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LUNG CONNECT

ONCOGENE-ADDICTED NSCLC HIGHLIGHTS FROM ESMO 2025

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DEVELOPED BY LUNG CONNECT

This programme is developed by LUNG CONNECT, an international group of experts in the field of thoracic oncology and brought to you alongside PRECISION ONCOLOGY CONNECT, an international group of experts in the field of detection and treatment of targetable genetic/genomic alterations in various cancers

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Expert disclosures:

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CLINICAL TAKEAWAYS

- **SOHO-01:** Sevabertinib produces rapid, durable, and clinically meaningful responses with manageable toxicity in pretreated and treatment-naïve patients with advanced *HER2*-mutant NSCLC. These results support sevabertinib as a potential new oral targeted therapy for this molecular subset
- **Beamion LUNG1:** Zongertinib demonstrates strong and clinically meaningful efficacy with manageable toxicity, supporting its role as a targeted treatment option for *HER2*-driven NSCLC
- **LOXO-RAS-20001:** Olomorasib provides evidence of meaningful intracranial activity, highlighting progress in addressing brain metastases in patients with *KRAS* G12C-mutant NSCLC and active, untreated brain metastases
- **FURMO-003:** Firmonertinib continues to show promising clinical activity in EGFR exon 20 insertion (ex20ins) NSCLC, with an acceptable safety profile and ongoing phase 3 development
- **OptiTROP-Lung04:** Sacitizumab tirumotecan (sac-TMT) demonstrated statistically significant and clinically meaningful improvements in PFS and OS compared to platinum-based chemotherapy (PBC) providing support for sac-TMT as a potential new treatment option for patients with *EGFR*-mutant NSCLC and EGFR-TKI resistance

NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

EDUCATIONAL OBJECTIVES

- Understand the **clinical trial data and emerging profiles** of therapies for the treatment of molecularly driven lung cancer, including treatments for HER2-directed NSCLC

NSCLC, non-small cell lung cancer

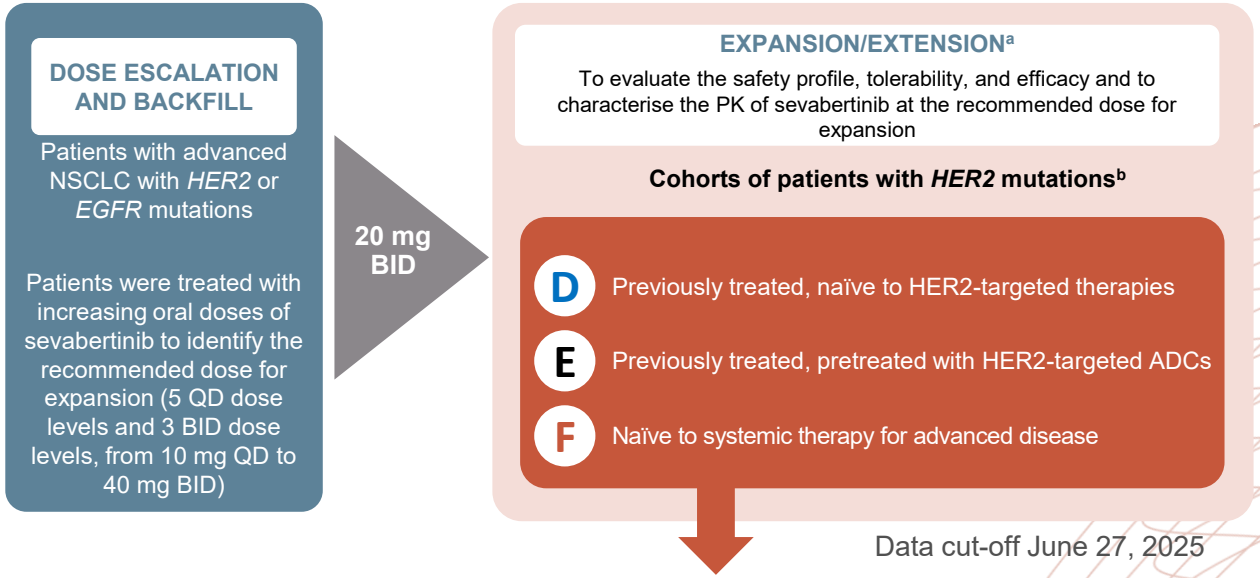
SEVABERTINIB (BAY 2927088) IN ADVANCED *HER2*-MUTANT NSCLC: RESULTS FROM THE SOHO-01 STUDY

Le X, et al. Abstract LBA75, ESMO 2025

NSCLC, non-small cell lung cancer

SOHO-01: BACKGROUND AND STUDY DESIGN

- *HER2*-activating mutations have been reported in approximately 1-4% of patients with NSCLC and are associated with a poor prognosis[1-3,9,10]
- *HER2* tyrosine kinase domain (TKD) mutations are the most common, with the Y772_A775dup (YVMA) ex20ins being the most frequent in NSCLC[4,5,6]
- Sevabertinib (BAY 2927088) is an oral, reversible TKI that potently inhibits *HER2*-activating mutations[3,7]
- Encouraging anti-tumour activity and manageable safety were observed in patients with NSCLC harbouring a *HER2*-activating mutation treated with sevabertinib[3,7]
- The FDA has granted Breakthrough Therapy designation for BAY 2927088 for previously-treated patients with advanced NSCLC and activating *HER2* mutations[3,8]
- Here we report results from cohorts of the ongoing, open-label, multicentre phase 1/2 SOHO-01 (NCT05099172)[9,10]



