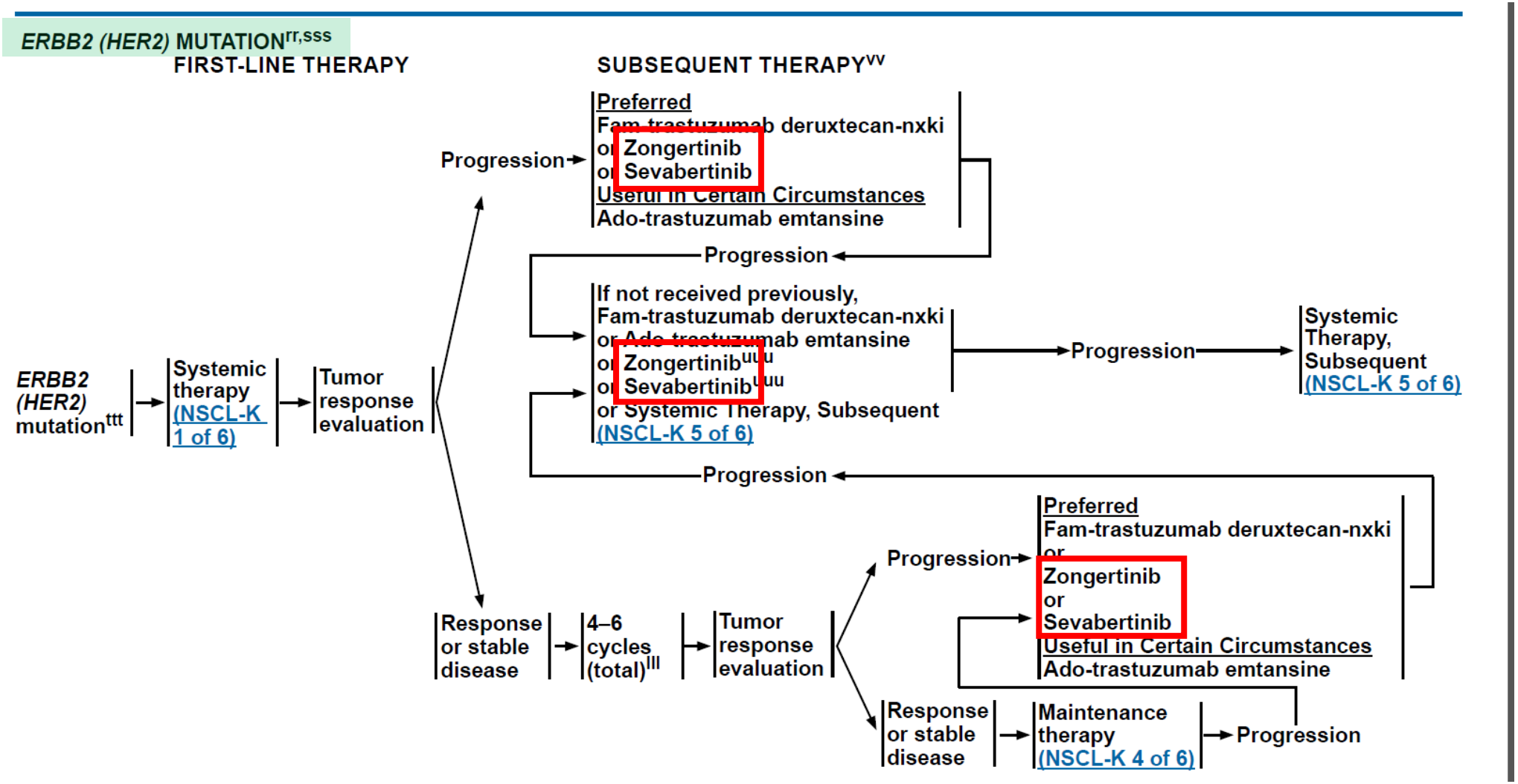

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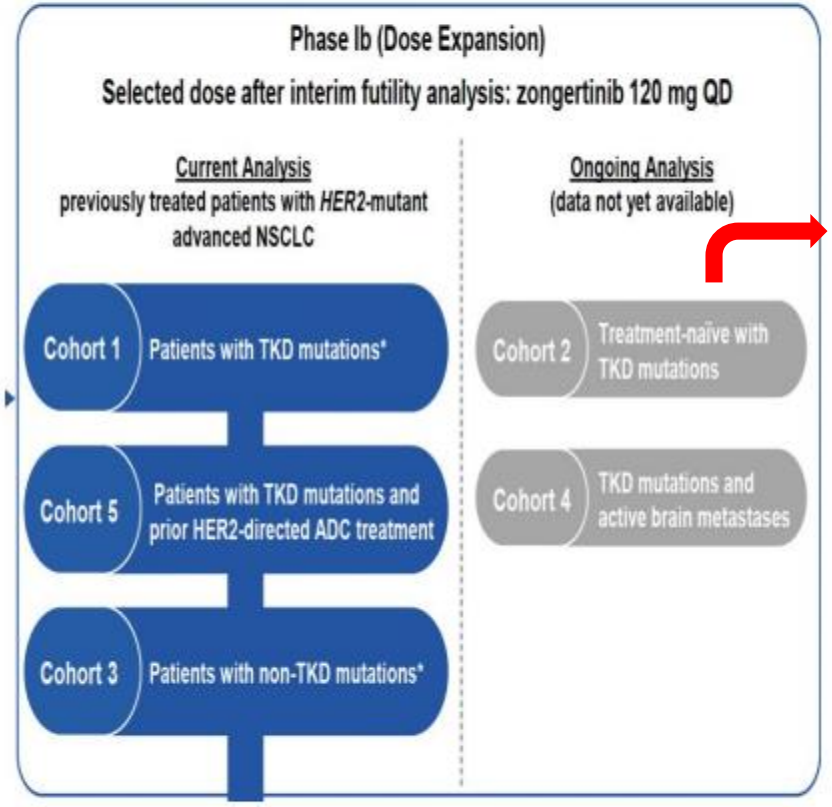
BEAMION LUNG-1 PHASE IB

FDA Approved



BERLIN 2025 ESMO congress

Zongertinib as First-Line Treatment in Patients with Advanced *HER2*-Mutant NSCLC: Beamion LUNG-1

Sanjay Popat,[1,2] Noboru Yamamoto,[3] Nicolas Girard,[4,5] Yi-Long Wu,[6] Gerrina Ruiter,[7,8] Egbert F. Smit,[8,9] Kiyotaka Yoh,[10] Hai-Yan Tu,[6] Jon Zugazagoitia,[11] Joshua K. Sabari,[12] Thomas Wehler,[13] Ernest Nadal,[14] Julia Stöhr,[15] Behbood Sadrolhefazi,[16] Hartmut Luess,[17] John V. Heymach[18]

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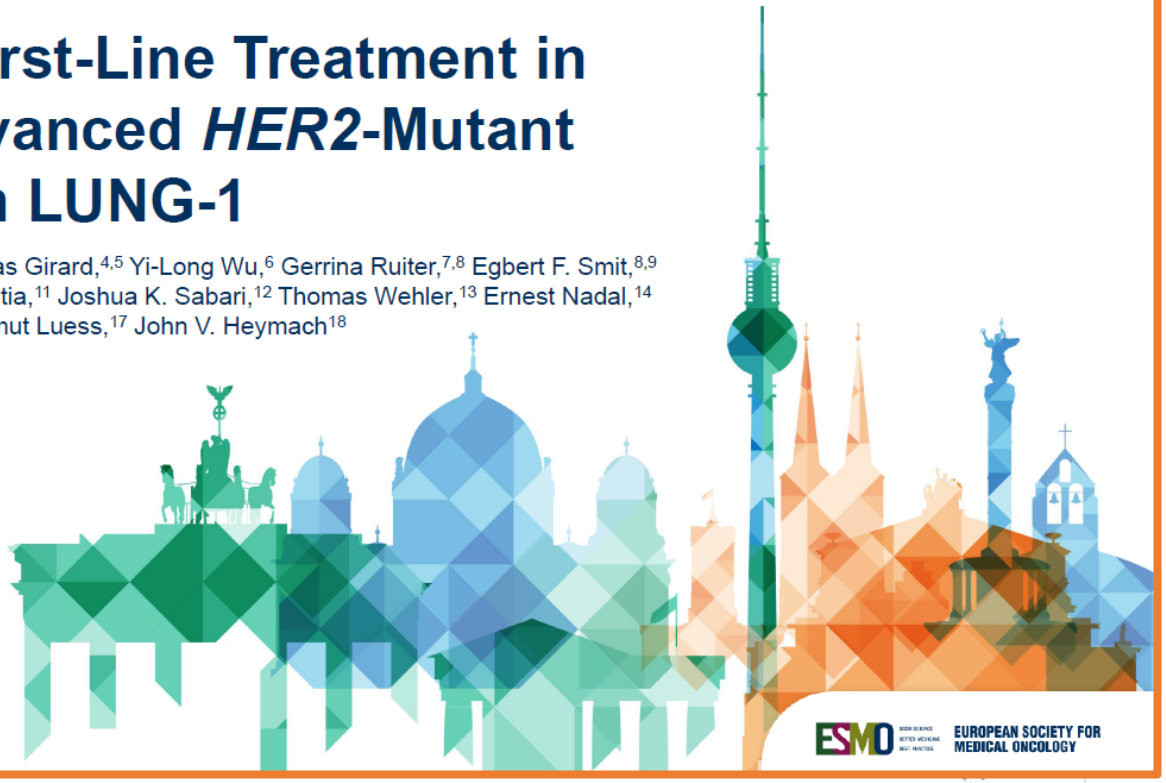
October 17–21, 2025



Heymach J AACR 2025, NEJM 2025

Sevabertinib (BAY 2927088) in advanced *HER2*-mutant non-small cell lung cancer (NSCLC): results from the SOHO-01 study

Xiuning Le, MD, PhD
MD Anderson Cancer Center, Houston, TX, USA

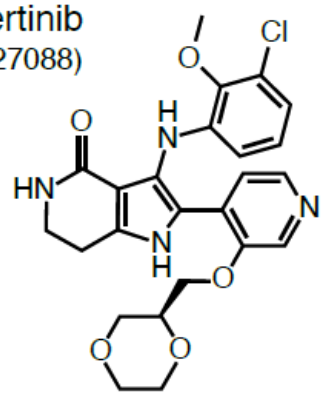
October 17, 2025

Xiuning Le,[1] Tae Min Kim,[2] Herbert H. Loong,[3,4] Arsela Prelaj,[5] Boon Cher Goh,[6,7] Lin Li,[8] Yong Fang,[9] Shun Lu,[10] Xiaorong Dong,[11] Lin Wu,[12] Yuki Shinno,[13] Gennaro Daniele,[14] Tsung-Ying Yang,[15] Hye Ryun Kim,[16,17] Gerrina Ruiter,[18] Jun Zhao,[19] Silvia Novello,[20] Liyun Miao,[21] Pasi A. Jänne,[22] Koichi Goto,[23] Dominik Rüttinger,[24] Tine Descamps,[25] Jan Christoph Brase,[26] Weichao Bao,[27] Rui Li,[27] Nicoletta Brega,[26] Paolo Grassi,[28] Nicolas Girard,[29] Daniel Shao-Weng Tan,[30,31] for the SOHO-01 investigators

[1]MD Anderson Cancer Center, Houston, TX, USA; [2]Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea; [3]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong SAR, China; [4]Phase 1 Clinical Trial Centre, The Chinese University of Hong Kong, Hong Kong SAR, China; [5]Oncologia Medica Toracica Dept., Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy; [6]Department of Hematology-Oncology, National University Cancer Institute, Singapore, Singapore; [7]Cancer Science Institute of Singapore, National University of Singapore, Singapore, Singapore; [8]Department of Medical Oncology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China; [9]Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China; [10]Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [11]Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [12]Department of Thoracic Medical Oncology, Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [13]National Cancer Center Hospital, Chuo-ku, Tokyo, Japan; [14]Phase 1 Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [15]Department of Chest Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [16]Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Seoul, South Korea; [17]Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul, South Korea; [18]Departments of Clinical Pharmacology and Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [19]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department I of Thoracic Oncology, Peking University Cancer Hospital & Institute, Beijing, China; [20]Department of Oncology, Azienda Ospedaliero-Universitaria San Luigi Gonzaga, Orbassano, Turin, Italy; [21]Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, China; [22]Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [23]National Cancer Center Hospital East, Kashiwa, Japan; [24]Bayer AG, Berlin, Germany; [25]Bayer plc, Reading, UK; [26]Bayer Consumer Care AG, Basel, Switzerland; [27]Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA; [28]Bayer S.p.A., Milan, Italy; [29]Institut Curie, Paris, France; [30]National Cancer Centre Singapore, Singapore, Singapore; [31]Duke-NUS Medical School, Singapore, Singapore

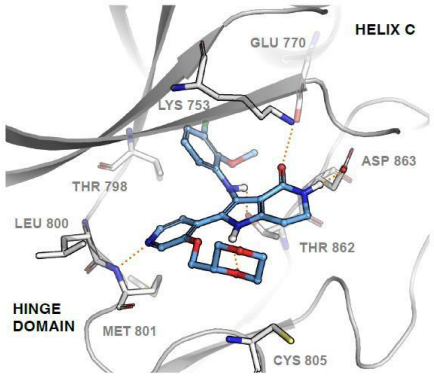
Sevabertinib is an oral, reversible HER2 TKI

Sevabertinib
(BAY 2927088)

