Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Therapeutic Targets Beyond EGFR for Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, June 30, 2026

5:00 PM – 6:00 PM ET

Faculty

John V Heymach, MD, PhD

Maurice Pérol, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

Faculty

John V Heymach, MD, PhD
Professor and Chair
Thoracic/Head and Neck Medical Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Maurice Pérol, MD
Head of Thoracic Oncology Program
Department of Medical Oncology
Léon Bérard Centre
Lyon, France

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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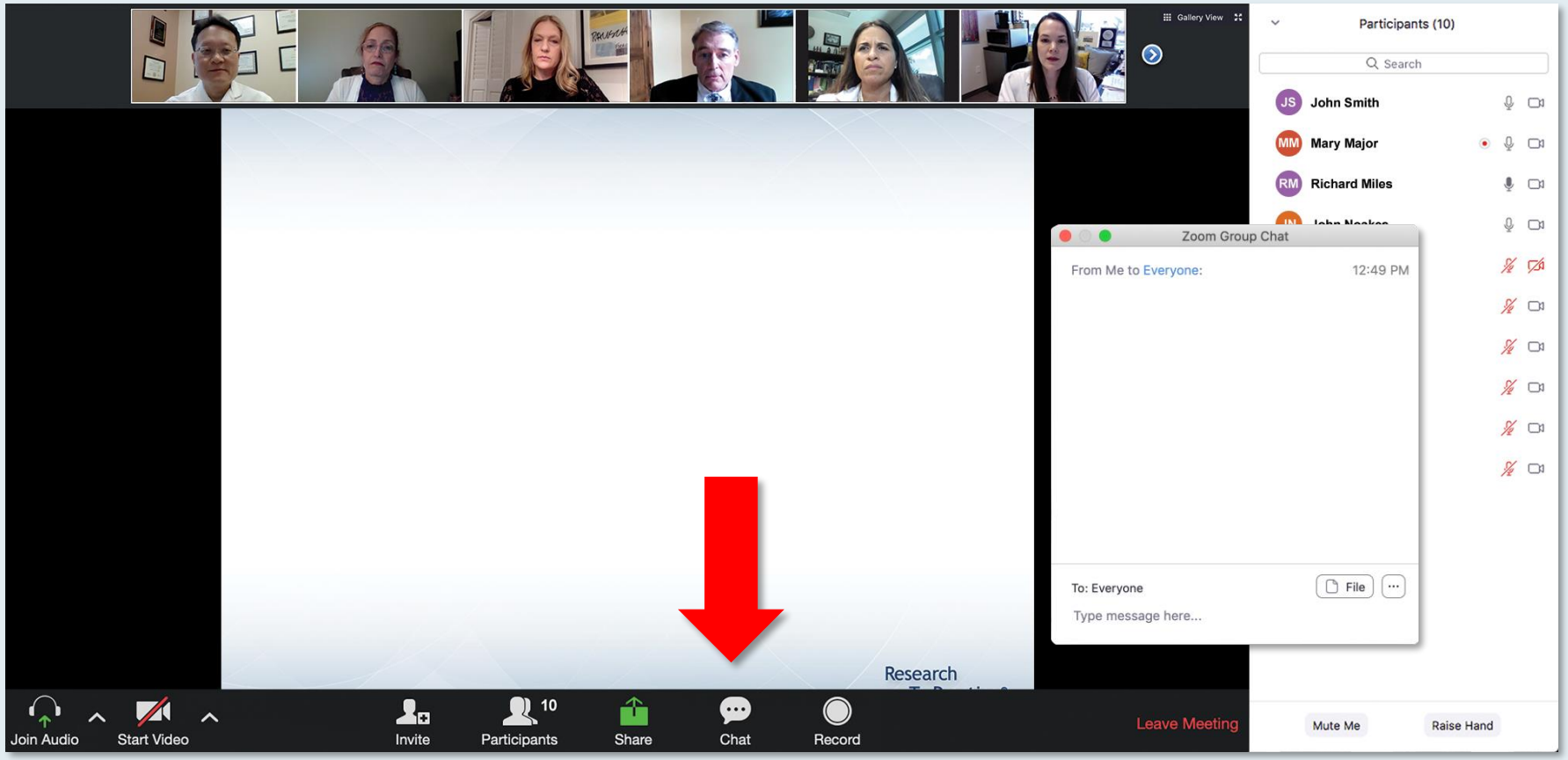
We Encourage Clinicians in Practice to Submit Questions



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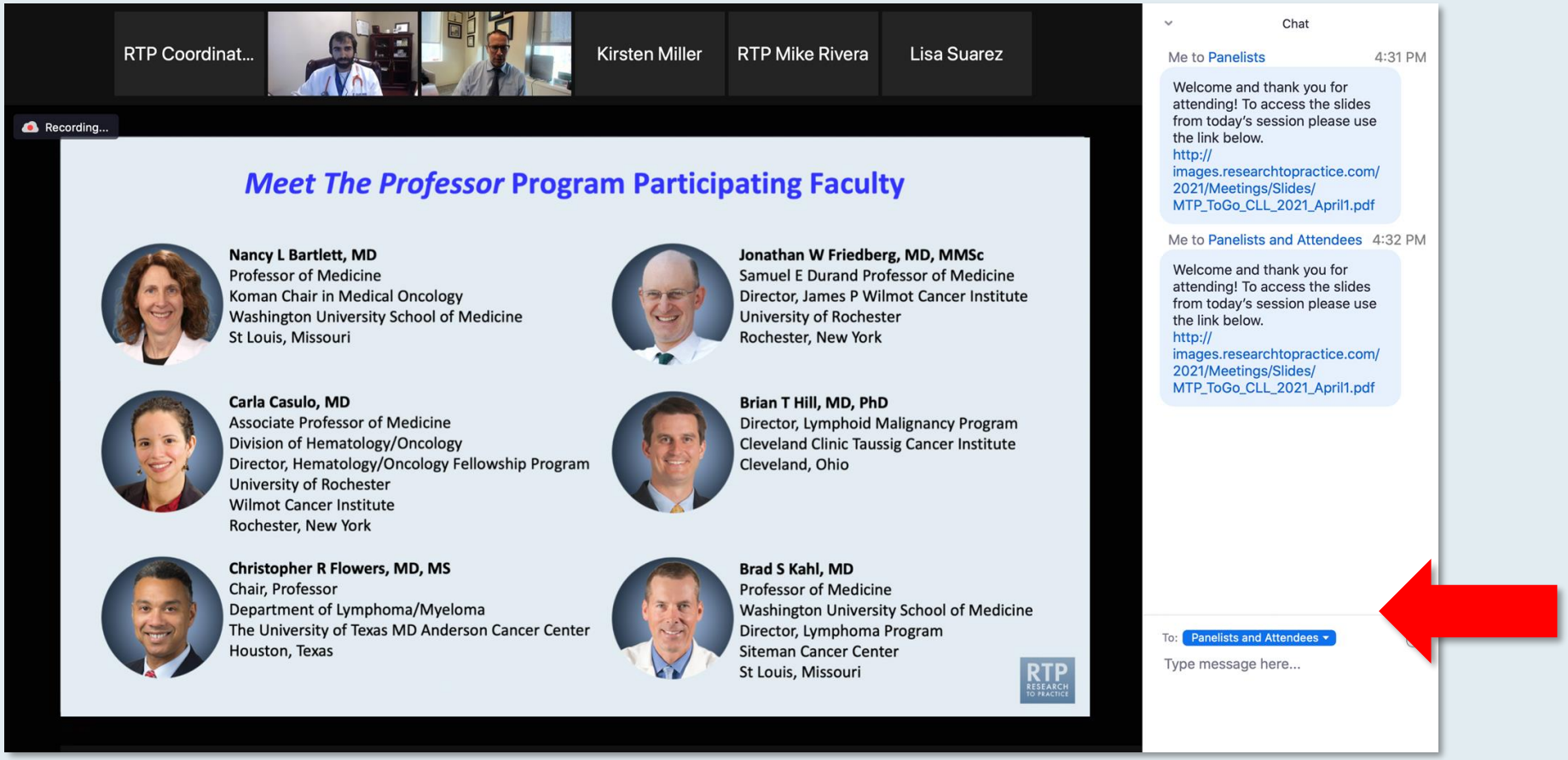

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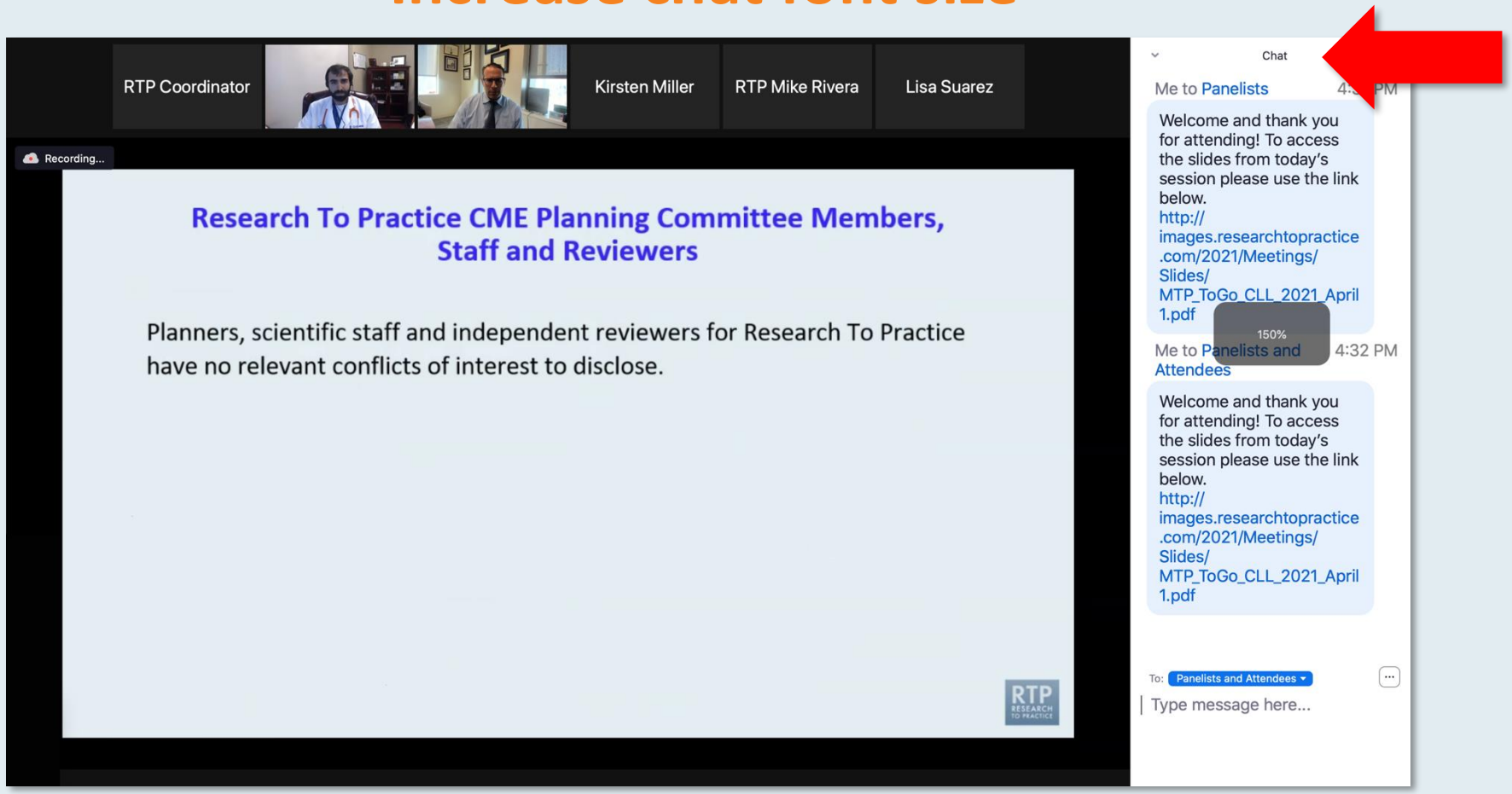

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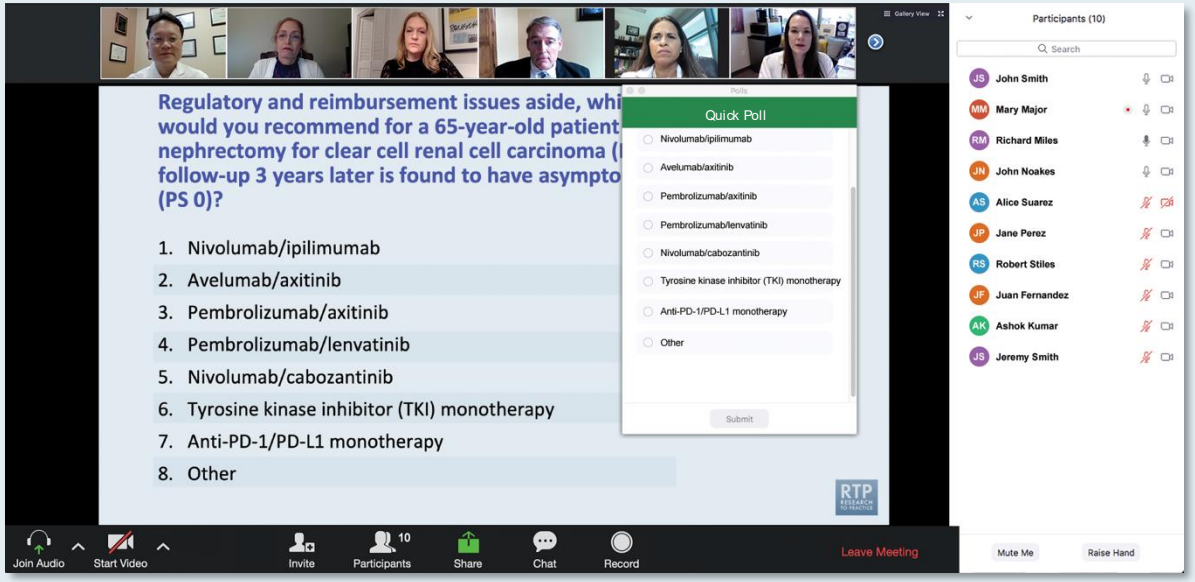

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WITH DR NEIL LOVE

EGFR-Mutant Non-Small Cell Lung Cancer — Year in Review Series on Relevant New Datasets and Advances

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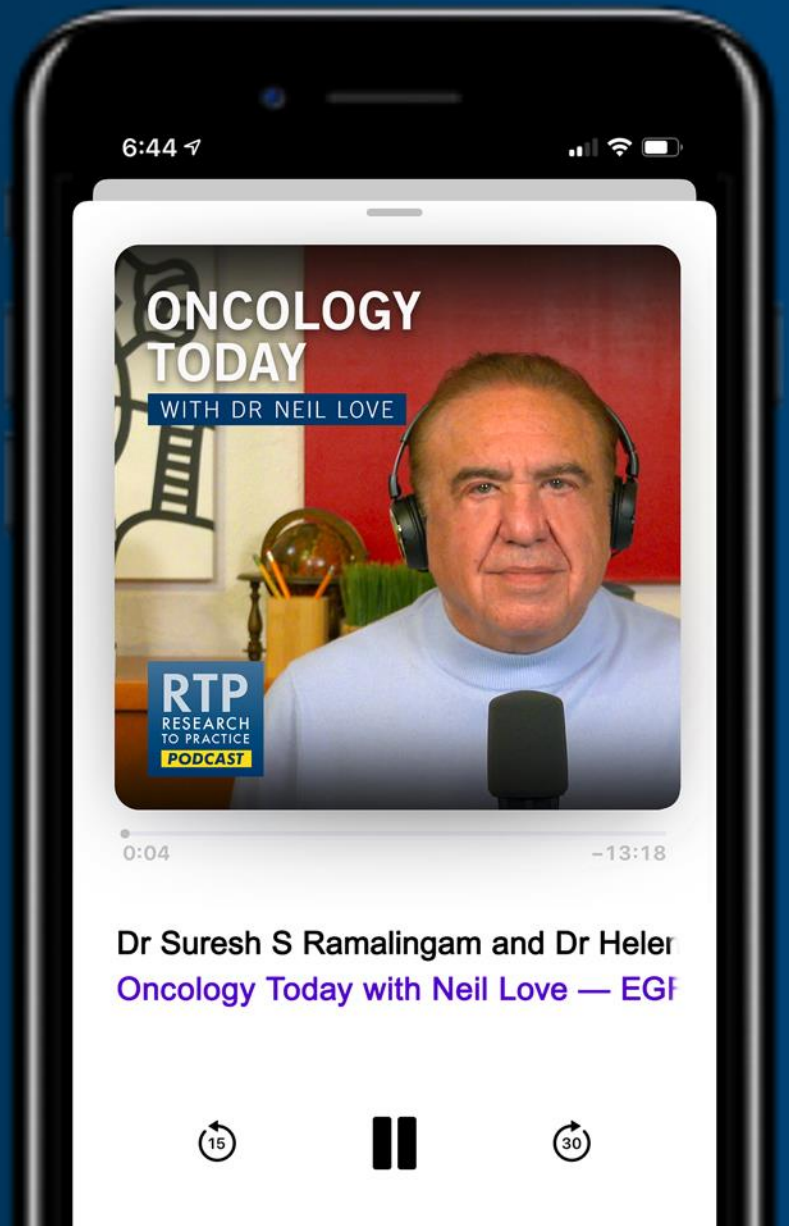

Patterns of Care: Exploring How Community Oncologists Manage HR-Positive, HER2-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 1, 2026

5:00 PM – 6:00 PM ET

Faculty

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Reshma L Mahtani, DO

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

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Neil Love, MD

RTP Year in Review 2026

Patterns of Care: Exploring How Community Oncologists Manage Metastatic Triple-Negative Breast Cancer

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Professor Peter Schmid, FRCP, MD, PhD

Melinda Telli, MD, FASCO

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Join Us In Person or Virtually

Integrating New Advances into the Care of Patients with Cancer

A Multitumor Symposium in Partnership with the American Oncology Network

Saturday, August 22, 2026

JW Marriott Nashville | Nashville, Tennessee

Chronic Lymphocytic Leukemia
9:00 AM – 9:50 AM CT

Gastroesophageal Cancers
9:50 AM – 10:40 AM CT

Gynecologic Cancers
10:55 AM – 11:45 AM CT

Diffuse Large B-Cell Lymphoma
12:35 PM – 1:25 PM CT

Lung Cancer
1:25 PM – 2:15 PM CT

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Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

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MODULE 5: **ROS1 Fusions**

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Information on how to obtain CME, ABIM MOC and ABS credit will be provided in the Zoom chat room.
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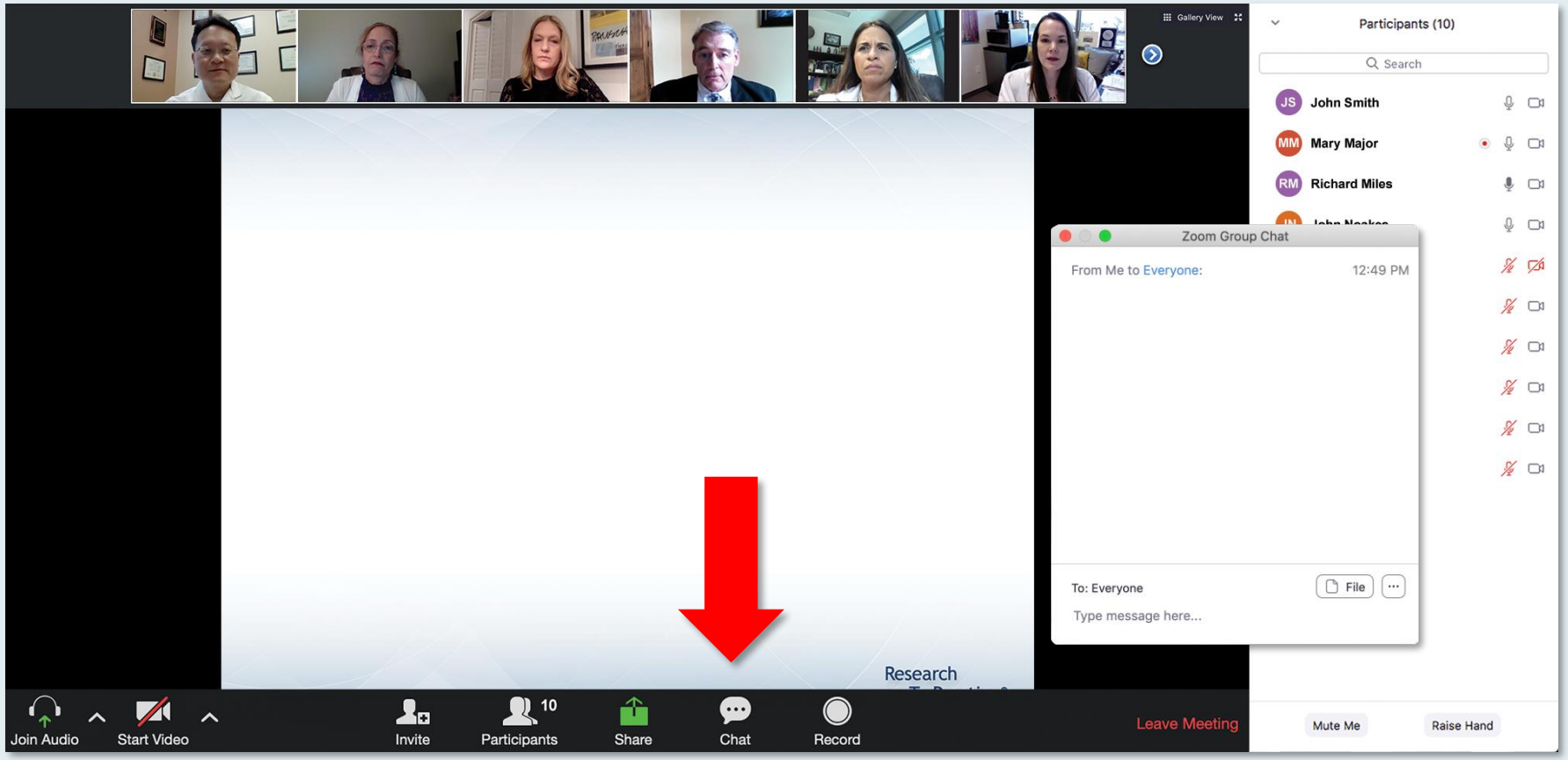

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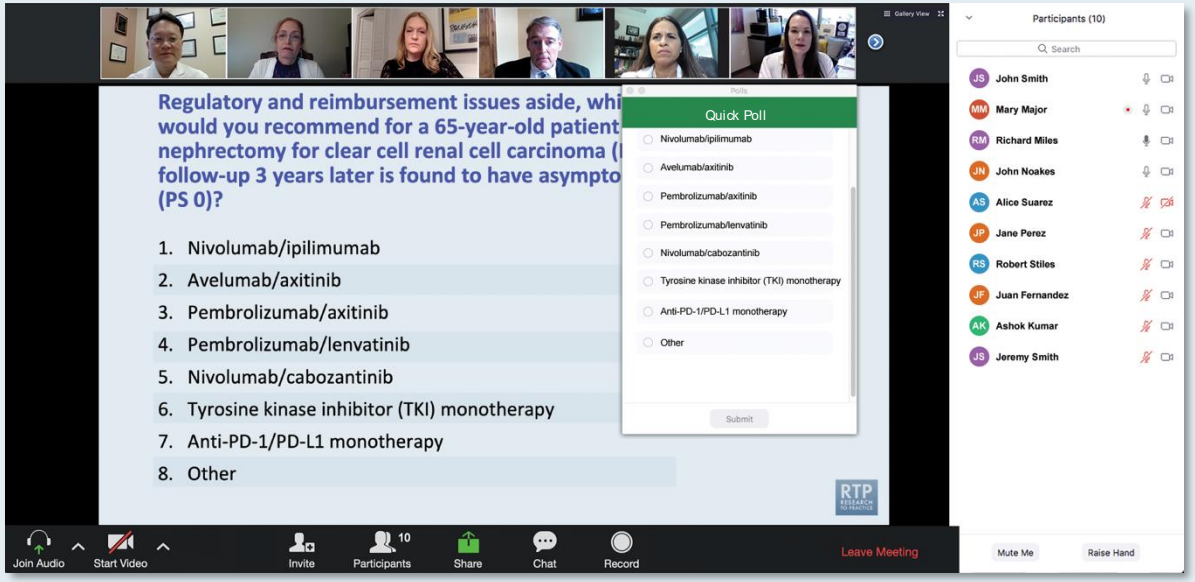

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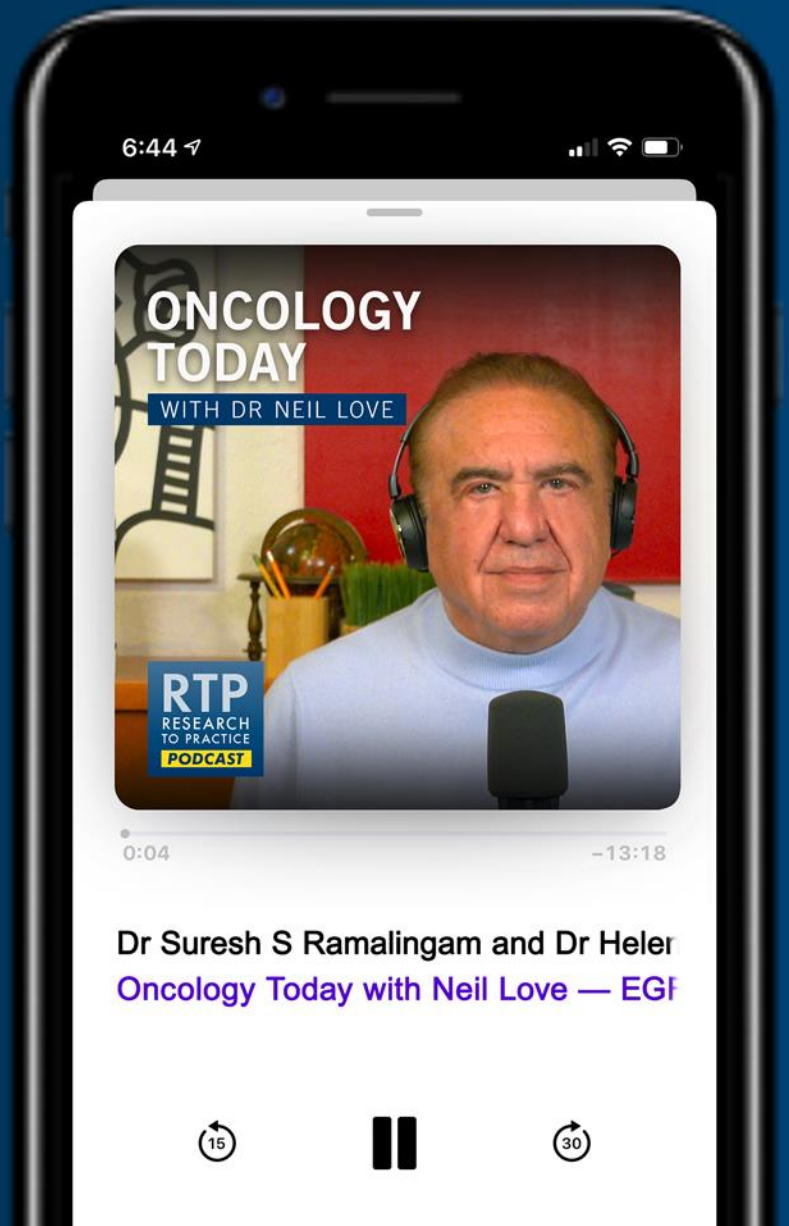

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Therapeutic Approaches Targeting HER2, MET and KRAS G12C

John Heymach, M.D., Ph.D.
Chair, Dept. of Thoracic/Head and Neck Medical Oncology
Ruth Legett Jones Distinguished Chair

Update in Therapeutic Approaches Targeting ALK, ROS1 and RET

Maurice Pérol
Department of Medical Oncology
Léon Bérard Cancer Center
Lyon, France

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Key Datasets

John V Heymach, MD, PhD

- Heymach JV et al. **Zongertinib** in **previously treated *HER2*-mutant** non-small-cell lung cancer. *N Engl J Med* 2025;392(23):2321-33.
- Ruiter G et al. **Zongertinib** in patients with **previously treated HER2-mutant** NSCLC and **brain metastases** at baseline: **Beamion LUNG-1**. WCLC 2025;Abstract PT2.12.03.
- Heymach JV et al. **First-line zongertinib** in advanced **HER2-mutant** non-small-cell lung cancer. *N Engl J Med* 2026;394(17):1675-84.
- Loong HH et al. SOHO-01: **Updated safety and efficacy** of **sevabertinib** in patients with advanced **HER2-mutant** non-small cell lung cancer (NSCLC). ASCO 2026;Abstract 8622.
- Heymach JV et al. **Zongertinib** in **treatment-naïve** patients with **HER2-mutant** NSCLC, including those with **active brain metastases: Beamion LUNG-1**. ELCC 2026;Abstract 6MO.
- Jänne PA et al. **Final analysis** results and patient-reported outcomes from DESTINY-Lung02 — A dose-blinded, randomized, phase 2 study of **trastuzumab deruxtecan** in patients with **HER2-mutant** metastatic NSCLC. *J Thorac Oncol* 2025;20(12):1814-28.
- Planchard D et al. **Trastuzumab deruxtecan** in patients with **HER2-overexpressing** NSCLC: Results from part 1 of the open-label, multicenter, phase **1b DESTINY-Lung03 trial**. *J Thorac Oncol* 2026; 21(5):103541.

Key Datasets

John V Heymach, MD, PhD (continued)

- Barlesi F et al. **Adagrasib** versus docetaxel in **KRAS^{G12C}-mutated** non-small-cell lung cancer **(KRYSTAL-12)**: A randomised, open-label, phase 3 trial. *Lancet* 2025;406(10503):615-26.
- Negrao MV et al. Efficacy and safety of **1L olomorasib + chemoimmunotherapy** in **KRAS G12C-mutant** NSCLC: Results from **LOXO-RAS-20001 and SUNRAY-01**. WCLC 2025;Abstract OA08.02.
- Johnson ML et al. Efficacy and safety of **1L olomorasib plus pembrolizumab** in **KRAS G12C-mutant** NSCLC: Results from **LOXO-RAS-20001 and SUNRAY-01**. WCLC 2025;Abstract MA02.06.
- Skoulidis F et al. **First-line (1L) divarasib plus pembrolizumab (pembro)** in advanced or metastatic ***KRAS* G12C+** non-small cell lung cancer (NSCLC): Results from the **Krascendo-170** study. ASCO 2026;Abstract 8510.
- Sacher AG et al. Single-agent **divarasib** in patients with **KRAS G12C-positive** non-small cell lung cancer: **Long-term follow-up** of a phase I study. *J Clin Oncol* 2025;43(30):3249-53.
- Girard N et al. **Telisotuzumab vedotin** monotherapy in patients with **previously treated c-Met protein–overexpressing** nonsquamous EGFR wildtype advanced NSCLC: **Updated analysis** of the **LUMINOSITY** trial. ELCC 2025;Abstract 18P.