Data cut-off June 27, 2025

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

ADC, antibody-drug conjugate; BICR, blinded independent central review; BID, twice daily; DCR, disease control rate; DoR, duration of response; FDA, Food and Drug Administration; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; PK, pharmacokinetics; QD, once a day; RECIST, Response Evaluation Criteria in Solid Tumours; TKI, tyrosine kinase inhibitor

1. Riudavets M, et al. ESMO Open 2021;6:100260; 2. Remon J, et al. Cancer Treat Rev. 2020;90:102105; 3. Girard N, et al. J Clin Oncol 2024;42(suppl 17). Abstr LBA8598; 4. Hong L, et al. NPJ Precis Oncol 2024;8:217: doi: 10.1038/s41698-024-00720-9; 5. Liu Z, et al. Onco Targets Ther 2018;11:7323-31; 6. Yang S, et al. Transl Lung Cancer Res. 2021;10:753-65; 7. Loong HHF, et al. Ann Oncol. 2023;34(suppl 2):S761-S762 (Abstract 1320MO); 8. Bayer receives U.S. FDA Breakthrough Therapy designation for BAY 2927088 for non-small cell lung cancer harboring HER2 activating mutations. Available here (accessed June 2025); 9. Le X, et al. Abstract LBA75, ESMO 2025. Oral presentation; 10. Le X, et al. N Engl J Med 2025; DOI: 10.1056/NEJMoa2511065

SOHO-01: EFFICACY RESULTS

Efficacy per BICR Outcome, n (%)	Cohort D (previously treated) (n=81)	Cohort E (previous HER2 ADCs) (n=55)	Cohort F (treatment naïve) (n=73)
Confirmed best overall response:			
CR	2 (2)	3 (5)	3 (4)
PR	50 (62)	18 (33)	49 (67)
SD	20 (25)	23 (42)	16 (22)
PD	6 (7)	7 (13)	2 (3)
NE[a]	3 (4)	4 (7)	1 (1)
Not available[b]	–	–	2 (3)
ORR[c] [95% CI]	52 (64) [53-75]	21 (38) [25-52]	52 (71) [59-81]
DCR[d] [95% CI]	66 (81) [71-89]	39 (71) [57-82]	65 (89) [80-95]
Median DoR (95% CI), months	9.2 (6.3-13.5)	8.5 (5.6-16.4)	11.0 (8.1-NE)
Median PFS (95% CI), months	8.3 (6.9-12.3)	5.5 (4.3-8.3)	NE (9.6-NE)
Median follow-up (range), months	13.8 (1-32)	11.6 (2-22)	9.9 (<1-15)

Data cut-off June 27, 2025; [a] Requirement for CR, PR, SD, or PD was not met; [b] Patients with no post-baseline tumour assessment but who discontinued due to drug-related toxicity, death, or progression by clinical judgement 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 weeks

- Among patients with *HER2* TKD mutations, those with Y772_A775dup (YVMA) had an ORR of 78% and a higher median PFS (12.2 vs 7.0 months) than those with other *HER2* TKD mutations

ADC, antibody-drug conjugate; BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TKD, tyrosine kinase domain

Le X, et al. Abstract LBA75, ESMO 2025. Oral presentation

SOHO-01: EFFICACY RESULTS

- Brain metastases were present in 22% (Cohort D) and 27% (Cohort E) of previously treated patients and 12% of treatment naïve patients (Cohort F)
- Similar systemic responses were observed in patients with and without brain metastases

ORR (RECIST v1.1)	Cohort D[b]	Cohort E[c]	Cohort F[d]	Total
Brain metastases at baseline, n/N (%)[a]	18/81 (22)	15/55 (27)	9/73 (12)	42/209 (20)
ORR by BICR (RECIST v1.1), n/N (%)				
All patients	52/81 (64)	21/55 (38)	52/73 (71)	125/209 (60)
Brain metastases	11/18 (61)	4/15 (27)	7/9 (78)	22/42 (52)
No brain metastases	41/63 (65)	17/40 (43)	45/64 (70)	103/167 (62)
CNS progression	**Cohort D[b]**	**Cohort E[c]**	**Cohort F[d]**	**Total**
Brain metastases at baseline, n/N (%)[a]	18/81 (22)	15/55 (27)	9/73 (12)	42/209 (20)
Post-baseline progression in brain	4/18 (22)	3/15 (20)	0/9 (0)	7/42 (17)
No brain metastases at baseline, n/N (%) Post-baseline progression in brain	63/81 (78) 4/63 (6)	40/55 (73) 2/40 (5)	64/73 (88) 2/64 (3)	167/209 (80) 8/167 (5)
Post-baseline progression in brain	4/63 (6)	2/40 (5)	2/64 (3)	8/167 (5)

- In patients who did not have brain metastases,~5% developed new lesions in the brain as the progression site

Analysis cut-off date was June 27, 2025. Brain metastases were evaluated as site of first radiological progression in brain by BICR and RECIST v1.1