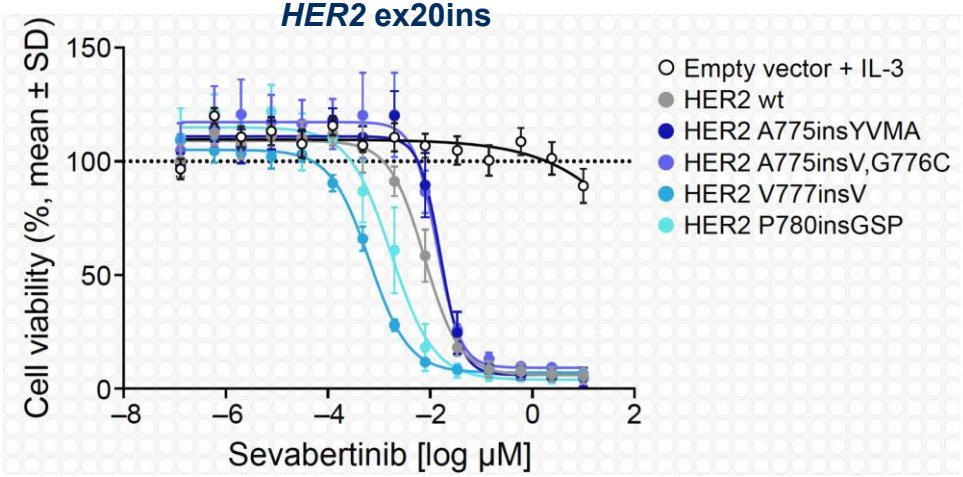


- Sevabertinib is an oral, reversible TKI that potently inhibits activating *HER2* (*ERBB2*) mutations and has demonstrated efficacy against *HER2* insertions and missense mutations, secondary resistance including irreversible binding site mutation (C805S), and gatekeeper mutations (T798M/T798I)[1]
- Sevabertinib has anti-tumor activity and a manageable safety profile in patients with *HER2*-mutant NSCLC[2]
- In May 2025, the FDA granted NDA Priority Review for sevabertinib in patients with previously treated *HER2*-mutant NSCLC[3]

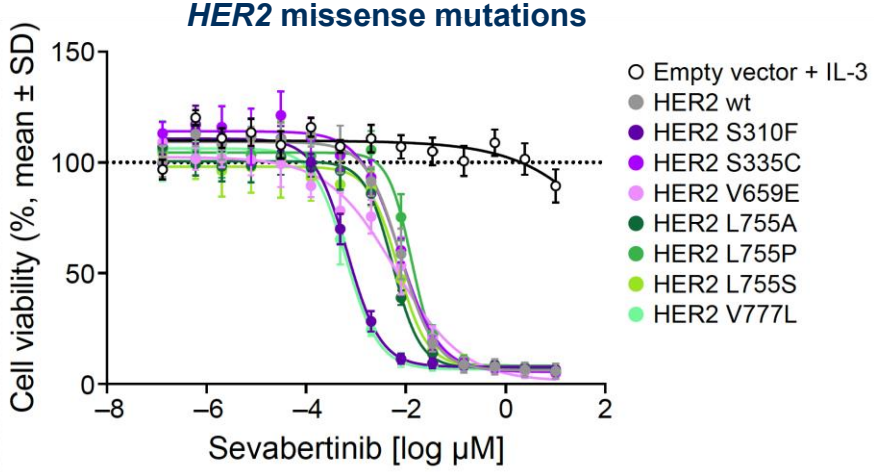
Sevabertinib proposed binding mode



***HER2* ex20ins**



***HER2* missense mutations**



Figures adapted with permission from Siegel F et al. *Cancer Discov* 2025; doi: 10.1158/2159-8290.CD-25-0605

1. Siegel F et al. *Cancer Discov* 2025; doi: 10.1158/2159-8290.CD-25-0605; 2. Girard N et al. *J Clin Oncol* 2024; 42 (17 Suppl): LBA8598; 3. Bayer. Sevabertinib (BAY 2927088) granted FDA Priority Review for the treatment of patients with HER2-mutant non-small cell lung cancer. May 28, 2025. https://www.bayer.com/en/us/news-stories/sevabertinib/. Accessed October 2025

SOHO-01 study design (NCT05099172)

DOSE ESCALATION AND BACKFILL

Patients with advanced NSCLC with *HER2* or *EGFR* mutations

Patients were treated with increasing oral doses of sevabertinib to identify the RDE (5 QD dose levels and 3 BID dose levels, from 10 mg QD to 40 mg BID)

20 mg BID

EXPANSION AND EXTENSION[a]
Cohorts of patients with *HER2* mutations[b]

To evaluate the safety, tolerability, and efficacy, and to characterize the pharmacokinetics, of sevabertinib at the RDE

- **D** Previously treated, naïve to HER2-targeted therapies
- **E** Previously treated with HER2-targeted ADCs
- **F** Naïve to systemic therapy for advanced disease

Cut-off date: June 27, 2025

Efficacy and safety from expansion / extension Cohorts D, E, and F

PRIMARY ENDPOINT (extension phase)

- ORR per RECIST v1.1 by BICR

SECONDARY ENDPOINTS

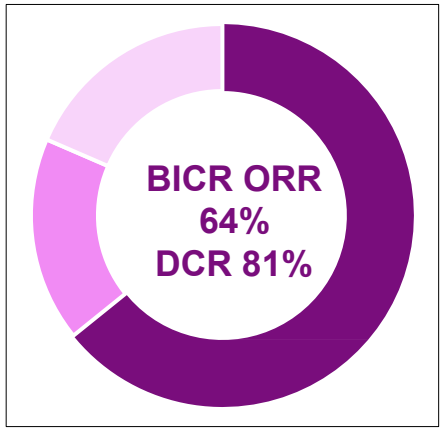
- DoR, DCR, and PFS (per RECIST v1.1) by BICR and investigator assessment
- Safety and tolerability

[a]Patients from dose escalation / backfill treated with 20 mg BID and who met the same eligibility criteria were combined for statistical analysis; [b]Cohorts of patients with *EGFR* mutations are not shown

Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

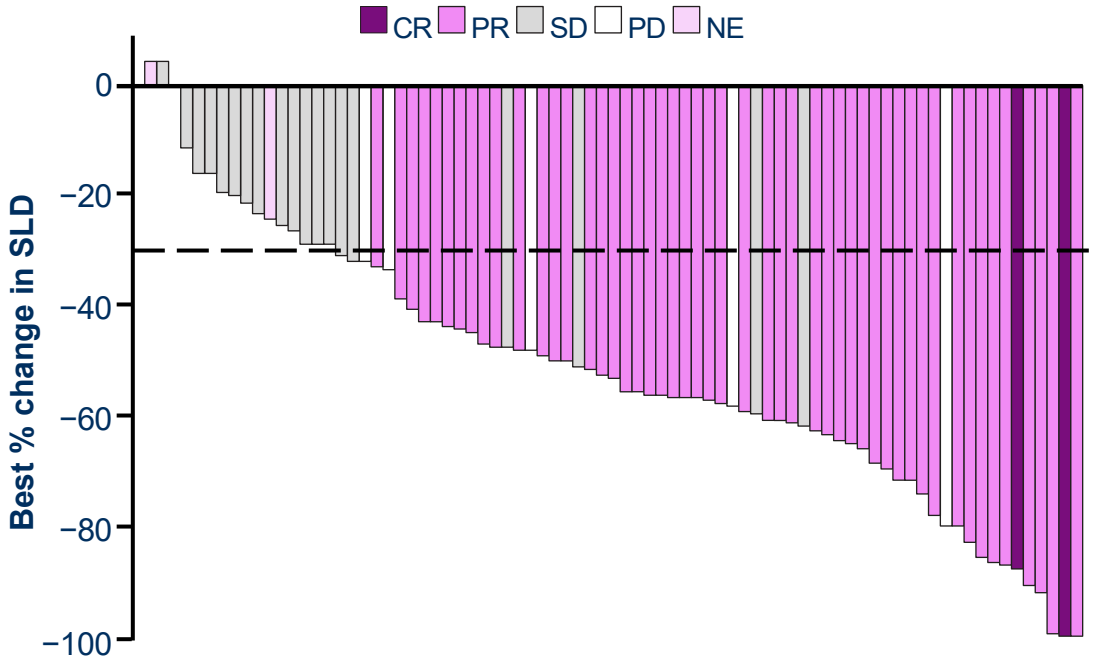
Cohort D (previously treated, *n*=81): Objective response (ORR) by BICR

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]
DCR[c] [95% CI]	**66 (81)** [71, 89]
DoR, median (months) [95% CI]	**9.2** [6.3, 13.5]
PFS, median (months) [95% CI]	**8.3** [6.9, 12.3]

Best overall response (RECIST v1.1 by BICR)



Analysis cut-off date was June 27, 2025. Data for patients without target lesion measurements are not shown in the waterfall plo
[a]Requirement for CR, PR, SD, or PD was not met; [b]Confirmed CR or confirmed PR; [c]Confirmed CR, confirmed PR, or SD for ≥12 weeks

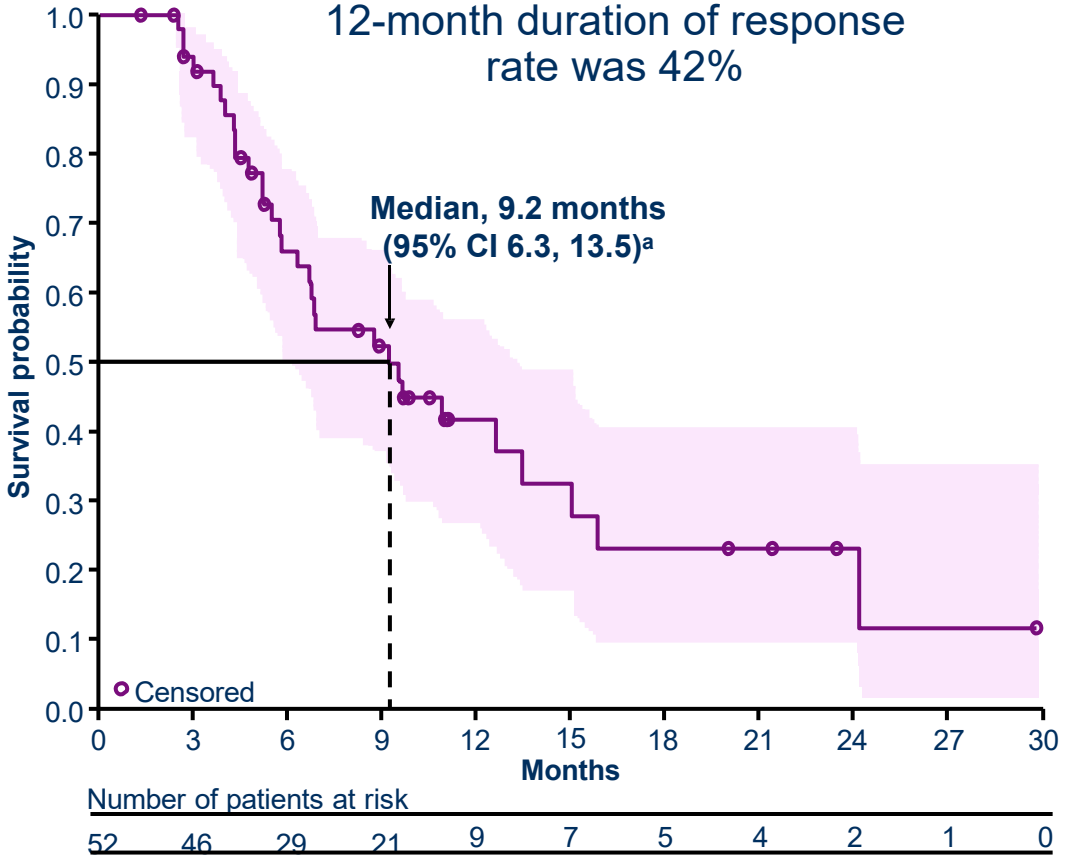
Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