Key Datasets

Maurice Pérol, MD

- Dziadziuszko R et al. **Updated results** from the phase **III ALINA study** of **adjuvant alectinib** vs chemotherapy (chemo) in patients (pts) with **early-stage ALK+** non-small cell lung cancer (NSCLC). ESMO 2025;Abstract 1787MO.
- Peters S et al. **Alectinib** versus crizotinib in **previously untreated ALK-positive** advanced non-small cell lung cancer: **Final overall survival analysis** of the phase III **ALEX** study. *Ann Oncol* 2026 Jan;37(1):92-103.
- Mok T et al. **Lorlatinib** vs crizotinib as **first-line treatment** for advanced ***ALK*+** non-small cell lung cancer: 7-year update from the phase 3 **CROWN** study. ASCO 2026;Abstract 8502.
- Lin J et al. **ALKOVE-1**: Efficacy and safety of **neladalkib** in patients with **advanced *ALK*+** NSCLC. ASCO 2026;Abstract 8503.
- Cho BC et al. **Repotrectinib** in patients with **ROS1 fusion-positive (ROS1+)** NSCLC: **Long-term follow-up** from the phase 1/2 **TRIDENT-1** trial. WCLC 2025;Abstract MA02.03.
- Bazhenova L et al. **Taletrectinib** in **TKI-naïve** patients with **ROS1+** NSCLC: **Updated data** from **TRUST-I and TRUST-II**. AACR 2026;Abstract CT300.
- Liu G et al. **Taletrectinib** in **TKI-pretreated patients** with **ROS1+** non-small cell lung cancer: **Updated data** from **TRUST-I and TRUST-II**. AACR 2026;Abstract CT244.

Key Datasets

Maurice Pérol, MD (continued)

- Drilon AE et al. Pivotal **ARROS-1 efficacy and safety** data: Zidesamtinib in TKI pre-treated patients with advanced/metastatic ROS1+ NSCLC. WCLC 2025;Abstract PL02.15.
- Gautschi O et al. **Selpercatinib** in **RET fusion-positive** non-small cell lung cancer: Final safety and efficacy, including overall survival, from **the LIBRETTO-001 phase I/II trial**. *J Clin Oncol* 2025;43(15):1758-64.
- Goldman J et al. Event-free survival with **adjuvant selpercatinib** in stage IB-IIIA *RET* fusion-positive NSCLC: Primary results of the phase 3 **LIBRETTO-432 trial**. ASCO 2026;Abstract LBA3.
- Besse B et al. **Final efficacy and safety data** from the phase I/II **ARROW study** of **pralsetinib** in patients with advanced ***RET* fusion-positive** non-small cell lung cancer. *J Clin Oncol* 2026 May;44(13):1190-7.
- Popat S et al. Efficacy and safety of **pralsetinib** as **first-line treatment** of ***RET* fusion-positive** advanced or metastatic non–small cell lung cancer (NSCLC): The phase 3 **AcceleRET-Lung study**. ASCO 2026;Abstract 8504.

Year in Review:
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INTRODUCTION: **Relative Impact of Targeted Treatment**

MODULE 1: **HER2 Alterations**

MODULE 2: **KRAS Mutations**

MODULE 3: **MET Overexpression**

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RTP Year in Review 2026

ROS1 TKIs in TKI-naive *ROS1* fusion+ NSCLC

	Crizotinib Profile 1001	Entrectinib ALKA 372-001 STARTRK-1 STARTRK-2	Ceritinib Korean Phase II	Brigatinib Barossa Phase II	Lorlatinib Phase I/II	Foritinib Phase IIb Cohort 1	Repotrectinib TRIDENT-1 Phase I/II	Taletrectinib TRUST I + II Phase II	Zidesamtinib ARROS Phase I/II
N	53	168	30	28	21	56	71	157	35
ORR	**72%**	**67.9%**	**67%**	**71.4%**	**62%**	**88%**	**79%**	**89.8%**	**89%**
Median PFS	**19.3 m**	**15.7 m**	**19.3 m**	**12.0 m**	**21.0 m**	**22.1 m**	**31.1 m**	**46.1 m**	**NR**
CNS activity IC-ORR	NR	25/48 (52.1%) Measurable and non-measurable	2/5 (40%) Measurable and non-measurable	0/3 Measurable	7/11 (64%) Measurable and non-measurable	19/21 (90%) Measurable and non-measurable	8/9 (89%) Measurable	13/17 (76.5%) Measurable	5/6 (83%) Measurable

Non-comparative data, for informational/descriptive purposes. Comparisons between trials should not be made due to differences in study design and patient populations.

Shaw A, Ann Oncol 2019; Fan Y, J Thorac Oncol 2022;17(suppl):Abstr MA13.04; Lim, JCO 2017; Shaw A, Lancet Oncol 2019; Drilon A, WCLC 2025; Li W, ELCC 2023. Krebs M, ESMO 2024; Pérol M, JCO 2025; Niho,S, ESMO Open 2024; Yang JJ, Lancet Oncol 2024; Lu S, Signal Transduct Target Ther 2023; Bazhenova L et al., AACR 2026.

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Therapeutic Targets Beyond EGFR for Non-Small Cell Lung Cancer

INTRODUCTION: Relative Impact of Targeted Treatment

MODULE 1: HER2 Alterations

MODULE 2: KRAS Mutations

MODULE 3: MET Overexpression

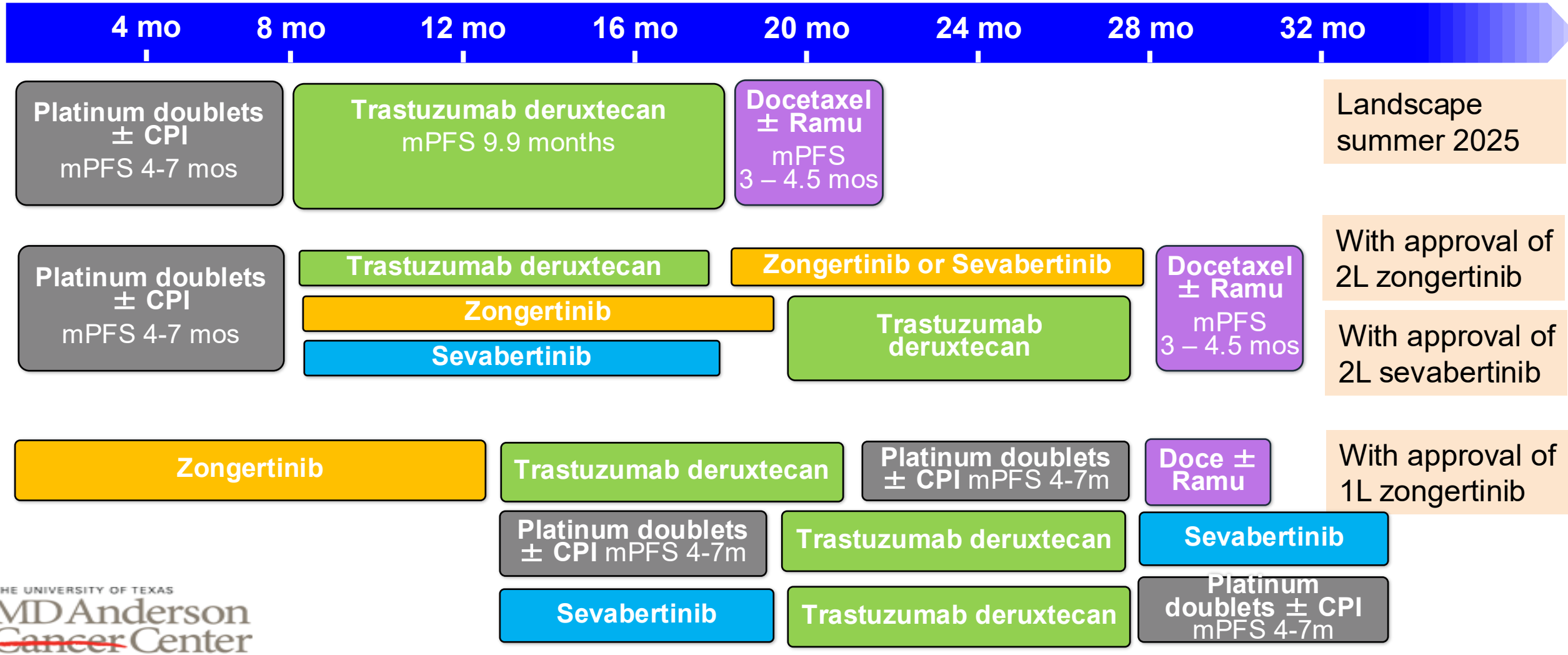
MODULE 4: ALK Fusions

MODULE 5: ROS1 Fusions

MODULE 6: RET Fusions

RTP Year in Review 2026

Evolution of the *HER2* mutant NSCLC landscape with new approvals: 1L, 2L zongertinib, 2L sevabertinib



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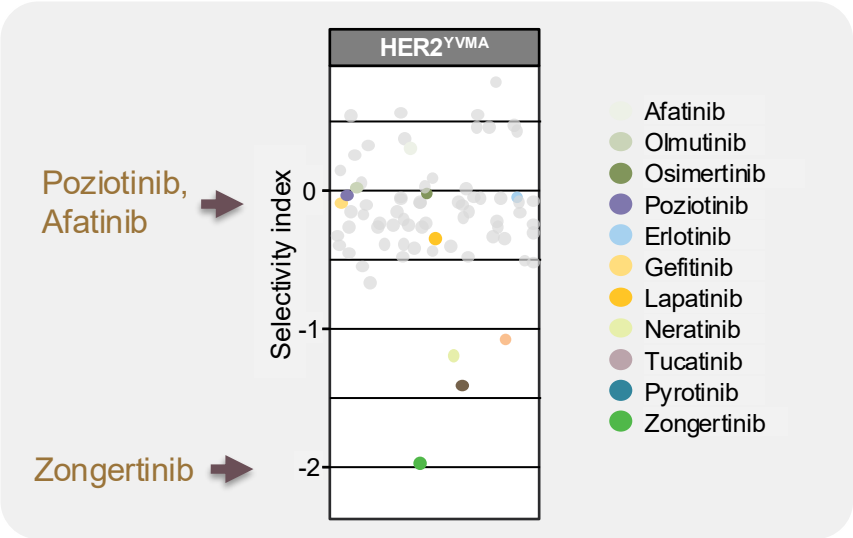
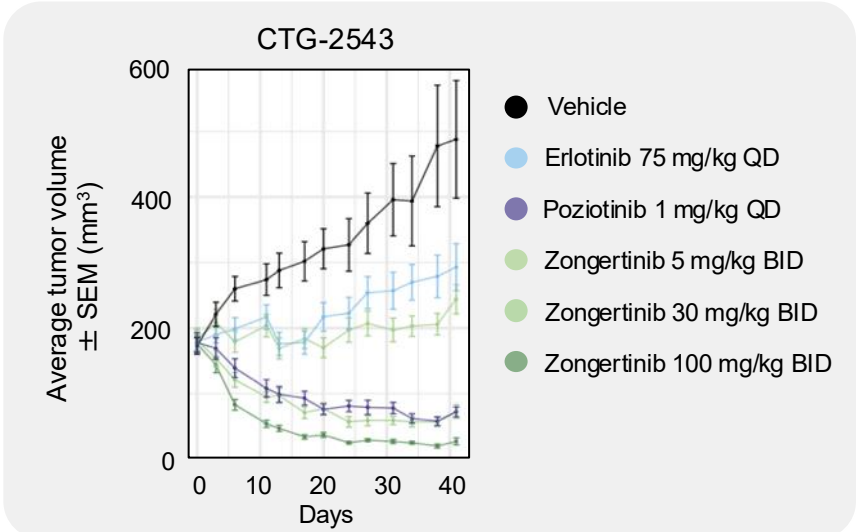
Zongertinib is an oral, HER2-specific, EGFR-sparing TKI

- Zongertinib is highly selective for mutant HER2 over EGFR wild-type[1]



- Zongertinib resulted in tumor regressions in a patient-derived NSCLC xenograft model carrying a *HER2* exon 20 insertion (HER2^{YVMA})[1]



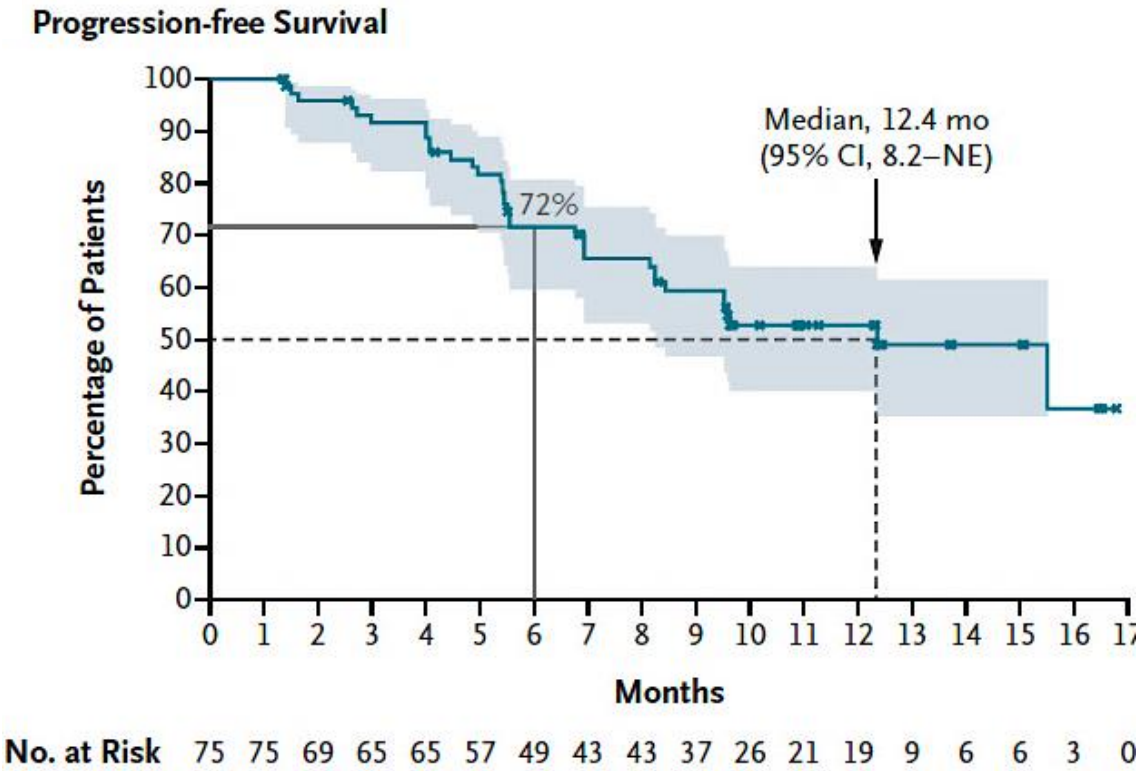
Zongertinib is a potent, covalent TKI that selectively inhibits HER2 while sparing EGFR wild-type, thereby potentially limiting associated toxicities

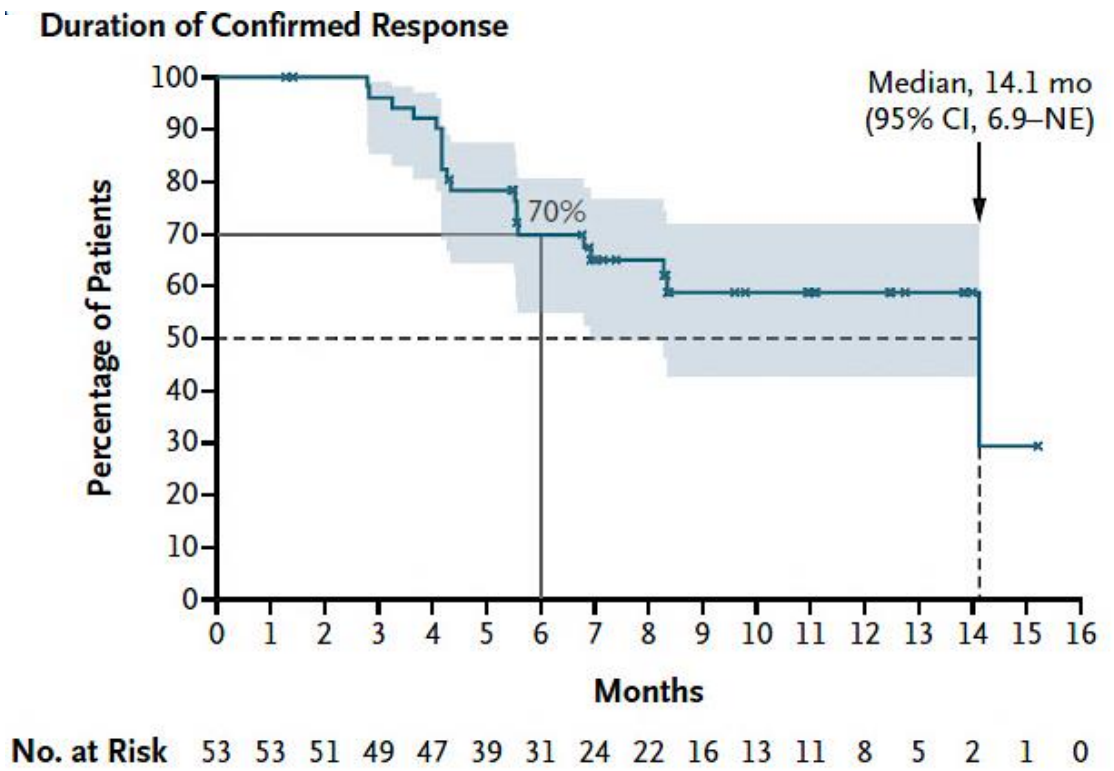
1. Wilding B et al. Cancer Discov. 2025;15:119–38

Zongertinib in patients with TKD *HER2* mutations (Cohort 1, N=75): median PFS and mDoR

mPFS: 12.4 months (8.2–NE)

mDOR: 14.1 months (6.9–NE)





Median follow-up was 11.3 months (95% CI, 10.2–12.3)

August 8, 2025: FDA grants accelerated approval to zongertinib for non-squamous NSCLC with HER2 TKD activating mutations

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Heymach et al. NEJM 2025

Zongertinib in previously treated *HER2*-mutant NSCLC with brain metastases at baseline

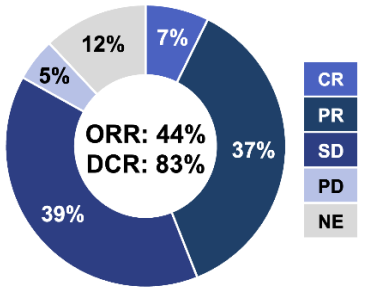
Confirmed intracranial response by RANO-BM

Pooled analysis of 58 patients with stable, asymptomatic or active brain metastases in Cohorts 1 and 4 (Cohort1: 28; Cohort 4: 30)*

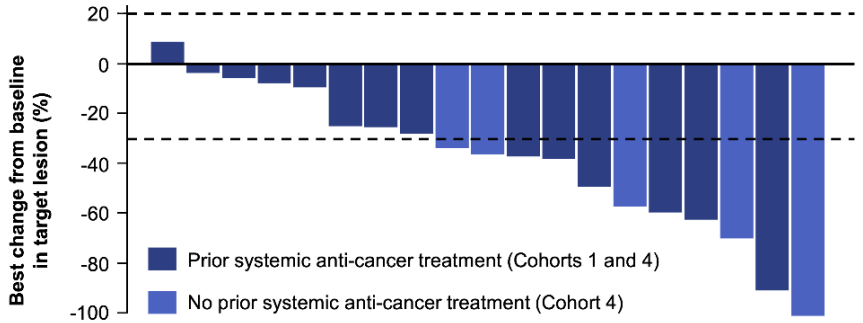
	n = 58
ORR, %	**41%**
CR, %	9
PR, %	33
DCR, %	**83%**
SD, %	41
PD, %	7
NE, %	10

Median PFS	95% CI
8.2 months	4.5–12.3

Pooled analysis of 41 patients who had not received prior brain radiotherapy in Cohorts 1 and 4



Median PFS	95% CI
8.1 months	4.1–12.3



Overall, 95% (18/19) of evaluable patients experienced a reduction in brain lesion size from baseline.

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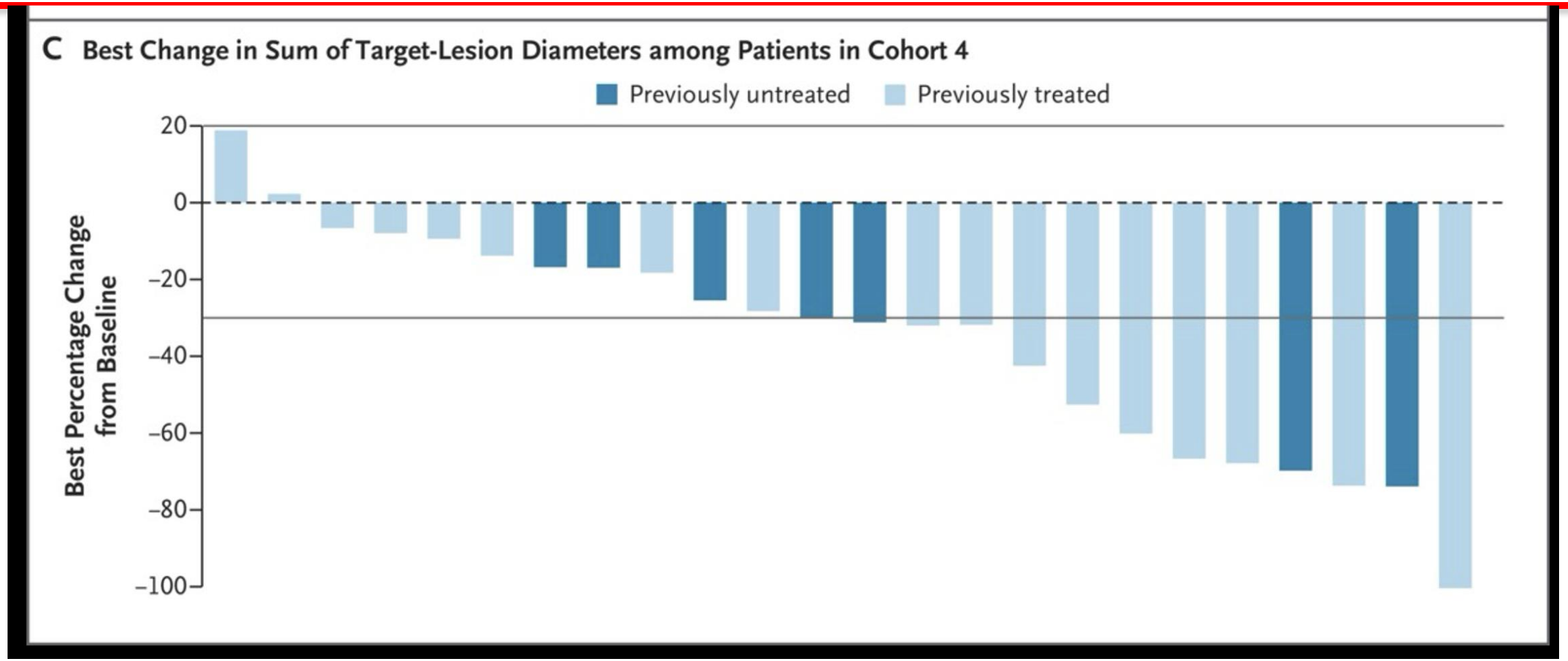
*Included patients who had received prior brain radiotherapy.

Ruiter G et al. WCLC 2025;Abstract PT2.12.03.

Zongertinib in previously treated *HER2*-mutant NSCLC with brain metastases



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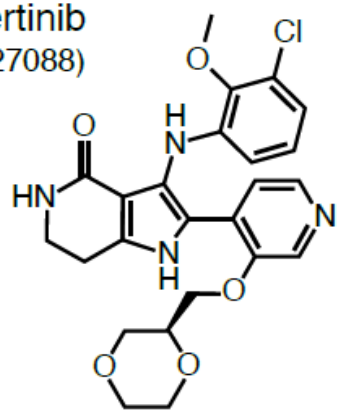
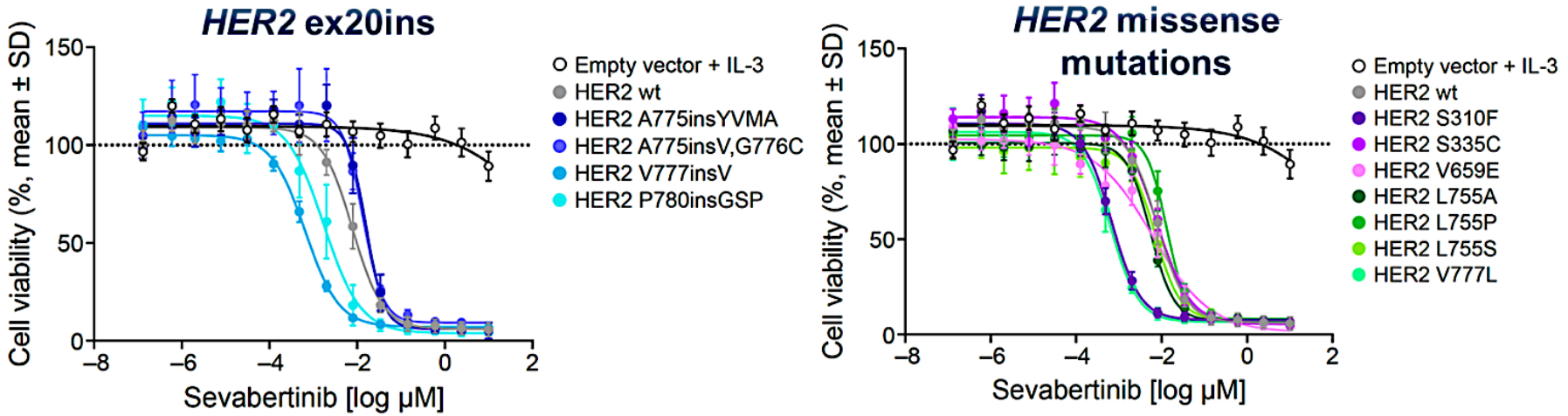
Heymach J et al. NEJM 2026;394:1675-1684.

Sevabertinib is an oral, reversible HER2 TKI

- 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
(BAY 2927088)





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1. Siegel F et al. Cancer Discov 2025;16(1):81-94. 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 June 2026.

Le et al., ESMO 2025

Sevabertinib in previously treated *HER2*-mutant NSCLC (SOHO1, Cohorts D, F)

Cohort D: Patients previously treated with systemic therapy but naïve to HER2 ex20ins-targeted therapy

Cohort F: Patients naïve to systemic treatment for locally advanced or metastatic disease

	Cohort D			Cohort F		
	Treated patients with non-squamous histology and *HER2* TKD mutation (*n*=70)	Treated patients with non-squamous histology and *HER2* YVMA mutation (*n*=49)	All treated patients (*n*=81)	Treated patients with non-squamous histology and *HER2* TKD mutation (*n*=69)	Treated patients with non-squamous histology and *HER2* YVMA mutation (*n*=55)	All treated patients (*n*=73)
ORR, % (95% CI)[a]	73 (61, 83)	78 (63, 88)	67 (55, 77)	75 (64, 85)	75 (61, 85)	75 (64, 85)
DCR, % (95% CI)[b]	84 (74, 92)	88 (75, 95)	81 (71, 89)	90 (80, 96)	89 (78, 96)	89 (80, 95)
mDoR, months (95% CI)	9.5 (6.3, 13.5)[c]	9.5 (6.3, 15.0)[d]	9.5 (6.3, 13.5)[e]	15.1 (8.8, NE[f])[c]	15.1 (8.8, NE[f])[d]	12.2 (8.8, NE[f])[e]
mPFS, months (95% CI)	9.6 (6.9, 14.5)	12.2 (6.9, 16.5)	8.3 (6.9, 12.3)	13.5 (10.0, NE[f])	16.4 (9.9, NE[f])	13.5 (10.0, NE[f])

[a]Patients with confirmed CR or PR; [b]Patients with confirmed CR or PR or stable disease for ⩾12 weeks; [c]Subset of patients with confirmed CR or PR (Cohort D, *n*=51; Cohort F, *n*=52); [d]Subset of patients with confirmed CR or PR (Cohort D, *n*=38; Cohort F, *n*=41); [e]Subset of patients with confirmed CR or PR (Cohort D, *n*=54; Cohort F, *n*=55); [f]Value cannot be estimated
CI, confidence interval; CR, complete response; DCR, disease control rate; mDoR, median duration of response; mPFS, median progression-free survival; NE, not estimable; PR, partial response

Nov. 19, 2025: Sevabertinib receives FDA approval for HER mutant NSCLC (TKD mutations)

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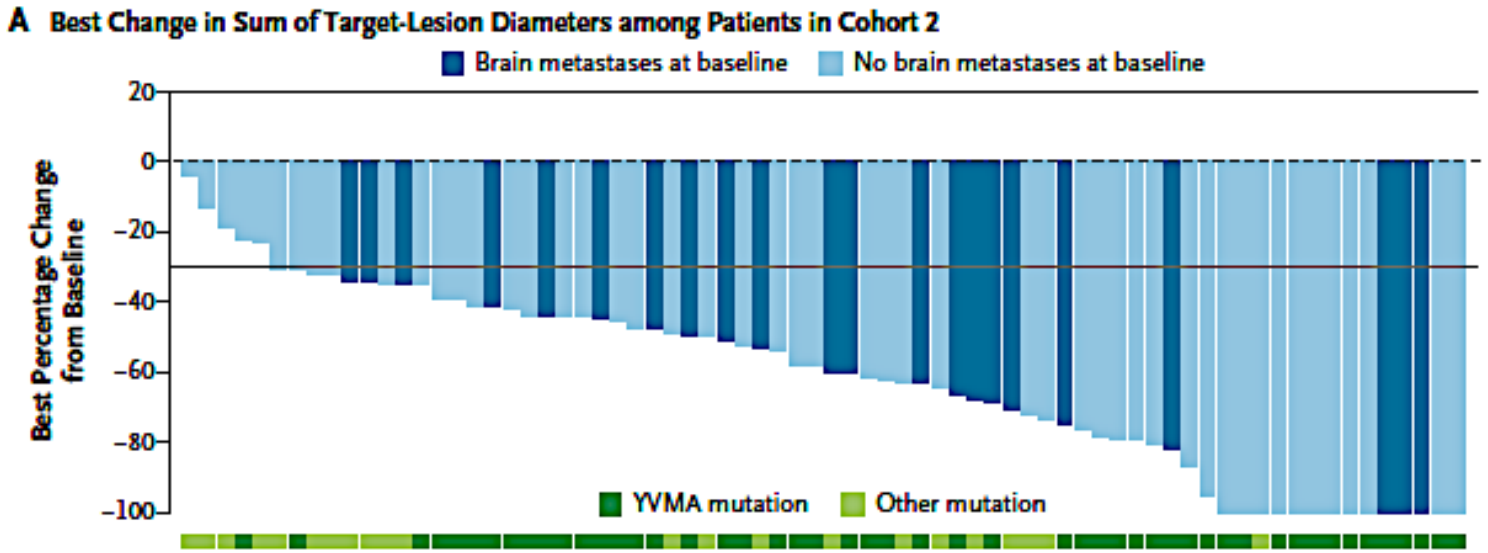
Loong HH et al. ASCO 2026; abstract 8622.