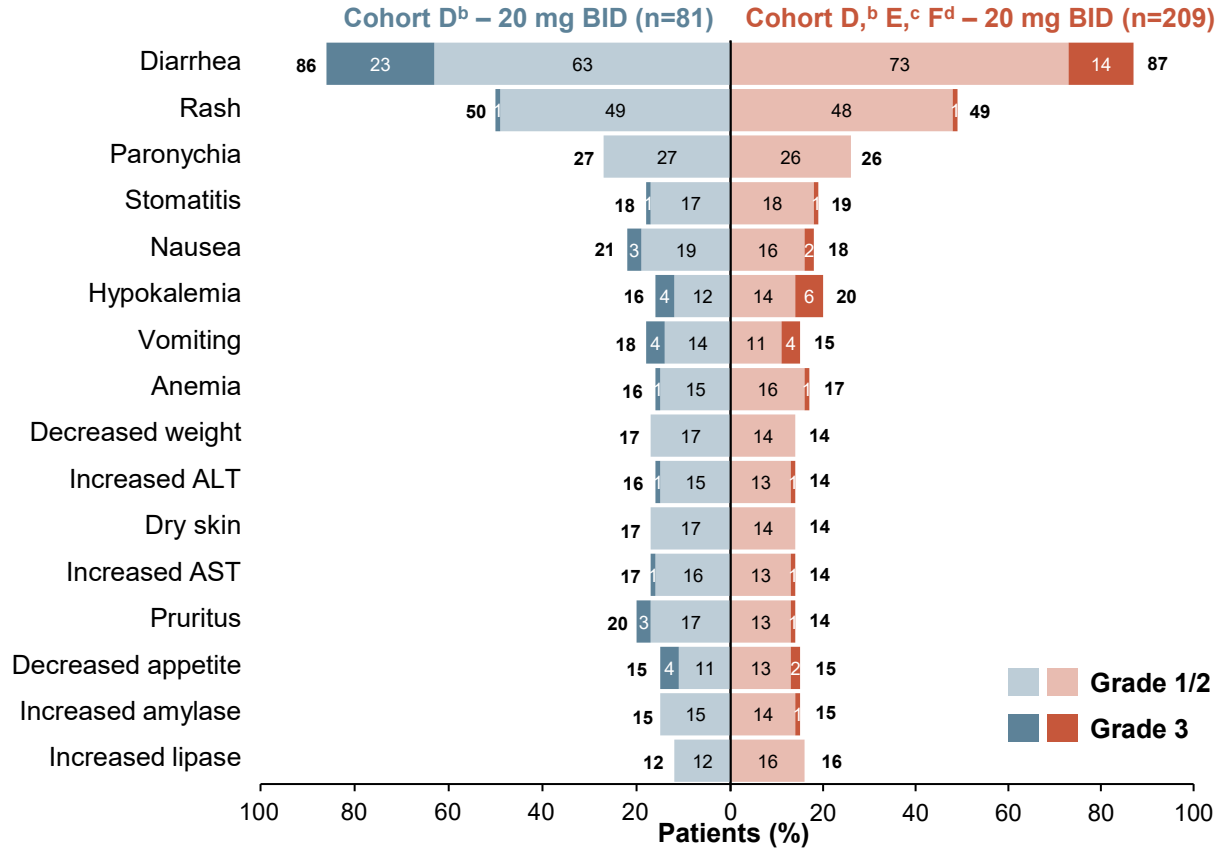
[a] Patients with any and/or non-target lesions having anatomical location of brain according to investigator assessment, including previously treated and asymptomatic brain metastases at baseline;
[b] Patients were naïve to *HER2*-targeted therapies; [c] Patients were pretreated with *HER2*-targeted ADCs;
[d] Patients were naïve to systemic therapy for advanced disease

ADC, antibody drug conjugate; BICR, blinded central independent review; CNS, central nervous system; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumours

Le X, et al. Abstract LBA75, ESMO 2025. Oral presentation

SOHO-01: SAFETY RESULTS

MOST FREQUENT TRAEs (≥10% OF TOTAL)



- Drug-related AEs were reported in 96%, 100%, and 97% of patients in Cohorts D, E, and F, respectively
- Diarrhea was the most commonly reported TRAE, mostly grade 1/2 (grade 3: 14%)
- TRAEs led to treatment discontinuation in 3% of patients; none due to diarrhea
- There were no reports of interstitial lung disease or pneumonitis

Analysis cut-off date was June 27, 2025. Grade categories do not necessarily equal total due to rounding

[a] MedDRA v28.0, CTCAE v5.0; [b] Patients were naïve to *HER2*-targeted therapies; [c] Patients were pretreated with *HER2*-targeted ADCs; [d] Patients were naïve to systemic therapy for advanced disease; [e] Grade 4 events of dyspnea, hypokalemia, and elevated ALT were reported, and 1 grade 5 event of cardiorespiratory arrest (this patient had baseline cardiopulmonary comorbidities and experienced renal failure, and the role of sevabertinib and renal failure in this outcome remains unclear and was reported by the investigator as "possibly related" to the study drug)