Cohort D (previously treated, *n*=81): DoR and PFS by BICR

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

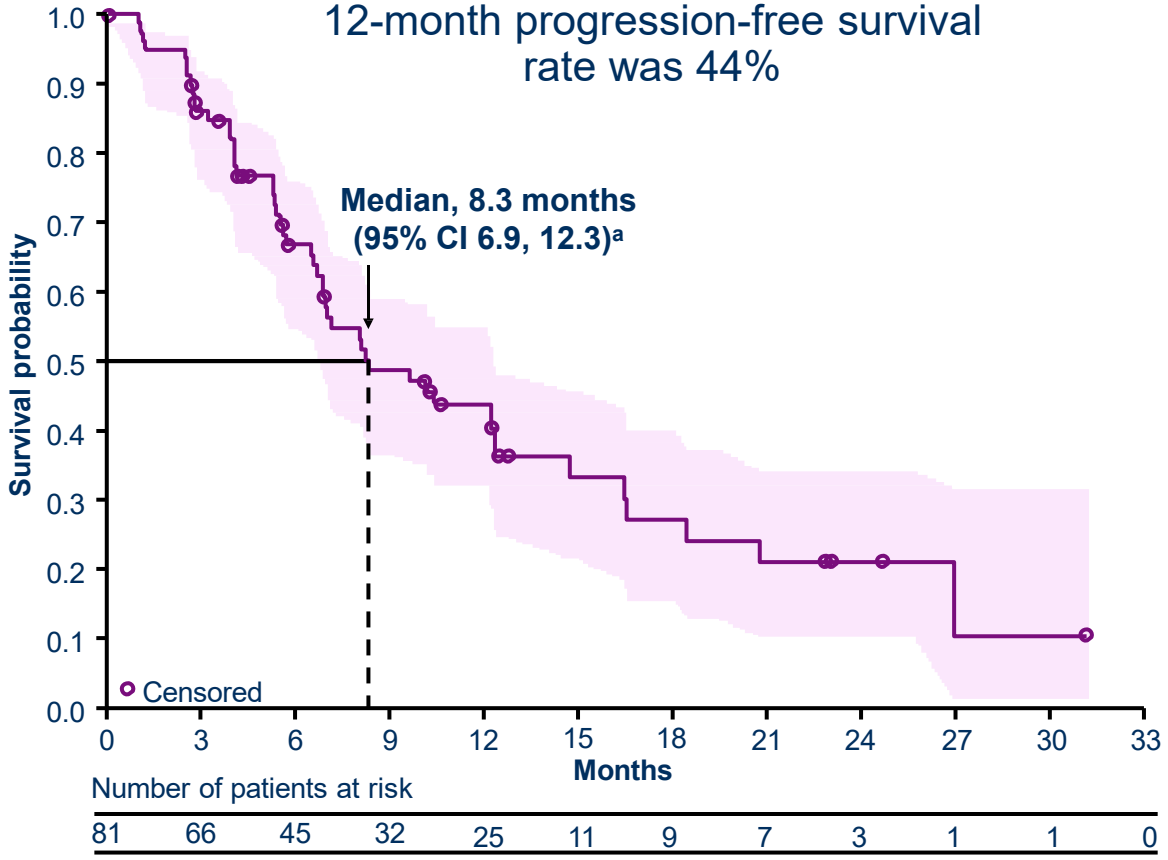
Duration of response

12-month duration of response rate was 42%



Progression-free survival

12-month progression-free survival rate was 44%

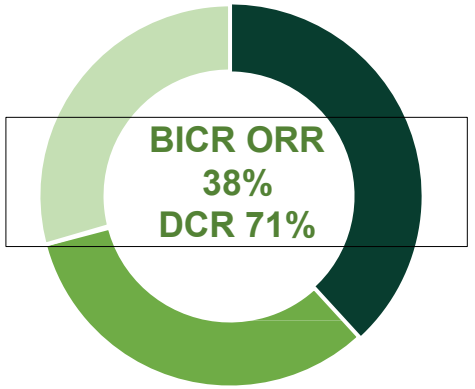


Analysis cut-off date was June 27, 2025
[a]Shading represents 95% CI

Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

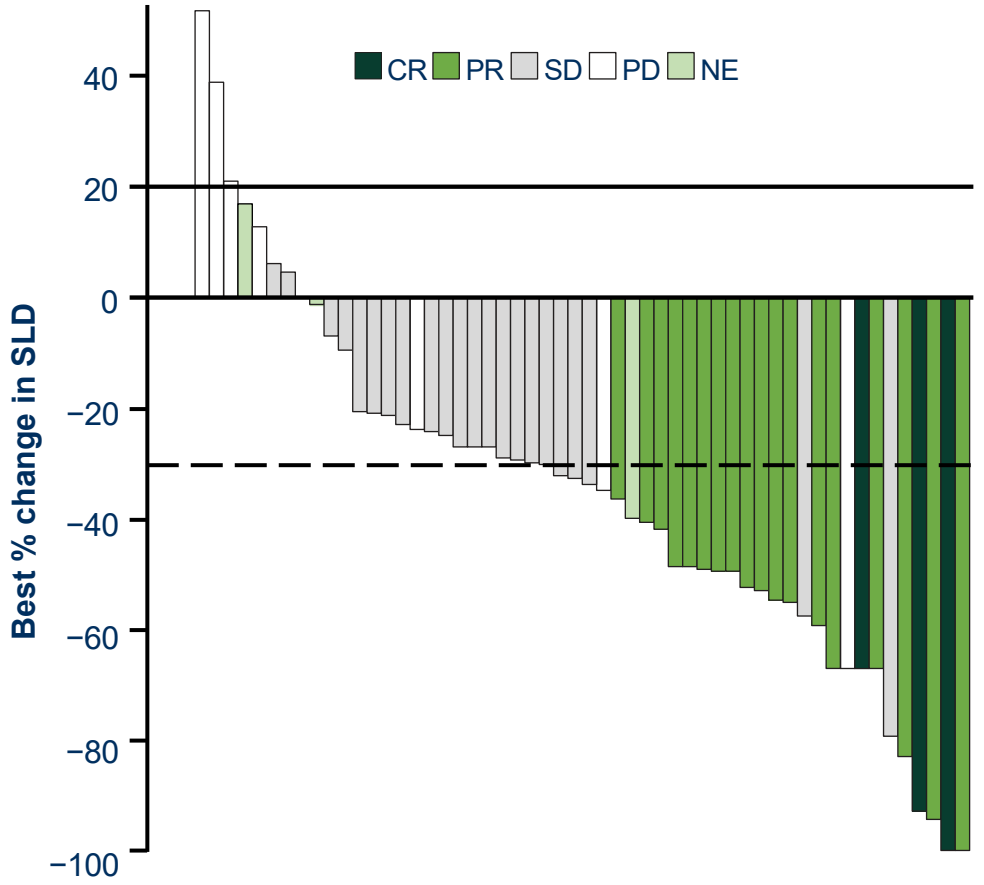
Cohort E (previous HER2 ADCs, *n*=55): Objective response by BICR

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]

Best overall response (RECIST v1.1 by BICR)



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

Analysis cut-off date was June 27, 2025. Data for patients without target lesion measurements are not shown in the waterfall plot

[a]Requirement for CR, PR, SD, or PD was not met; [b]Confirmed CR or confirmed PR; [c]Confirmed CR, confirmed PR, or SD for ≥12 weeks

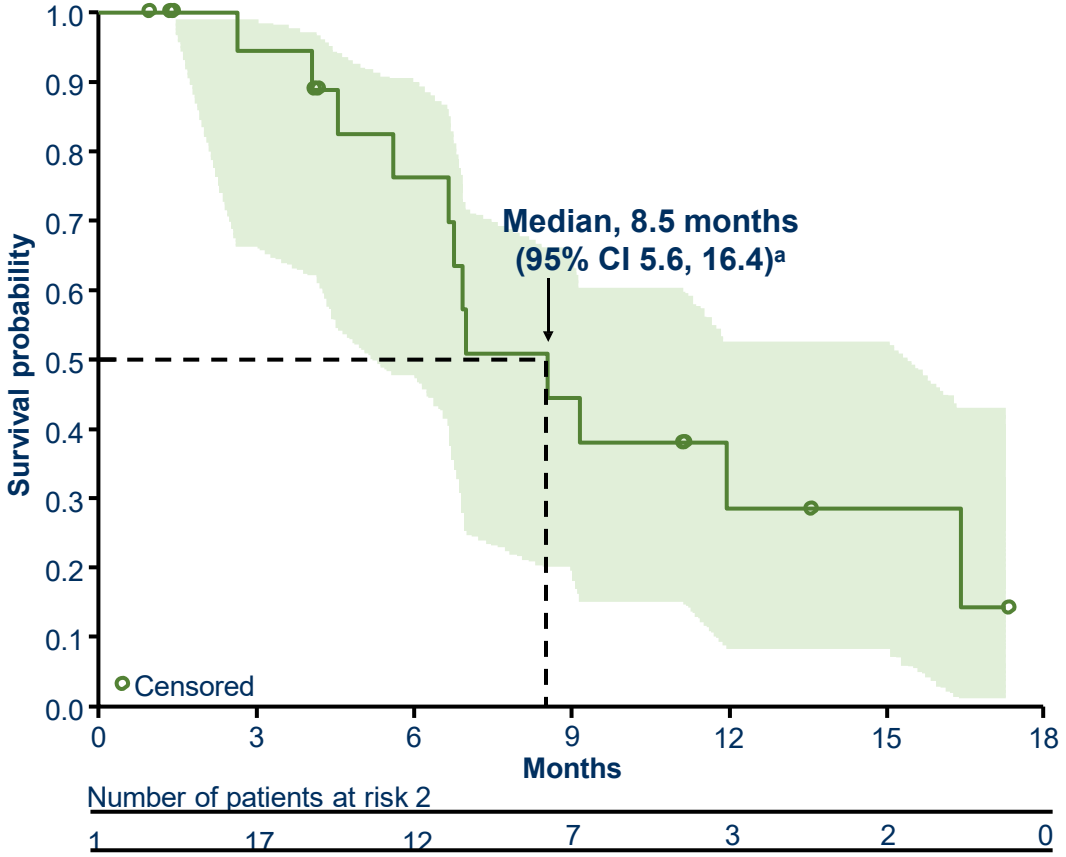
Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

Cohort E (previous HER2 ADCs, *n*=55): DoR and PFS by BICR

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

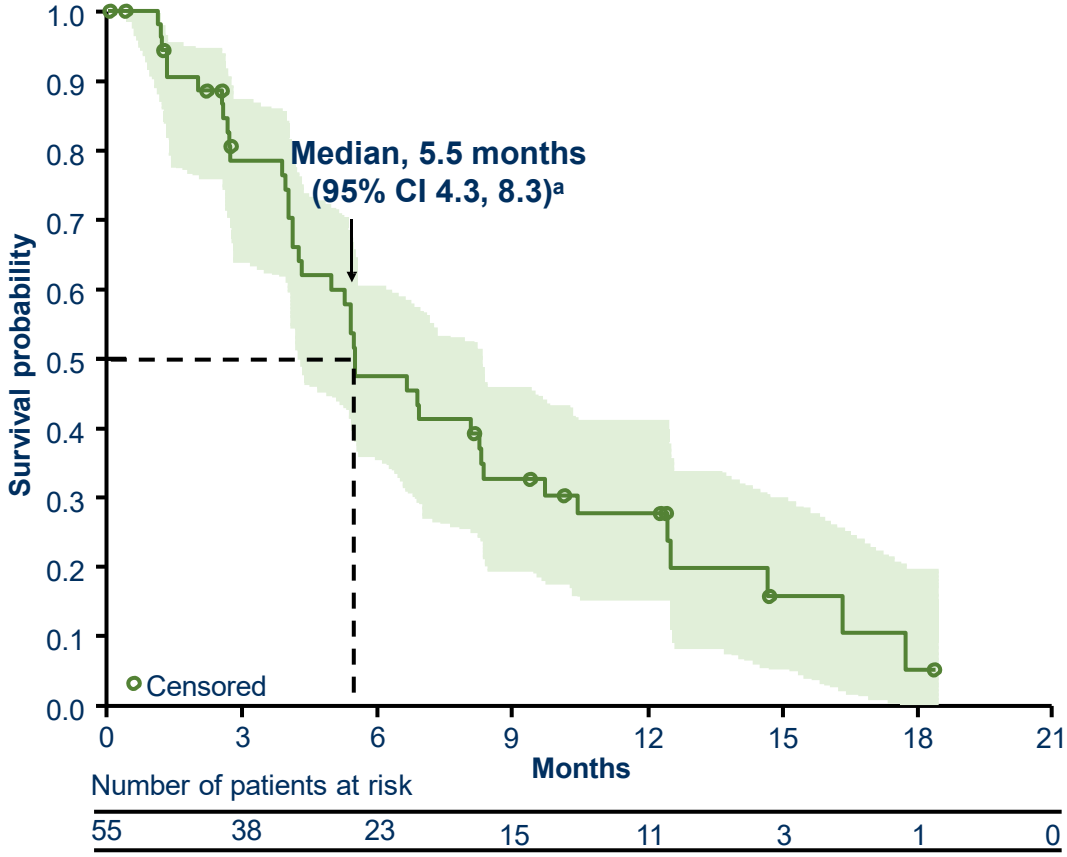
Duration of response

12-month duration of response rate was 29%



Progression-free survival

12-month progression-free survival rate was 28%



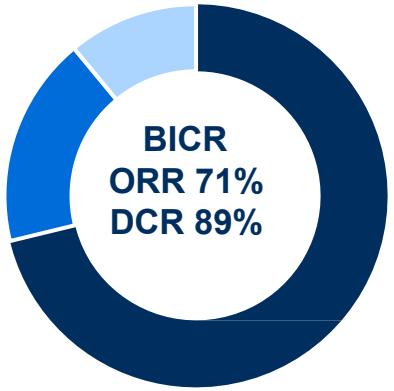
Analysis cut-off date was June 27, 2025

[a]Shading represents 95% CI

Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

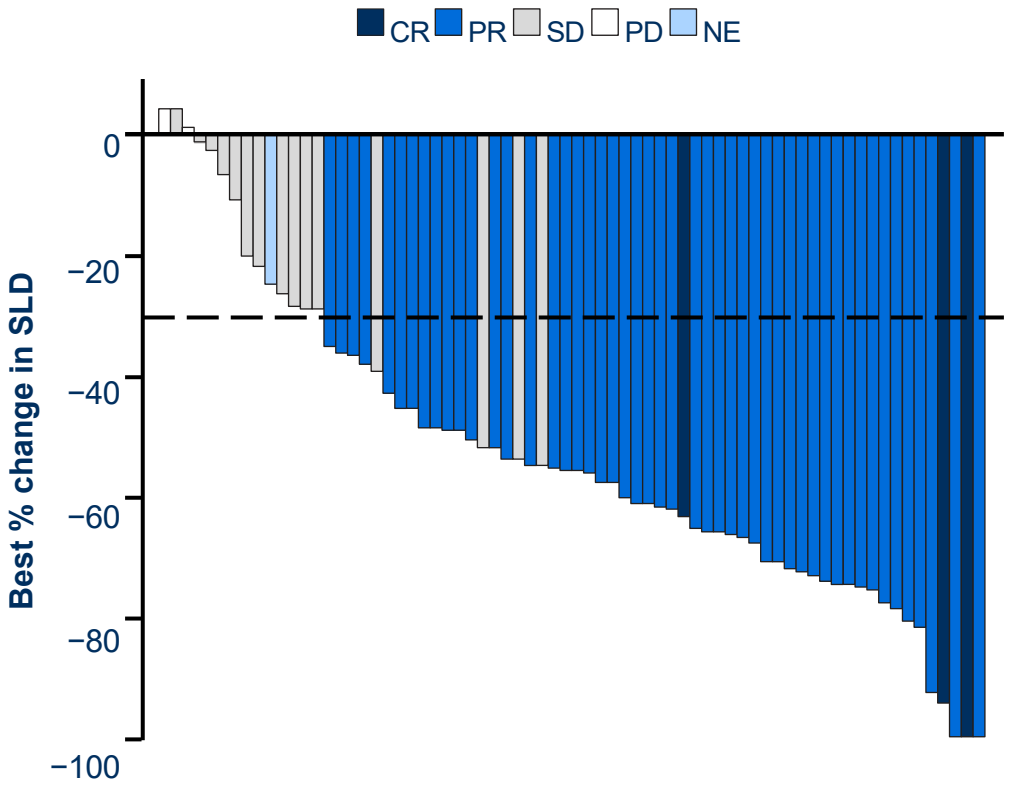
Cohort F (treatment-naïve, *n*=73): Objective response by BICR

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]

Best overall response (RECIST v1.1 by BICR)



Analysis cut-off date was June 27, 2025. Data for patients without target lesion measurements are not shown in the waterfall plot

[a]Requirement for CR, PR, SD, or PD was not met; [b]Patients who have no post-baseline tumor assessment, but who discontinued due to a drug-related toxicity, death, or progression by clinical judgmen before disease was re-evaluated and were therefore considered evaluable (considered as non-responder); [c]Confirmed CR or confirmed PR; [d]Confirmed CR, confirmed PR, or SD for ≥12 week s