Zongertinib in 1L *HER2*-mutant NSCLC

ORR 76%

Confirmed response by BICR (RECIST v1.1)	Cohort 2: Treatment-naïve patients N = 74
ORR	**76%**
CR, n (%)	8 (11)
PR, n (%)	48 (65)
DCR	**96%**
SD, n (%)	15 (20)
PD, n (%)	1 (1)*

- Median time to objective response was 1.4 months (95% CI, 1.1 to 6.9)



February 26, 2026: FDA granted accelerated approval to zongertinib as 1L for HER2 mutant NSCLC harboring HER2 (ERBB2) tyrosine kinase domain activating mutations.

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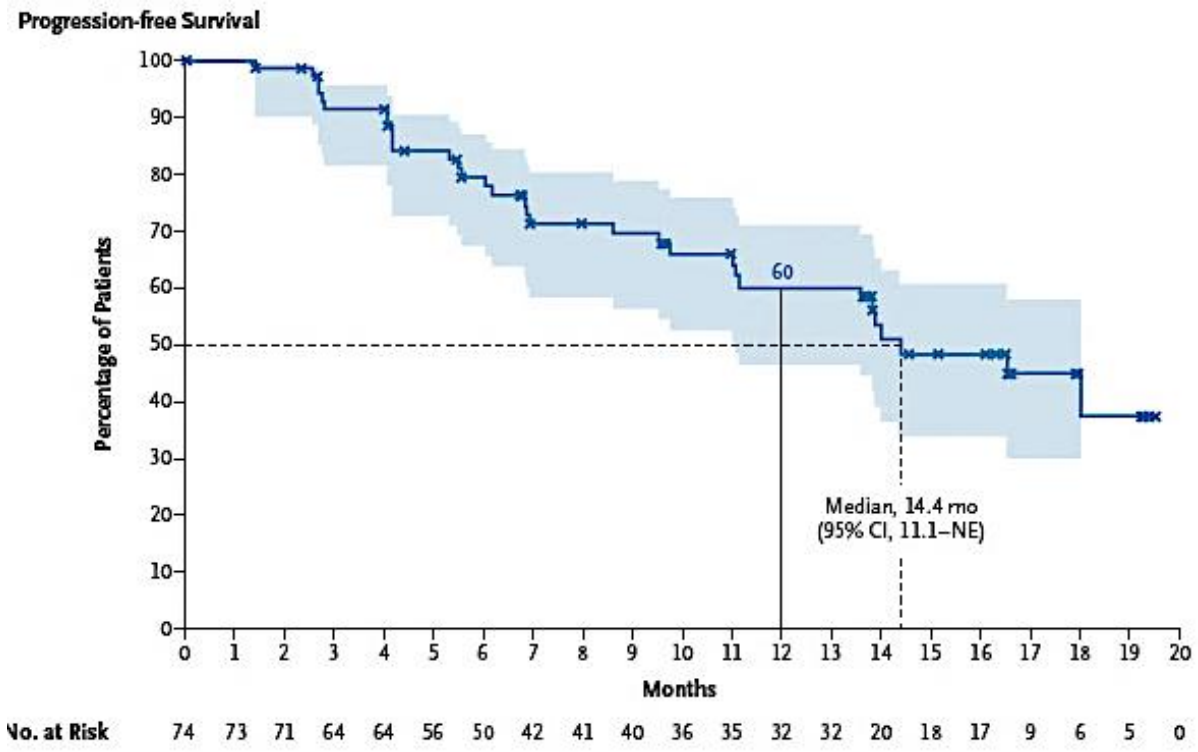
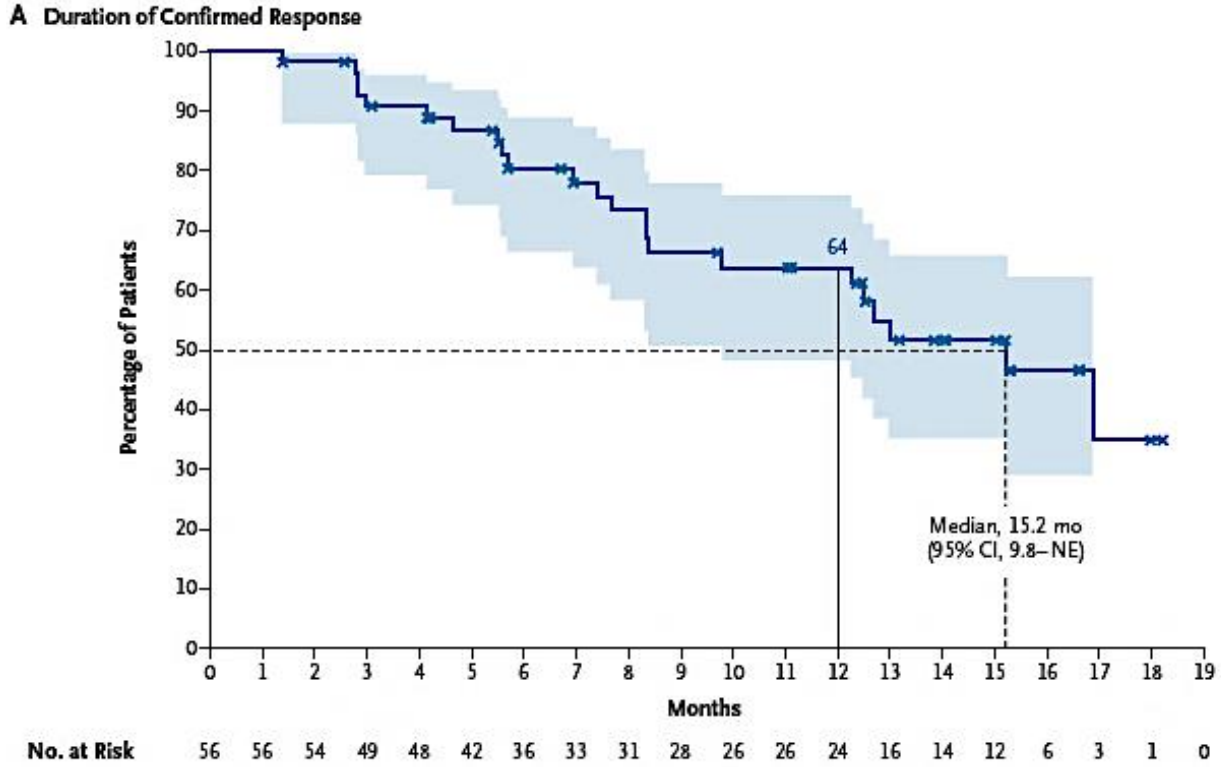
Heymach NEJM 2026; Heymach ELCC 2026

Zongertinib in 1L *HER2*-mutant NSCLC

mPFS 14.4 months



mDoR 15.2 months



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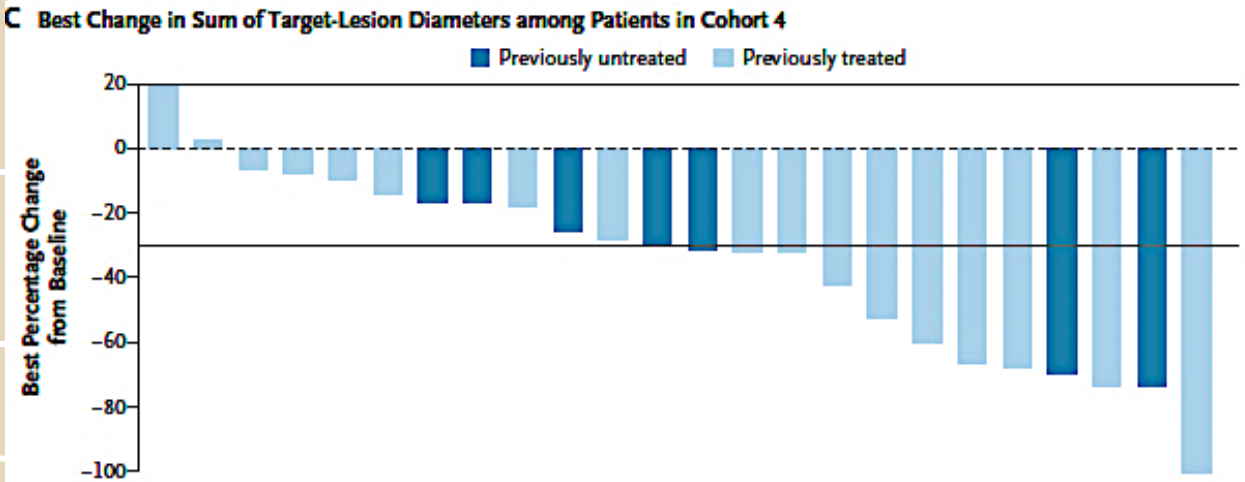
Heymach NEJM 2026; Heymach ELCC 2026

Zongertinib in 1L *HER2*-mutant NSCLC: Intracranial Tumor Response

ORR 47% (59% in those with no prior RT)

Confirmed intracranial response by BICR (RANO-BM)	Cohort 4: Active brain metastases	
	N = 30	No prior brain RT and confirmed measurable intracranial disease n = 17
ORR	**47%**	**59%**
CR, n (%)	2 (7)	1 (6)
PR, n (%)	12 (40)	9 (53)
DCR	**87%**	**94%**
SD, n (%)	12 (40)	6 (35)
NE, n (%)	4 (13)	1 (6)
Median DoR	**6.9 months**	**6.2 months**
95% CI	2.9–NE	2.7–NE
Median PFS	**8.2 months**	NE
95% CI	4.1–11.3	NE



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Heymach NEJM 2026; Heymach ELCC 2026

Beamion LUNG-1 Study Design

Phase Ib (dose expansion): patients with advanced *HER2*-mutant NSCLC
In Phase Ia, the MTD was not reached at 360 mg QD
In Phase Ib, the selected dose after interim futility analysis was zongertinib 120 mg QD

Current analysis

Cohort 2 — **Treatment-naïve patients with TKD mutations**

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

Cohort 4 — **Treatment-naïve or previously treated patients with TKD mutations and active brain metastases at baseline**

Primary endpoint: Objective response in CNS lesions by BICR (RANO-BM)

Here we present the efficacy and safety of zongertinib 120 mg as 1L therapy, as well as findings in patients with active brain metastases

Additional cohorts not included in the current analysis

Cohort 1 — Previously treated patients with TKD mutations

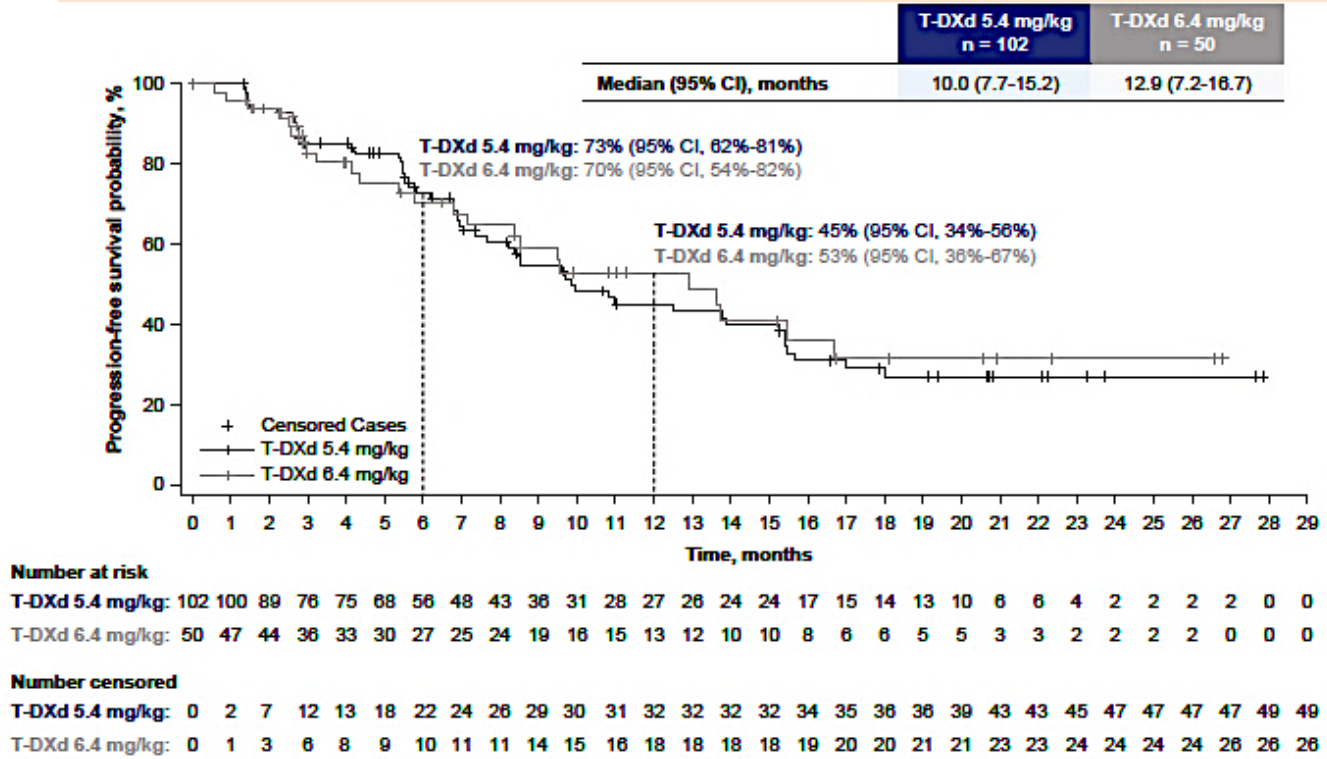
Cohort 3 — Previously treated patients with non-TKD mutations

Cohort 5 — Patients previously treated with HER2-directed ADC and with TKD mutations

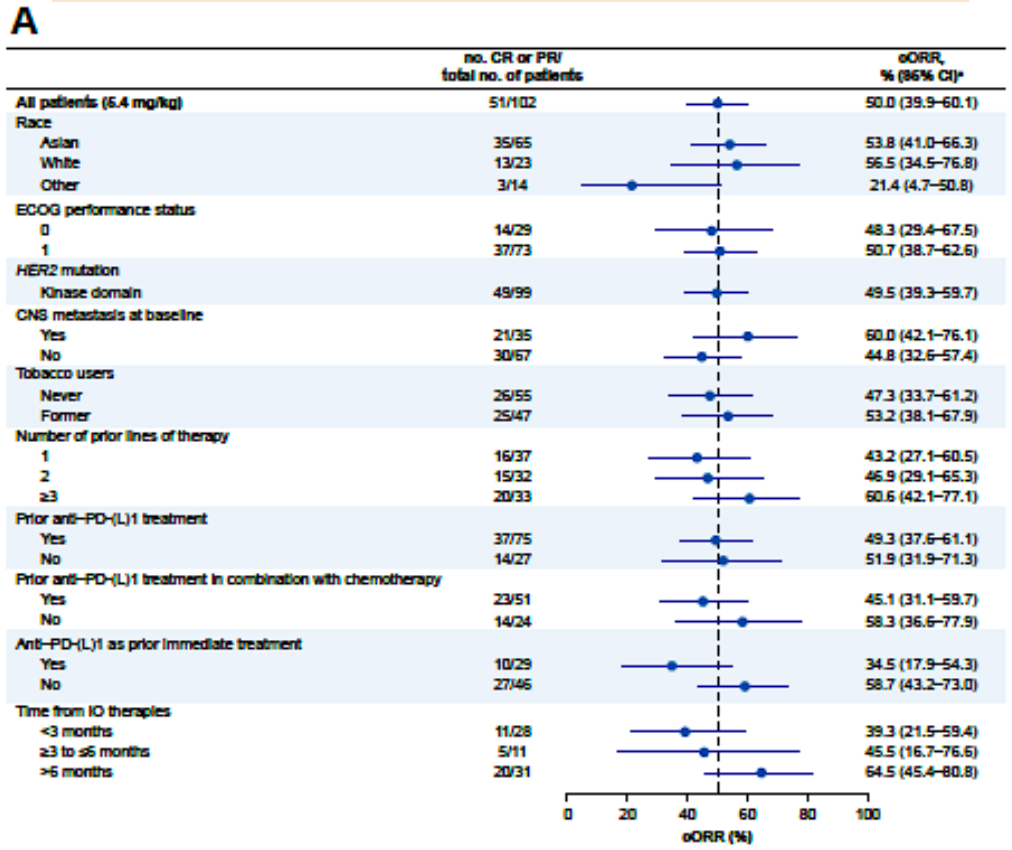
Heymach et al, ELCC 2026

Final analysis from DESTINY-Lung02-A RP2 Study of Trastuzumab Deruxtecan in 2L+ *HER2*-mutant NSCLC

mPFS, 5.4 mg/kg: 10.0 (7.7-15.2)
Confirmed ORR: 50%



ORR by subgroups



Janne et al JTO 2025

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Final analysis from DESTINY-Lung02-A RP2 Study of Trastuzumab Deruxtecan in 2L+ *HER2*-mutant NSCLC

ILD: 14.9% (all grade) at 5.4 mg/kg dose

Table 3. Adjudicated Drug-Related ILD[a]

Adjudicated Drug-Related ILD Variable	T-DXd 5.4 mg/kg n = 101[b]	T-DXd 6.4 mg/kg n = 50[b]
Any grade, n (%)	15 (14.9)	16 (32.0)
Grade 1	4 (4.0)	3 (6.0)
Grade 2	9 (8.9)	11 (22.0)
Grade 3	1 (1.0)	1 (2.0)
Grade 4	0	0
Grade 5	1 (1.0)[c]	1 (2.0)[c]
Grade ≥3	2 (2.0)	2 (4.0)
Outcome of ILD events,[d,e] n/N (%)		
Fatal	1/15 (6.7)	1/16 (6.3)
Not recovered/not resolved	3/15 (20.0)	6/16 (37.5)
Recovering/resolving	1/15 (6.7)	0
Recovered/resolved with sequelae	0	1/16 (6.3)
Recovered/resolved	10/15 (66.7)	8/16 (50.0)

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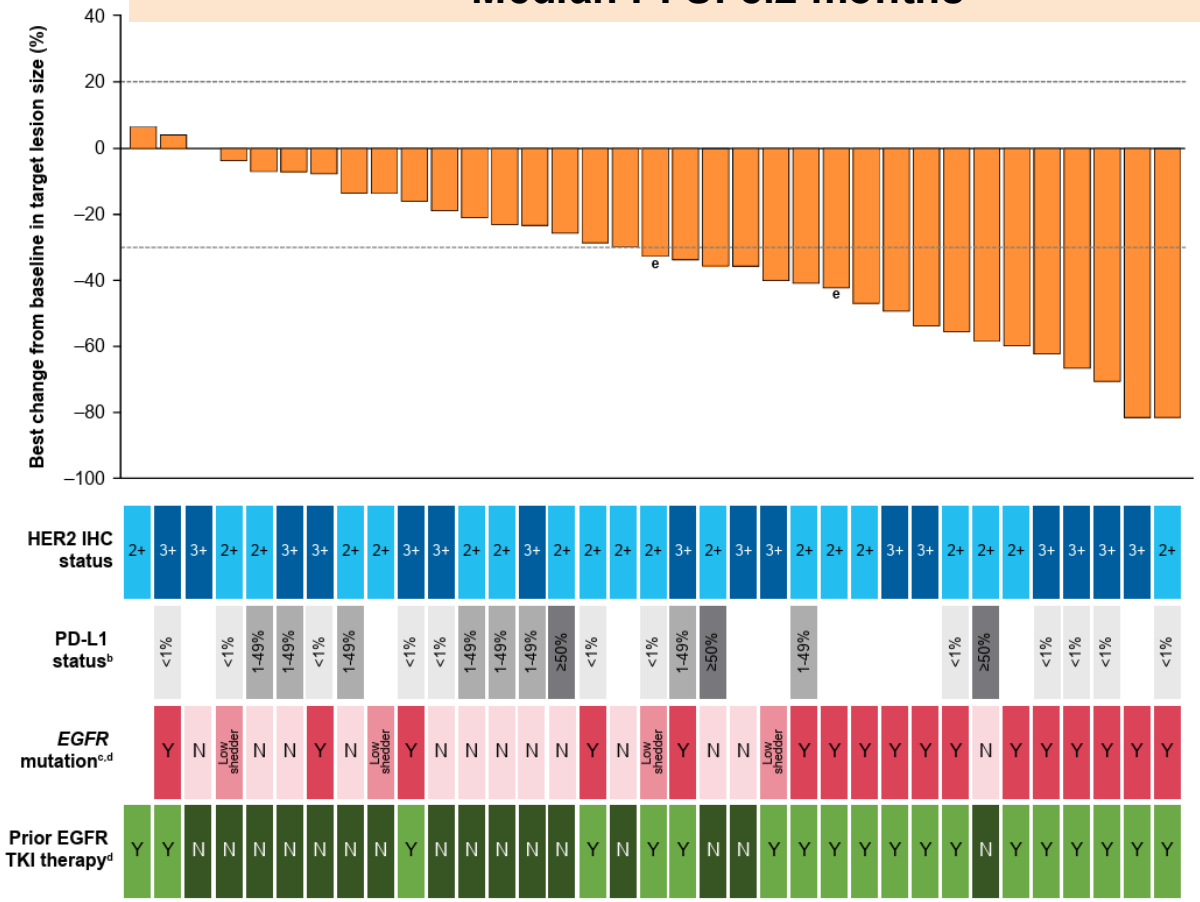
Janne et al JTO 2025

Trastuzumab deruxtecan in HER2-overexpressing NSCLC: DESTINY-Lung03 (part 1, T-DXd mono)

Confirmed ORR: 44.4%; Median DOR: 11.0 months; Median PFS: 8.2 months



- Drug-related AEs: 34 (94.4%)
- Grade ≥3 drug-related AEs: 15 (41.7%)
- Drug-related SAEs: 6 (16.7%)
- Discontinuation: 3 (8.3%)
- One patient (2.8%) died due to a drug-related AE (neutropenic colitis)
- Adjudicated drug-related ILD/pneumonitis: 2 (5.6%)
- LVEF decrease: 1 (2.8%)

Planchard D et al. *J Thorac Oncol* 2026;21(5):103541

Year in Review:
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RTP Year in Review 2026

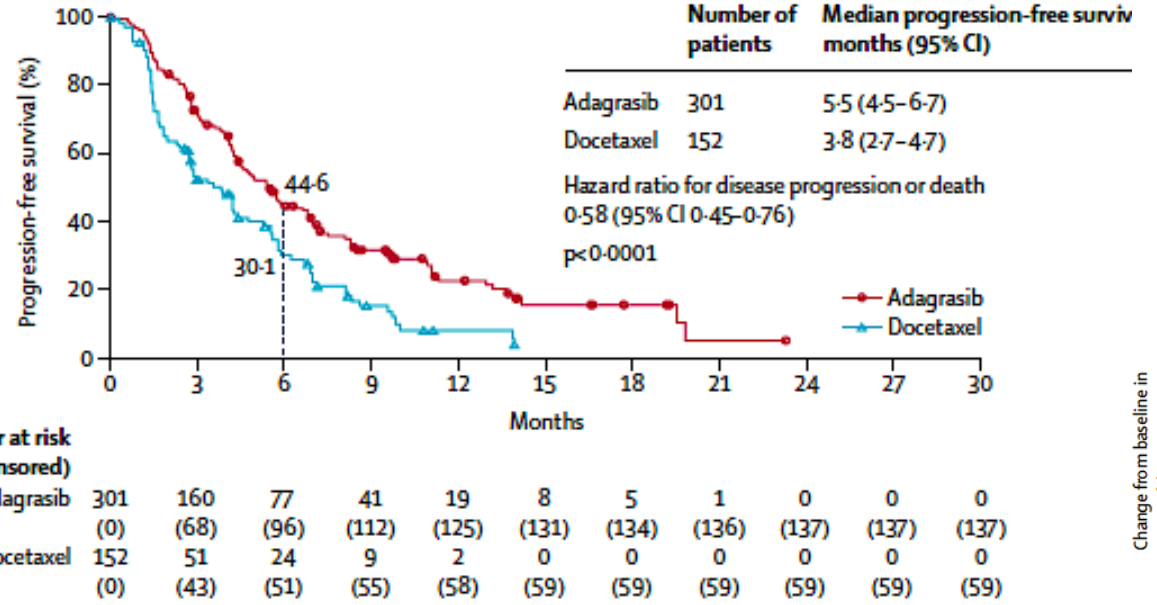
KRYSTAL-12: RP3 of adagrasib vs docetaxel in previously treated *KRAS* G12C mutant NSCLC

	Ada	Doc
mPFS (mo)	5.5	3.8

PFS HR 0.58 (p<0.001)

	Ada	Doc
ORR(%)	32	9
mDoR (mo)	8.3	5.5

A



	Number of patients	Median progression-free survival months (95% CI)
Adagrasib	301	5·5 (4·5–6·7)
Docetaxel	152	3·8 (2·7–4·7)

Hazard ratio for disease progression or death 0·58 (95% CI 0·45–0·76)

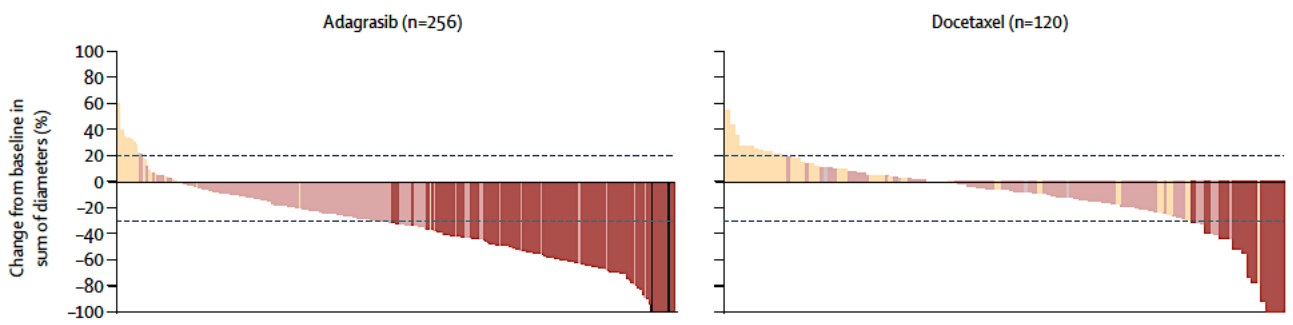
p<0·0001

Number at risk (censored)

Adagrasib	301 (0)	160 (68)	77 (96)	41 (112)	19 (125)	8 (131)	5 (134)	1 (136)	0 (137)	0 (137)	0 (137)
Docetaxel	152 (0)	51 (43)	24 (51)	9 (55)	2 (58)	0 (59)	0 (59)	0 (59)	0 (59)	0 (59)	0 (59)

A

Tumour response	Adagrasib (n=301)	Docetaxel (n=152)
Objective response	96 (32%)	14 (9%)
Complete response	3 (1%)	0
Partial response	93 (31%)	14 (9%)
Disease control rate	236 (78%)	89 (59%)
Median duration of response, months (95% CI)	8·3 (6·1–10·4)	5·5 (2·9–8·5)
Patients with a response who had ongoing responses at 6 months, % (95% CI)	64% (50·9–74·0)	39% (12·6–65·3)



Bottom line: Met its primary endpoint; slightly larger improvement in mPFS (1.7m) than CB200. FDA approved 2022; EMA 2024.

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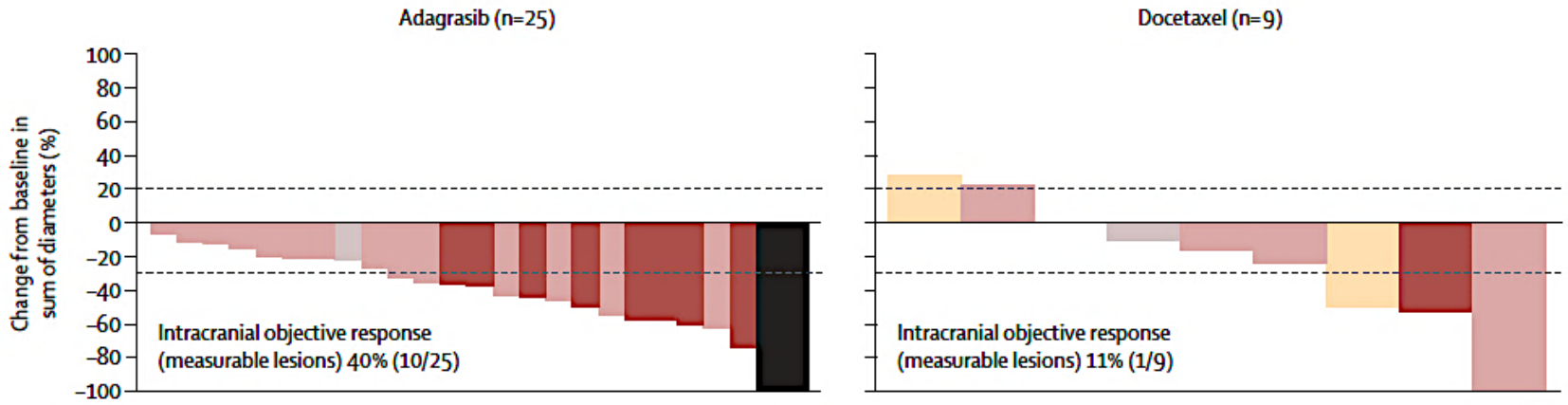
Barlesi F et al. Lancet 2025;406(10503):615-26.