ADC, antibody-drug conjugate; AE, adverse event; ALT, alanine transferase; AST, aspartate aminotransferase; BID, twice daily; CTCAE, Common Terminology for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities; TRAE, treatment-related adverse event

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SOHO-01: SUMMARY

- Sevabertinib showed robust and durable responses in pretreated and treatment-naïve patients with advanced *HER2*-mutant NSCLC
- Sevabertinib had a manageable safety profile with the most common side effect being diarrhea. There were no reported cases of pneumonitis
- These data support sevabertinib as a potential practice-changing, new targeted therapy for patients with *HER2*-mutant NSCLC
- The phase 3, SOHO-02 trial (NCT06452277) investigating the safety and efficacy of sevabertinib in the 1st line setting for locally advanced or metastatic NSCLC is ongoing

Clinical perspective

- Sevabertinib produces rapid, durable, and clinically meaningful responses with manageable toxicity in pretreated and treatment-naïve pts with advanced *HER2*-mutant NSCLC. These results support sevabertinib as a potential new oral targeted therapy for this molecular subset

NSCLC non-small cell lung cancer

Le X, et al. Abstract LBA75, ESMO 2025. Oral presentation

ZONGERTINIB AS 1ST LINE TREATMENT IN PATIENTS WITH ADVANCED *HER2*-MUTANT NSCLC: BEAMION LUNG 1

Popat S, et al. Abstract LBA74, ESMO 2025

NSCLC, non-small cell lung cancer

BEAMION LUNG-1: BACKGROUND AND STUDY DESIGN

- ***HER2*-activating mutations** have been reported in approximately 2-4% of patients with NSCLC and are associated with poor prognosis[1]
- **Zongertinib, a novel HER2-specific TKI**, binds selectively and covalently to the HER2 TKD while sparing wild-type EGFR and limiting EGFR-related AEs[2]
- **Beamion LUNG-1,** a phase 1a/1b, open-label trial, is evaluating the safety and efficacy of zongertinib in patients with *HER2* aberration-positive solid tumours (phase 1a) and *HER2* mutation-positive NSCLC (phase 1b). **The findings from phase 1b Cohort 2 are reported[3]**

Phase 1b (dose expansion): patients with advanced *HER2*-mutant NSCLC

In phase 1a, the MTD was not reached at 360 mg QD
In phase 1b, the selected dose after interim futility analysis was zongertinib 120 mg QD

Current analysis

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

Primary endpoint: ORR by BICR (RECIST v1.1)

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

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

Here we present the efficacy and safety of zongertinib 120 mg given as a 1st line therapy

Additional cohorts not included in the current analysis

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

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

AE, adverse event; ADC, antibody-drug conjugate; BICR, blinded central independent review; CNS, central nervous system; DC, disease control; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; QD, once a day; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours; TKD, tyrosine kinase domain; TKI, tyrosine kinase inhibitor

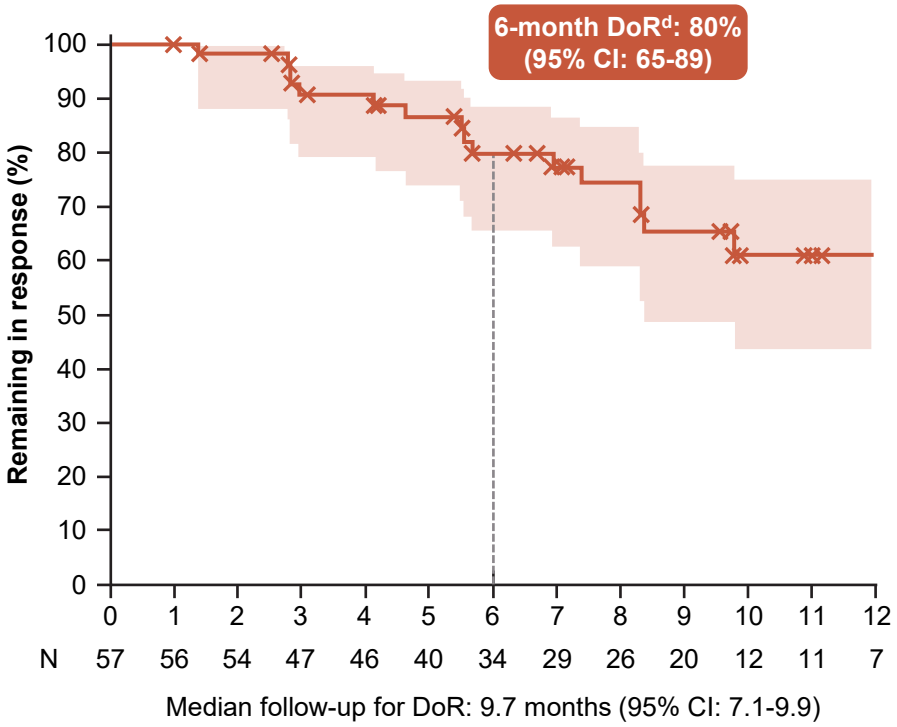
1. Nutzinger J, et al. Lung Cancer 2023;186:107385; 2. Wilding B, et al. Cancer Discov 2025;15:119-38; 3. Popat S, et al. Abstract LBA74, ESMO 2025. Oral presentation