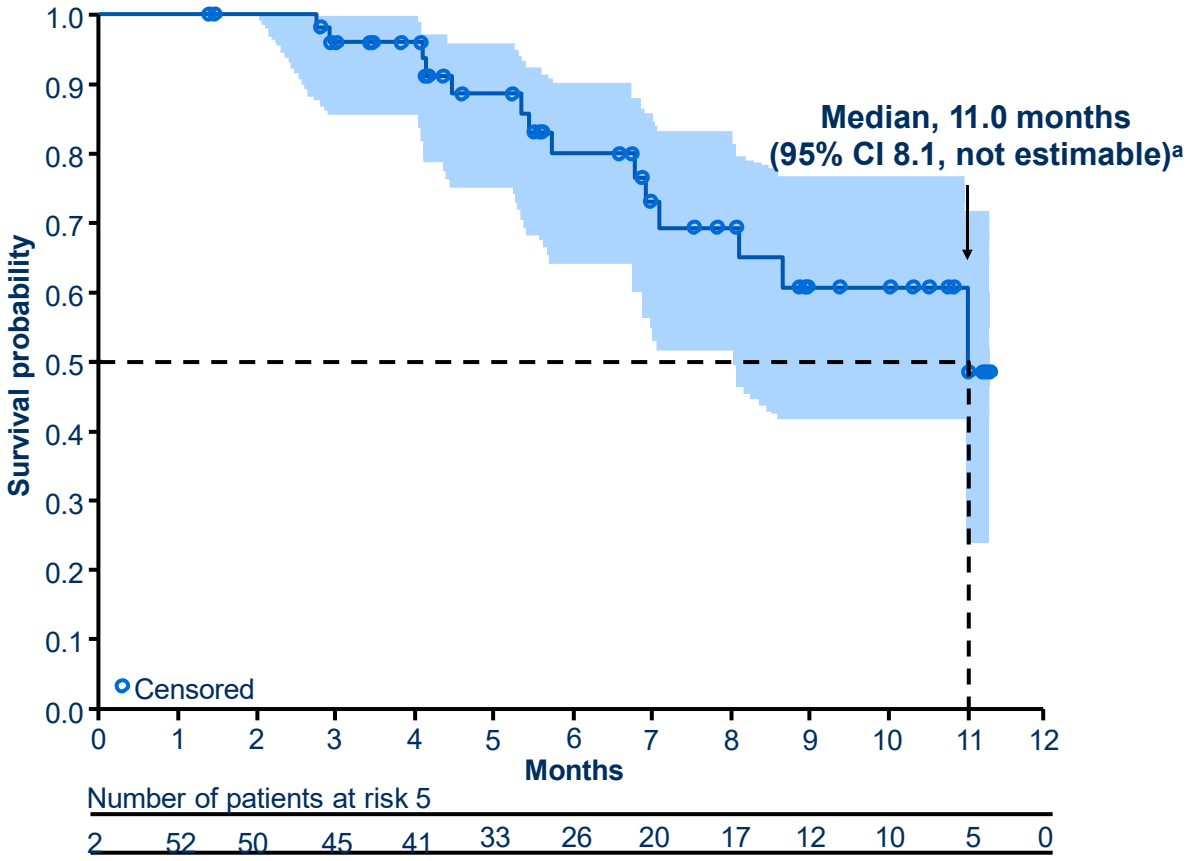
Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

Cohort F (treatment-naïve, *n*=73): DoR and PFS by BICR

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

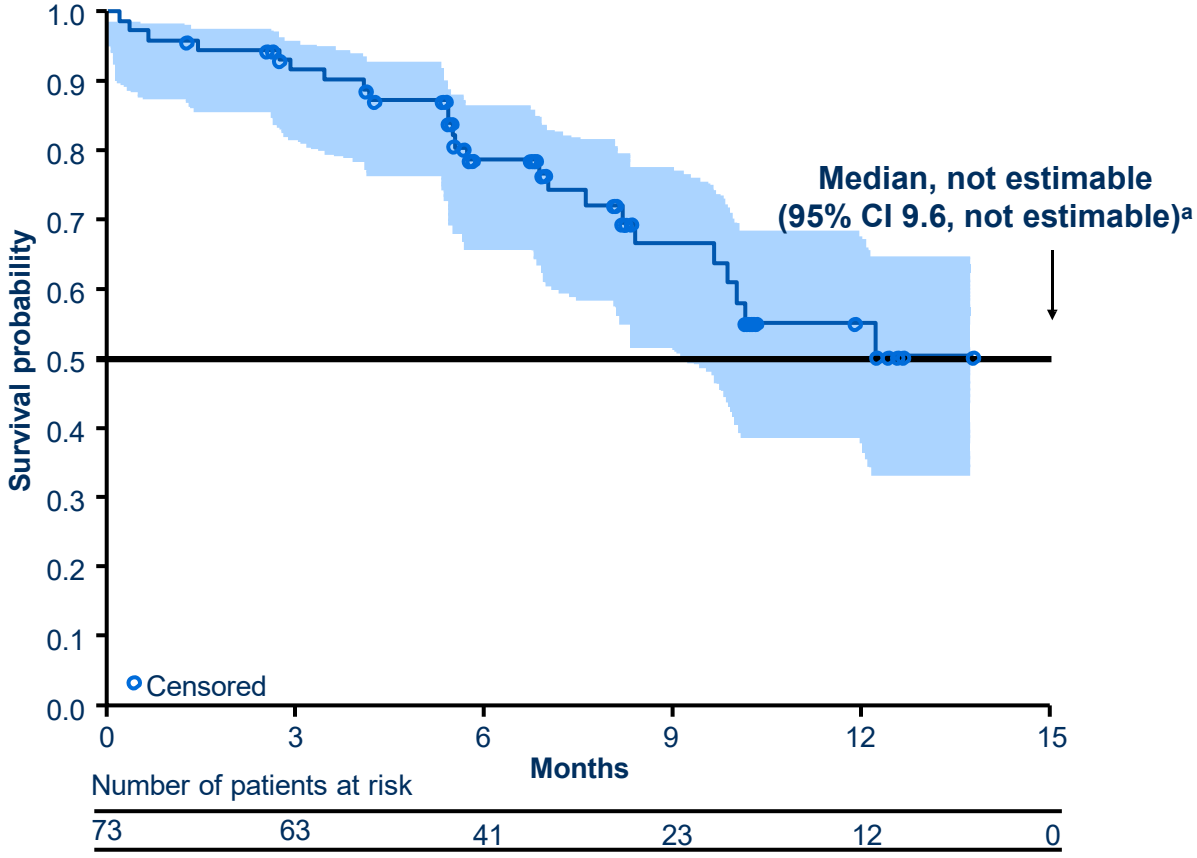
Duration of response

12-month duration of response rate was not estimable due to censored data
38 patients (73%) were censored



Progression-free survival

12-month progression-free survival rate was 55%
49 patients (67%) were censored

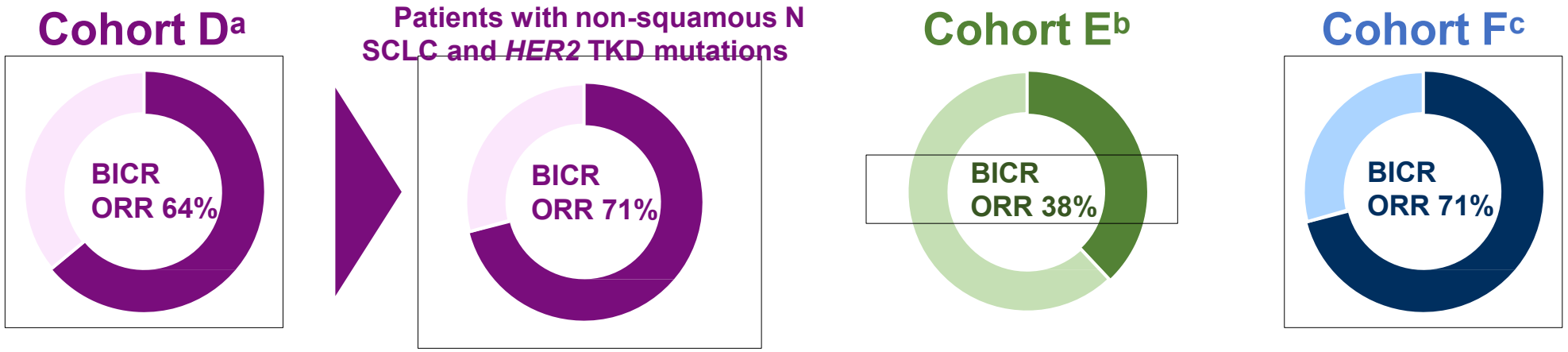


Analysis cut-off date was June 27, 2025
[a]Shading represents 95% CI

Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

Conclusions

- Sevabertinib demonstrated robust and durable responses in patients with *HER2*-mutant advanced NSCLC in both pretreated and first-line settings



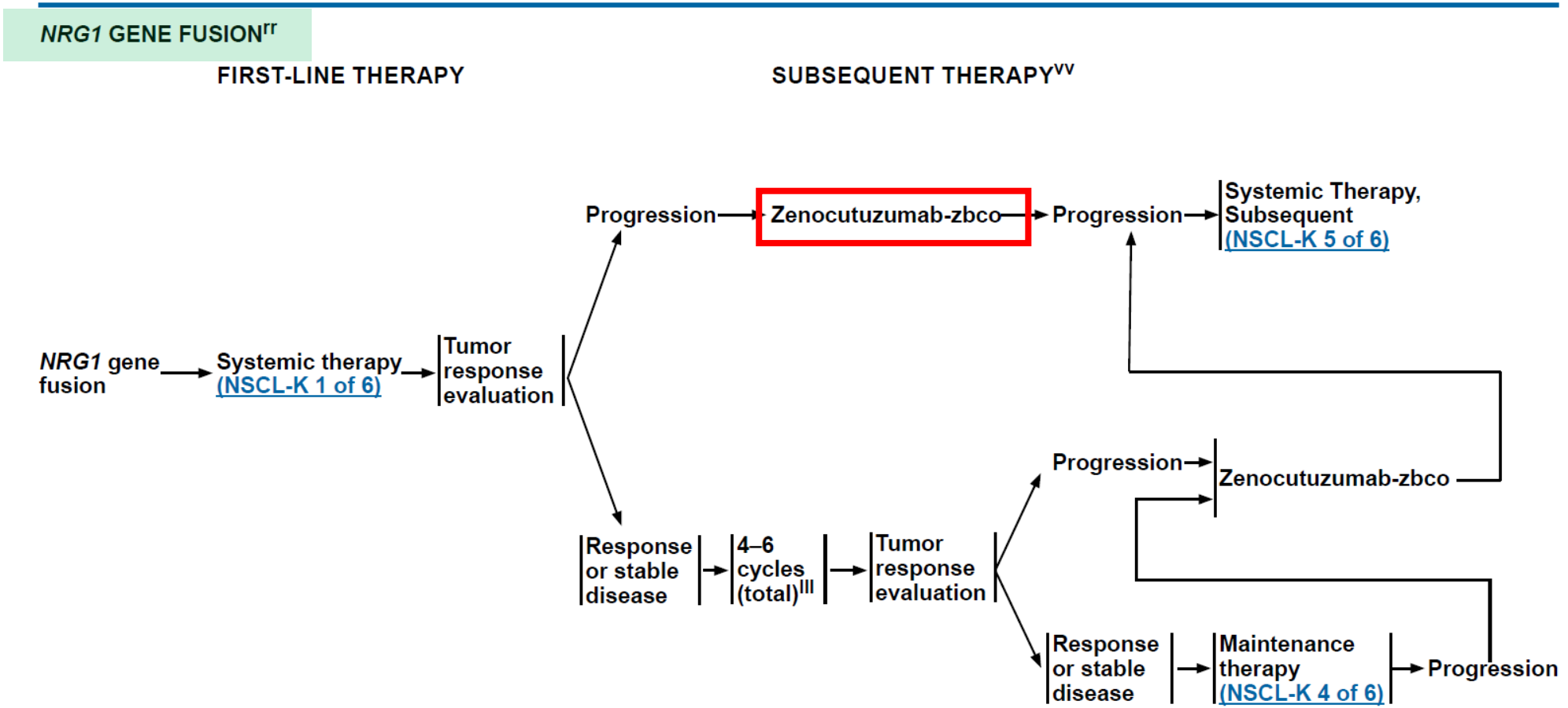
- The most common side effect of sevabertinib was diarrhea, which was manageable; there were no reported cases of interstitial lung disease (ILD) or pneumonitis
- These data support sevabertinib as a potential new targeted therapy for patients with *HER2*-mutant NSCLC
- The safety and efficacy of sevabertinib as first-line therapy for locally advanced or metastatic NSCLC with *HER2* mutations are being investigated in the ongoing Phase III, randomized SOHO-02 trial (NCT06452277)

Analysis cut-off date was June 27, 2025

[a]Patients were naïve to HER2-targeted therapies; [b]Patients were pretreated with HER2-targeted ADCs; [c]Patients were naïve to systemic therapy for advanced disease

Presented by: Xiuning Le, MD, PhD **MD Anderson Cancer Center**

NCCN Guidelines (NSCLC) ver3. 2026

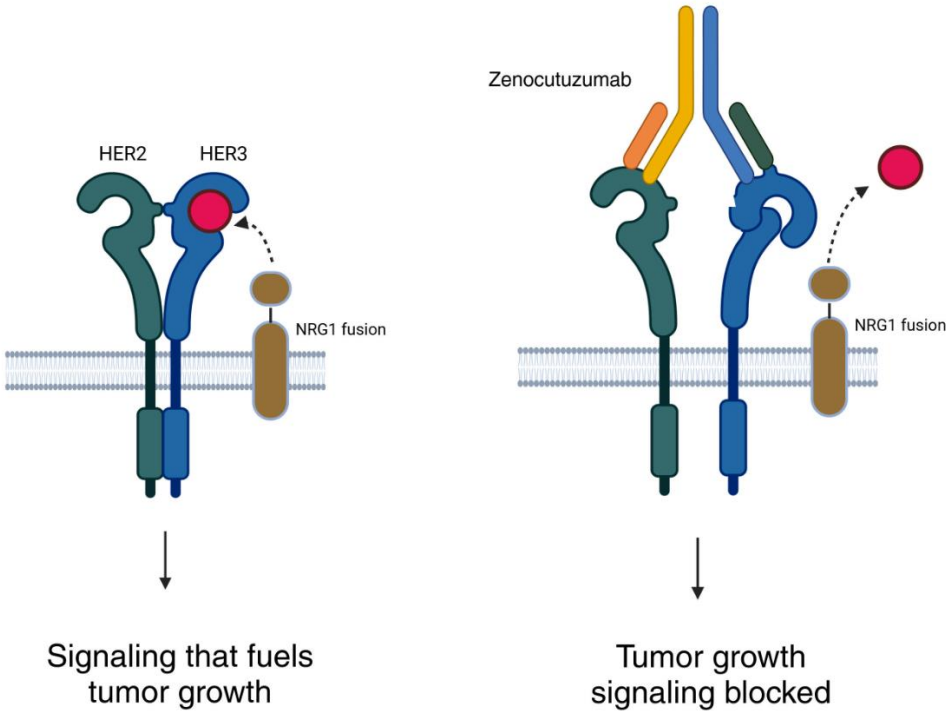


NCCN Guideline (NSCLC). 2026. Version 3.