KRYSTAL-12: Intracranial activity of adagrasib vs sotorasib

	Ada	Doc
IC ORR(%)	24	11
IC control rate	82%	56%

Intracranial response (measurable or non-measurable lesions)	Adagrasib (n=78)	Docetaxel (n=36)
Intracranial objective response	19 (24%)	4 (11%)
Complete response	11 (14%)	3 (8%)
Partial response	8 (10%)	1 (3%)
Intracranial disease control rate	64 (82%)	20 (56%)



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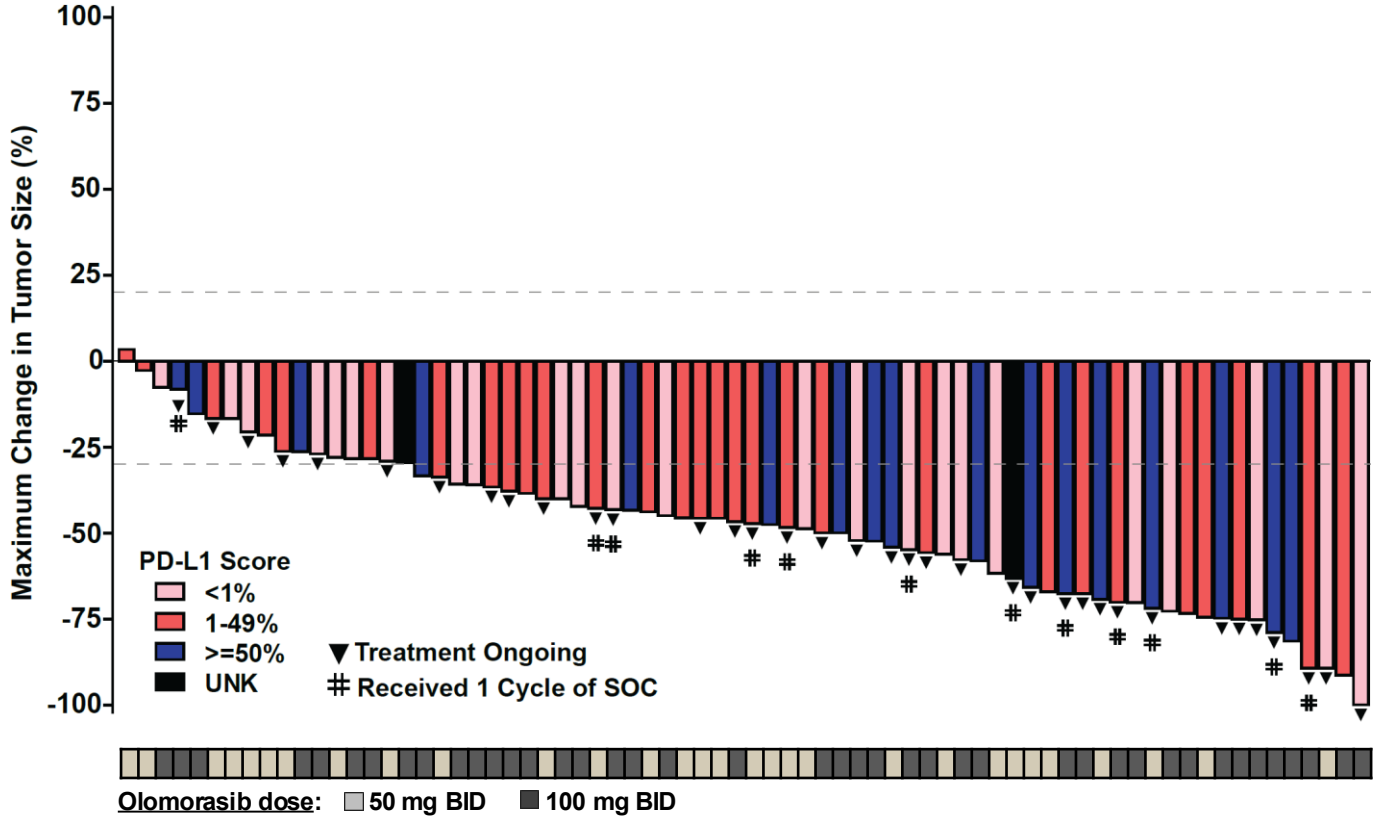
Barlesi F et al. Lancet 2025;406(10503):615-26.

Efficacy of 1L Olomorasib+ Pembro +Pemetrexed+Platinum in *KRAS* G12C NSCLC

ORR: 61% (all PD-L1)



Olomorasib + Pembrolizumab + Pemetrexed + Platinum				
Efficacy Evaluable Patients[a]	**All pts PD-L1 0-100% N = 77[b]**	**Pts with PD-L1 <1% N = 26**	**Pts with PD-L1 1-49% N = 31**	**Pts with PD-L1 ≥50% N = 18**
ORR, (%) (95% CI)	**61 (49.2, 72.0)**	**50 (29.9, 70.1)**	**68 (48.6, 83.3)**	**67 (41.0, 86.7)**
BOR, n (%)				
CR	1 (1)	-	1 (3)	-
PR[b]	46 (60)	13 (50)	20 (65)	12 (67)
SD	22 (29)	9 (35)	8 (26)	5 (28)
PD	3 (4)	2 (8)	-	-
NE	5 (7)	2 (8)	2 (7)	1 (6)
DCR, (%) (95% CI)	90 (80.6, 95.4)	85 (65.1, 95.6)	94 (78.6, 99.2)	94 72.7, 99.9)

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Negrao et al WCLC 2025

Efficacy and Safety of 1L Olomo + pembro in *KRAS* G12C-Mutant NSCLC: Results From LOXO-RAS-20001 and SUNRAY-01

Table. Response and Time-To-Event Endpoints in the Efficacy Evaluable Population

	Olomorasib (50 mg or 100 mg BID) + Pembrolizumab	
Endpoint	All Pts (PD-L1 0-100%) N = 82	Pts with PD-L1 ≥50%* N = 52
ORR†, % (n/N)	71 (58/82)	79 (41/52)
BOR, n (%)		
CR†	2 (2)	0 (0)
PR†	56 (68)	41 (79)
SD	17 (21)	7 (14)
PD	4 (5)	2 (4)
NE	3 (4)	2 (4)
DCR, % (n/N)	92 (75/82)	92 (48/52)
mDOR, months (95% CI)	NE (10.5-NE)	NE (10.5-NE)
mPFS, months (95% CI)	NE (12.0-NE)	NE (12.0-NE)
6-month PFS rate, % (95% CI)	77 (65-86)	83 (69-91)

†Includes responses confirmed and pending. *Target population in Phase 3 study.

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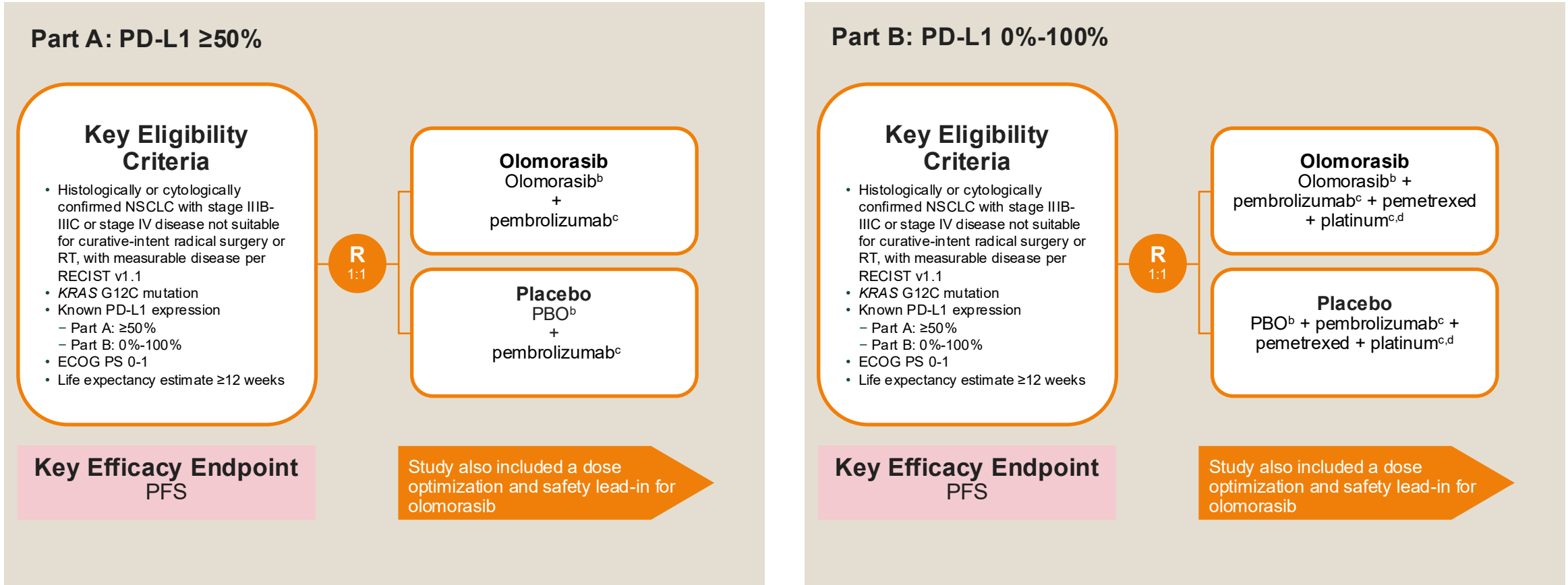
Johnson et al WCLC 2025

SUNRAY 01: RP3 of Olomorasib in 1L



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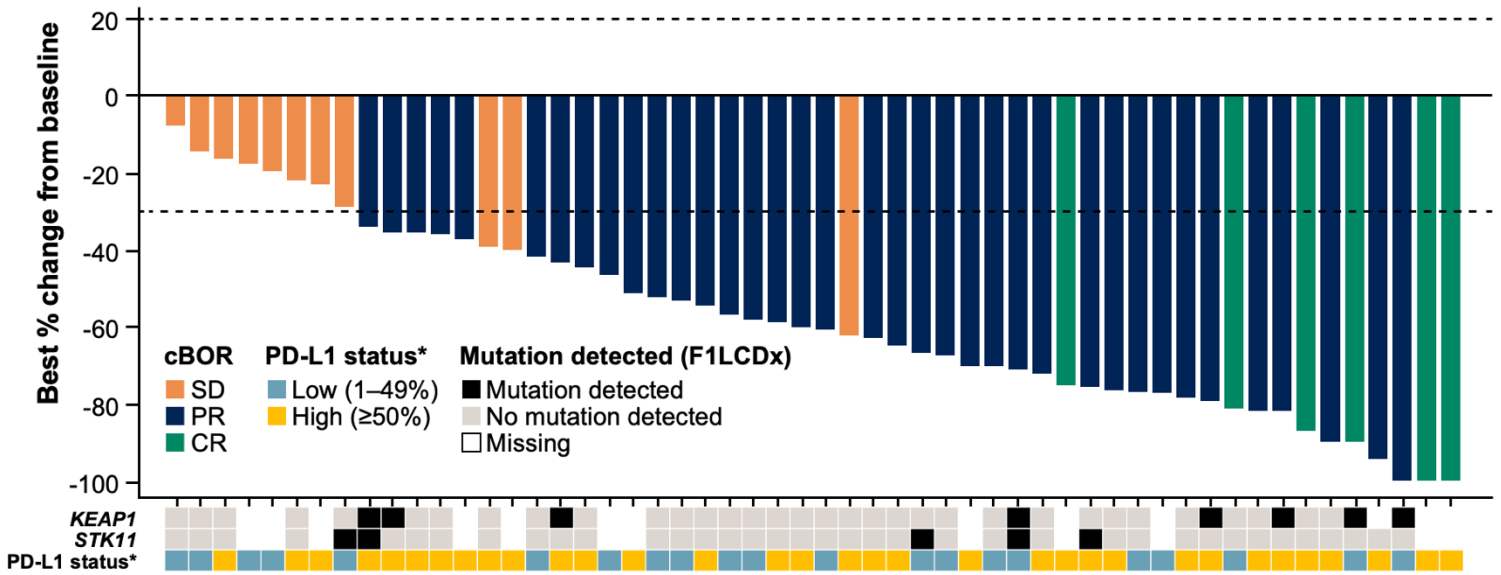
Nishio M et al. ASCO 2024. Abstract TPS218; https://clinicaltrials.gov/study/NCT06119581

1L divarasib plus pembrolizumab in *KRAS G12C*+ NSCLC: the Krascendo 170 study

PD-L1 positive cohort (≥1%)
Confirmed ORR: 72.9%
mPFS: 19.3 months; data were immature



n (%) unless specified	Divarasib + pembrolizumab (N=59)†
Confirmed ORR [95% CI]	43 (72.9) [59.7–83.6]
CR	6 (10.2)
PR	37 (62.7)
SD	11 (18.6)
PD	0
Not evaluable/missing	5 (8.5)
Median time to first response, days (range)	43 (36–164)
Median DoR, months (95% CI)	NE (14.5–NE)

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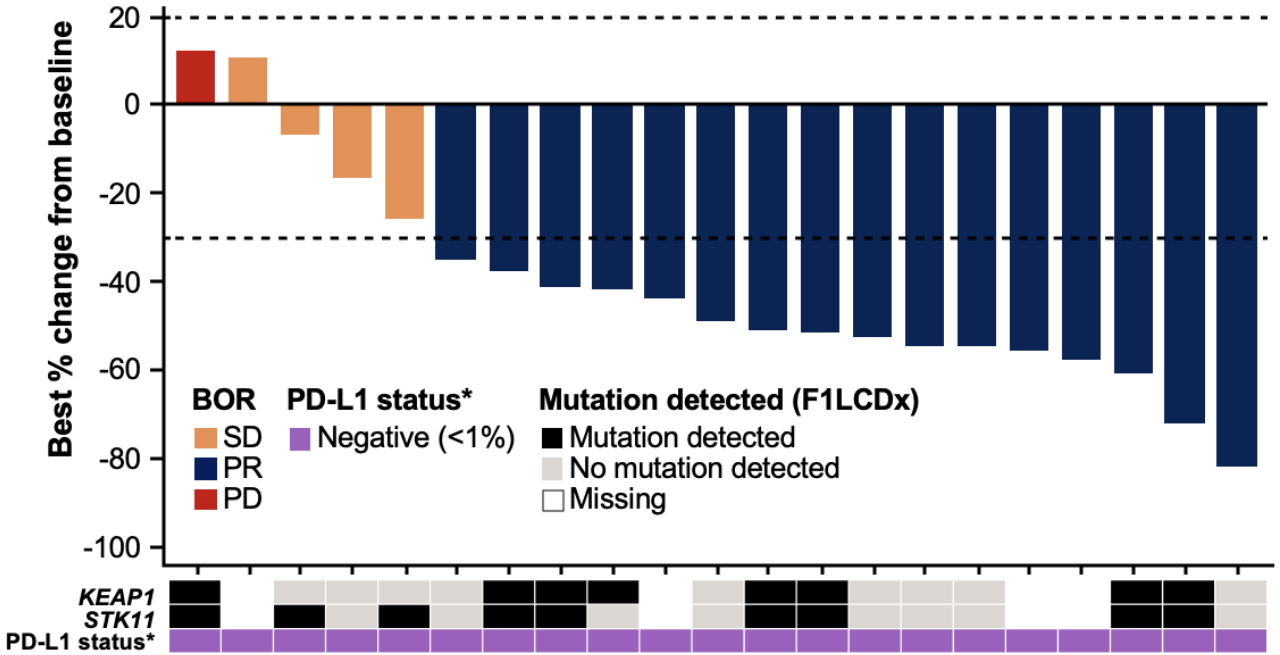
Skoulidis F et al. ASCO 2026; Abstract 8510

1L divarasib plus pembrolizumab in *KRAS G12C*+ mNSCLC: the Krascendo 170 study

PD-L1 negative cohort (<1%)

Unconfirmed ORR: 69.6%



n (%) unless specified	Divarasib + pembrolizumab (N=23)
Unconfirmed† ORR [95% CI]	16 (69.6) [47.1–86.8]
CR	0
PR	16 (69.6)
SD	4 (17.4)
PD	1 (4.3)
Not evaluable/missing	2 (8.7)
Median time to first response, days (range)	40.5 (36–120)

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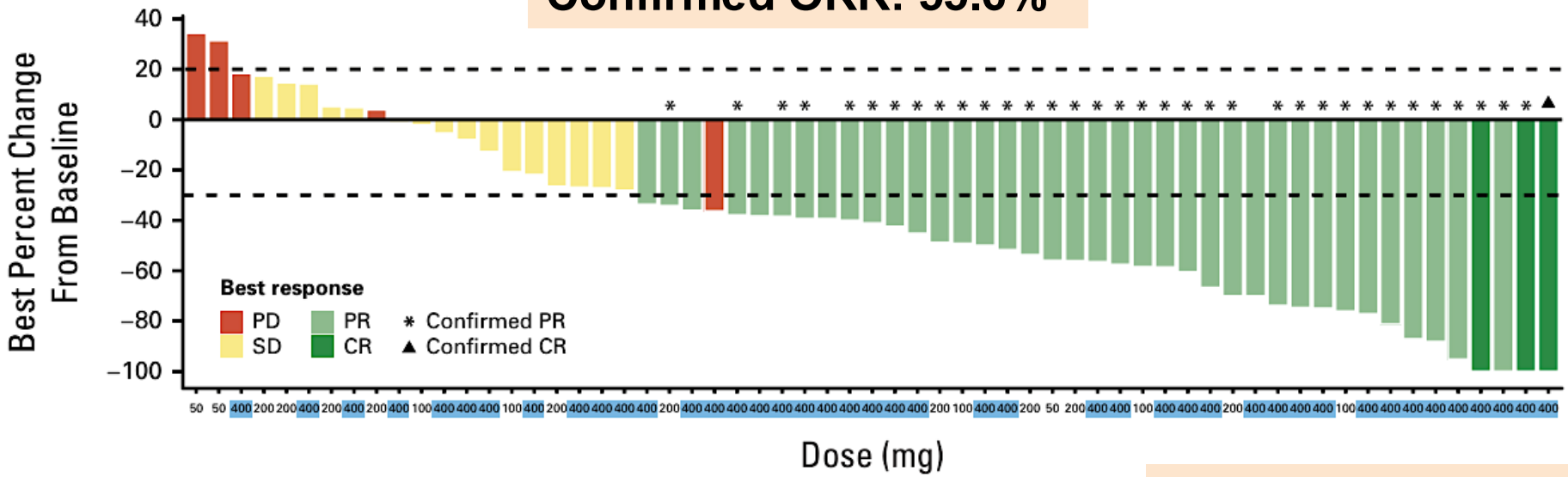
Making Cancer History®

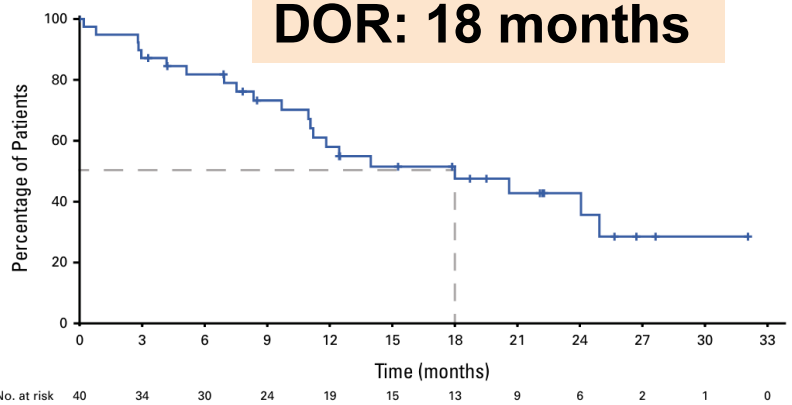
Skoulidis F et al. ASCO 2026; Abstract 8510

Single-agent divarasib in advanced *KRAS G12C*+ NSCLC

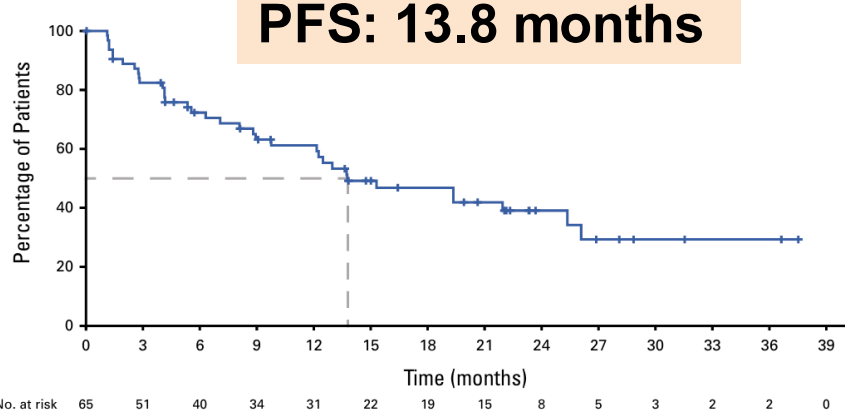
Confirmed ORR: 55.6%



DOR: 18 months



PFS: 13.8 months



Sacher AG et al. J Clin Oncol 2025;43(30):3249-53.

Year in Review:
Therapeutic Targets Beyond EGFR for Non-Small Cell Lung Cancer

INTRODUCTION: Relative Impact of Targeted Treatment

MODULE 1: HER2 Alterations

MODULE 2: KRAS Mutations

MODULE 3: MET Overexpression

MODULE 4: ALK Fusions

MODULE 5: ROS1 Fusions

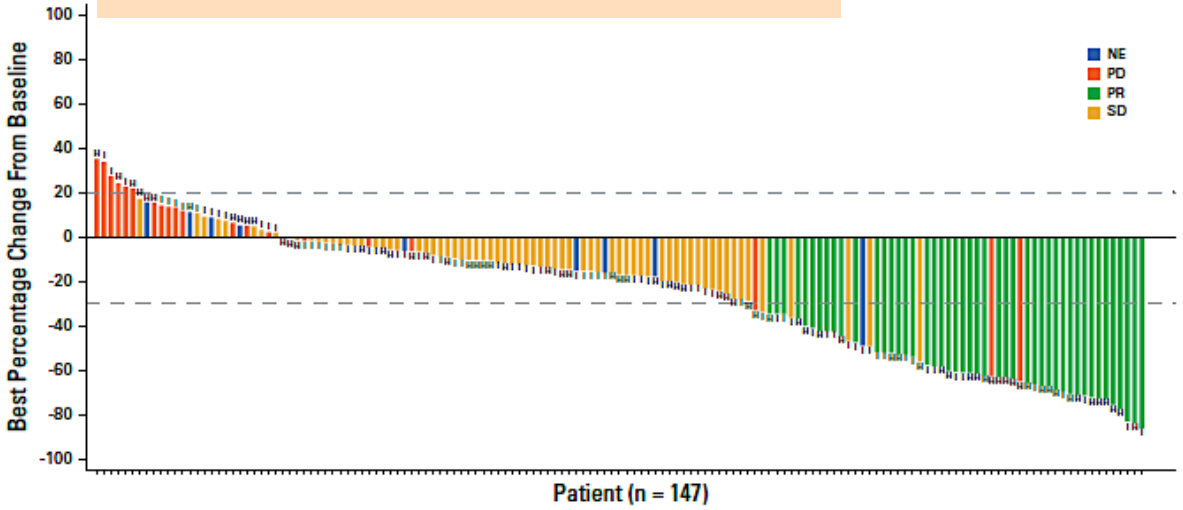
MODULE 6: RET Fusions

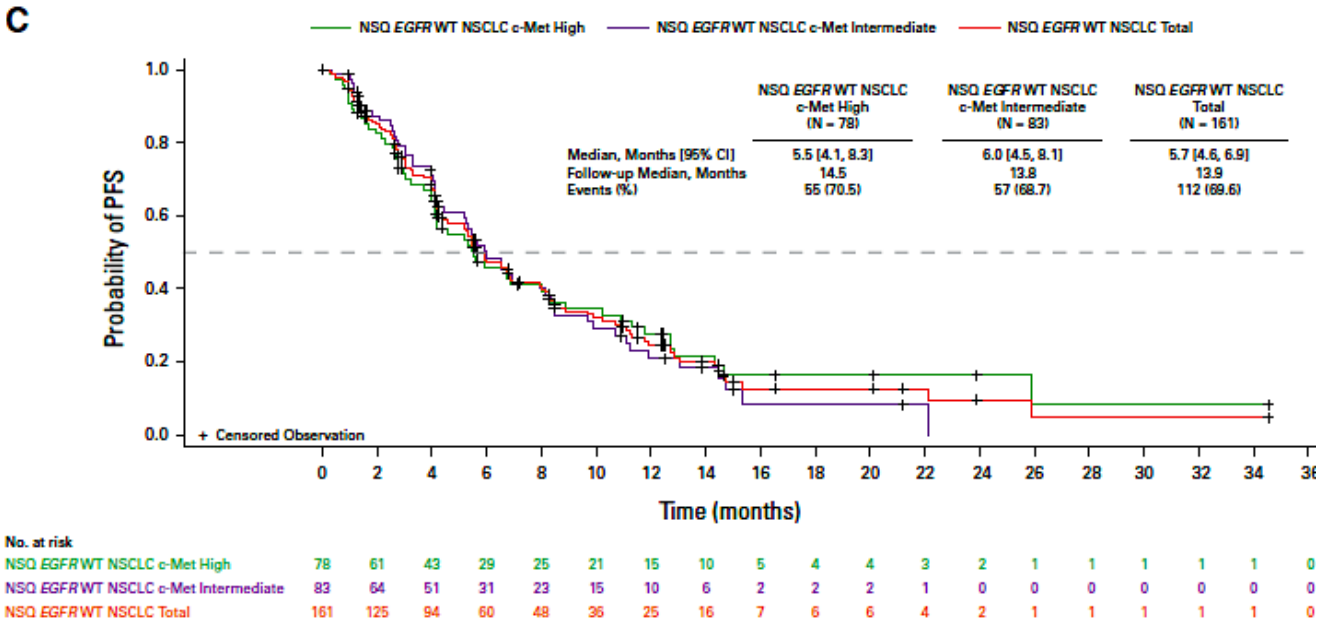
RTP Year in Review 2026

The LUMINOSITY trial: Teliso-V in previously treated patients with c-MET overexpression (wtEGFR)

	ORR%
Overall	28.6%
c-MET high:	34.6%
c-MET int:	22.9%

mPFS 5.7m; not correlated with expression level





c-Met protein overexpression in NSQ EGFRwt: high ≥50% tumor cells with 3+ staining; intermediate ≥25%–<50%

May 14, 2025: FDA granted accelerated approval to Teliso-V for previously non-SQ NSCLC with high c-Met protein overexpression [≥50% of tumor cells with strong (3+) staining], as determined by an FDA-approved test,

Cancer Center
Making Cancer History®

Camidge et al, JCO 2024

Updated results of LUMINOSITY trial: Teliso-V in previously treated patients with c-MET overexpression (wtEGFR)

	ORR%	mPFS (m)	mOS
Overall	29.2%	5.6	14.2
c-MET high:	34.5%	5.5	14.3
c-MET int:	23.8%	5.9	14.2

Most common TRAE:
peripheral sensory neuropathy (31%, 7% ≥Gr3),
peripheral edema (16%)
fatigue (14%).

	c-Met High n = 84	c-Met Int n = 84	c-Met OE Total
ORR,[a] n (%) [95% CI]	29 (34.5) [24.5, 45.7]	20 (23.8) [15.2, 34.3]	49 (29.2) [22.4, 36.7]
Median DOR,[a] mo [95%$_a$ CI]	7,2 [4.2, 12.0]	7.2 [4.7, 11.5]	7.2 [5.5, 11.0]
DOR[a] ≥6 mo, n/no, of responders (%)	17/29 (58.6)	9/20 (45.0)	26/49 (53.1)
Median PFS,[a] mo [95% CI]	5.5 [4.1, 6.8]	5.9 [4.5, 8.1]	5.6 [46, 6.8]
Median OS, mo [95% CI]	14,3 [9.0, 25.4]	14.2 [9.6, 16.4]	14.2 [9.9, 16.4]

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Girard N et al. ELCC 2025;Abstract 18P.

Year in Review:
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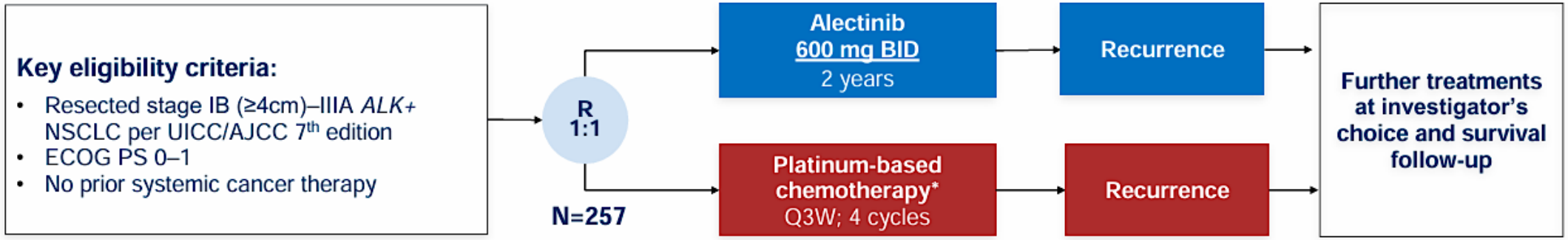
RTP Year in Review 2026

ALINA Updated Analysis
Adjuvant alectinib *vs* chemotherapy in patients with early-stage *ALK*+ NSCLC



Stratification factors:
- Stage: IB (≥ 4cm) vs II vs IIIA
- Race: Asian vs non-Asian†

Primary endpoint
- DFS per investigator tested hierarchically: Stage II–IIIA → stage IB–IIIA (ITT)

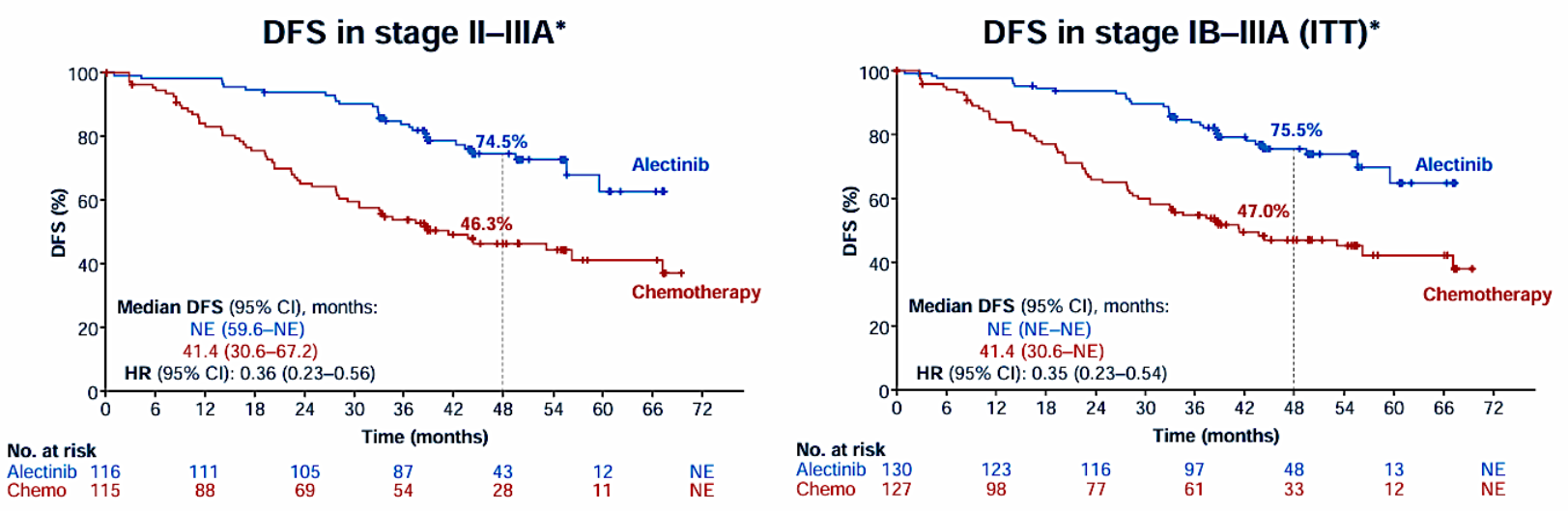
Other endpoints
- CNS-DFS, OS, safety

Characteristic[1,2]	Alectinib (n=130)	Chemotherapy (n=127)
Median age <65 / ≥65 years, %	54 years 79 / 21	57 years 73 / 27
Sex: female / male, %	58 / 42	46 / 54
Smoking status: never / former / current, %	65 / 32 / 4	55 / 43 / 2
Race: Asian / non-Asian, %	55 / 45	56 / 44
ECOG PS: 0 / 1, %	55 / 45	51 / 49
Stage at diagnosis per AJCC 7th edition: IB / II / IIIA, %	11 / 36 / 53	9 / 35 / 55
Stage at diagnosis per AJCC 8th edition: IB* / IIA / IIB / IIIA / IIIB, %	5 / 8 / 31 / 51 / 5	4 / 3 / 35 / 54 / 5
Nodal status: N0 / N1 / N2, %	16 / 35 / 49	14 / 34 / 52
Histology: squamous / non-squamous, %	5 / 95	2 / 98
Surgical procedure: Lobectomy / other†, %	97 / 3	92 / 8