BEAMION LUNG-1: EFFICACY DATA

- As of May 8, 2025, 74 patients had received zongertinib (median age: 67 years [range: 35-88], 50% female)

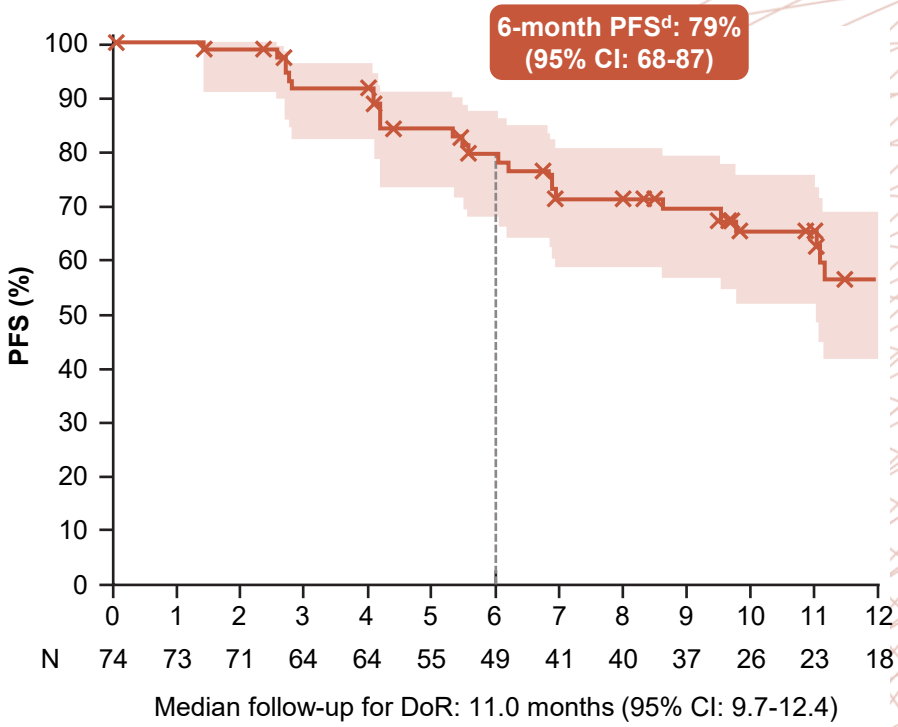
Confirmed response by BICR (RECIST v1.1)	N=74[a]
ORR	**77%**
95% CI	66-85
p value[b]	<0.0001
CR, n (%)	6 (8)
PR, n (%)	51 (69)
DCR	**96%**
95% CI	89-99
SD, n (%)	14 (19)
PD, n (%)[c]	1 (1)

DoR RATES



Median follow-up for DoR: 9.7 months (95% CI: 7.1-9.9)

PFS[d] RATES



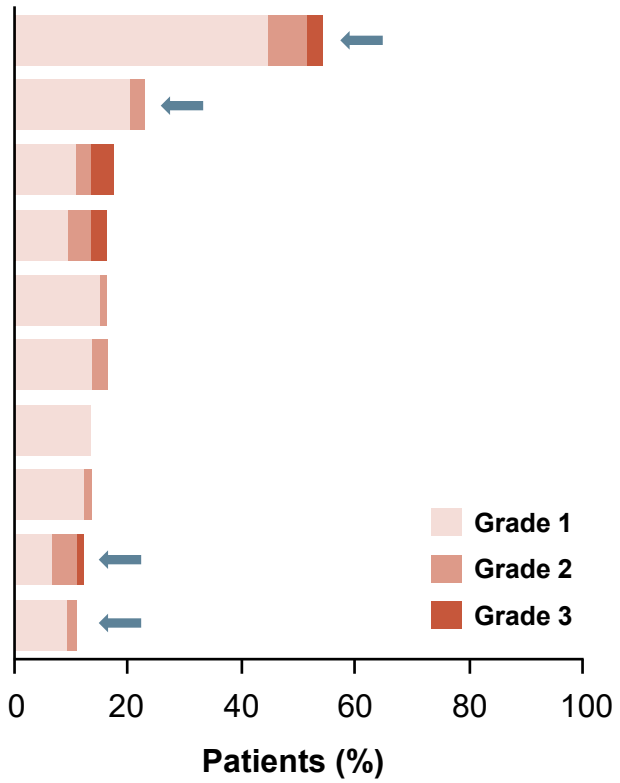
Median follow-up for DoR: 11.0 months (95% CI: 9.7-12.4)

[a] 2 patients were NE for response (images were not available); [b] Null hypothesis: ORR ≤40; [c] PD due to non-target lesion progression; [d] Median values are not yet mature
BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response;
NE, not evaluable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease

Popat S, et al. Abstract LBA74, ESMO 2025. Oral presentation

BEAMION LUNG-1: SAFETY DATA

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



- TRAEs were reported in 91% of patients (grade 3, in 18% of patients)
- There were no grade 4 or 5 TRAEs
- The most common TRAEs (all/grade 3) were diarrhea (54%/3%), ALT increased (18%/4%), AST increased (16%/3%), and dysgeusia and nausea (both 16%/0%)
- Two cases (3%) of ILD/ pneumonitis were reported (both grade 2)

[a] TRAEs as assessed by the investigator that occurred in ≥10% of patients; [b] Grouped terms