Efficacy of Zenocutuzumab in NRG1 Fusion-Positive Cancer (eNRGy study)

Open-label, registrational, Phase 1-2 clinical study

MOA of Zenocutuzumab



Baseline Characteristics

Primary tumor type — no. (%)	
Non–small-cell lung cancer§	94 (58)
Pancreatic cancer¶	36 (22)
Cholangiocarcinoma	10 (6)
Breast cancer‖	9 (6)
Colorectal cancer	6 (4)
Cancer of unknown primary site	2 (1)
Endometrial cancer	1 (1)
Gastric cancer	1 (1)
Ovarian cancer	1 (1)
Renal-cell carcinoma	1 (1)
Central nervous system metastasis — no. (%)	14 (9)
NRG1 fusion partner — no. (%)	
CD74	56 (35)
SLC3A2	22 (14)
ATP1B1	17 (11)
SDC4	12 (7)
RBPMS	5 (3)
Other**	49 (30)
Median no. of previous systemic therapies (range)	2 (0–10)
Previous systemic treatment — no. (%)	
None	14 (9)
Chemotherapy	142 (88)
Immunotherapy††	62 (39)
Targeted therapy‡‡	44 (27)
Hormonal therapy	8 (5)

Cited from NIH March 26, 2025, by Linda Wang;

N Engl J Med 2025;392:566-76

Efficacy of Zenocutuzumab in NRG1 Fusion-Positive Cancer (eNRGy study)

Open-label, registrational, Phase 1-2 clinical study

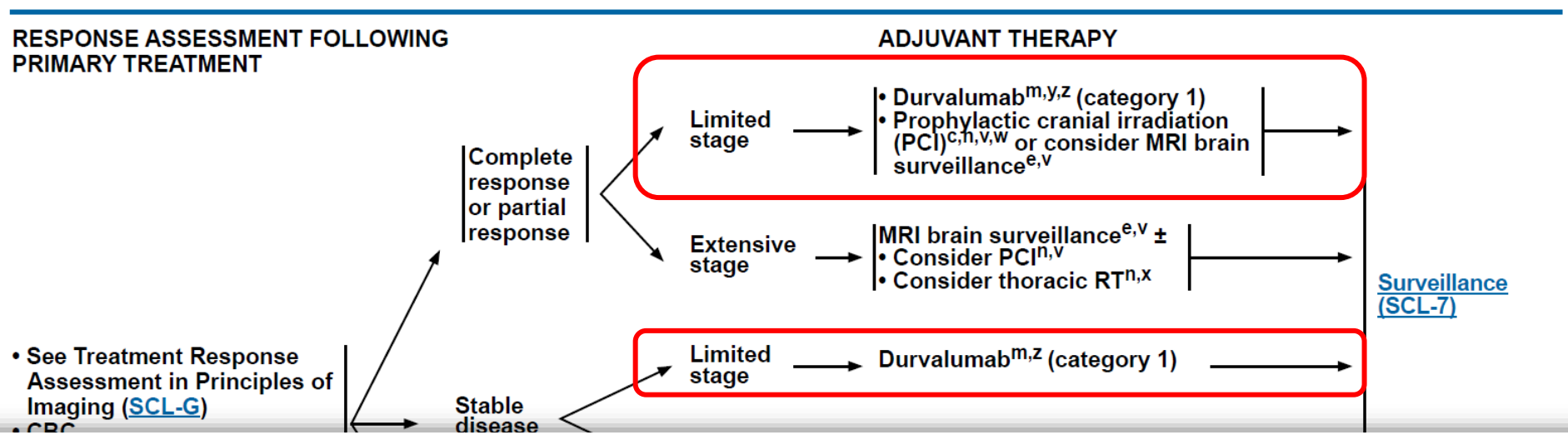
Efficacy of Zenocutuzumab in NRG1 Fusion-Positive Cancer across Multiple Tumor Types

Tumor Type	Investigator Assessment			Blinded Independent Central Review		
	Overall Response†		Median Duration of Response (Range)‡	Overall Response†		Median Duration of Response (Range)‡
	no./total no.	*% (95% CI)*	*mo*	*no./total no.*	*% (95% CI)*	*mo*
All *NRG1* fusion–positive tumor types§	47/158	30 (23 to 37)	11.1 (1.7+ to 29.5+)	50/160	31 (24 to 39)	11.5 (1.9+ to 29.5+)
Non–small-cell lung cancer	27/93	29 (20 to 39)	12.7 (1.8+ to 29.5+)	29/94	31 (22 to 41)	13.4 (1.9+ to 29.5+)
Pancreatic cancer	15/36	42 (25 to 59)	7.4 (2.1+ to 20.7)	16/36	44 (28 to 62)	9.1 (1.9+ to 16.6)
Cholangiocarcinoma	2/10	20 (2 to 56)	9.2 (7.4 to 11.1)	2/10	20 (2 to 56)	8.3 (3.7 to 12.9)
Breast cancer	1/7¶	14‖	1.7+	0/8	0	NA
Colorectal cancer	0/6	0	NA	1/6¶	17‖	11.7
Cancer of unknown primary site	0/2	0	NA	0/2	0	NA
Endometrial cancer	0/1	0	NA	0/1	0	NA
Gastric cancer	1/1¶	100‖	1.9+	1/1¶	100‖	1.9+
Ovarian cancer	1/1¶	100‖	12.8	1/1¶	100‖	12.8+
Renal-cell carcinoma	0/1	0	NA	0/1	0	NA

N Engl J Med 2025;392:566-76

Contents

Update treatment of LD of SCLC



PRINCIPLES OF SYSTEMIC THERAPY

PRIMARY OR ADJUVANT THERAPY FOR LIMITED STAGE SCLC:
Four cycles of cytotoxic chemotherapy are recommended. Planned cycle length should be every 21–28 days during concurrent RT. During cytotoxic chemotherapy + RT, Cisplatin/Etoposide is recommended (category 1). The use of myeloid growth factors is not recommended during concurrent cytotoxic chemotherapy therapy plus RT (category 1 for not using GM-CSF).[1]
Preferred • Cisplatin 75 mg/m² Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[2] • Cisplatin 60 mg/m² Day 1 and Etoposide 120 mg/m² Days 1, 2, 3[3] • Carboplatin area under the curve (AUC) 5–6 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[b,4]
• Consolidation Therapy ‣ Durvalumab 1500 mg Day 1 every 28 Days (category 1)[a,5]
Other Recommended • Cisplatin 25 mg/m² Days 1, 2, 3 and Etoposide 100 mg/m² Days 1, 2, 3[2]

NCCN Guideline (NSCLC). 2026. Version 3.

2024 ASCO ANNUAL MEETING

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

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

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

ADRIATIC study design

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

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

N=730

R‡

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

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

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

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

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

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

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

Other secondary endpoints:
- OS/PFS landmarks
- Safety

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

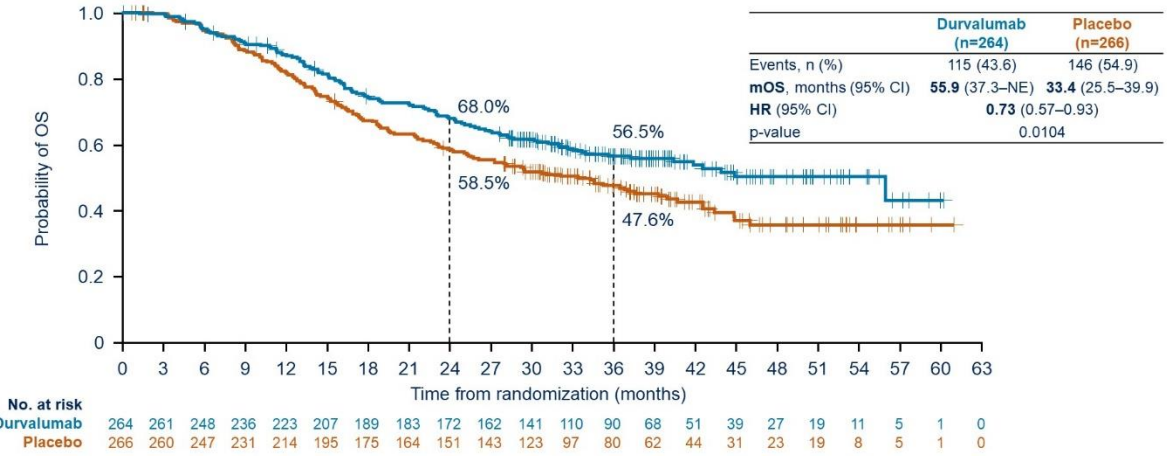
BICR, blinded independent central review; BID, twice daily; CT, chemotherapy; D, durvalumab; PCI, prophylactic cranial irradiation; PS, performance status; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; T, tremelimumab; WHO, World Health Organization.

ADRIATIC study design

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

Overall survival (dual primary endpoint)

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



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

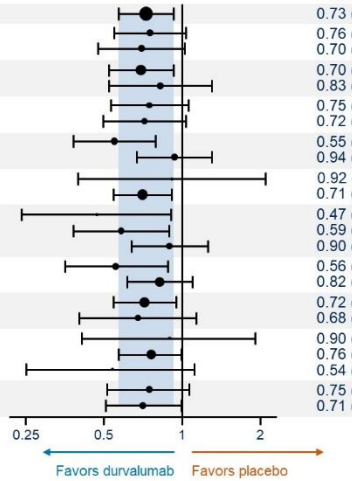
No. at risk																				
Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

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

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

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)



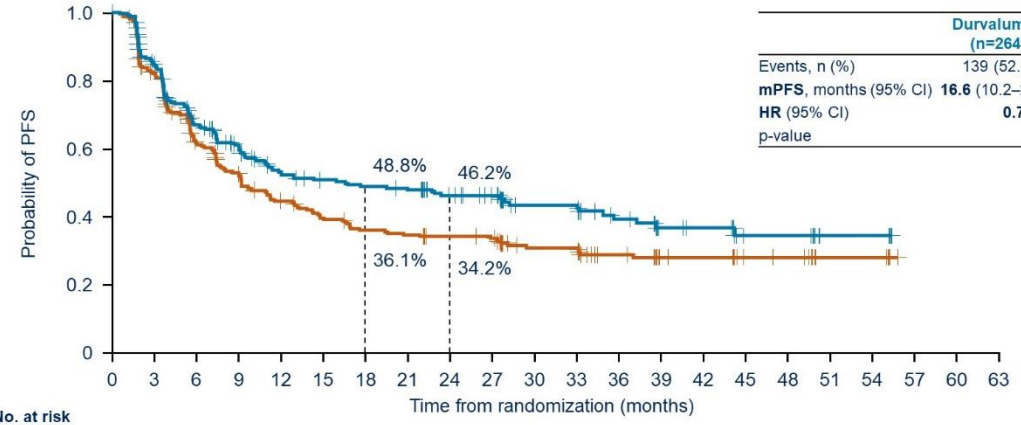
*End of chemotherapy or radiotherapy, whichever was latest.
Intention-to-treat analysis stratified, subgroup analyses unstratified. Not all prespecified subgroups are included in the plot.
Size of circle is proportional to number of events across both arms.

ADRIATIC study design

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

Progression-free survival* (dual primary endpoint)

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



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

No. at risk

Durvalumab	264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	0	0
Placebo	266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	0	0

*By BICR per RECIST v1.1.

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

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. Size of circle is proportional to number of events across both arms.

BARCELONA 2024 ESMO congress

Durvalumab as consolidation therapy in limited-stage SCLC (LS-SCLC): Outcomes by prior concurrent chemoradiotherapy (cCRT) regimen and prophylactic cranial irradiation (PCI) use in the ADRIATIC trial

Suresh Senan,[1] David Spigel,[2] Byoung Chul Cho,[3] Konstantin K. Laktionov,[4] Yoshitaka Zenke,[5] Ki Hyeong Lee,[6] Qiming Wang,[7] Alejandro Navarro,[8] Eva Lotte Buchmeier,[9] Sema Sezgin Goksu,[10] Andrzej Badzio,[11] Anhui Shi,[12] Davey B. Daniel,[13] Milada Zemanova,[14] Puneeth Iyengar,[15] Luis Paz-Ares,[16] Leah Szadkowski,[17] Priti Chugh,[18] W. Victoria Lai,[19] Ying Cheng[20]

[1]Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands; [2]Sarah Cannon Research Institute, Nashville, TN, USA; [3]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; [4]Federal State Budgetary Institution "N.N. Blokhin National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia; [5]National Cancer Center Hospital East, Kashiwa, Japan; [6]Chungbuk National University Hospital, Cheongju, South Korea; [7]The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, 450008, China; [8]Hospital Vall d'Hebron and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [9]Hospitals of the City of Cologne gGmbH, Cologne, Germany; [10]Akdeniz University Medical Faculty, Antalya, Türkiye; [11]Medical University of Gdansk, Gdansk, Poland; [12]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/ Beijing), Department of Radiation Oncology, Peking University Cancer Hospital & Institute, Beijing, China; [13]Tennessee Oncology PLLC, Nashville, TN, USA; [14]First Faculty of Medicine, Charles University, and General University Hospital, Prague, Czech Republic; [15]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [16]Hospital Universitario 12 de Octubre, CNIO-H120 Lung Cancer Unit, Ciberonc and Universidad Complutense, Madrid, Spain; [17]AstraZeneca, Mississauga, ON, Canada; [18]AstraZeneca, Waltham, MA, USA; [19]AstraZeneca, New York, NY, USA; [20]Jilin Cancer Hospital, Changchun, China.