Median follow up of 4 years

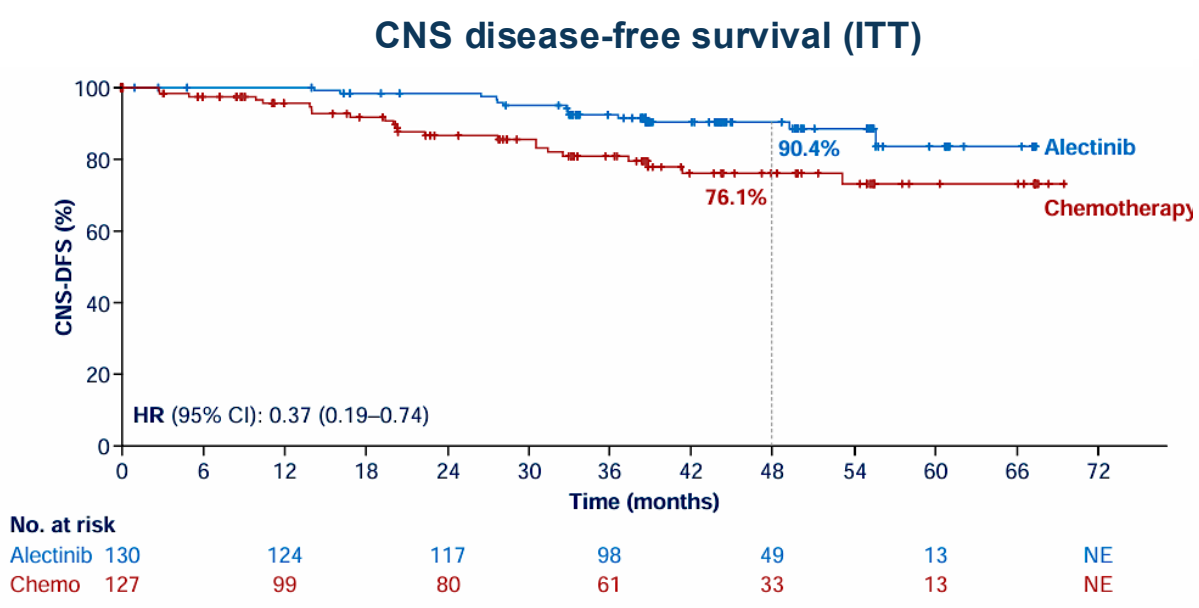
Dziadziuszko R et al., ESMO 2025

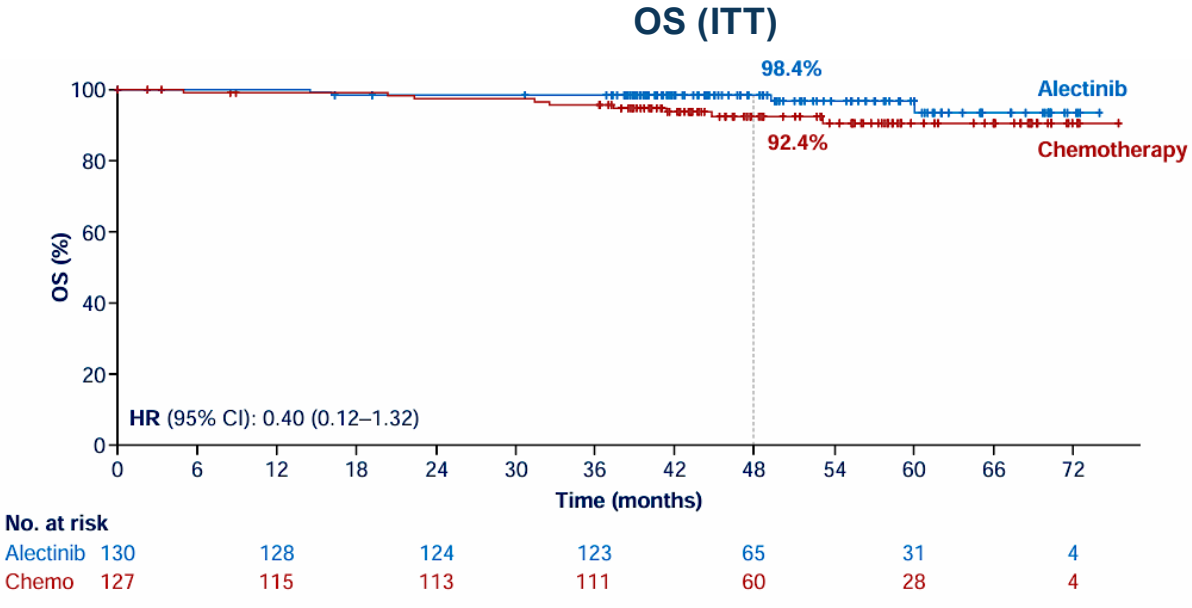
ALINA Updated Analysis
Adjuvant alectinib *vs* chemotherapy in patients with early-stage *ALK*+ NSCLC



Post-recurrence therapy in control arm:

- systemic therapy 85% (ALK TKI 81.7%, chemotherapy 5%)
- radiotherapy 16.7%
- surgery 5%



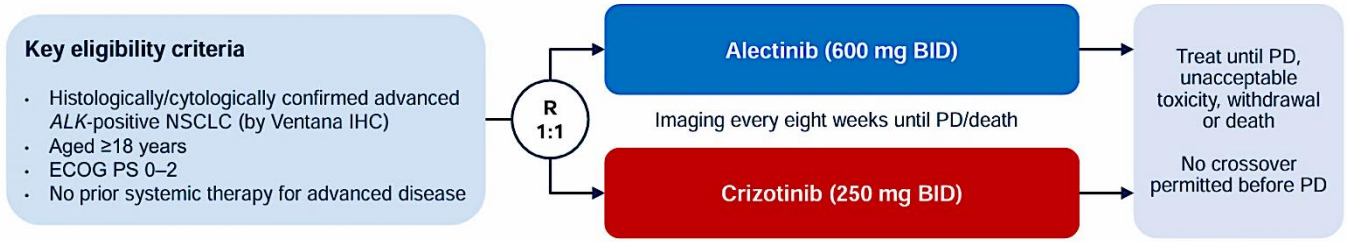


Dziadziuszko R et al., ESMO 2025

ALINA Updated Analysis
Adjuvant alectinib *vs* chemotherapy in patients with early-stage *ALK*+ NSCLC

- Alectinib continues to demonstrate a durable DFS benefit over CT, including reduction of CNS relapses
- OS data are still immature with a trend favoring the alectinib arm (82% of patients received ALK TKI at recurrence in the control arm)
- There is still no DFS plateau at 4 years in the control arm (late relapses can occur)
- More recurrences at the time of alectinib discontinuation in the experimental arm
- Results reinforcing alectinib as the SoC after surgical resection of *ALK*+ NSCLC

ALEX: study of alectinib *vs* crizotinib in advanced *ALK*+ NSCLC
Final overall survival and safety analysis



Stratification factors
- ECOG PS (0 or 1 vs 2)
- Race (Asian vs non-Asian)
- Baseline CNS metastases (yes vs no)

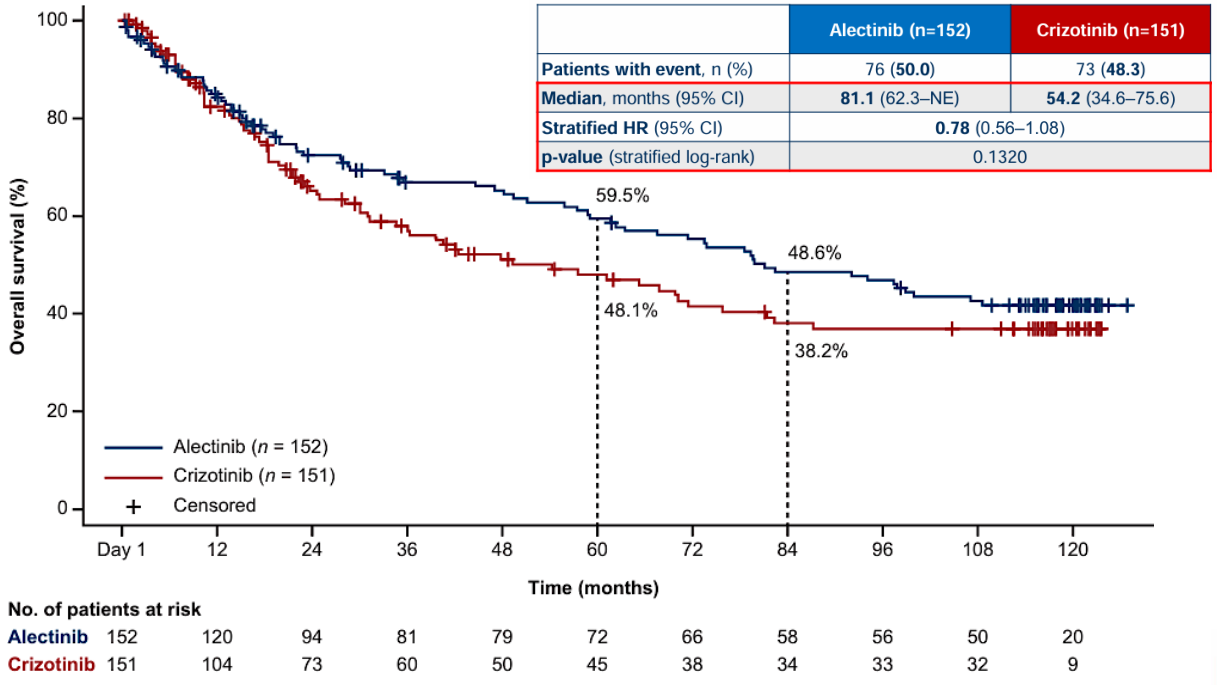
Primary endpoint
- PFS per investigator using RECIST v1.1

Secondary endpoints
- PFS by IRC
- Time to CNS progression
- ORR
- DoR
- OS; safety

Characteristic	Alectinib (n=152)	Crizotinib (n=151)
Median age, years (range)	**58.0** (25-88)	**54.0** (18-91)
Sex, n (%)		
Male	68 (**44.7**)	64 (**42.4**)
Female	84 (**55.3**)	87 (**57.6**)
Race, n (%)		
Asian	69 (**45.4**)	69 (**45.7**)
Non-Asian	83 (**54.6**)	82 (**54.3**)
ECOG PS, n (%)		
0 or 1	142 (**93.4**)	141 (**93.4**)
2	10 (**6.6**)	10 (**6.6**)
Disease stage, n (%)		
IIIB	4 (**2.6**)	6 (**4.0**)
IV	148 (**97.4**)	145 (**96.0**)
CNS metastases (by IRC), n (%)		
Yes	64 (**42.1**)	58 (**38.4**)
No	88 (**57.9**)	93 (**61.6**)
Prior brain radiation, n (%)		
Yes	26 (**17.1**)	21 (**13.9**)
No	126 (**82.9**)	130 (**86.1**)

Mok T et al., ESMO 2025: Peters S et al., Ann Oncol 2026

ALEX: study of alectinib *vs* crizotinib in advanced *ALK*+ NSCLC
Final overall survival and safety analysis



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

No. of patients at risk

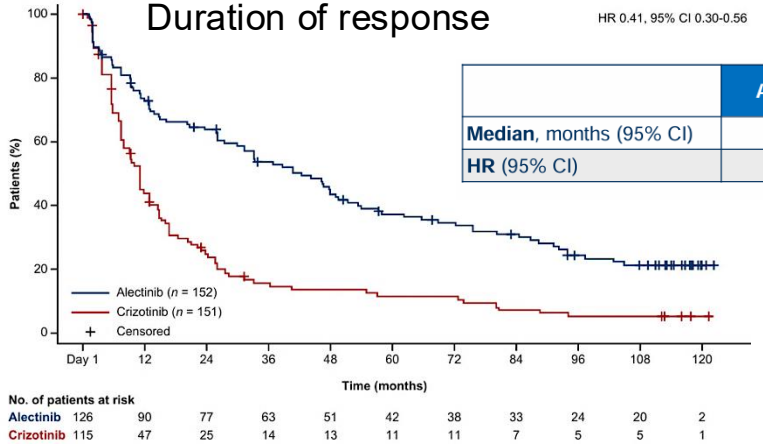
Alectinib	152	120	94	81	79	72	66	58	56	50	20
Crizotinib	151	104	73	60	50	45	38	34	33	32	9

Subsequent anticancer therapy

n (%)	Alectinib (n=152)	Crizotinib (n=151)
≥1 subsequent therapy	57 (**37.5**)	72 (**47.7**)
Lorlatinib	28 (**18.4**)	18 (**11.9**)
Brigatinib	16 (**10.5**)	16 (**10.6**)
Crizotinib	14 (**9.2**)	10 (**6.6**)
Alectinib	13 (**8.6**)	38 (**25.2**)
Ceritinib	10 (**6.6**)	29 (**19.2**)
Ensartinib	1 (**0.7**)	0
NVL 655	1 (**0.7**)	0
APG 2449	0	1 (**0.7**)

- No new safety signal with longer follow up

Duration of response



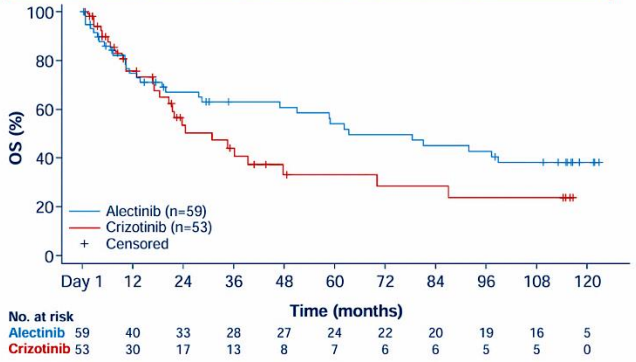
	Alectinib (n=126)	Crizotinib (n=115)
Median, months (95% CI)	**42.3** (31.3–51.3)	**11.1** (7.9–13.0)
HR (95% CI)	**0.41** (0.30–0.56)	

No. of patients at risk

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

Patients with CNS metastases at baseline

- Median OS: 63.4 months with alectinib vs 30.9 months with crizotinib (HR 0.68; 95% CI 0.40–1.15)

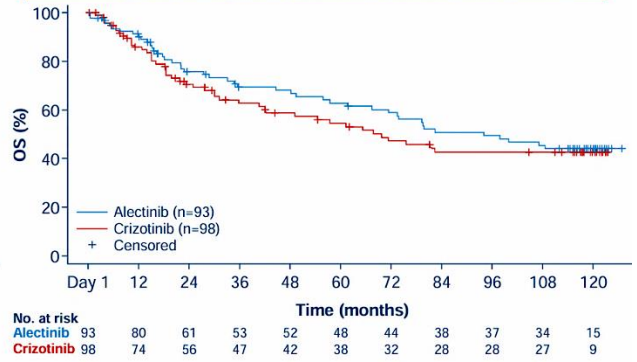


No. at risk

Alectinib	59	40	33	28	27	24	22	20	19	16	5
Crizotinib	53	30	17	13	8	7	6	6	5	5	0

Patients without CNS metastases at baseline

- Median OS: 94.0 months with alectinib vs 69.8 months with crizotinib (HR 0.87; 95% CI 0.58–1.32)



No. at risk

Alectinib	93	80	61	53	52	48	44	38	37	34	15
Crizotinib	98	74	56	47	42	38	32	28	28	27	9

Mok T et al., ESMO 2025: Peters S et al., Ann Oncol 2026

ALEX: study of alectinib *vs* crizotinib in advanced *ALK*+ NSCLC
Final overall survival and safety analysis

- Confirmation of the impact of 2nd generation ALK TKI on the natural history of the disease (median OS at 81.1 months)
- Substantial but statistically not significant OS benefit despite the lack of cross over (only 25% of patients in the crizotinib arm received alectinib) and the relative low proportion of patients benefiting from subsequent therapy
- Impressive duration of response with alectinib
- No new safety signal but 17.8% of patients had to discontinue alectinib for safety reasons

Lorlatinib *vs* crizotinib as first-line treatment for advanced *ALK*+ NSCLC: 7-year update from the phase 3 CROWN study

- Key eligibility criteria
- Stage IIIB/IV ALK+ NSCLC
- No prior systemic treatment for metastatic disease
- ECOG PS 0-2
- Asymptomatic treated or untreated CNS metastases were permitted
- ≥1 extracranial measurable target lesion (RECIST 1.1) with no prior radiation required

Randomized 1:1 N=296

Lorlatinib 100 mg once daily n=149

Stratified by:
- Presence of brain metastases (yes vs no)
- Ethnicity (Asian vs non-Asian)

Crizotinib 250 mg twice daily n=147

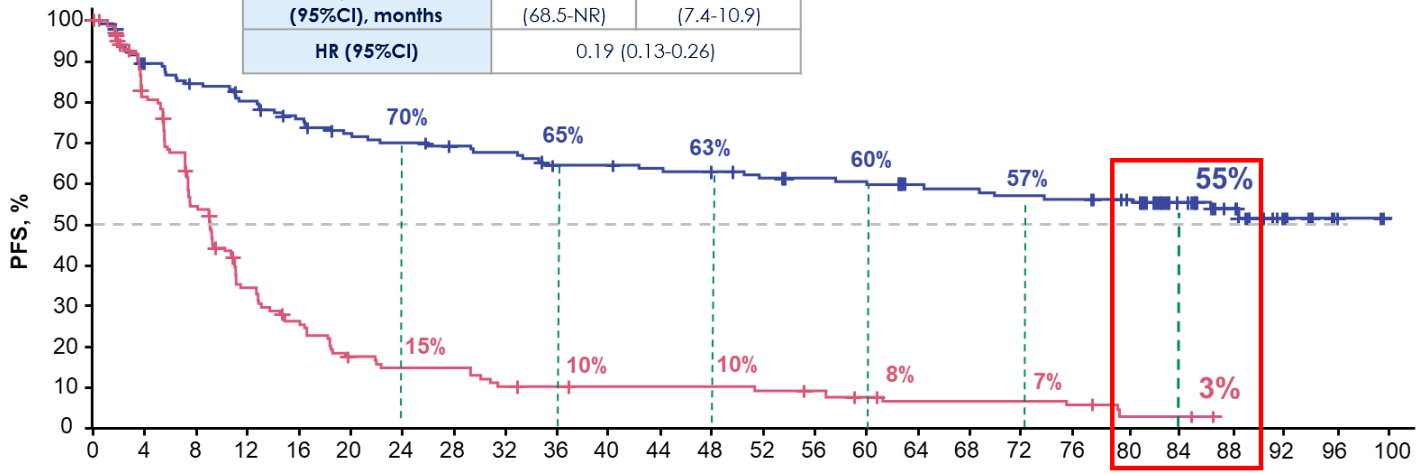
Primary endpoint
- PFSa by BICR

Key secondary endpoint
- OS

Other secondary endpoints
- PFS by investigator
- ORR by BICR and investigator
- IC ORR, IC TTP, DOR, IC DOR, TTR and IC TTR by BICR and investigator
- Safety
- Quality of life
- Biomarker analyses

No crossover between treatment arms was permitted

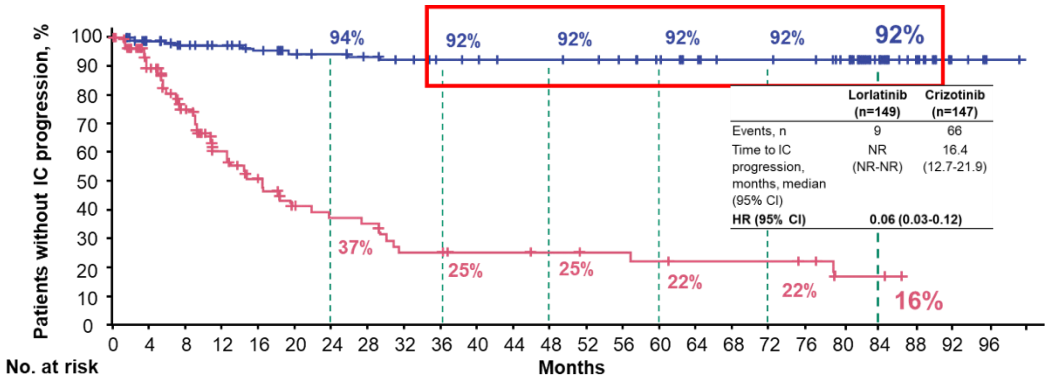
	Lorlatinib (n=149)	Crizotinib (n=147)
Events, n	62	119
PFS, median (95%CI), months	NR (68.5-NR)	9.1 (7.4-10.9)
HR (95%CI)	0.19 (0.13-0.26)	



No. at risk

Lorlatinib	149	126	118	111	103	96	93	89	87	81	81	79	78	75	73	71	69	68	66	65	62	38	28	9	2	0
Crizotinib	147	107	70	42	30	19	16	16	11	10	9	9	9	8	8	7	6	6	6	5	2	2	0	0	0	0

Time to IC Progression in the ITT Population

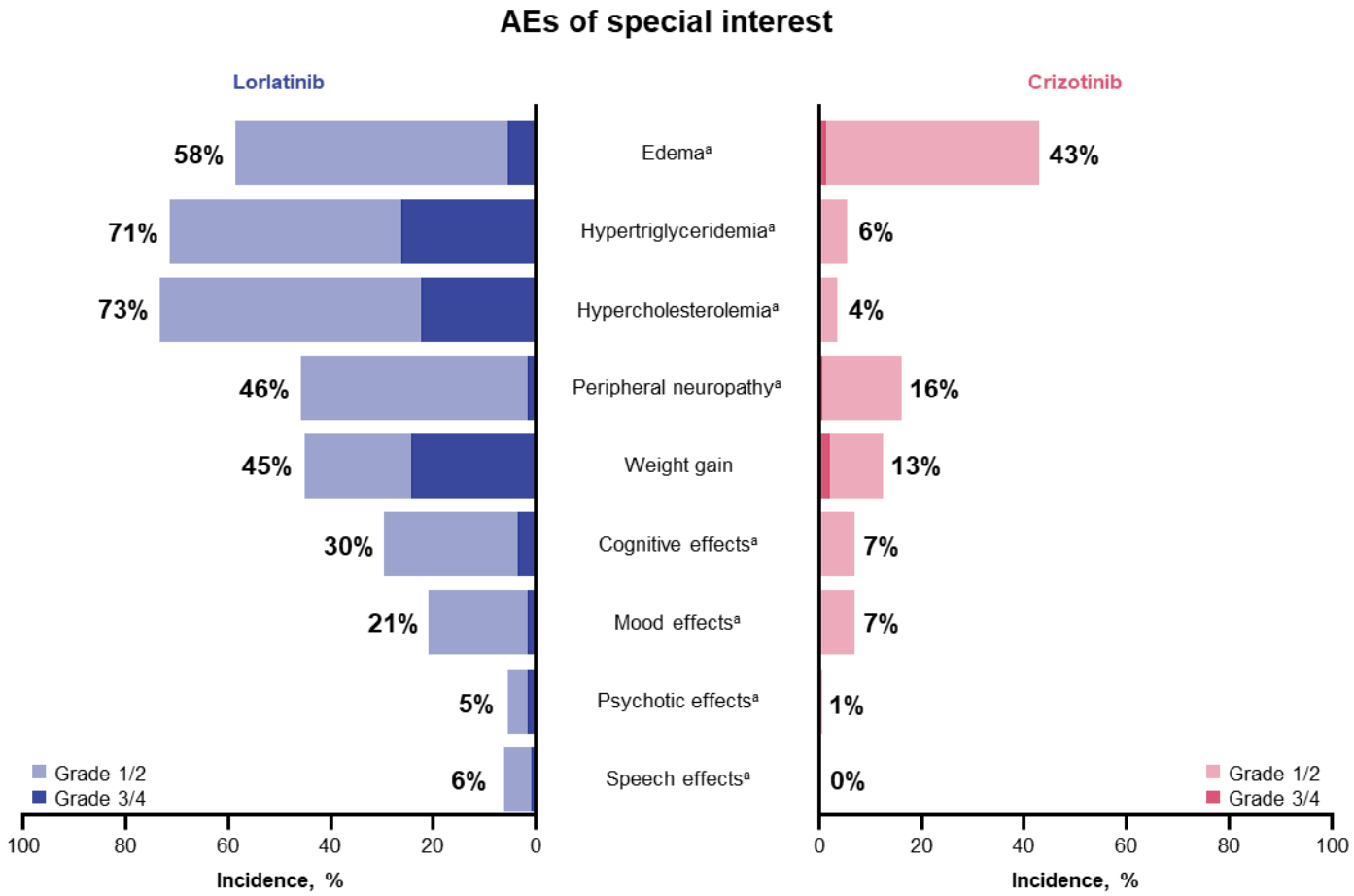


No. at risk

Lorlatinib	149	128	119	112	105	98	96	92	89	86	84	81	81	78	78	76	72	69	69	68	64	41	29	9	2
Crizotinib	147	107	75	46	34	22	19	18	12	12	10	10	9	8	8	7	6	6	6	5	2	2	0	0	0

Mok T et al., ASCO 2026; Shaw A et al., Ann Oncol 2026

Lorlatinib *vs* crizotinib as first-line treatment for advanced *ALK*+ NSCLC: 7-year update from the phase 3 CROWN study



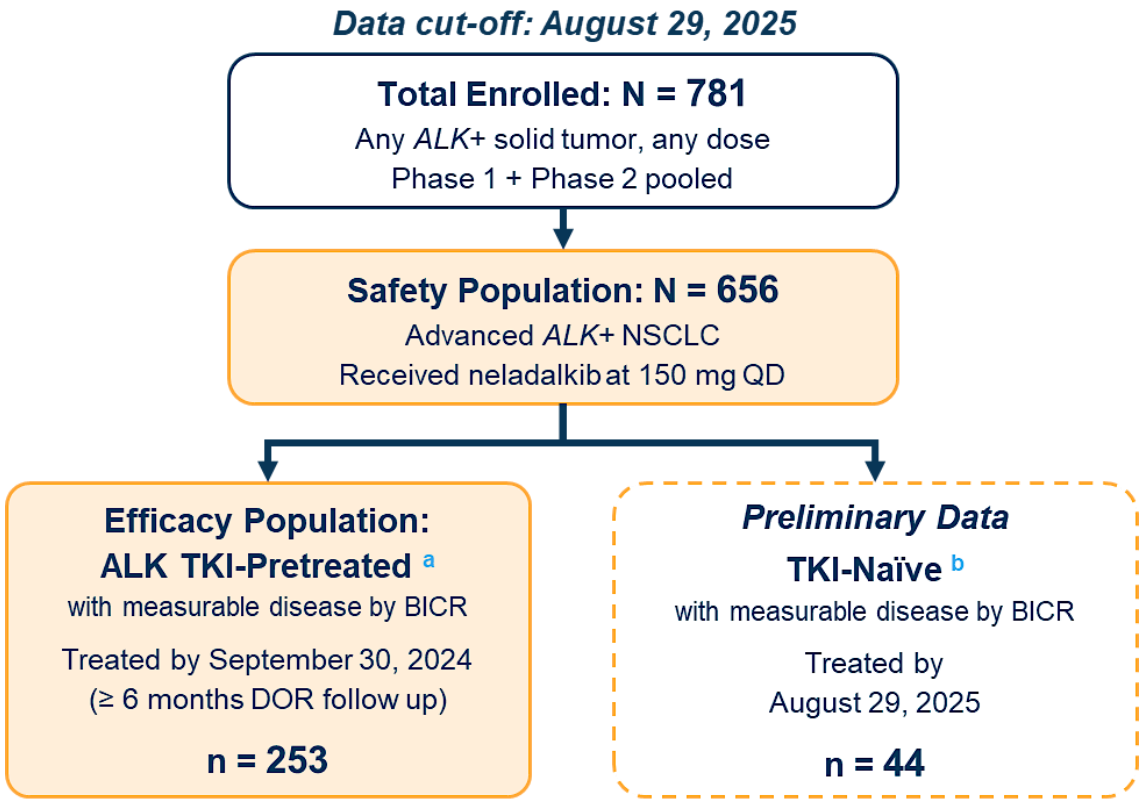
- No increase in frequency of grade 3 or 4 AEs since the 5-year analysis (77%)
  - Majority were due to an increase in lipid values
- No increase in cardiovascular AEs compared with crizotinib
- Frequency of CNS AEs was consistent with longer follow-up; most were grade 1 or 2
- Dose reductions in 34% of patients in the lorlatinib group
- All treatment-related discontinuations (5%) occurred within the first 26 months

Mok T et al., ASCO 2026: Shaw A et al., Ann Oncol 2026

Lorlatinib *vs* crizotinib as first-line treatment for advanced *ALK*+ NSCLC: 7-year update from the phase 3 CROWN study

- 7-year PFS rate of 55% with lorlatinib with a trend toward a plateau is extremely impressive
- Results making lorlatinib as the undeniable SoC in first-line treatment of *ALK*+ advanced NSCLC
- Management of toxicity is not trivial with insufficient follow up to evaluate long term consequences of hyperlipemia, approximately 25% of grade 3 weight gain (> 20% from baseline), 46% of neuropathy and 30% of cognitive effects
- Dose reductions appear the main way to manage toxicities without impact on PFS
- No *ALK* resistance mutations detected on lorlatinib
- The majority of PD events occurred within the 1st year: early progressors have more *TP53* and co-mutations at baseline

ALKOVE-1:
Efficacy and safety of neladalkib in patients with advanced *ALK*+ NSCLC



Treatment History		ALK TKI-Pretreated [a] Efficacy Population N = 253
Prior anticancer therapy, median (range)		3 (1 – 11)
Chemotherapy		128 (51%)
Prior ALK TKIs [f]		
1G	crizotinib	67 (26%)
2G	any 2G	240 (95%)
	alectinib	220 (87%)
	brigatinib	55 (22%)
	ceritinib	27 (11%)
	ensartinib	3 (1%)
3G	lorlatinib	190 (75%)
Lorlatinib-naïve [g, h]		**63 (25%)**
	≥1 prior 2G	**63/63 (100%)**
	1 ALK TKI (alectinib)	**44/63 (70%)**
	≥ 2 ALK TKIs	**17/63 (27%)**
Lorlatinib-experienced		**190 (75%)**
	≥2 ALK TKIs, including 2G and lorlatinib	**177/190 (93%)**
	≥3 ALK TKIs, including 2G and lorlatinib	**69/190 (36%)**