ALT, alanine transferase; AST, aspartate aminotransferase; ILD, interstitial lung disease; TRAE, treatment-related adverse events

Popat S, et al. Abstract LBA74, ESMO 2025. Oral presentation

BEAMION LUNG-1: SUMMARY

- First-line zongertinib elicited strong and clinically meaningful efficacy with a manageable safety profile in treatment-naïve patients with advanced *HER2*-mutant NSCLC
- Zongertinib is being further investigated in the randomised, phase 3 Beamion LUNG-2 study in patients with unresectable, locally advanced, or metastatic *HER2*-mutant NSCLC

Clinical perspective

- Zongertinib demonstrates strong and clinically meaningful efficacy with manageable toxicity, supporting its role as a targeted treatment option for *HER2*-driven NSCLC

NSCLC, non-small cell lung cancer

Popat S, et al. Abstract LBA74, ESMO 2025. Oral presentation

INTRACRANIAL EFFICACY OF OLOMORASIB, A NEXT-GENERATION KRAS G12C INHIBITOR, IN PATIENTS WITH *KRAS* G12C-MUTANT NSCLC WITH ACTIVE, UNTREATED BRAIN METASTASES (LOXO-RAS-20001)

Cassier P, et al. Abstract 1846MO, ESMO 2025

NSCLC, non-small cell lung cancer

LOXO-RAS-20001: BACKGROUND AND STUDY DESIGN

- Brain metastases commonly occur in patients with *KRAS* G12C-mutant NSCLC and are associated with a poor prognosis[1]
- **Olomorasib** is a potent, selective **next-generation *KRAS* G12C inhibitor** which has demonstrated **safety and systemic efficacy in NSCLC,**[2,3] and has demonstrated **preliminary intracranial activity in NSCLC patients with brain metastases**[4]
- Olomorasib in combination with pembrolizumab recently received Breakthrough Therapy designation from the FDA for 1st line treatment in patients with advanced or metastatic NSCLC with a *KRAS* G12C mutation and PD-L1 ≥50%[5]
- Updated results are presented on the intracranial efficacy of olomorasib in patients with *KRAS* G12C-mutant NSCLC with active, untreated brain metastases from the phase 1/2 LOXO-RAS-20001 (NCT04956640) study[6]

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

Cohort B8 eligibility

- Age ≥ 18 years
- ECOG PS 0 or 1
- Measurable intracranial disease per mRECIST v1.1
- Locally advanced/metastatic NSCLC
- Presence of a *KRAS* G12C mutation
- **At least 1 untreated, active, brain lesion (≥5 mm)**
- No prior KRAS G12C inhibitor
- Leptomeningeal disease was excluded

Key objectives

- Safety and tolerability
- PK
- Intracranial ORR and DoR
- ORR, DoR, DCR, and PFS per mRECIST v1.1

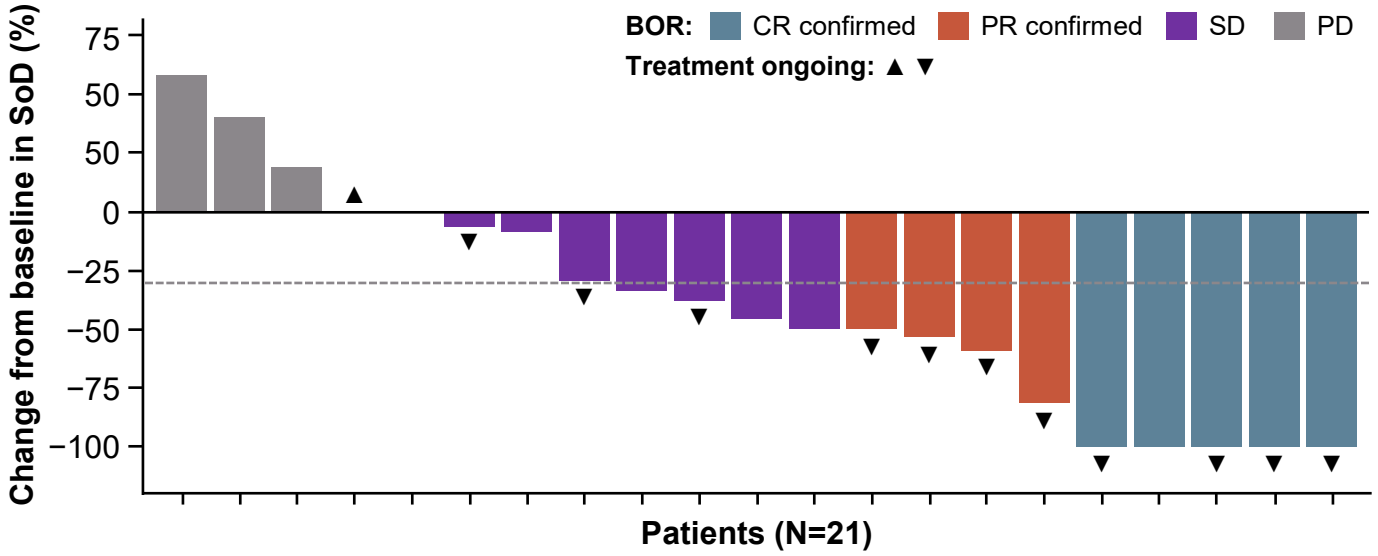
BID, twice daily; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, Food and Drug Administration; KRAS, Kirsten rat sarcoma viral oncogene homologue; mRECIST, modified Response Evaluation Criteria in Solid Tumours; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; PK, pharmacokinetics