Phase 3 ADRIATIC trial subgroup analyses

Post-hoc analyses of durvalumab versus placebo in prespecified subgroups defined by PCI use and prior cCRT-related variables

PCI/cCRT components (in line with standards of care)*

- PCI delivered before randomisation, as clinically indicated
- Four cycles of platinum (cisplatin or carboplatin) and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks‡

ITT population	Durvalumab (n = 264)	Placebo (n = 266)
Received PCI, %	54	54
Carboplatin / cisplatin CT,§ %	34 / 66	33 / 67
BID / QD thoracic RT, %	26 / 74	30 / 70

- Analyses of OS, PFS, and safety with durvalumab vs placebo in subgroups of patients who received:
  - PCI or no PCI
  - Carboplatin- or cisplatin-based CT
  - BID or QD RT
- Multivariable analyses: for each subgroup, HRs for durvalumab vs placebo were calculated from an unstratified multivariable Cox proportional hazards model with a treatment-by-subgroup (PCI, CT, or RT) interaction term that was adjusted for PCI, CT, RT, time from cCRT to randomisation, response to cCRT, age, sex, WHO PS, and disease stage

BID, twice daily; CT, chemotherapy; Gy, gray; HR, hazard ratio; ITT, intention-to-treat; QD, once daily; RT, radiotherapy.

*The components and delivery of standard of care may vary based on patient characteristics and region.
†If disease control was achieved and no additional benefit was expected with an additional cycle of CT, in the opinion of the investigator.
‡RT must commence no later than end of cycle 2 of CT. §Based on the first cycle of CT.

Conclusions

- **Consolidation durvalumab consistently improved OS and PFS vs placebo across presented subgroups**
  - Magnitude of benefit with durvalumab vs placebo was consistent within PCI and RT subgroups and varied somewhat between CT subgroups
    - Multivariable analyses showed no significant interactions between durvalumab treatment effect and PCI or cCRT subgroups
- **Safety profiles were generally consistent across all subgroups**

Durvalumab demonstrated consistent benefit vs placebo irrespective of prior PCI use and cCRT components, further supporting consolidation durvalumab as the new standard of care in LS-SCLC

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Small Cell Lung Cancer

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Four cycles of cytotoxic chemotherapy are recommended, but some patients may receive up to 6 cycles based on response and tolerability after 4 cycles.
Preferred
• Carboplatin AUC 5 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3 and Atezolizumab 1200 mg Day 1 every 21 Days x 4 Atezolizumab 1200 mg Day 1, every 21 Days (category 1 for all)[d,e,l,6]
• Carboplatin AUC 5 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3 and Atezolizumab 1200 mg Day 1 every 21 Days x 4 Atezolizumab 1680 mg Day 1, every 28 Days[d,e,k]
• Carboplatin AUC 5 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3 and Atezolizumab 1200 mg Day 1 every 21 Days x 4 cycles followed by maintenance Lurbinectedin 3.2 mg/m² and Atezolizumab 1200 mg Day 1, every 21 Days[l,m,48]
• Carboplatin AUC 5–6 Day 1 and Etoposide 80–100 mg/m² Days 1, 2, 3 and Durvalumab 1500 mg Day 1 every 21 Days x 4 cycle Durvalumab 1500 mg Day 1 every 28 Days (category 1 for all)[d,e,f,7]
• Cisplatin 75–80 mg/m² Day 1 and Etoposide 80–100 mg/m² Days 1, 2, 3 and Durvalumab 1500 mg Day 1 every 21 Days x 4 cyc Durvalumab 1500 mg Day 1 every 28 Days (category 1 for all)[d,e,f,7]
Other Recommended
• Carboplatin AUC 5–6 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[8]
• Cisplatin 75 mg/m² Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[9]
• Cisplatin 80 mg/m² Day 1 and Etoposide 80 mg/m² Days 1, 2, 3[10]
• Cisplatin 25 mg/m² Days 1, 2, 3 and Etoposide 100 mg/m² Days 1, 2, 3[11]
Useful in Certain Circumstances
• Carboplatin AUC 5 Day 1 and Irinotecan 50 mg/m² Days 1, 8, 15[12]
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• Cisplatin 30 mg/m² Days 1, 8 and Irinotecan 65 mg/m² Days 1, 8[14]

IMpower-133

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Footnotes (SCL-E 2 of 6)
Subsequent Systemic Therapy (SCL-E 3 of 6)
Response Assessment (SCL-E 4 of 6)
References (SCL-E 5 of 6)

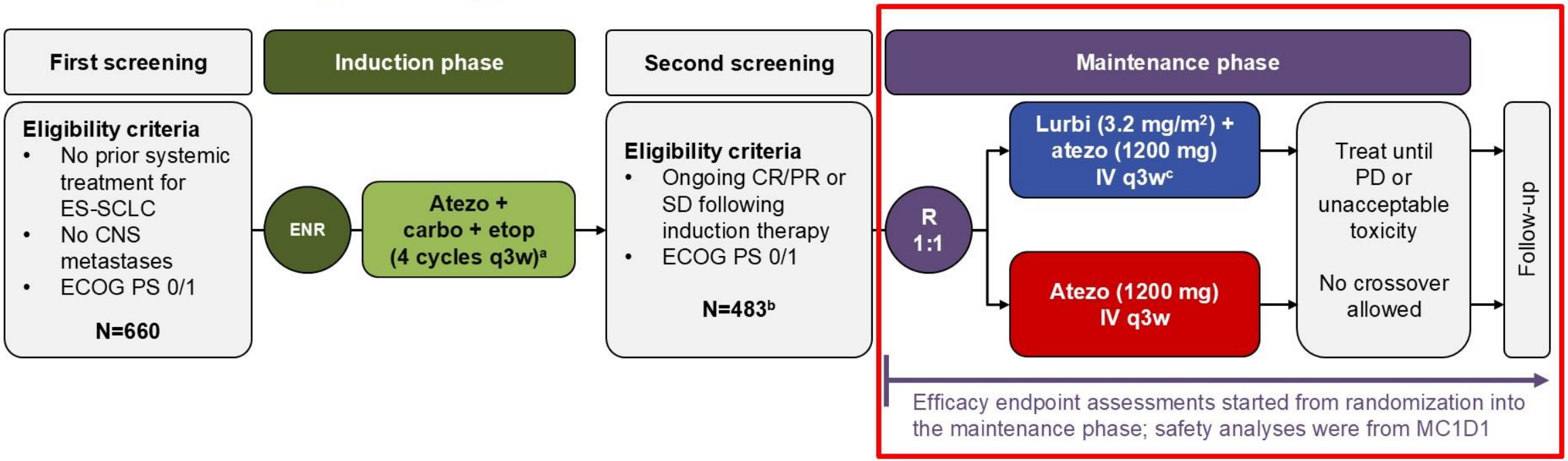
2025 ASCO ANNUAL MEETING

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

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

[1]Hospital Universitario 12 de Octubre, H12O-CNIO Lung Cancer Unit, Universidad Complutense and Ciberonc, Madrid, Spain; [2]Fox Chase Cancer Center, Philadelphia, PA, USA; [3]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [4]University Hospital CHUV, Lausanne, Switzerland; [5]Yale School of Medicine, New Haven, CT, USA; [6]Wielkopolska Center of Pulmonology and Thoracic Surgery of Eugenia and Janusz Zeyland, Poznan, Poland; [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [8]The John Paul II Specialist Hospital, Kraków, Poland; [9]Hospital Universitario Virgen del Rocío, Seville, Spain; [10]Chungbuk National University Hospital, Cheongju, South Korea; [11]Tennessee Oncology, Sarah Cannon Research Institute, Nashville, TN, USA; [12]University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Türkiye; [13]Klinik für Pneumologie, Evangelische Lungenklinik Berlin, Berlin, Germany; [14]Genentech Inc, South San Francisco, CA, USA; [15]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Jazz Pharmaceuticals plc, Dublin, Ireland; [17]Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany

IMforte study design



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

Primary endpoints
IRF-PFS and OS

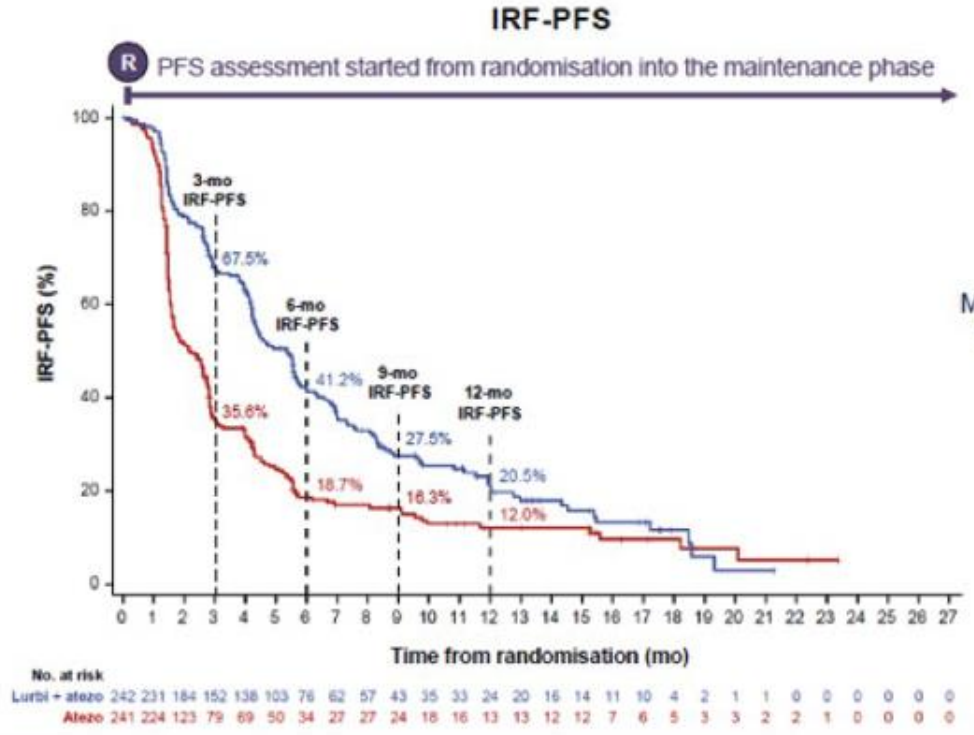
Secondary endpoints included
INV-PFS, ORR, DOR, and safety

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

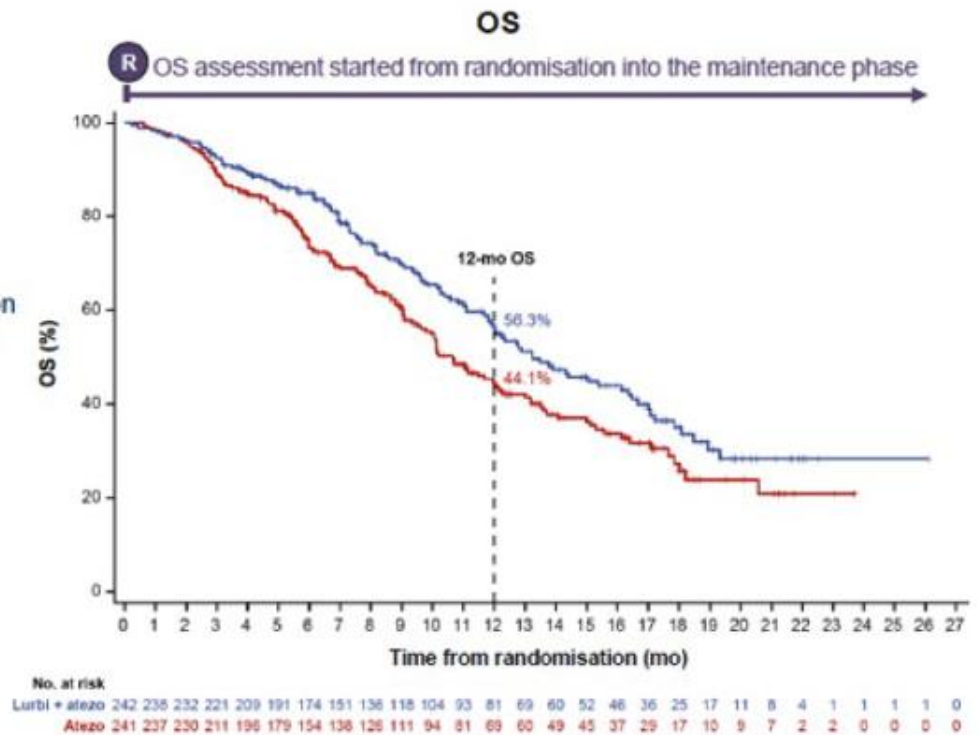
ClinicalTrials.gov ID: NCT05091567.
[a] Administered per standard dose. [b] 73% of patients continued from induction to maintenance. [c] With **prophylactic granulocyte colony-stimulating factor** and anti-emetics.
atezo, atezolizumab; BL, baseline; carbo, carboplatin; CNS, central nervous system; ECOG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

IMforte Study

PFS and OS from randomization into maintenance phase



Median time from induction C1D1 to randomisation: **3.2 mo** in each arm



	Lurbi + atezo (n = 242)	Atezo (n = 241)	HR (95% CI)	*P* value
Median PFS, mo	5.4	2.1	0.54 (0.43, 0.67)	< .0001

	Lurbi + atezo (n = 242)	Atezo (n = 241)	HR (95% CI)	*P* value
Median OS, mo	13.2	10.6	0.73 (0.57-0.95)	.0174

Paz-Ares L, et al. ASCO 2025. Presentation LBA8505.

Update treatment of ED of SCLC

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PRIMARY THERAPY FOR EXTENSIVE STAGE SCLC[c]:

Four cycles of cytotoxic chemotherapy are recommended, but some patients may receive up to 6 cycles based on response and tolerability after 4 cycles.