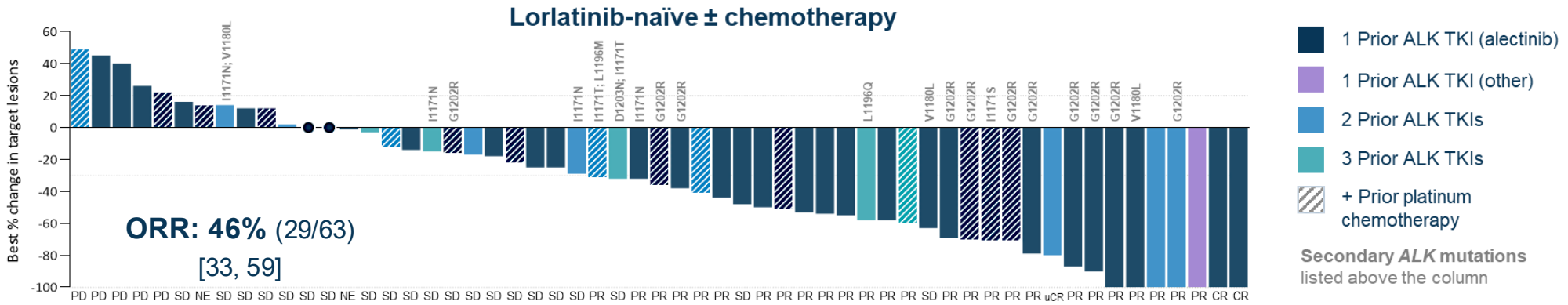
Lin J et al., ASCO 2026

ALKOVE-1:
Efficacy and safety of neladalkib in patients with advanced *ALK*+ NSCLC

PHASE 2: Neladalkib 150 mg QD (RP2D)

PATIENT POPULATION	PRIOR ALK TKI	PRIOR LINES CHEMO/I-O
ALK+ NSCLC	**1 prior 2G** *(ceritinib, alectinib, or brigatinib)*	0-2
	2-3 prior, any generation *(crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib [a])*	0-2
	1 prior 3G *(lorlatinib)*	≤ 1
	None (TKI-naïve)	≤ 1
	Any *(not eligible for other cohorts)*	Any
Other *ALK*+ Solid Tumors	**≥ 1 prior ALK TKI or systemic therapy** (or for whom no satisfactory standard therapy exists)	Any

ORR, % (n/N) [95%CI]	**31%** (79/253) [26, 37]
Median DOR [95% CI]	**NR** [14.5, NE], 1-yr: 64%
Median PFS [95% CI]	**4.7** [4.4, 6.5]
IC-ORR, % (n/N) [95% CI]	**32%** (29/92) [22,42]

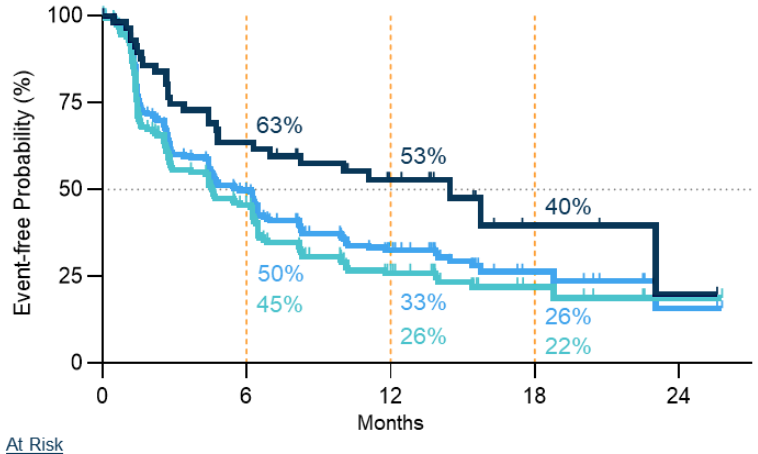


Lin J et al., ASCO 2026

ALKOVE-1:
Efficacy and safety of neladalkib in patients with advanced *ALK*+ NSCLC

Advanced *ALK*+ NSCLC RECIST v1.1 by BICR	Lorlatinib-experienced (1–5 prior ALK TKIs ± chemotherapy) **N = 190**
ORR, % (n/N) [95% CI]	**26%** (50/190) [20, 33]
Median DoR [95% CI]	**4.6** [2.8, 6.2]
Median PFS [95% CI]	**17.6** [6.9, NE]

Kaplan-Meier Plot of PFS
ALK TKI-Pretreated



All Treatment-Emergent Adverse Events (TEAEs) in ≥ 15% of TKI-Naïve or TKI-Pretreated Patients with Advanced *ALK*+ NSCLC Receiving Neladalkib 150 mg QD (N = 656)

Preferred Term	Any Grade	Grade ≥3
ALT increased	47%	20%
AST increased	44%	16%
Constipation	28%	0.2%
Dysgeusia	23%	0
Peripheral edema	18%	0.3%
Cough	16%	0.5%
Nausea	16%	0.8%

TKI-Pretreated with *ALK* G1202R mutation RECIST 1.1, BICR [95% CI]	Any prior ALK TKI ± chemotherapy [a] N = 47	Lorlatinib-naive ± chemotherapy N = 12	Lorlatinib-experienced ± chemotherapy N = 35
ORR, % (n/N)	**68%** (32/47) [b] [53, 81]	**83%** (10/12) [52, 98]	**63%** (22/35) [b] [45, 79]

ALK TKI-naïve, BICR	Response-evaluable N = 44
ORR, % (n/N)	**86%** (38/44) [a]
CR, % (n/N)	9% (4/44) [b]
% DOR ≥ 12 months [95% CI] [c]	**91%** [70, 98]

Lin J et al., ASCO 2026

ALKOVE-1:
Efficacy and safety of neladalkib in patients with advanced *ALK*+ NSCLC

- Neladalkib is an active new-generation ALK TKI with a good CNS penetration

- In pre-treated patients
  - Activity mainly in patients treated with 1st and 2nd generation TKIs as first-line of prior treatment: ORR 31%, median DoR not reached
  - Activity is modest in lorlatinib pre-treated patients (ORR 26%, median PFS 4.6 months)
  - The lack of ALK-dependent mechanisms of resistance after lorlatinib in 1st line suggests a low level of activity in this setting

- Neladalkib should be placed as a 1st line treatment
  - Preliminary evidence of high level of activity with CNS penetration
  - Lower toxicity burden in comparison with lorlatinib
  - The ALKAZAR phase III trial is ongoing with alectinib as the comparator

Year in Review:
Therapeutic Targets Beyond EGFR for Non-Small Cell Lung Cancer

INTRODUCTION: Relative Impact of Targeted Treatment

MODULE 1: HER2 Alterations

MODULE 2: KRAS Mutations

MODULE 3: MET Overexpression

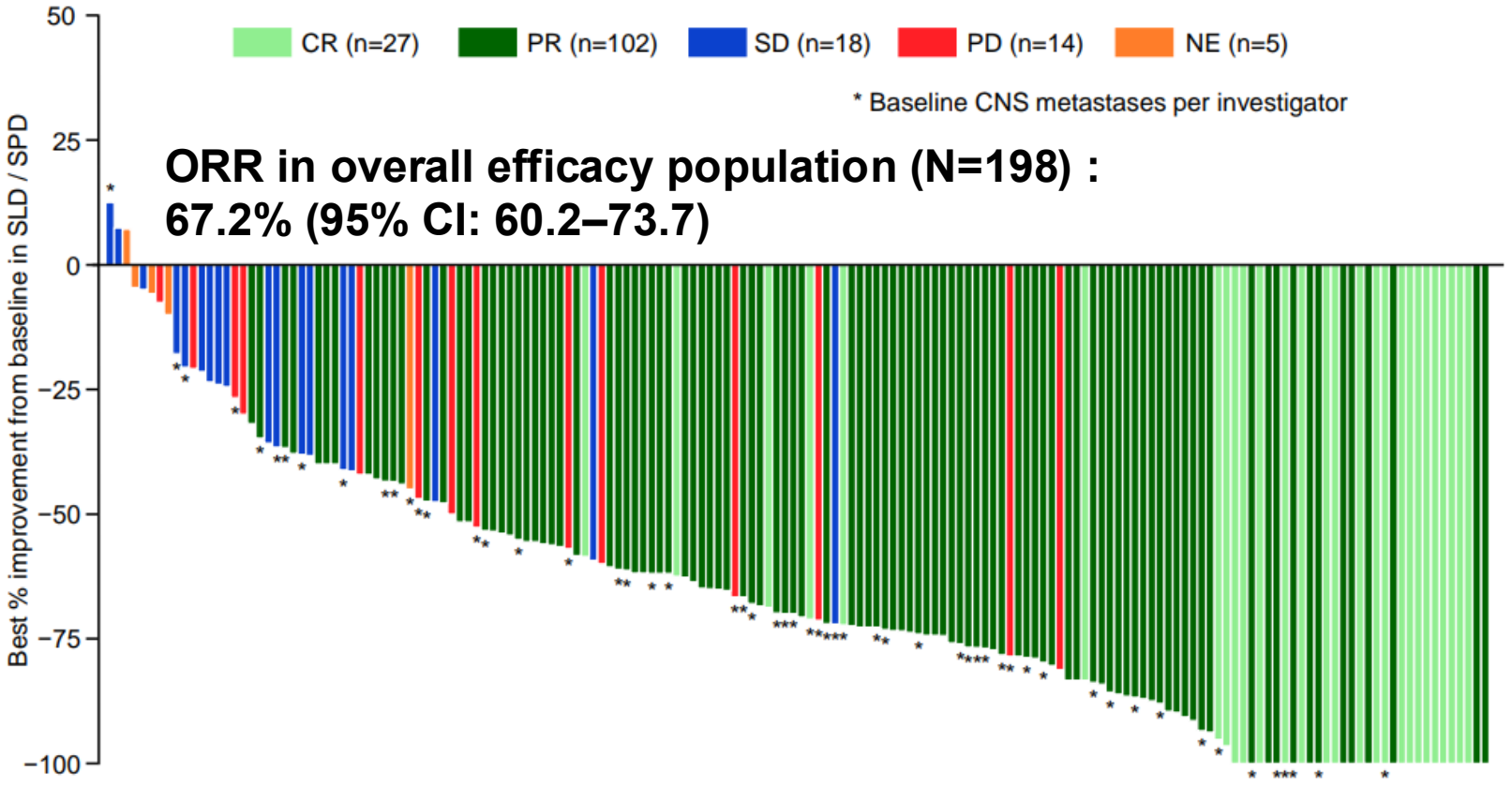
MODULE 4: ALK Fusions

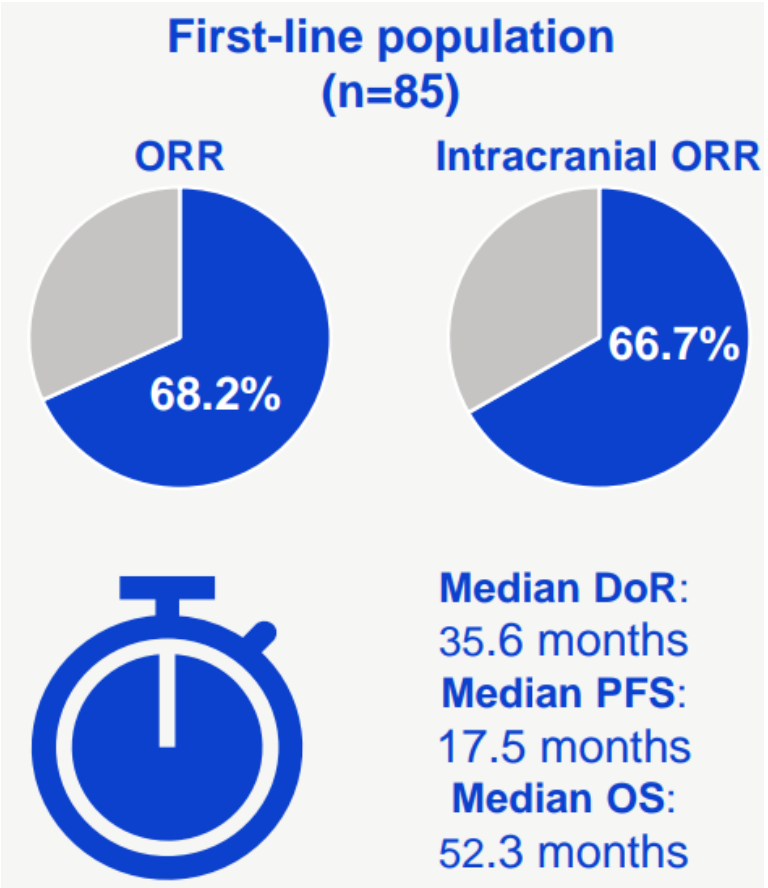
MODULE 5: ROS1 Fusions

MODULE 6: RET Fusions

RTP Year in Review 2026

Entrectinib in Patients with *ROS1* Fusion-Positive NSCLC Updated Analysis of STARTRK-1 and -2 and ALKA-372-001





Krebs MG et al., ESMO 2024

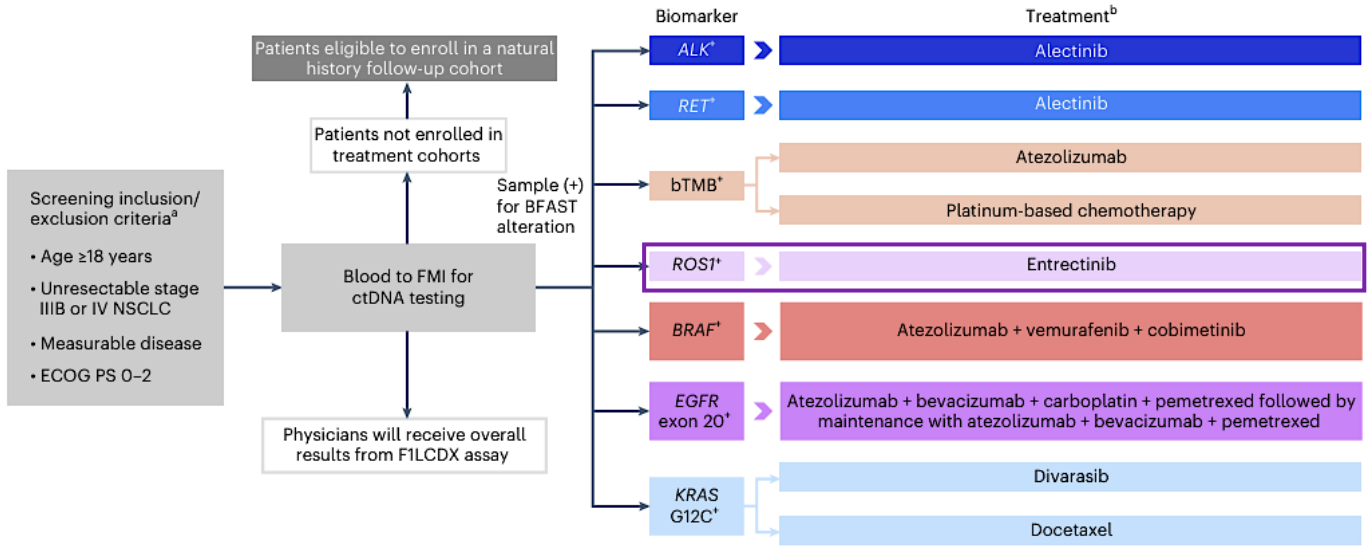
Entrectinib in Patients with *ROS1* Fusion-Positive NSCLC
Updated Analysis of STARTRK-1 and -2 and ALKA-372-001

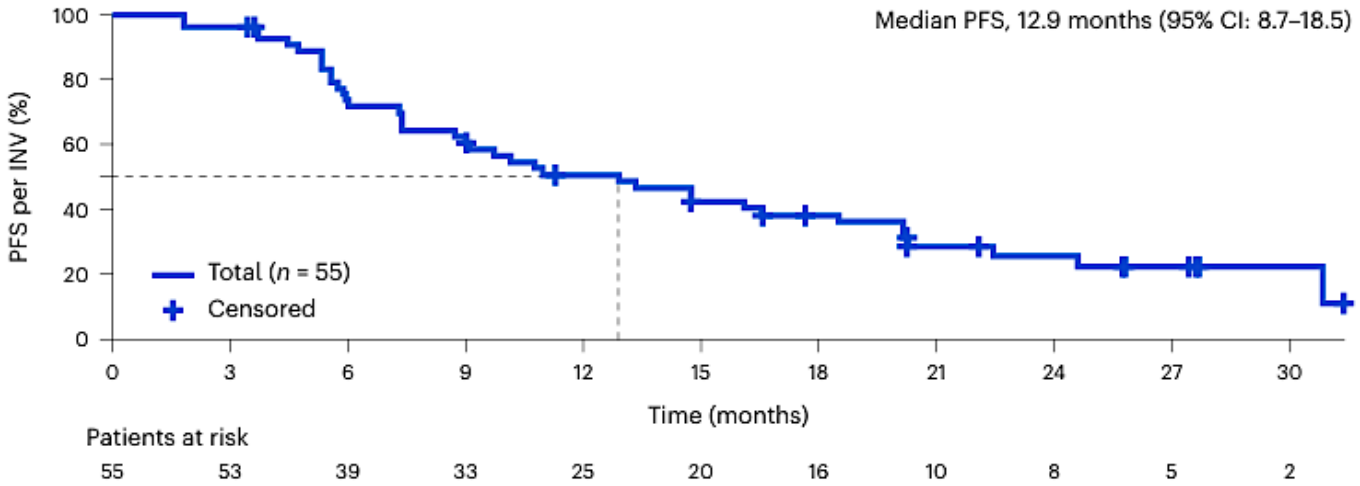
n (%)	Safety-evaluable population (N=247)
Treatment-related AE	234 (94.7)
Treatment-related serious AE	41 (16.6)
Treatment-related grade ≥3 AE	113 (45.7)
AE leading to dose reduction	86 (34.8)
Treatment-related AE leading to dose reduction	85 (34.4)
Treatment-related AE leading to discontinuation	17 (6.9)
AE leading to death	22 (8.9)

	Grade 1–2	Grade 3	Grade 4
Dysgeusia	56 (42%)	1 (<1%)	0
Dizziness	43 (32%)	1 (<1%)	0
Constipation	44 (33%)	0	0
Diarrhoea	35 (26%)	3 (2%)	0
Weight increase	26 (19%)	10 (7%)	0
Fatigue	32 (24%)	0	0
Paraesthesia	23 (17%)	0	0
Nausea	23 (17%)	0	0
Peripheral oedema	22 (16%)	0	0
Myalgia	19 (14%)	2 (2%)	0
Vomiting	19 (14%)	0	0
Blood creatinine increase	17 (13%)	1 (<1%)	0
Aspartate aminotransferase increase	14 (10%)	2 (2%)	0
Alanine aminotransferase increase	13 (10%)	3 (2%)	0

Fan Y, et al. J Thorac Oncol 2022;17(suppl):Abstr MA13.04; Drilon A et al., Lancet Oncol 2020; Krebs M et al., ESMO 2024

Update on entrectinib in advanced *ROS1*+ NSCLC: BFAST Trial





N = 54	IRF assessment
ORR, 95% CI	81.5% (68.6-90.8)
Median DoR, 95% CI	16.7 m (5.6-24.0)
Median time to CNS progression, 95% CI	NE (NE), 86.4% at 12 m
Median PFS, 95% CI	14.8 m (7.2-24.0)
Median OS	31.2 m (20.2-NE)

	ROS1-positive NSCLC (*n*=55)
Patients with ≥1 TRAE, *n* (%)	51 (92.7)
Patients with ≥1 serious TRAE, *n* (%)	7 (12.7)
Patients with TRAE leading to, *n* (%)	
Dose reduction	20 (36.4)
Dose interruption	11 (20)
Dose discontinuation	3 (5.5)
Patients with AE leading to death[a], *n* (%)	2 (3.6)
Patients with grade 3–5 AE, *n* (%)	31 (56.4)
Patients with grade 3–5 AE with incidence of ≥2%, *n* (%)	
Weight increase	4 (7.3)
Syncope	3 (5.5)
Pleural effusion	3 (5.5)
Dizziness	2 (3.6)
Cardiac failure	2 (3.6)
Pulmonary embolism	2 (3.6)
Urinary tract infection	2 (3.6)

Peters S et al., Nature Med 2024

Entrectinib in advanced *ROS1*+ NSCLC

- High systemic activity (ORR 75-80%)
- High CNS penetration
- But in comparison with new generation of ROS1 inhibitors
  - Shorter duration of response
  - Shorter PFS
  - Safety profile less favorable (TRB inhibition) with weight gain, dizziness, dysgeusia
- Ongoing phase III trial *vs* crizotinib

Updated analysis of Trident-1: repotrectinib in *ROS1*+ NSCLC

Phase 1/2 patient eligibility

- Locally advanced or metastatic solid tumors harboring *ROS1* or *NTRK1-3* gene fusion
- Asymptomatic CNS metastases allowed

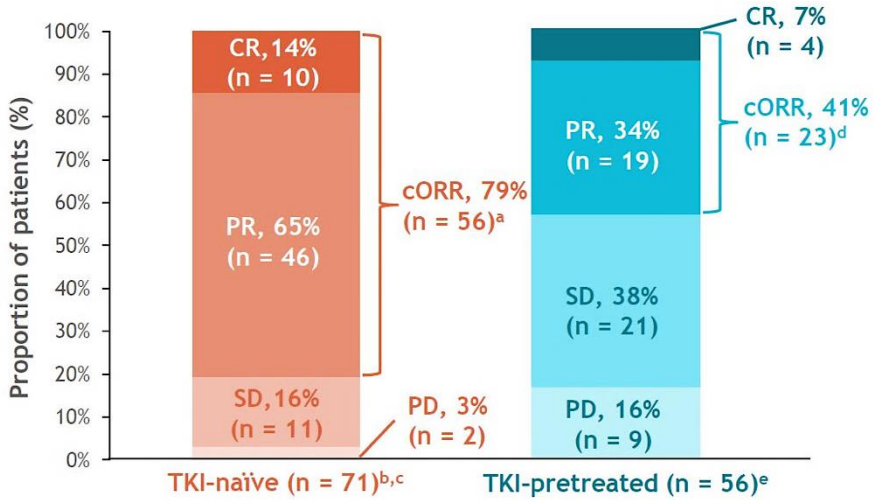
Phase 1[a] dose escalation cohorts — RP2D: 160 mg QD × 14 days, then 160 mg BID[b]

Phase 2 dose expansion cohorts[c]

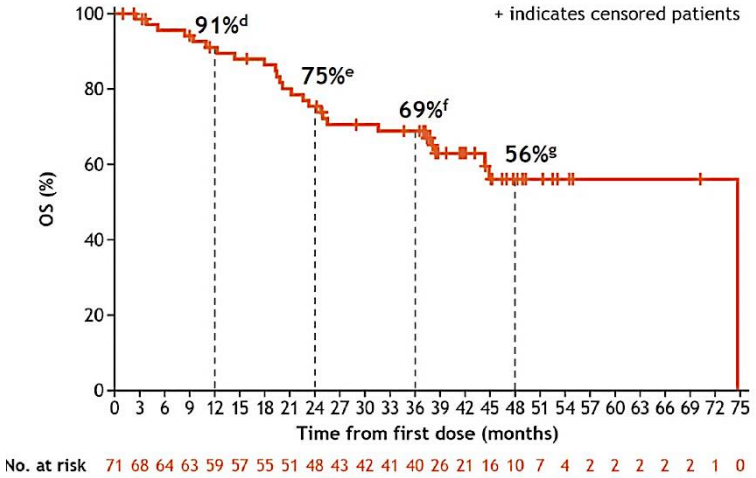
ROS1+ locally advanced or metastatic NSCLC

- **ROS1 TKI-naïve**
- **ROS1 TKI-pretreated[d]**

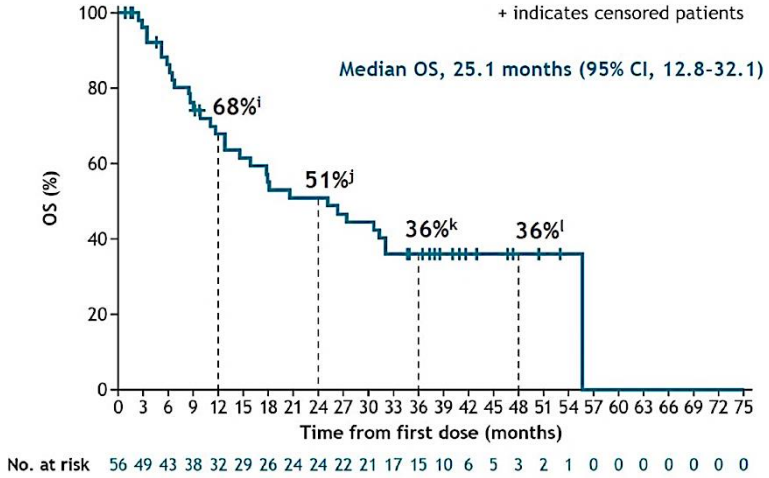
Phase 2 primary endpoint[e]: cORR by BICR using RECIST v1.1



TKI-naïve patients in the primary efficacy population[c]



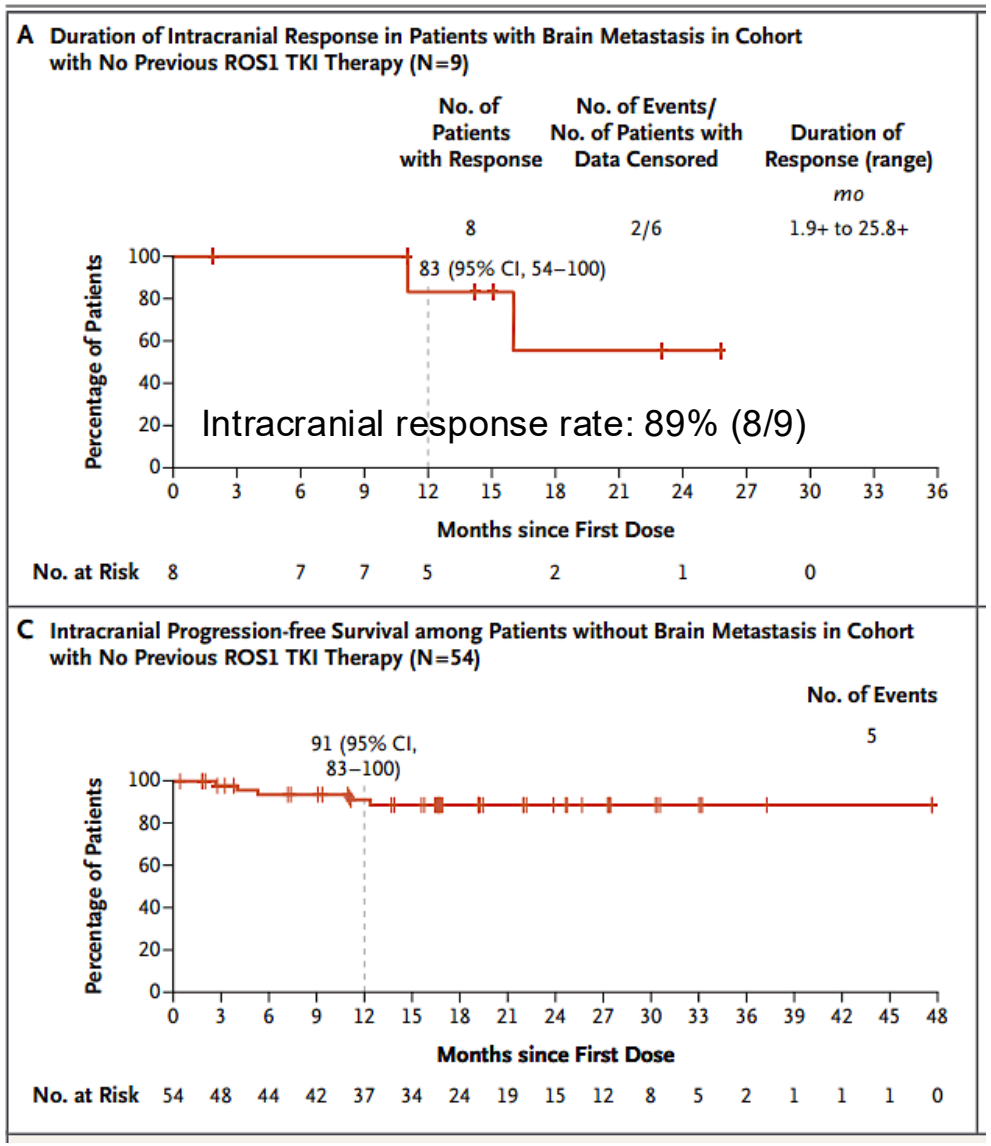
TKI-pretreated patients in the primary efficacy population[h]



- TKI pretreated = 1 prior TKI
- Median PFS
  - TKI-naïve: 31.1 months (21.9-NE)
  - TKI-pretreated: 8.6 months (5.5-14.5)
- Median DoR
  - TKI-naïve: 36.8 months (27.4-NE)
  - TKI-pretreated: 17.8 months (7.5-31.4)
- IC-ORR
  - TKI-naïve: 89% (8/9)
  - TKI-pretreated: 38% (5/13)

Cho B et al., WCLC 2025

Repotrectinib in TKI-naive *ROS1*+ advanced NSCLC



	Any Grade	Grade ≥3
Any event	422 (99)	216 (51)
Event occurring in ≥15% of patients		
Dizziness	264 (62)	11 (3)
Dysgeusia	224 (53)	0
Constipation	162 (38)	1 (<1)
Anemia	160 (38)	33 (8)
Paresthesia	143 (34)	3 (1)
Dyspnea	117 (27)	27 (6)†
Increased alanine aminotransferase level	99 (23)	8 (2)
Fatigue	95 (22)	4 (1)
Ataxia	90 (21)	1 (<1)
Increased aspartate aminotransferase level	89 (21)	9 (2)
Nausea	85 (20)	3 (1)
Muscular weakness	85 (20)	8 (2)
Headache	79 (19)	0
Increased blood creatine kinase level	75 (18)	15 (4)
Weight increase	67 (16)	11 (3)
Memory impairment	65 (15)	1 (<1)
Cough	64 (15)	1 (<1)
Event that led to treatment discontinuation	31 (7)	0
Event that led to dose reduction	163 (38)	0
Event that led to dose interruption	213 (50)	0
Any serious event	147 (35)	0

Drilon A et al., NEJM 2023

Repotrectinib in *ROS1*+ advanced NSCLC

- Highly active second generation agent in TKI-naïve *ROS1*+ advanced NSCLC
  - ORR 79%, median DoR 36.8 months, median PFS 31.1 months
  - High level of activity in CNS with CNS-protective effect
  - Management of toxicity related to TRK-B inhibition is an issue (all grades dizziness 62%, dysgeusia 53%, ataxia 21%, muscular weakness 20%) leading to dose interruptions in 50% of patients and dose reduction in 38% of patients
- Interesting activity after 1 prior TKI (ORR 41%, median DoR 17.8 months) with coverage of G2032R mutation but with relatively short PFS
- Ongoing phase III trial (Trident-3) *vs* crizotinib

Taletrectinib in *ROS1*+ NSCLC: Pooled Analysis of Two Phase 2 Trials

Key Eligibility Criteria for Pivotal Cohorts[1–3]

Inclusion criteria

- Locally advanced or metastatic NSCLC
- Age ≥18 years[a]
- ECOG PS 0–1
- Evidence of ROS1 fusion
- Stable CNS involvement allowed[b]
- At least one measurable lesion per RECIST v1.1

Exclusion criteria

- Anticancer therapy ≤2 weeks
- Radiotherapy ≤14 days
- Major surgery ≤4 weeks
- History of interstitial lung disease

ROS1 TKI-naïve (n=160)

ROS1 TKI-pretreated (n=113)[c]

Taletrectinib 600 mg once daily[d]