1. Vassell E, et al. Eur J Cancer 2021;159:227-36; 2. Fujiwara Y, et al. Abstract OA14.04. WCLC 2024. Oral presentation; 3. Dragnev KH, et al. J Clin Oncol 2025;43:8519-8519; 4. Heist RS, et al. J Clin Oncol 2024;42:3007-3007 (ASCO 2024 oral presentation); 5. Olomorasib Receives FDA Breakthrough Therapy Designation for KRAS G12C-Mutant NSCLC – OncoDaily. Accessed 19-Oct-2025; 6. Cassier P, et al. Abstract 1846MO, ESMO 2025. Oral presentation

LOXO-RAS-20001: EFFICACY RESULTS

- As of DCO[a], 21 patients (median age: 65 years [range, 42-80]) were treated.
  17 patients had prior systemic therapy with 12 patients having ≥2 lines of therapy. 12 patients (57%) had 1 target IC lesions, and 9 patients (43%) had 2-5.

INTRACRANIAL RESPONSE RATE[a]



- Intracranial ORR:
  43% (95% CI: 21.8-66.0)
- Intracranial rate of DoR
  ≥6 months: 100%
- 5 patients (24%) had an intracranial complete response
- DCR: 86%

[a] Data cut-off: June 6, 2025.

BOR, best overall response; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters

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LOXO-RAS-20001: SAFETY RESULTS

- The most common TRAEs (>15%) were low-grade diarrhea, fatigue, and nausea

OLOMORASIB (150 mg BID, N=201)[a]

Parameter, n (%)	Most common TRAEs	
	Any grade	Grade ≥3
Any TRAE	140 (70)	14 (7)
Diarrhoea	56 (28)	1 (1)
Nausea	24 (12)	–
Fatigue	19 (9)	1 (1)
ALT increased	19 (9)	2 (1)
AST increased	19 (9)	3 (2)

Safety profile in the subpopulation of NSCLC patients with brain metastases (n=21) is consistent with the overall population receiving monotherapy at 150 mg BID, with no safety concerns identified

- TRAEs led to dose reductions of olomorasib in 15 patients (7.5%)
- TRAEs led to permanent discontinuation of olomorasib in 2 patients (1.0%)

Data cut-off: April 29, 2025

[a] Includes 201 patients with all solid tumours treated in LOXO-RAS-2001 with olomorasib 150 mg BID

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; NSCLC, non-small cell lung cancer; TRAE, treatment related adverse event

Cassier P, et al. Abstract 1846MO, ESMO 2025. Oral presentation

LOXO-RAS-20001: SUMMARY

- Olomorasib continues to demonstrate promising intracranial activity and disease control in patients with *KRAS* G12C-mutant NSCLC and active, untreated brain metastases
- These results support continued clinical development of olomorasib in patients with *KRAS* G12C-mutant NSCLC including in patients with brain metastases
- TRAEs were consistent with the known safety profile of olomorasib monotherapy and could be managed through dose adjustments
- Two global registrational studies investigating olomorasib in combination with immunotherapy in 1st line metastatic and early-stage NSCLC are ongoing (NCT06119581 and NCT06890598)

Clinical perspective

- Olomorasib provides evidence of meaningful intracranial activity, highlighting progress in addressing brain metastases in patients with *KRAS* G12C-mutant NSCLC and active, untreated brain metastases

NSCLC, non-small cell lung cancer; TRAEs, treatment-related adverse events

Cassier P, et al. Abstract 1846MO, ESMO 2025. Oral presentation

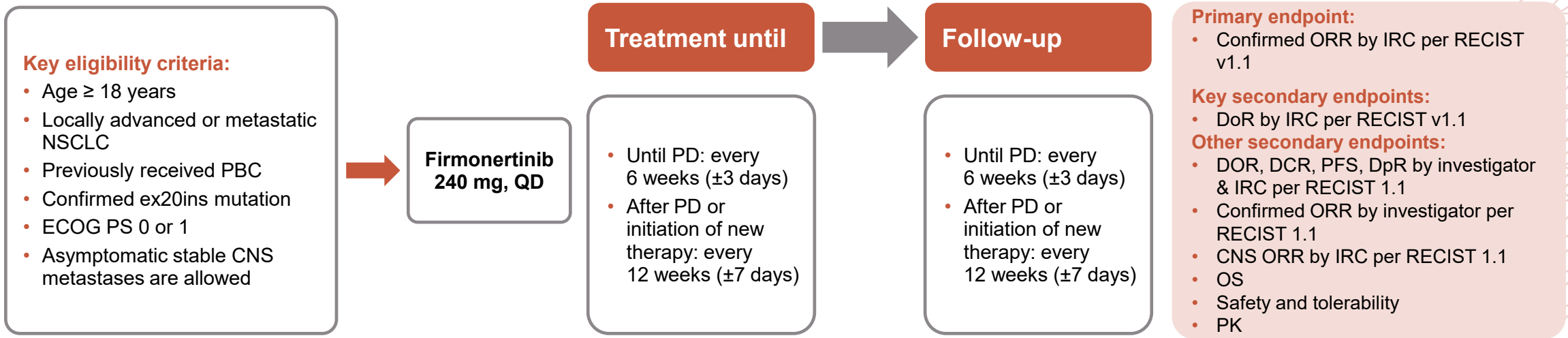
FURMO-003: PHASE 2 STUDY OF FIRMONERTINIB IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED OR METASTATIC NSCLC WITH *EGFR* EXON 20 INSERTION MUTATIONS