Preferred

- Carboplatin AUC 5 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3 and Atezolizumab 1200 mg Day 1 every 21 Days x 4 cy
  Atezolizumab 1200 mg Day 1, every 21 Days (category 1 for all)[d,e,k,6]
- Carboplatin AUC 5 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3 and Atezolizumab 1200 mg Day 1 every 21 Days x 4 cy
  Atezolizumab 1680 mg Day 1, every 28 Days[d,e,k]
- Carboplatin AUC 5 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3 and Atezolizumab 1200 mg Day 1 every 21 Days x 4 cycles follo ance
  Lurbinectedin 3.2 mg/m² and Atezolizumab 1200 mg Day 1, every 21 Days[l,m,48]
- Carboplatin AUC 5–6 Day 1 and Etoposide 80–100 mg/m² Days 1, 2, 3 and Durvalumab 1500 mg Day 1 every 21 Days x 4 cycles
  Durvalumab 1500 mg Day 1 every 28 Days (category 1 for all)[d,e,f,7]
- Cisplatin 75–80 mg/m² Day 1 and Etoposide 80–100 mg/m² Days 1, 2, 3 and Durvalumab 1500 mg Day 1 every 21 Days x 4 cycle
  Durvalumab 1500 mg Day 1 every 28 Days (category 1 for all)[d,e,f,7]

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Other Recommended

- Carboplatin AUC 5–6 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[8]
- Cisplatin 75 mg/m² Day 1 and Etoposide 100 mg/m² Days 1, 2, 3[9]
- Cisplatin 80 mg/m² Day 1 and Etoposide 80 mg/m² Days 1, 2, 3[10]
- Cisplatin 25 mg/m² Days 1, 2, 3 and Etoposide 100 mg/m² Days 1, 2, 3[11]

Useful in Certain Circumstances

- Carboplatin AUC 5 Day 1 and Irinotecan 50 mg/m² Days 1, 8, 15[12]
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- Cisplatin 30 mg/m² Days 1, 8 and Irinotecan 65 mg/m² Days 1, 8[14]

Footnotes (SCL-E 2 of 6)
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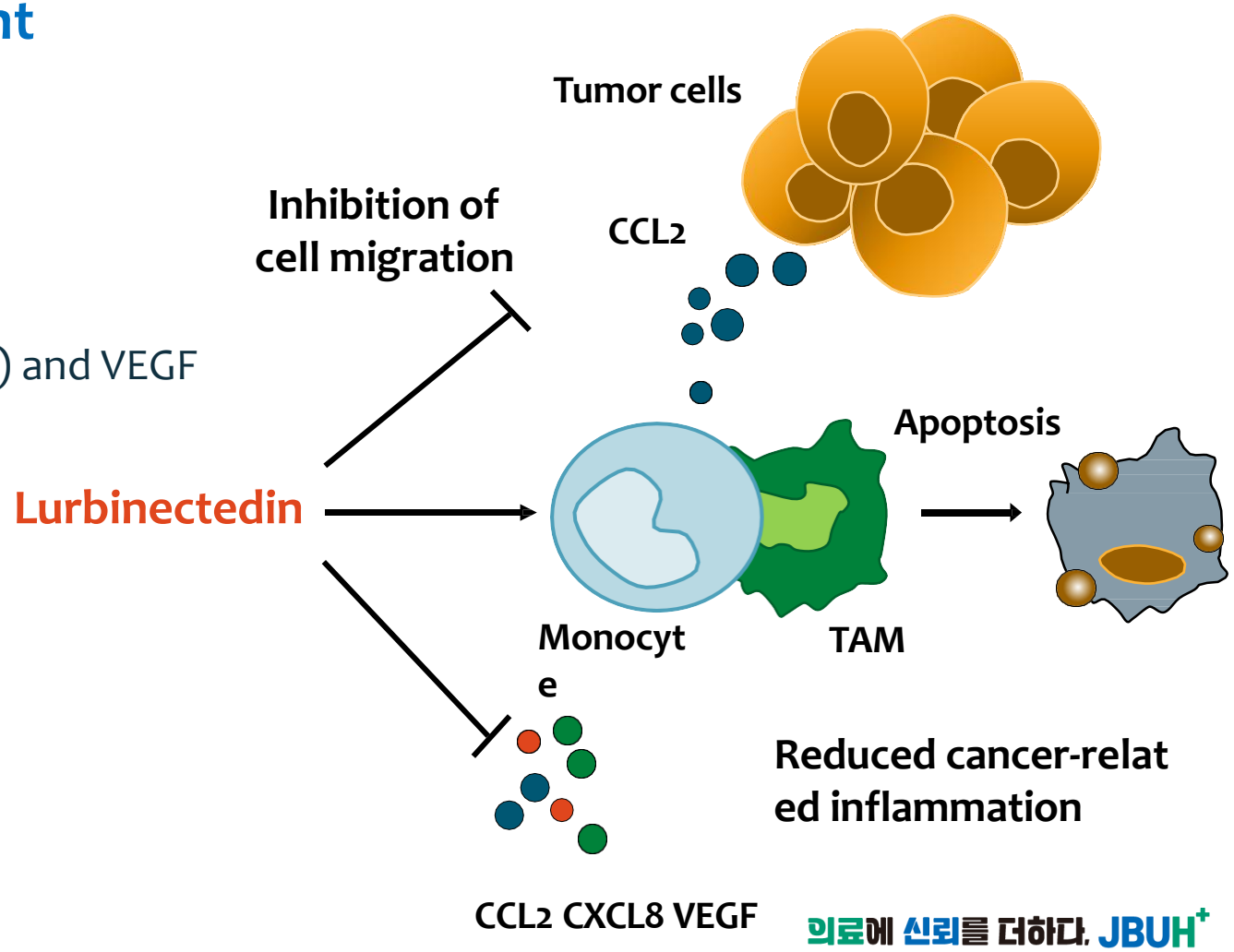
Lurbinectedin

- **Effects on the tumor microenviroment**

Based on a preclinical study:

- Induce apoptosis in tumor-associated macrophapes
- Reduce macrophage infiltration
- Reduce inflammatory chemokines (CCL2 and CXCLB) and VEGF



SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)[g]
Consider dose reduction or growth factor support for patients with PS 2

CHEMOTHERAPY-FREE INTERVAL (CTFI) >6 MONTHS

Preferred Regimens
- Clinical trial enrollment
- Re-treatment with platinum-based doublet[h,15-19]

Other Recommended Regimens
- Lurbinectedin[20,21]
- Topotecan oral (PO) or intravenous (IV)[22-25]
- Irinotecan[i,25,26]
- Tarlatamab-dlle[j,28]

CTFI ≤6 MONTHS

Preferred Regimens
- Clinical trial enrollment
- Lurbinectedin[20,21]
- Topotecan oral (PO) or intravenous (IV)[17,22-25]
- Irinotecan[i,25,26]
- Tarlatamab-dlle[j,28]
- Re-treatment with platinum-based doublet may be considered for CTFI 3–6 months[h,17-19]

Other Recommended Regimens
- Nivolumab[k] or pembrolizumab (if not previously treated with an ICI)[d,29-33]
- Paclitaxel[34,35]
- Temozolomide[36,37]
- Cyclophosphamide/doxorubicin/vincristine (CAV)[22]
- Docetaxel[38]
- Gemcitabine[27,39,40]
- Oral etoposide[41,42]

02 Update treatment of ED of SCLC

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SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)[g]
Consider dose reduction or growth factor support for patients with PS 2

Preferred

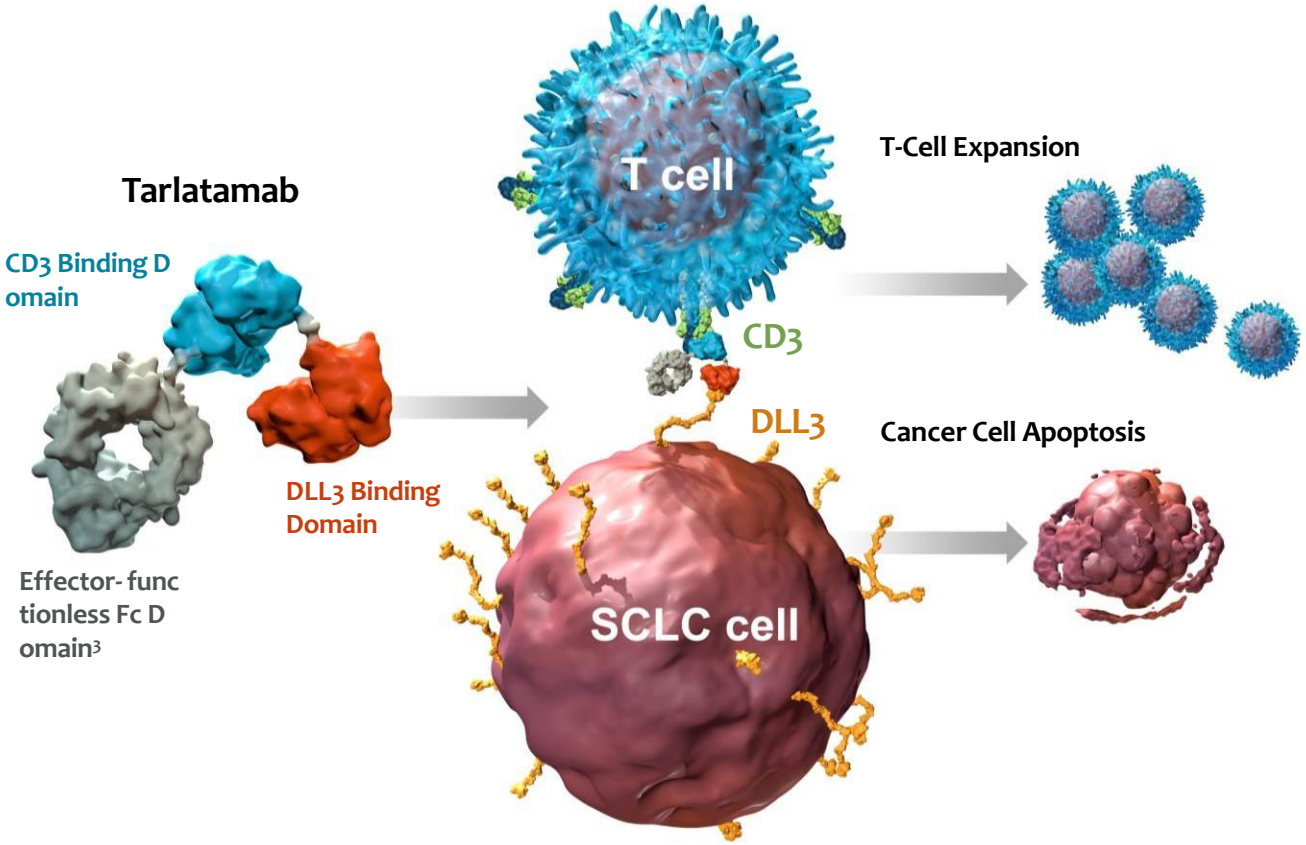
- Tarlatamab-dlle[j,27] (category 1)
- Clinical trial enrollment
- Irinotecan[i,25,26]
- Lurbinectedin (if not previously used)[20,21]
- If prolonged disease free time, re-treatment with platinum-based doublet with or without immunotherapy[15-19]
- Topotecan Oral (PO) or Intravenous (IV)[17,22-25]

Other Recommended

- CAV (Cyclophosphamide/Doxorubicin/Vincristine)[22]
- Docetaxel[36]
- Gemcitabine[37,38,39]
- Nivolumab[n] or Pembrolizumab (if not previously treated with an ICI)[d,28-31]
- Oral Etoposide[40,41]
- Paclitaxel[32,33]
- Temozolomide[34,35]

NCCN Guideline Small cell lung cancer version 4. 2025 Available from:https://www.nccn.org/guidelines/

Tarlatamab is a BiTE® (Bispecific T-Cell Engager) Immunotherapy



Tarlatamab Mechanism of Action[1]

- Tarlatamab binds both DLL3 on cancer cells and CD3 on T cells, leading to T-cell mediated cancer cell lysis[1]
- Binding creates a cytolytic synapse between T cells and cancer cells, and can activate T cells without relying on MHC I[2,3]

CD3, cluster of differentiation 3; **DLL3**, Delta-like ligand 3; **Fc**, fragment crystallizable; **MHC I**, major histocompatibility complex class I; **SCLC**, small cell lung cancer.

1. Owen DH, et al. *J Hematol Oncol*. 2019;12:61. 2. Nagorsen D, et al. *Exp. Cell Res.* 2011; 317:1255-1260. 3. Giffin MJ, et al. *Clin Cancer Res*. 2021;27:1526-1537.

DeLLphi-301

Phase 2, open-label study (NCT05060016)

Key Inclusion Criteria

- R/R SCLC
- Previous treatment with ≥ 2 lines (including platinum-doublet)
- ECOG PS 0–1
- Measurable disease
- Treated and stable brain me tastases allowed

R 1:1

Part 1: Dose Evaluation

Tarlatamab 10 mg IV infusion (n = 88)
1 mg on Day 1, followed by 10 mg on Days 8 and 15, and Q2W thereafter*,†

Tarlatamab 100 mg IV infusion (n = 88)
1 mg on Day 1, followed by 100 mg on Days 8 and 15, and Q2W thereafter*,†

ITT analysis set

Dose Selection‡

Part 2: Dose Expansion

Tarlatamab 10 mg (n = 12)
Same dosing as in Part 1

Part 3: Reduced Inpatient Monitoring Period

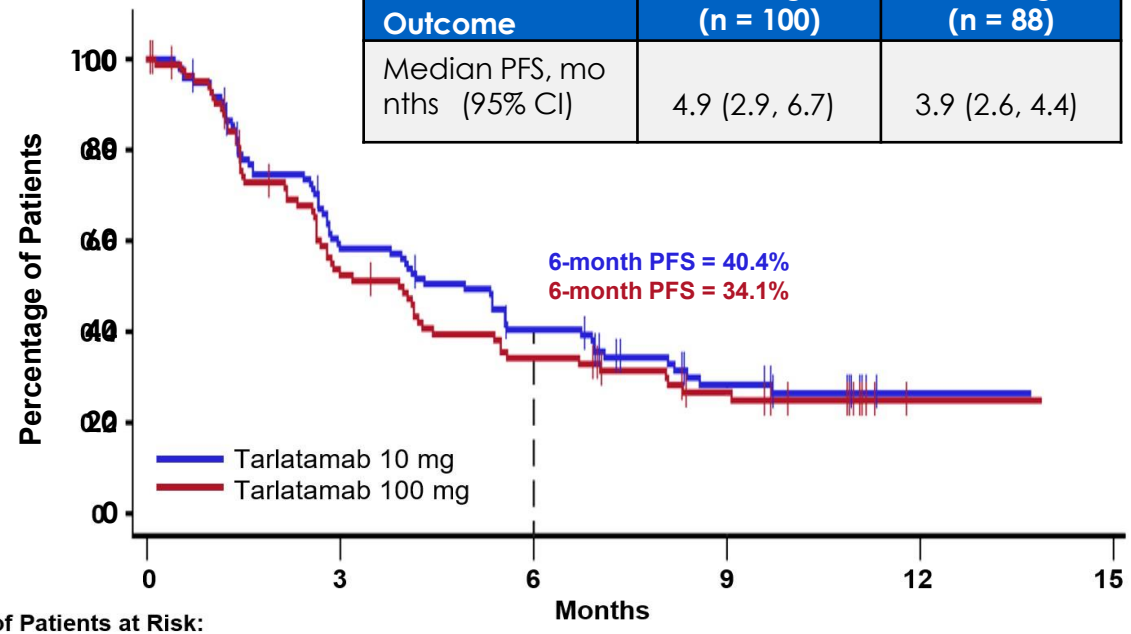
Tarlatamab 10 mg (n = 34)
Same dosing as in Part 1

Primary Efficacy Endpoint: ORR per RECIST 1.1 by BICR
Key Secondary Endpoints: DOR, DCR, PFS per RECIST 1.1 by BICR, OS, adverse events during the treatment period

*Dexamethasone was administered on days 1 and 8 of cycle 1, and IV hydration was administered following all tarlatamab doses in cycle 1. †28-day cycles. ‡Once 30 patients per dose level had the opportunity to confirm an objective response after the first post-treatment scan or up to13 weeks of follow-up, whichever occurred first.
BICR, blinded independent central review; **DCR**, disease control rate; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ITT**, intention-to-treat; **IV**, intravenous; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **R**, randomization; **R/R**, relapse/refractory; **RECIST**, Response Evaluation Criteria in Solid Tumors; **SCLC**, small cell lung cancer.
1. Ahn MJ, et al. *N Engl J Med*. 2023;389:2063-2075. 2. Ahn MJ, et al. *N Engl J Med*. 2023;389:2063-2075; Appendix.