Study Endpoints

Primary

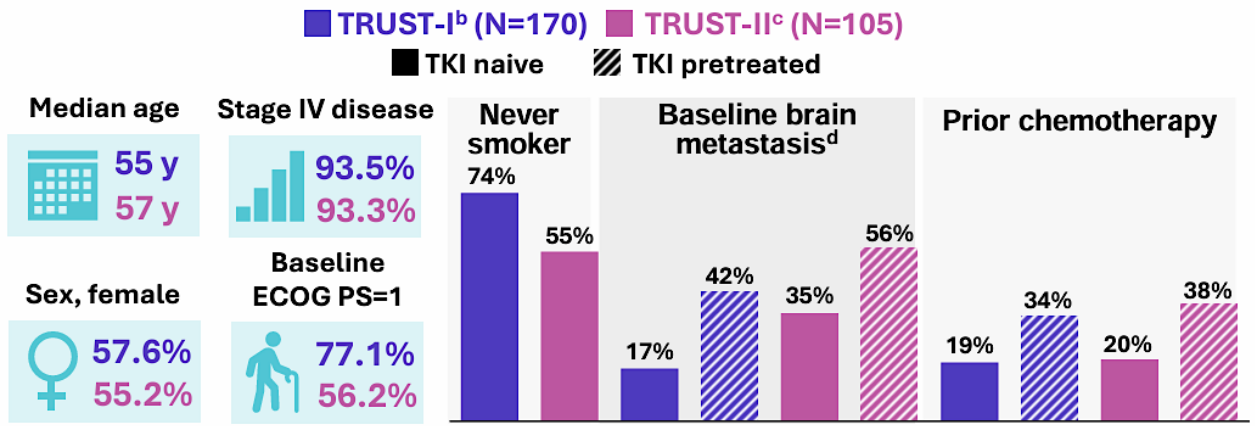
- **IRC-assessed cORR per RECIST v1.1**

Secondary

- IC-cORR per mRECIST v1.1
- DOR
- PFS
- Safety

Study populations

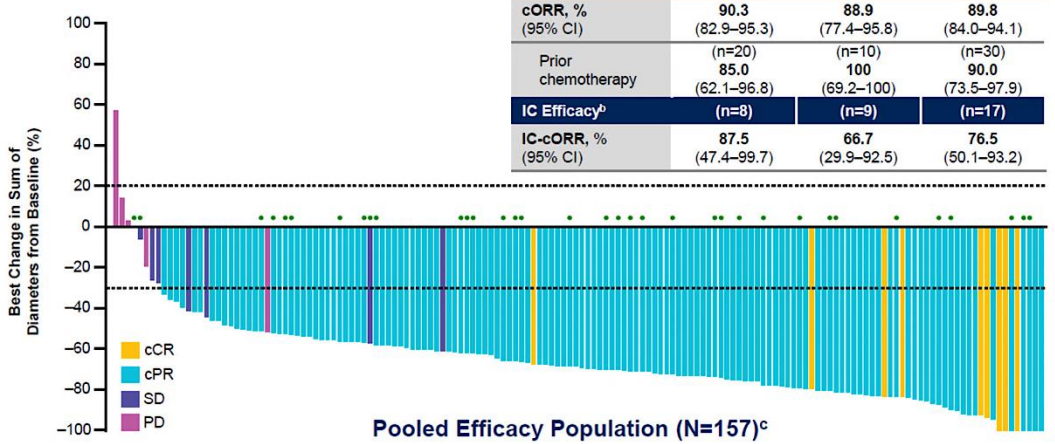
- Efficacy: Response evaluable population (REP) included patients with ROS1+ NSCLC with ≥1 measurable lesion(s) at baseline per RECIST V1.1 by IRC and who received ≥1 dose(s) of taletrectinib; TKI-naïve (n=160) and TKI-pretreated (n=113)
- Safety: Patients with ROS1+ NSCLC who received ≥1 dose(s) of taletrectinib 600 mg (n=337)



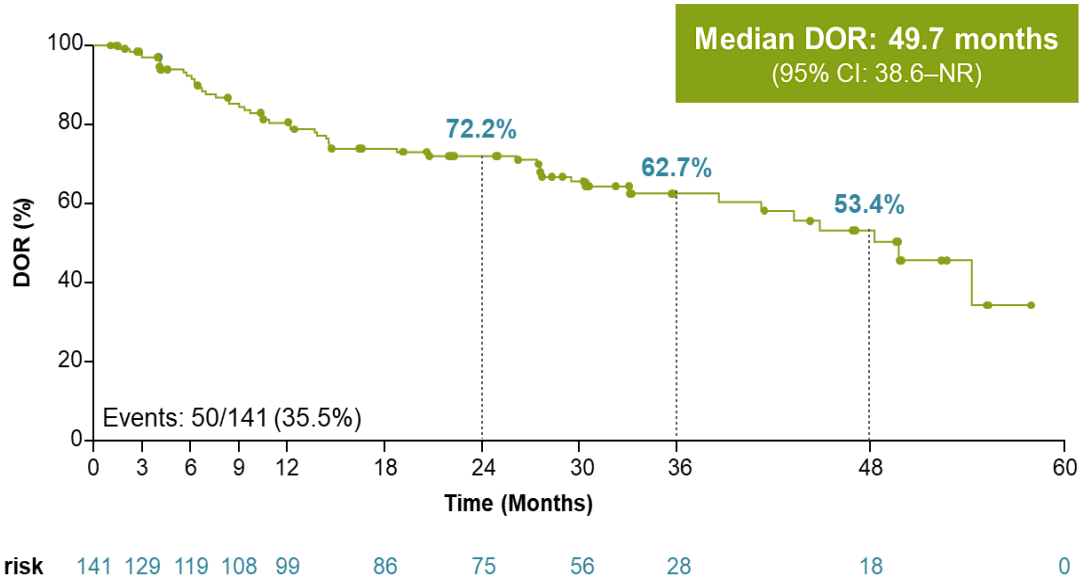
1. Pérol M, et al. *J Clin Oncol*. 2025. **2.** ClinicalTrials.gov. NCT04919811 . **3.** Li W, et al. *J Clin Oncol*. 2024.

Taletrectinib in *ROS1*+ NSCLC: Pooled Analysis of Two Phase 2 Trials
TKI-naïve patients

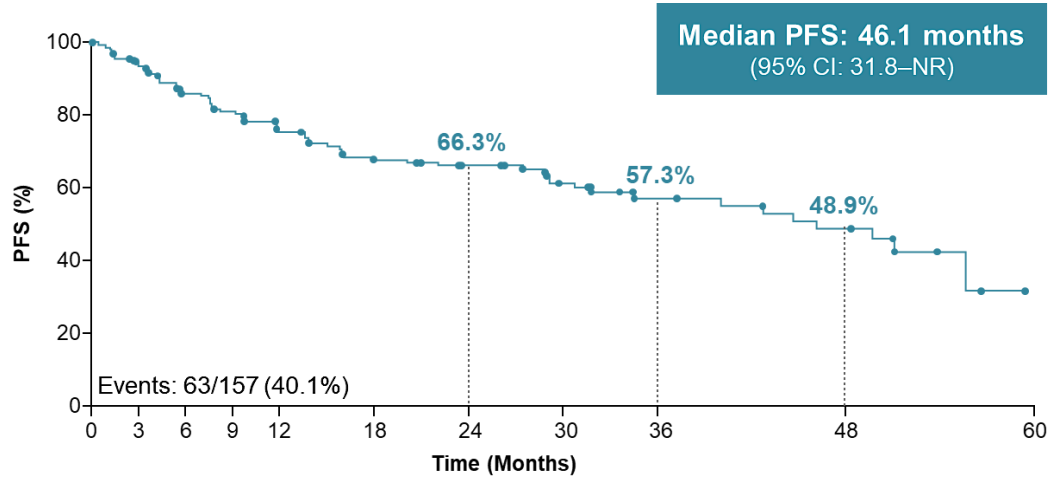
Efficacy[a]	TRUST-I (n=103)	TRUST-II (n=54)	Pooled (N=157)
cORR, % (95% CI)	90.3 (82.9–95.3)	88.9 (77.4–95.8)	89.8 (84.0–94.1)
Prior chemotherapy	(n=20) 85.0 (62.1–96.8)	(n=10) 100 (69.2–100)	(n=30) 90.0 (73.5–97.9)
IC Efficacy[b]	**(n=8)**	**(n=9)**	**(n=17)**
IC-cORR, % (95% CI)	87.5 (47.4–99.7)	66.7 (29.9–92.5)	76.5 (50.1–93.2)



Data cutoff: August 31, 2025

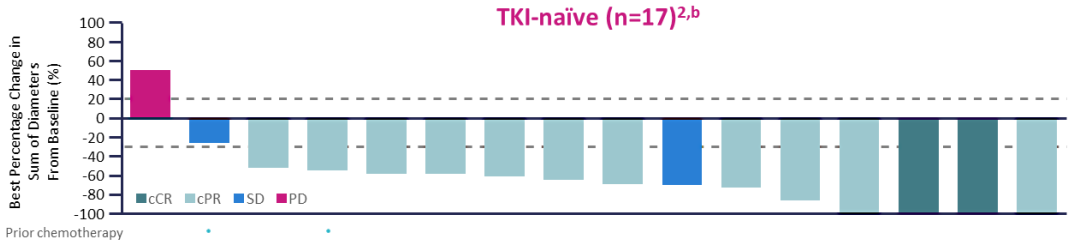


No. at risk											
	141	129	119	108	99	86	75	56	28	18	0



No. at risk											
	157	141	123	115	103	87	76	60	30	23	0

IC-cORR[1,2]
76.5%
95% CI: 50.1–93.2



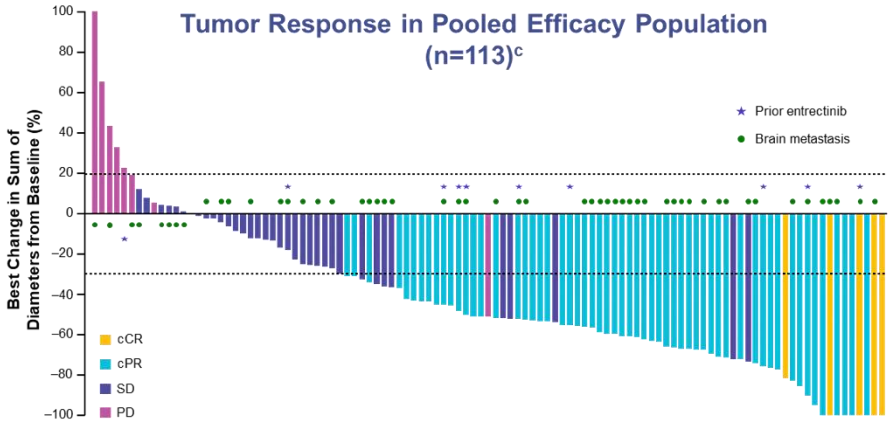
Bazhenova L et al., AACR 2026

Taletrectinib in *ROS1*+ NSCLC: Pooled Analysis of Two Phase 2 Trials
TKI-pretreated patients (crizotinib or entrectinib)

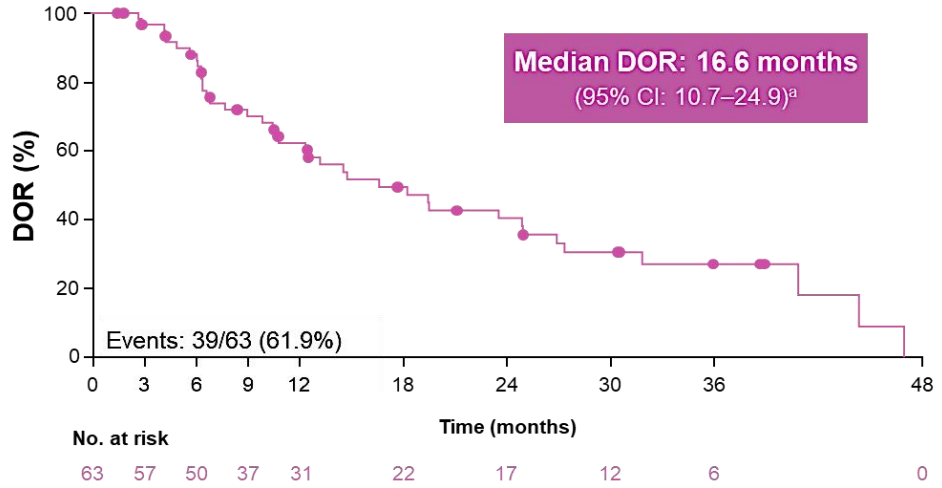
Tumor Response in TKI-Pretreated Patients

Efficacy[a]	TRUST-I (n=66)	TRUST-II (n=47)	Pooled Efficacy Population (N=113)
cORR, % (95% CI)	**51.5** (38.9–64.0)[b]	**61.7** (46.4–75.5)	**55.8** (46.1–65.1)
Prior chemotherapy	(n=23) **43.5** (23.2–65.5)	(n=19) **78.9** (54.4–94.0)	(n=42) **59.5** (43.3–74.4)

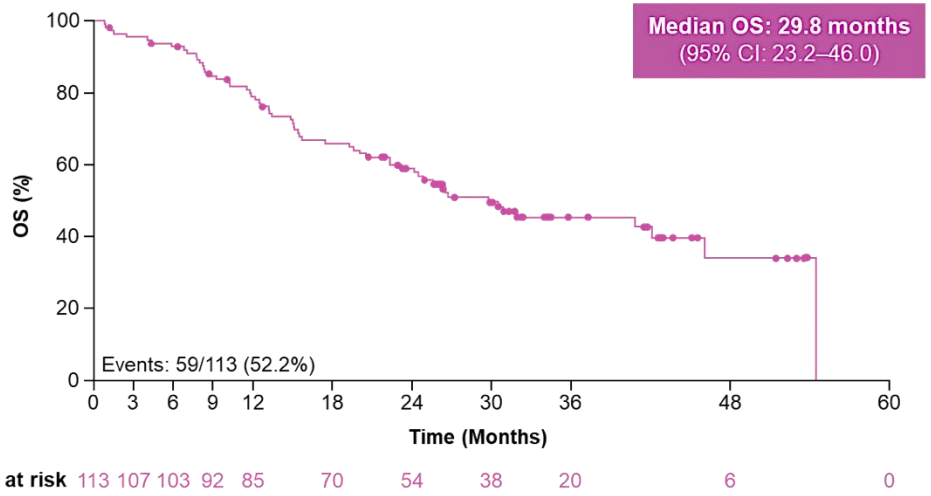
IC efficacy data are shown in the **Supplement**

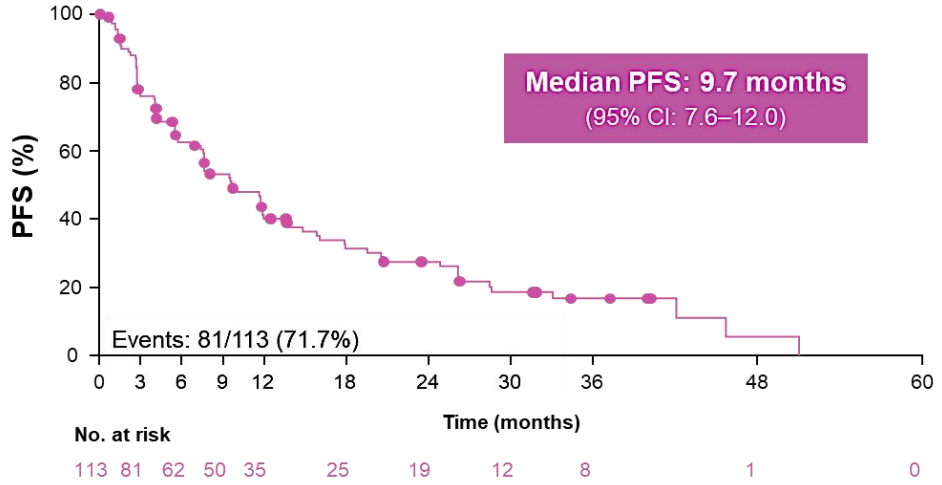


Pooled (N=113)
Median follow-up: 35.8 months



Pooled (N=113)
Median follow-up: 35.8 months





Liu G et al. AACR 2026

Taletrectinib Safety Profile in the Integrated Safety Analysis (N=363)

Most frequent TEAEs (≥20% of patients), n (%)	Any grade	Grade 1	Grade 2	Grade ≥3
AST increased	261 (71.9)	166 (45.7)	65 (17.9)	30 (8.3)
ALT increased	248 (68.3)	143 (39.4)	65 (17.9)	40 (11.0)
Diarrhea	234 (64.5)	181 (49.9)	44 (12.1)	9 (2.5)
Nausea	174 (47.9)	131 (36.1)	38 (10.5)	5 (1.4)
Vomiting	164 (45.2)	127 (35.0)	32 (8.8)	5 (1.4)
Anemia	139 (38.3)	80 (22.0)	44 (12.1)	15 (4.1)
Dizziness	78 (21.5)	67 (18.5)	10 (2.8)	1 (0.3)
Electrocardiogram QT prolonged	76 (20.9)	52 (14.3)	11 (3.0)	13 (3.6)
Constipation	74 (20.4)	62 (17.1)	12 (3.3)	0
Blood creatinine increased	73 (20.1)	62 (17.1)	11 (3.0)	0

- The most common (any grade) TEAEs were increased AST, increased ALT, diarrhea, nausea, and vomiting
- Rates of neurologic TEAEs were low and mostly Grade 1 or 2
  - **Dizziness**: 18.5% Grade 1; 2.8% Grade 2
  - **Dysgeusia**: 13.2% Grade 1; 2.2% Grade 2
- TEAEs led to dose interruptions in 42.7% of patients, dose reductions in 31.3%, and treatment discontinuations in 8.5%

Taletrectinib in *ROS1*+ NSCLC: Pooled Analysis of Two Phase 2 Trials

- Taletrectinib appears as a highly active agent in TKI-naïve ROS1+ advanced NSCLC
  - ORR 90.3%
  - Median DoR: 49.7 months
  - Median PFS : 46.1 months
  - Good CNS activity
- The tolerance profile is adapted to a long duration of first-line treatment
  - Short-term duration of GI toxicity
  - Transaminases elevation is managed with dose reductions
  - Without impact on PFS
- Data based on a majority of Asian patients without obvious differences with Caucasian patients

ARROS-1: A Global First-in-Human Phase 1/2 Clinical Trial of Zidesamtinib in Advanced *ROS1*+ NSCLC

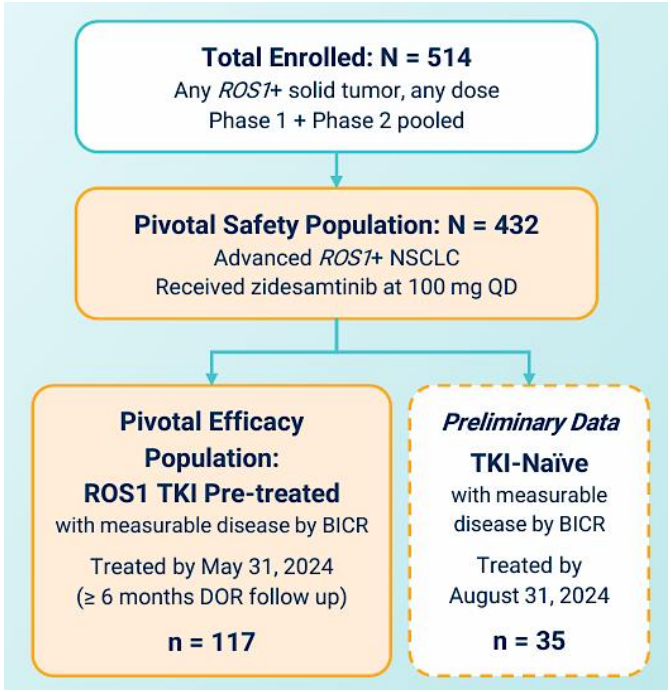
PHASE 1: Zidesamtinib dose escalation (25 – 150 mg QD) in ROS1 TKI pre-treated patients with advanced *ROS1*+ solid tumors

PHASE 2: Zidesamtinib 100 mg QD (RP2D)

ARROS-1 PHASE 2 PATIENT POPULATION	PRIOR ROS1 TKI	PRIOR CHEMO/I-O
ROS1+ NSCLC	ROS1 TKI-naïve [a]	≤ 1
	1 prior ROS1 TKI [b]	None
		1 [c]
	≥ 2 Prior ROS1 TKIs [d]	≤ 1
Any *ROS1*+ Solid Tumor [e]	Any	Any

PHASE 2 OBJECTIVES

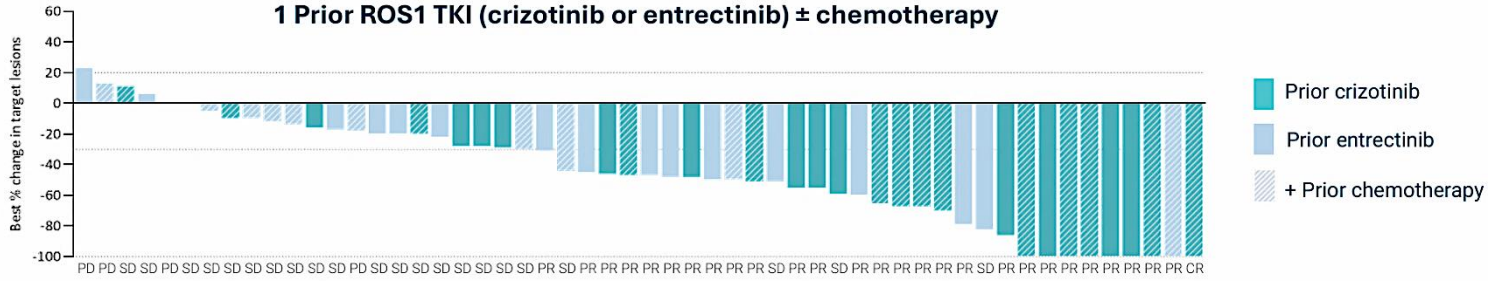
- **Primary:** ORR by blinded independent central review (BICR)
- **Secondary:** Additional efficacy measures (DOR, TTR, CBR, PFS, OS), intracranial activity, overall safety and tolerability, confirmation of PK profile, PROs



Treatment History	ROS1 TKI Pre-Treated [a] Pivotal Efficacy Population N = 117
Prior anticancer therapy, median (range)	2 (1 – 11)
Prior chemotherapy	62 (53%)
Prior ROS1 TKIs ± chemotherapy	
1 prior (crizotinib or entrectinib)	**55 (47%)**
Crizotinib	*28/55 (51%)*
Entrectinib	*27/55 (49%)*
1 prior (repotrectinib or taletrectinib)	4 (3%)
≥2 prior	**58 (50%)**
Lorlatinib, repotrectinib, or taletrectinib	***54/58 (93%)***
Lorlatinib	*43/58 (74%)*
Repotrectinib	*15/58 (26%)*
Taletrectinib	*5/58 (9%)*

Drilon A et al., WCLC 2025

ARROS-1
Zidesamtinib in TKI Pretreated Patients with Advanced *ROS1*+ NSCLC



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

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

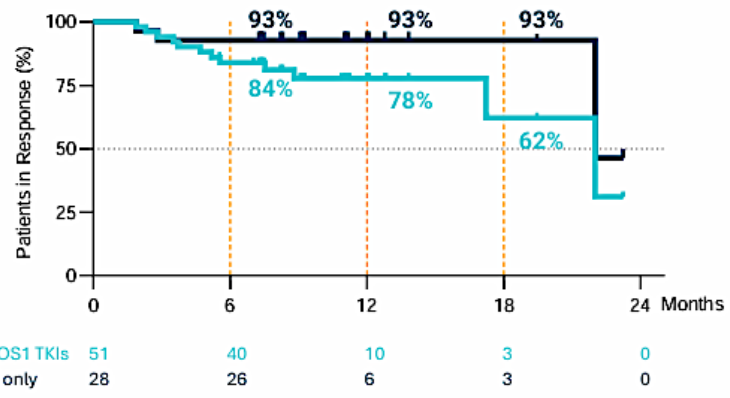
Responses were also observed in patients previously treated with:

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

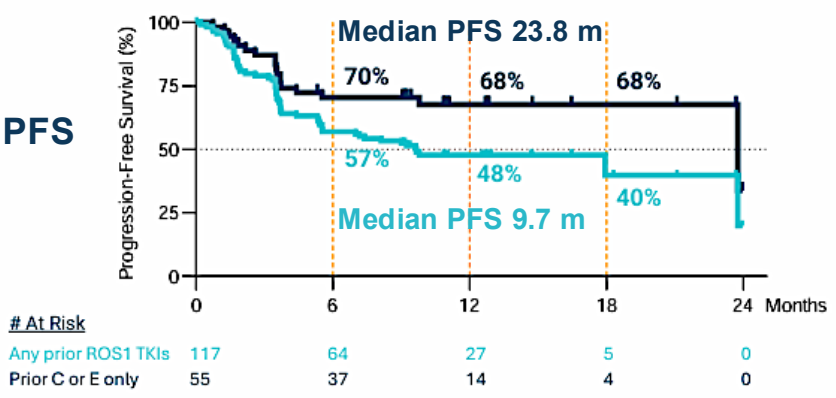
ROS1 G2032R Resistance Mutation		
Advanced *ROS1*+ NSCLC Analysis by BICR	Any prior ROS1 TKI ± chemotherapy	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy [a]
ORR, % (n/N) [95% CI]	**54%** (14/26) [33, 73]	**83%** (5/6) [36, 100]

Measurable CNS lesions by BICR at baseline		
Advanced *ROS1*+ NSCLC Analysis by BICR	Any prior ROS1 TKI ± chemotherapy	Prior crizotinib only ± chemotherapy
IC-ORR, % (n/N) [95% CI]	**48%** (27/56) [a] [35, 62]	**85%** (11/13) [55, 98]

DoR



PFS



Drilon A et al., WCLC 2025

ARROS-1
Zidesamtinib in TKI Pretreated Patients with Advanced *ROS1*+ NSCLC

All Treatment-Emergent Adverse Events (TEAEs) in ≥15% of Patients Treated with Zidesamtinib 100 mg QD (N = 432) [a]

Preferred or grouped term	Any Grade	Grade ≥ 3
Peripheral edema [b]	36%	0.7%
Constipation	17%	0%
Blood CPK increased	16%	3.5%
Fatigue [c]	16%	0.7%
Dyspnea [d]	15%	3.0%

[a] Patients received at least 1 dose of zidesamtinib at 100 mg QD with median duration of exposure of 5 months (range: 0, 32).

[b] Includes terms peripheral edema, peripheral swelling, edema, generalized edema.

[c] Includes terms fatigue, asthenia, malaise.

[d] Includes terms dyspnea, dyspnea exertional, orthopnea

Dose reduction due to TEAEs: 10% (43/432)

- Most common (>2 patients): peripheral edema (n=8), blood CPK increased (n=4), peripheral sensory neuropathy (n=4), arthralgia (n=3), paresthesia (n=3)

Discontinuation due to TEAE: 2% (10/432)

- Most common (>2 patients): pneumonia (n=3)

The only treatment-related adverse event in ≥15% of patients was peripheral edema [b] (29%)

Drilon A et al., WCLC 2025

ARROS-1
Zidesamtinib in TKI Pretreated Patients with Advanced ROS1+ NSCLC

- Zidesamtinib demonstrated in *ROS1*+ pretreated advanced NSCLC
  - Durable activity, including in heavily pre-treated patients (even after prior repotrectinib or taletrectinib) and patients with the ROS1 G2032R resistance mutation
  - Durable intracranial responses
  - With a favorable tolerance profile with low rates of dose reduction (10%) and treatment discontinuation (2%), consistent with the TRK sparing design
- Activity in TKI-naïve patients appears promising but needing a longer follow-up to be evaluated

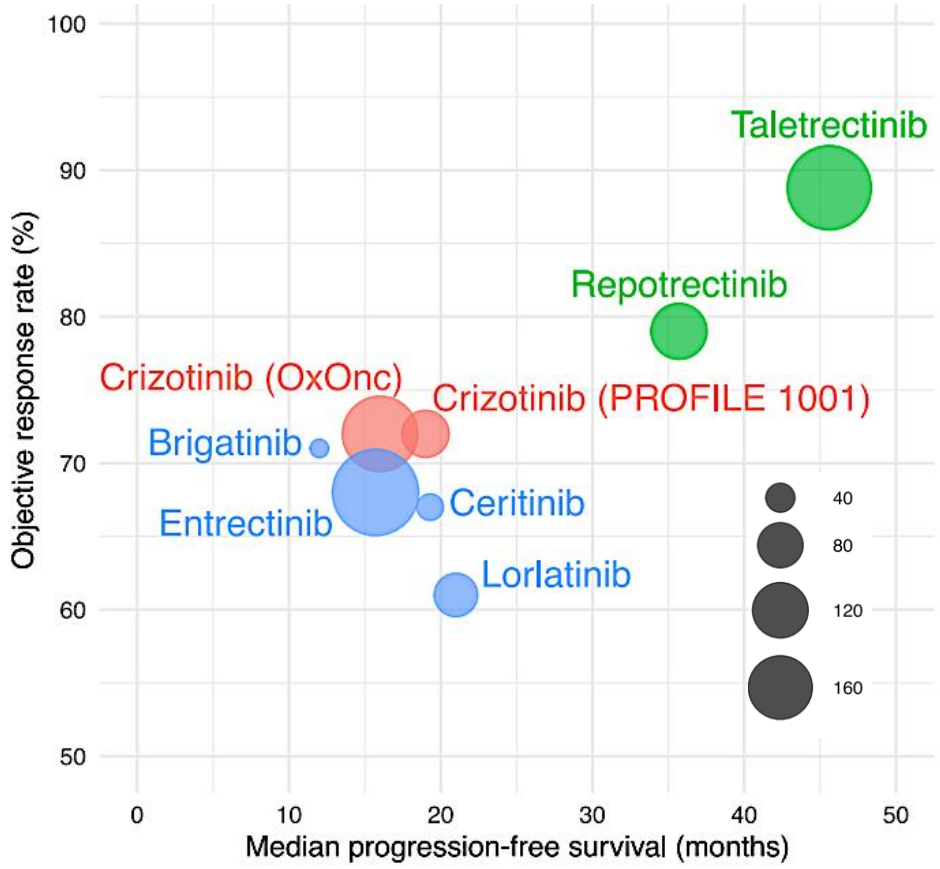
Frontline Treatment of *ROS1+* Advanced NSCLC

- Similar to *ALK+ NSCLC*, the choice of first-line treatment appears crucial in altering the natural history of the disease and improving patient survival
- The tolerance profile is also essential from the perspective of long-term treatment

ROS1+ advanced NSCLC → **New generation ROS1 TKI**

Systemic efficacy, CNS penetration, TRKB inhibition, tolerance profile

- Ongoing trials
  - NCT04603807: entrectinib *vs*. crizotinib in 1st line (PFS in pts with brain mets)
  - NCT06140836: repotrectinib *vs*. crizotinib in 1st line (PFS in ITT pts), Trident-3
  - NCT06564324: taletrectinib *vs*. crizotinib in 1st line (China)
  - NCT07154706, TRUST-IV: taletrectinib *vs*. placebo in adjuvant setting



Desilets A et al., Cancer 2025

Year in Review:
Therapeutic Targets Beyond EGFR for Non-Small Cell Lung Cancer

INTRODUCTION: **Relative Impact of Targeted Treatment**

MODULE 1: **HER2 Alterations**

MODULE 2: **KRAS Mutations**

MODULE 3: **MET Overexpression**

MODULE 4: **ALK Fusions**

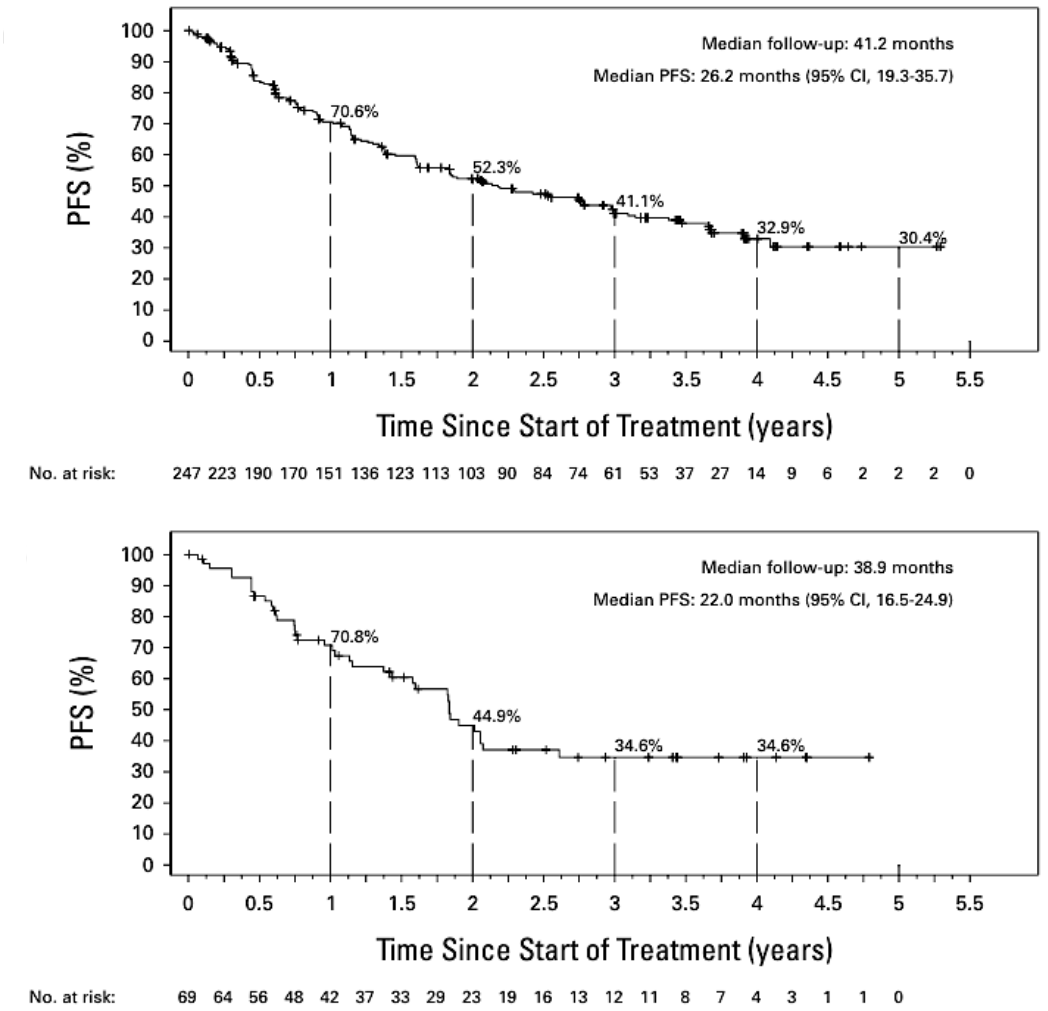
MODULE 5: **ROS1 Fusions**

MODULE 6: RET Fusions

RTP Year in Review 2026

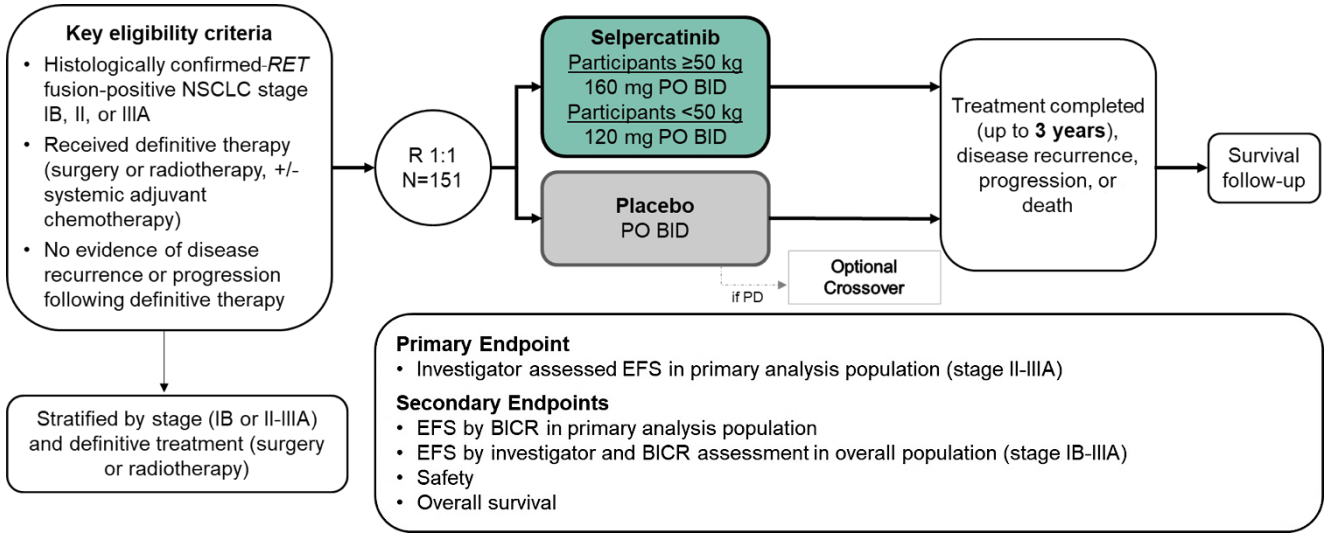
Selpercatinib: final results of the LIBRETTO-001 Phase I/II Trial

	Previous platinum CT	Treatment naïve
N	247	69
Median age	61.0	63.0
Female	56.7%	62.3%
Never smoker	66.8%	69.6%
ECOG PS 0/1/2, %	36.4/60.7/2.8	36.2/58.0/5.8
Median No of prior lines	2	0
RET fusion, % *KIF5B-RET* *CCDC6-RET* *NCOA4-RET*	 61.9 21.5 2.0	 69.6 14.5 1.4
ORR, % (95% CI)	61.5 (55.2-67.6)	82.6 (71.6-90.7)
DoR, months, median (95% CI)	31.6 (20.4-42.3)	20.3 (15.4-29.5)
PFS, months, median, (95% CI)	26.2 (19.3-35.7)	22.0 (16.5-24.9)
OS, months, median, (95% CI)	47.6 (35.9-NE)	NE (37.8-NE)

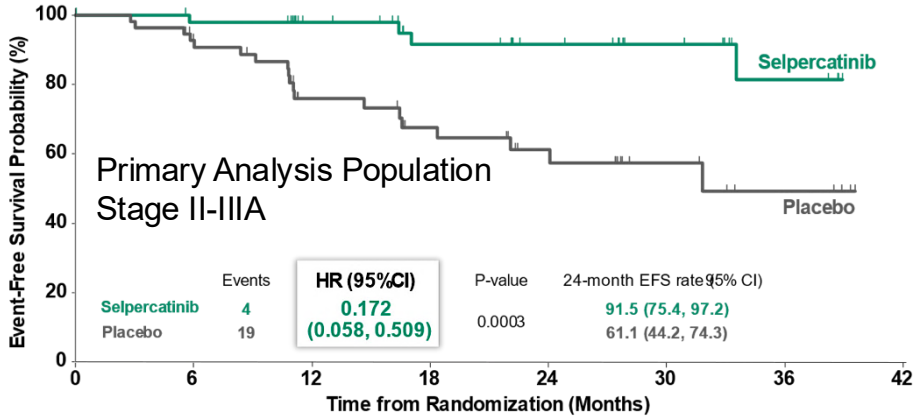


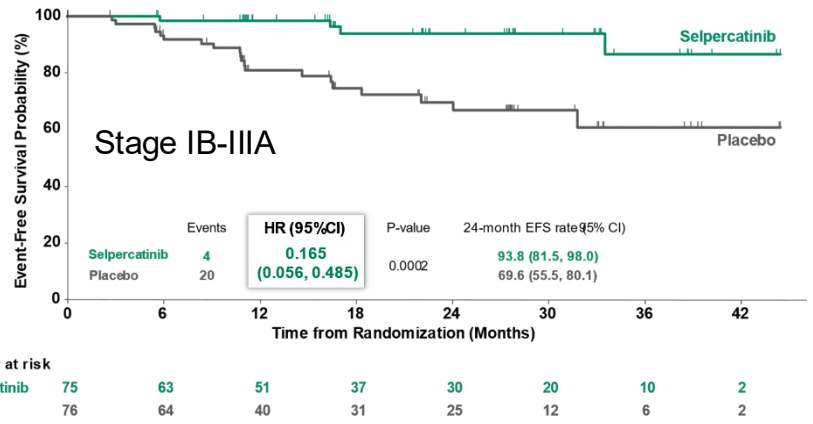
Gautschi O et al., JCO 2025

LIBRETTO-432 Trial: A multicenter, phase 3, double-blind, randomized, placebo-controlled study with adjuvant selpercatinib in stage IB-IIIA *RET* fusion-positive NSCLC



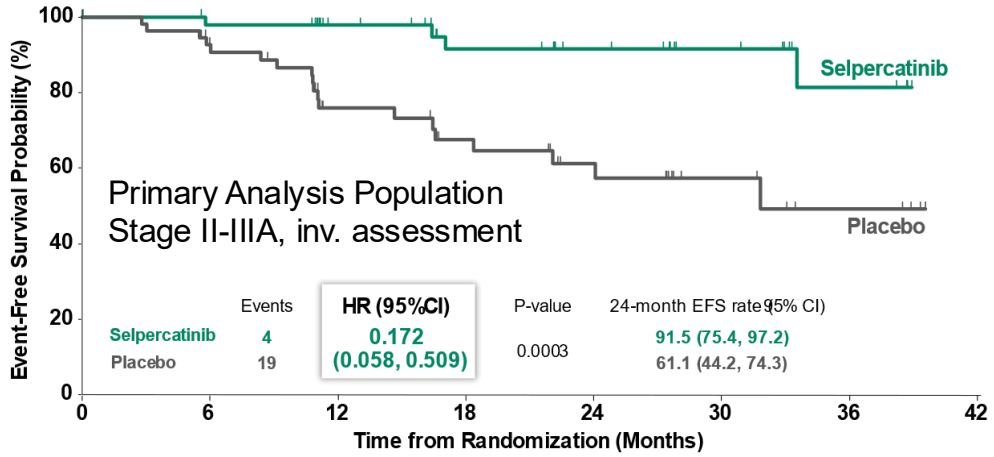
		Selpercatinib N=54	Placebo N=55
Age, years	Median (range)	59.5 (41.0-84.0)	61.0 (26.0-78.0)
Sex, n (%)	Female	34 (63.0)	30 (54.5)
	Male	20 (37.0)	25 (45.5)
Race, n (%)[a]	Asian	33 (61.1)	32 (58.2)
	White	21 (38.9)	21 (38.2)
Geographic Region, n (%)	East Asia	31 (57.4)	31 (56.4)
	Europe/North America	18 (33.3)	21 (38.2)
	Other	5 (9.3)	3 (5.5)
Smoking Status, n (%)	Never	37 (68.5)	38 (69.1)
	Former / Current	17 (31.5)	17 (30.9)
ECOG PS, n (%)[b]	0	30 (55.6)	36 (65.5)
	1	24 (44.4)	18 (32.7)
RET fusion, n (%)	KIF5B:: RET	33 (61.1)	34 (61.8)
	CCDC6:: RET	14 (25.9)	11 (20.0)
	Other	7 (13.0)	10 (18.2)
PD-L1, n (%)[c]	Negative	11 (20.4)	16 (29.1)
	Positive	25 (46.3)	28 (50.9)
	Unknown	17 (31.5)	11 (20.0)
Prior anti-cancer therapy, n (%)	Surgery	54 (100.0)	54 (98.2)
	Radiotherapy	2 (3.7)	6 (10.9)
	Systemic therapy	50 (92.6)	50 (90.9)





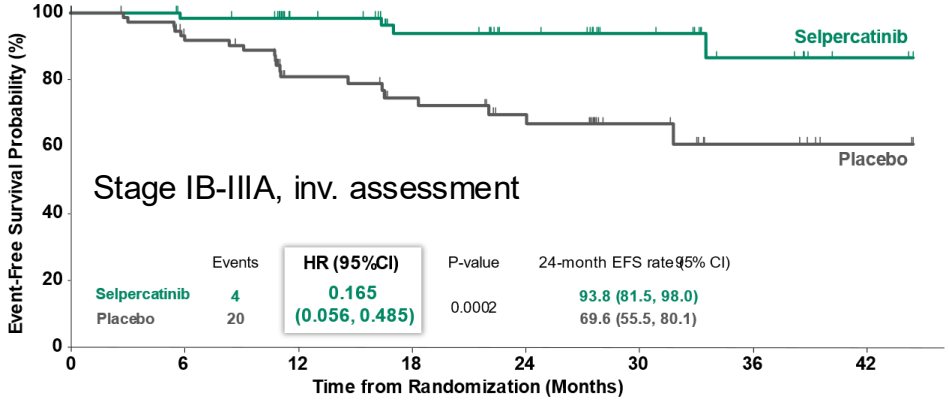
Goldman J et al., ASCO 2026; Wu YL et al., NEJM 2026

LIBRETTO-432 Trial: A multicenter, phase 3, double-blind, randomized, placebo-controlled study with adjuvant selpercatinib in stage IB-IIIA *RET* fusion-positive NSCLC



Number at risk

Selpercatinib	54	45	37	27	22	15	7	0
Placebo	55	47	28	22	16	8	4	0



Number at risk

Selpercatinib	75	63	51	37	30	20	10	2
Placebo	76	64	40	31	25	12	6	2

	Selpercatinib N=54	Placebo N=55
Number of EFS events, n	4	19
Locoregional	1	10
Local	1	3
Regional	0	7
Distant	5	18
Brain	1	3

	Selpercatinib N=75		Placebo N=76	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Patients with ≥1 TEAE (≥ 20%), no. (%)	75 (100.0)	50 (66.7)	74 (97.4)	18 (23.7)
ALT increase	47 (62.7)	13 (17.3)	14 (18.4)	1 (1.3)
AST increase	45 (60.0)	14 (18.7)	12 (15.8)	2 (2.6)
Diarrhea	29 (38.7)	3 (4.0)	13 (17.1)	0
Dry mouth	30 (40.0)	0	12 (15.8)	0
Cough	20 (26.7)	0	18 (23.7)	0
Bilirubin increase	20 (26.7)	1 (1.3)	11 (14.5)	0
Hypertension	23 (30.7)	8 (10.7)	8 (10.5)	2 (2.6)
Constipation	17 (22.7)	0	10 (13.2)	0
Hyperuricemia	15 (20.0)	0	8 (10.5)	0
Other AEs of special Interest				
Hypersensitivity	5 (6.7)	0	0	0
ECG QT prolongation	7 (9.3)	1 (1.3)	1 (1.3)	1 (1.3)

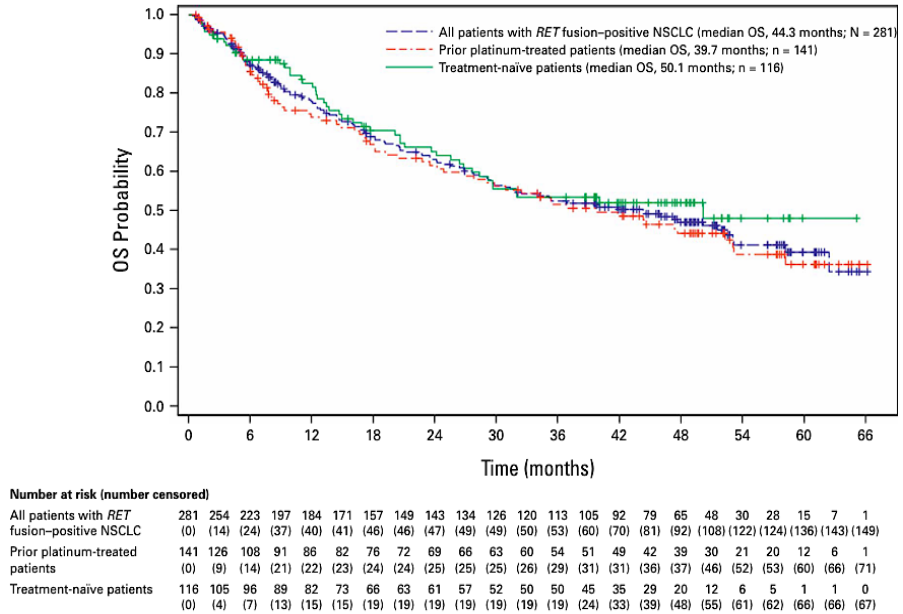
Goldman J et al., ASCO 2026; Wu YL et al., NEJM 2026

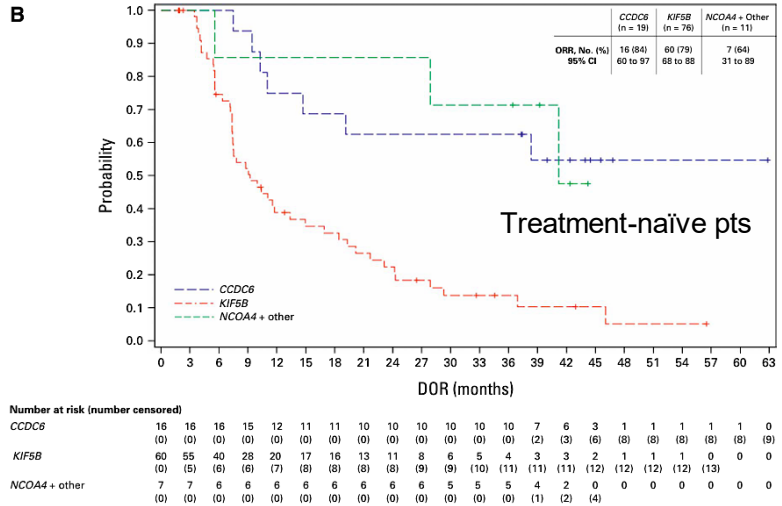
LIBRETTO-432 Trial: A multicenter, phase 3, double-blind, randomized, placebo-controlled study with adjuvant selpercatinib in stage IB-IIIA *RET* fusion-positive NSCLC

- Libretto-432 defines a new standard of care for early-stage RET fusion-positive NSCLC.
- Joining osimertinib and alectinib as proven adjuvant targeted therapies in early-stage NSCLC
- Role of adjuvant chemotherapy in this setting?
- Impact on OS needs a longer follow up
- Management of side-effects is not trivial
  - 66.7% of patients experienced grade > 3 TEAE
  - 17.3% discontinued selpercatinib
  - 77.3% required dose interruption
  - 54.7% required dose reduction
- Early-stage molecular testing must expand beyond EGFR, ALK, and PD-L1

Pralsetinib in patients with advanced *RET* fusion-positive NSCLC: Update from the ARROW trial

	Previous platinum CT	Treatment naïve
N	141	116
Median age	59.0	62.5
Female	60%	51%
Never smoker	63%	59%
ECOG PS 0/1/2, %	26/70/4	30/69/1
Median No of prior lines	2	0
RET fusion, % *KIF5B-RET* *CCDC6-RET* *NCOA4-RET*	 70 19 1	 70 16 1
ORR, % (95% CI)	63 (54-71)	78 (69-86)
DoR, months, median (95% CI)	31.8 (15.1-40.4)	13.4 (9.4-21.7)
PFS, months, median, (95% CI)	16.4 (11.4-23.5)	12.1 (9.2-16.6)
OS, months, median, (95% CI)	39.7 (27.8-53.2)	50.1 (28.3-NE)





AcceleRET-Lung: Open-Label Phase 3 Trial of Pralsetinib in 1L *RET* Fusion-Positive mNSCLC

- ***RET* fusion-positive mNSCLC**
- ECOG PS 0 or 1
- No prior systemic treatment
- Patients with CNS metastases were permitted if they were asymptomatic and on a stable dose of corticosteroids

Planned enrollment: N=226

R 1:1

- **Pralsetinib**
- **Optional crossover upon PD**
- **Investigator's choice of platinum-based chemotherapy (SOC)[a]**

Primary endpoint:

PFS by investigator assessment according to RECIST v1.1

Secondary endpoints:

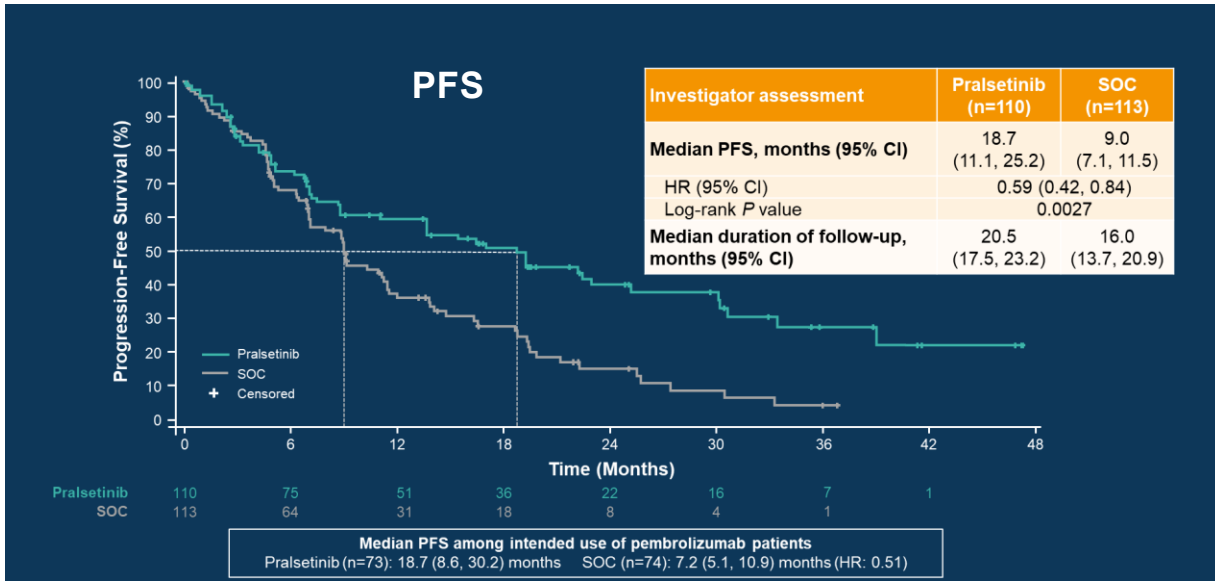
- Overall response rate: CR or PR, duration of response
- Overall survival, clinical benefit rate, disease control rate, safety/tolerability

Stratification factors

- History of brain metastasis (yes vs no)
- ECOG PS (0 vs 1)
- Intended use of pembrolizumab (yes vs no)

Statistical assumptions

- 133 PFS events targeted for 90% power to detect an HR of 0.57 corresponding to target median PFS:
  - Pralsetinib: 12.3 months
  - SOC: 7.0 months

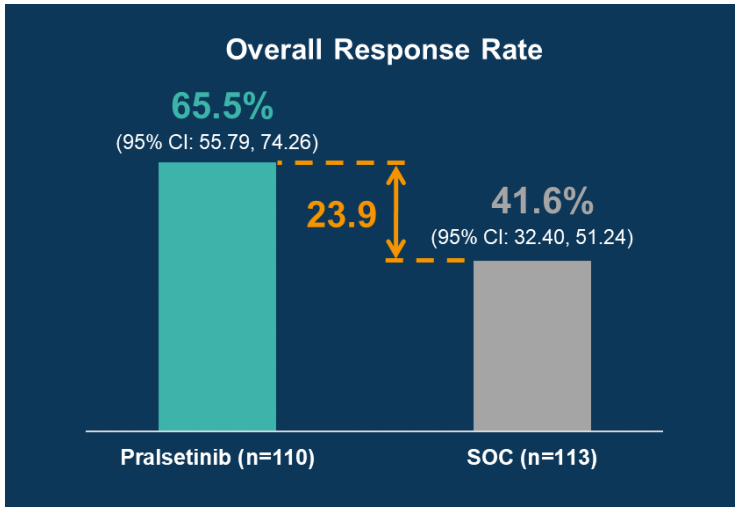


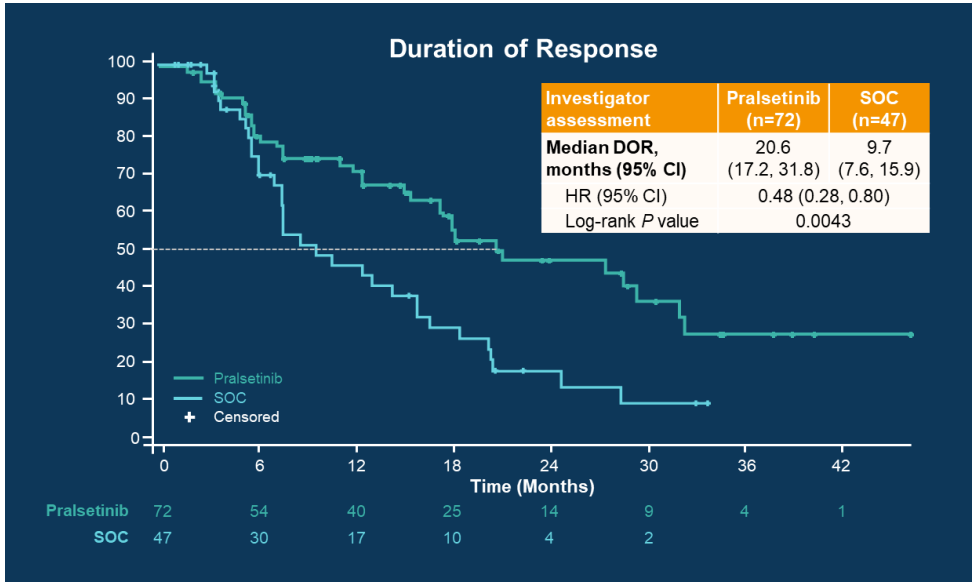
Investigator assessment	Pralsetinib (n=110)	SOC (n=113)
Median PFS, months (95% CI)	18.7 (11.1, 25.2)	9.0 (7.1, 11.5)
HR (95% CI)	0.59 (0.42, 0.84)	
Log-rank *P* value	0.0027	
Median duration of follow-up, months (95% CI)	20.5 (17.5, 23.2)	16.0 (13.7, 20.9)

Patient characteristics, n (%)		Pralsetinib n=110	SOC n=113
Age, years	Median (range)	62.0 (25-82)	63.0 (25-88)
Sex	Male	57 (52)	49 (43)
	Female	53 (48)	64 (57)
ECOG PS[b]	0	42 (38)	43 (38)
	1	68 (62)	68 (60)
Smoking status[c]	Never smoked	65 (59)	67 (59)
	Former smoker	33 (30)	39 (35)
	Current smoker	9 (8)	5 (4)
NSCLC histology	Adenocarcinoma	109 (99)	109 (97)
Disease stage[d]	IIIB or IIIC	4 (4)	3 (3)
	IV	31 (28)	49 (43)
	IVA	29 (26)	26 (23)
	IVB	45 (41)	33 (29)
History of metastases	CNS	30 (27)	33 (29)
Intended use of pembrolizumab if randomized to SOC	Yes	73 (66)	74 (66)

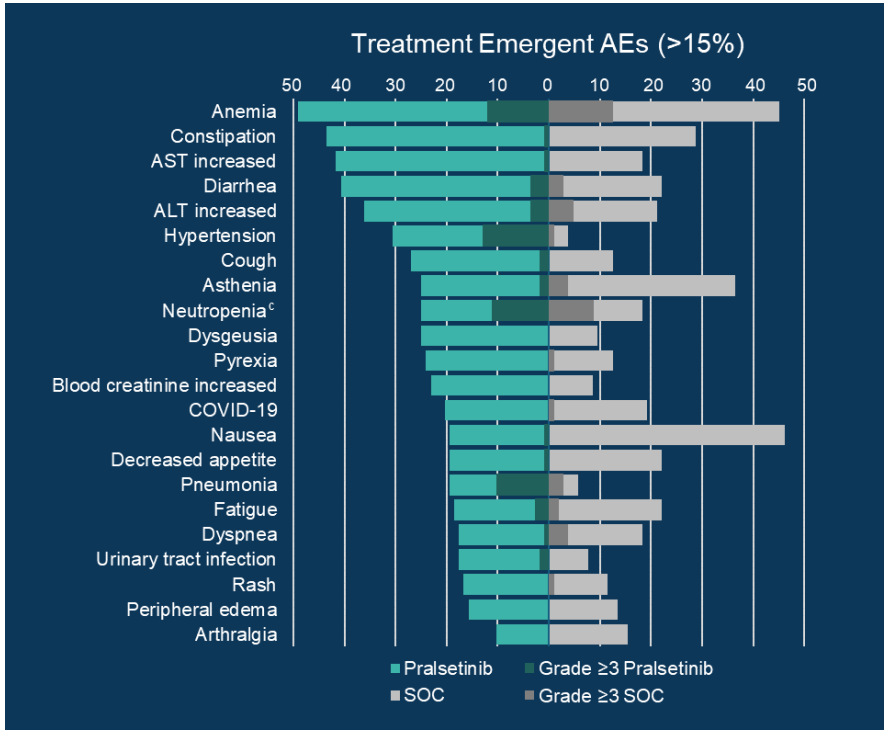
Popat S et al., ASCO 2026

AcceleRET-Lung: Open-Label Phase 3 Trial of Pralsetinib in 1L *RET* Fusion-Positive mNSCLC





Adverse events (main treatment period)	Pralsetinib (n=108)	SOC (n=104)
Patients with ≥1 AE	108 (100)	104 (100)
Related AEs	101 (93.5)	96 (92.3)
Serious AEs	67 (62.0)	38 (36.5)
Related serious AEs	23 (21.3)	9 (8.7)
Grade 3-5 AEs	84 (77.8)	60 (57.7)
Deaths due to AEs[b]	16 (14.8)	5 (4.8)
Deaths due to infections[b]	8 (7.4)	0
Grade ≥3 QT prolongation	3 (2.8)	0
AEs leading to withdrawal from treatment	18 (16.7)	25 (24.0)
AEs leading to dose modification/interruption	80 (74.1)	57 (54.8)



Popat S et al., ASCO 2026

Pralsetinib in *RET*+ advanced NSCLC

- Pralsetinib has undeniable efficacy in RET-positive NSCLC, demonstrating superiority over chemotherapy

- However, its tolerability profile—characterized by hematologic toxicity and a significant risk of opportunistic infections—makes its use difficult compared with selpercatinib, which has at least comparable efficacy and is better tolerated.

Patterns of Care: Exploring How Community Oncologists Manage HR-Positive, HER2-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 1, 2026

5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO

Reshma L Mahtani, DO

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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RTP Year in Review 2026