DeLLphi-301 PFS and OS

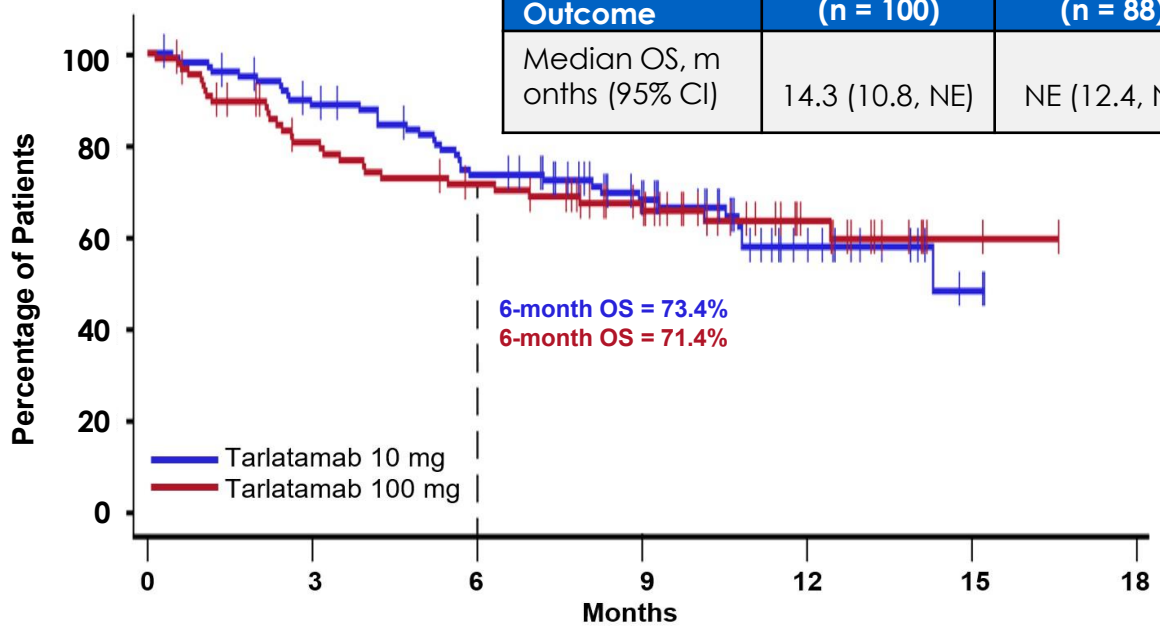
Outcome	Tarlatamab 10 mg (n = 100)	Tarlatamab 100 mg (n = 88)
Median PFS, months (95% CI)	4.9 (2.9, 6.7)	3.9 (2.6, 4.4)



Number of Patients at Risk:

Tarlatamab 10 mg	100	53	35	18	2	0
Tarlatamab 100 mg	88	41	26	15	3	0

Outcome	Tarlatamab 10 mg (n = 100)	Tarlatamab 100 mg (n = 88)
Median OS, months (95% CI)	14.3 (10.8, NE)	NE (12.4, NE)



Tarlatamab 10 mg	100	84	67	44	17	3	0
Tarlatamab 100 mg	88	62	53	39	16	2	0

OS data is not yet mature; at the last follow-up 57% of patients in the tarlatamab 10 mg group and 51% of patients in the tarlatamab 100 mg group were still alive

Median follow-up was 10.6 months for tarlatamab 10 mg and 10.3 months for tarlatamab 100 mg.
CI, confidence interval; **NE**, not evaluable; **OS**, overall survival; **PFS**, progression-free survival.

1. Ahn MJ, et al. *N Engl J Med*. 2023;389:2063-2075.

2025 ASCO ANNUAL MEETING

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

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

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

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

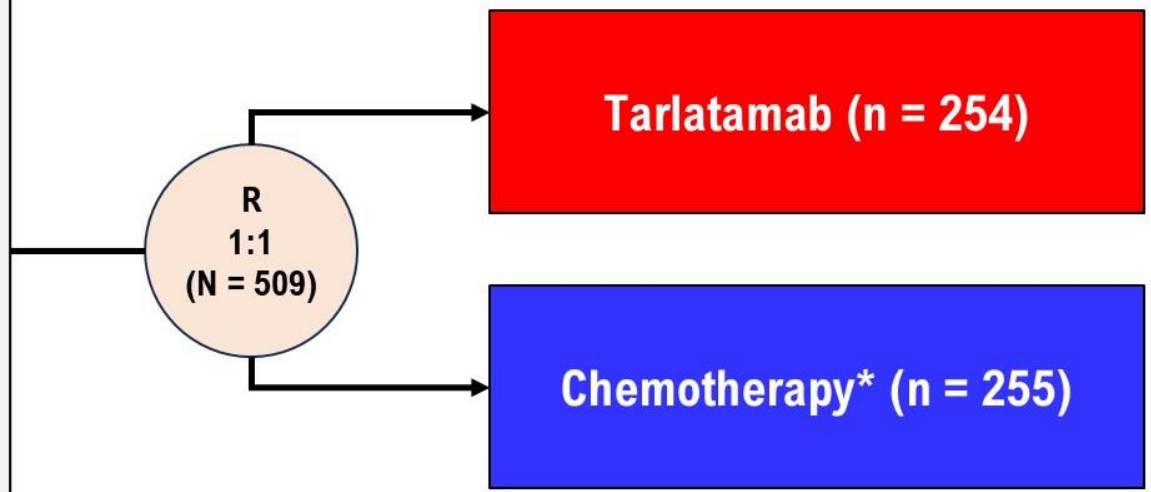
DeLLphi 304

Key inclusion criteria

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

Randomization stratified by

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

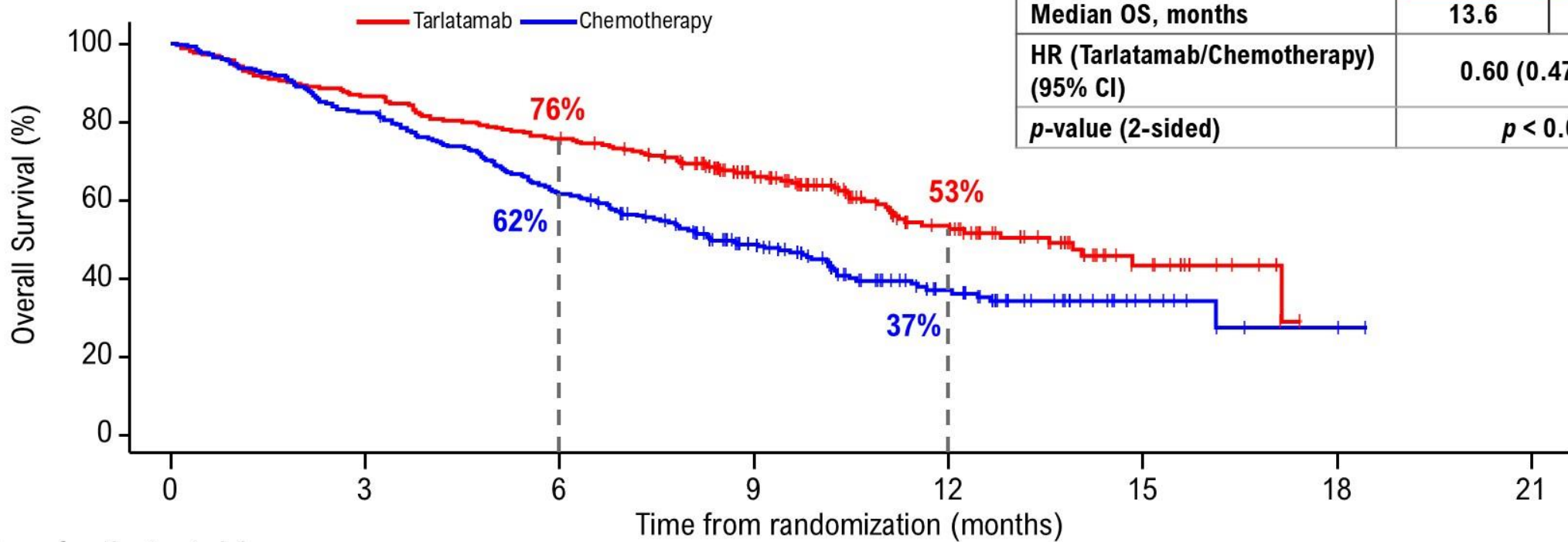


Primary Endpoint: Overall survival
Key Secondary Endpoints: Progression-free survival, patient-reported outcomes
Other Secondary Endpoints: Objective response, disease control, duration of response, safety

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

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

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



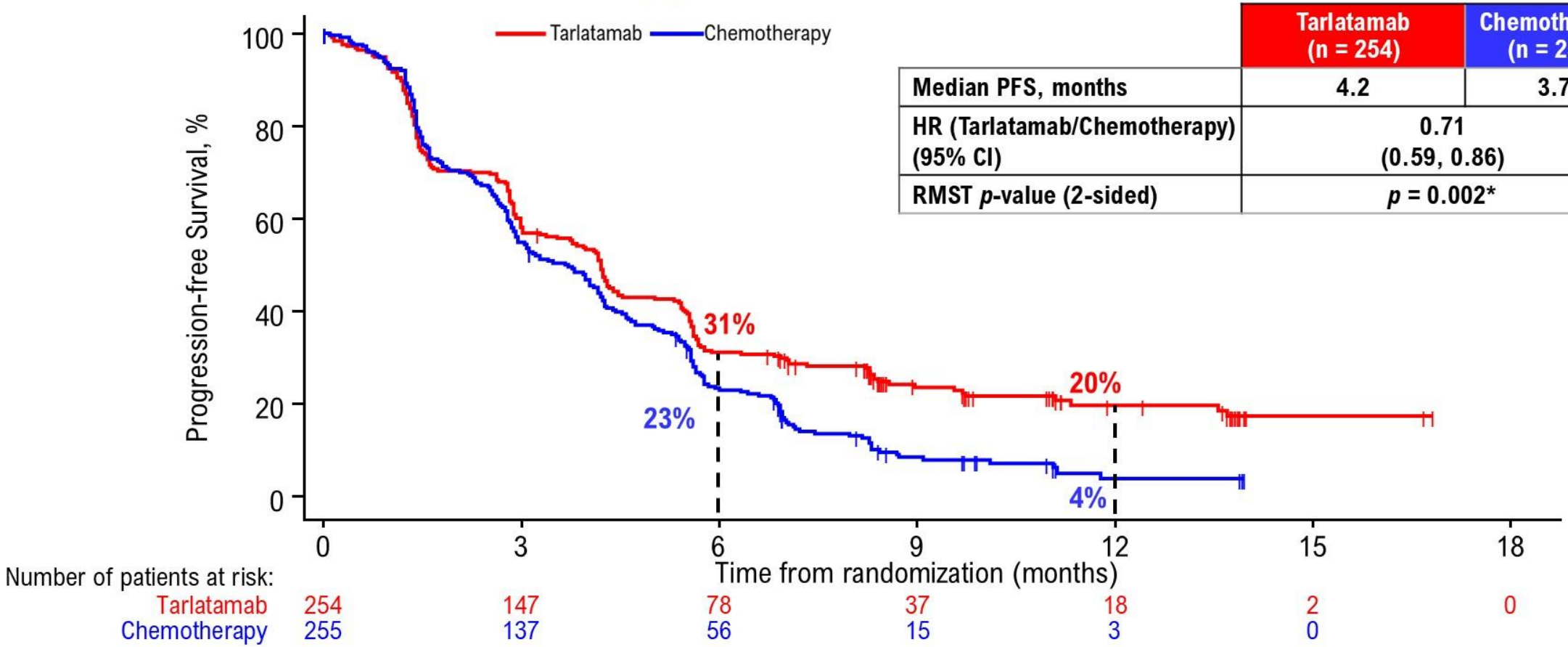
Number of patients at risk:

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

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

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.

Summary

- 1. NSCLC
  - Systematic EBUS & EUS for N2 subdivision
  - EGFR, ALK, and PD-L1 : TAT
  - Perioperative Tx : IO+CTx
  - Adjuvant Tx : Alectinib
  - CCRTx -> Osimertinib consolidation
  - Advanced Tx : Exon 20ins, ROS-1, HER2, NRG1

- 2. SCLC
  - LS : Durvalumab consolidation
  - ES : Atezolizumab+Lurbinectedin maintenance and Tarlatamab

의료에 신뢰를 더하다. JBUH+

감사합니다.