Liu Y, et al. Abstract 1848MO, ESMO 2025

NSCLC, non-small cell lung cancer

FURMO-003: BACKGROUND AND STUDY DESIGN

- Firmonertinib is an oral, third-generation EGFR inhibitor with broad activity and selectivity across *EGFR* mutations and has received FDA Breakthrough Therapy designation[1]
- FURMO-003 (NCT05466149) is a phase 2, multicentre, open-label study of firmonertinib 240 mg QD. Eligible patients had advanced/metastatic NSCLC with *EGFR* ex20ins mutations and received prior PBC. Initial results are presented[2]



CNS, central nervous system; DoR, duration of response; DpR, depth of response; ECOG PS, European Cooperative Oncology Group performance status; ex20ins, exon 20 insertion; FDA, Food and Drug Administration; IRC, independent review committee; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PBC, platinum-based chemotherapy; PD, progressive disease; PK, pharmacokinetics; QD, once a day; RECIST, Response Evaluation Criteria in Solid Tumours

1. FDA Grants Breakthrough Therapy Designation to Furmonertinib for EGFR Exon 20 Insertion+ NSCLC | OncLive . Accessed October 2025;
2. Liu Y, et al. Abstract 1848MO, ESMO 2025. Oral presentation

FURMO-003: EFFICACY RESULTS

- 71 patients were enrolled and treated (median age, 57.0 years; 50.7% female; 22.5% had CNS metastases; 76.1% ECOG PS 1
- 22 patients (31.0%) had received prior onco-immunotherapy and 43 patients (60.6%) prior targeted therapy

	N=70[b]
Best ORR,[a] % (95% CI)	51.4 (39.2-63.6)
Confirmed ORR,[c] % (95% CI)	44.3 (31.2-56.7)
Best tumour response, n (%)	
PR	31 (44.3)
SD	32 (45.7)
PD	6 (8.6)
NE	1 (1.4)
DCR (95% CI), %	90.0 (80.5-95.9)
Median DoR, months, (95% CI)	8.3 (5.6-9.7)
Median PFS, months, (95% CI)	8.3 (5.5-10.9)
Median OS[d], months, (95% CI)	21.2 (16.5-NE)

[a] Includes confirmed and unconfirmed responses; [b] Of the 71 patients in total, 1 patient was excluded from the efficacy analysis due to no ex20ins mutation; [c] 5 patients did not have measurable disease by IRC but were included in the primary analysis. The cORR was 47.0% if excluding 5 patients without measurable disease at baseline by IRC; [d] No grade 5/death due to TRAEs

cORR, confirmed overall response rate; CI, confidence interval; CNS, central nervous system; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; ex20ins, exon 20 insertion; IRC, independent review committee; NE, not evaluable; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TRAE, treatment-related adverse event

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FURMO-003: SAFETY RESULTS

TRAEs IN ≥20% OF PATIENTS

Preferred term (PT)	Any grade	Grade 3 or 4[b]
All TRAEs,[a] n (%)	67 (94.4)	15 (21.1)
Diarrhea	46 (64.8)	3 (4.2)
Anemia	28 (39.4)	0
Blood creatinine increased	24 (33.8)	0
AST increased	22 (31.0)	3 (4.2)
Appetite decreased	21 (29.6)	0
Rash	20 (28.2)	0
WBC count decreased	19 (26.8)	1 (1.4)
ALT increased	16 (22.5)	1 (1.4)
Stomatitis	16 (22.5)	0
Platelet count decreased	15 (21.2)	2 (2.8)

- The most common TRAEs were gastrointestinal and resolved with treatment interruption, dose reduction, or supportive care
- No grade 5/death due to TRAEs

[a] Most common TRAE with 20% as cut-off; CTCAE v5.0; [b] No grade 5/death due to TRAEs

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; TRAE, treatment-related adverse event; WBC, white blood cell

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FURMO-003: SUMMARY

- Firmonertinib demonstrates promising clinical activity and an acceptable safety profile in previously treated advanced/metastatic NSCLC patients with *EGFR* ex20ins mutations in China
- These results support firmonertinib as a potential treatment option for this patient population
- Firmonertinib is also under evaluation in a global, randomised, phase 3 trial for 1st line NSCLC patients with *EGFR* ex20ins mutations (FURVENT/FURMO-004; NCT05607550) and has completed enrolment

Clinical perspective

- Firmonertinib continues to show promising clinical activity in *EGFR* ex20ins NSCLC, with an acceptable safety profile and ongoing phase 3 development

Ex20ins, exon 20 insertion; NSCLC, non-small cell lung cancer

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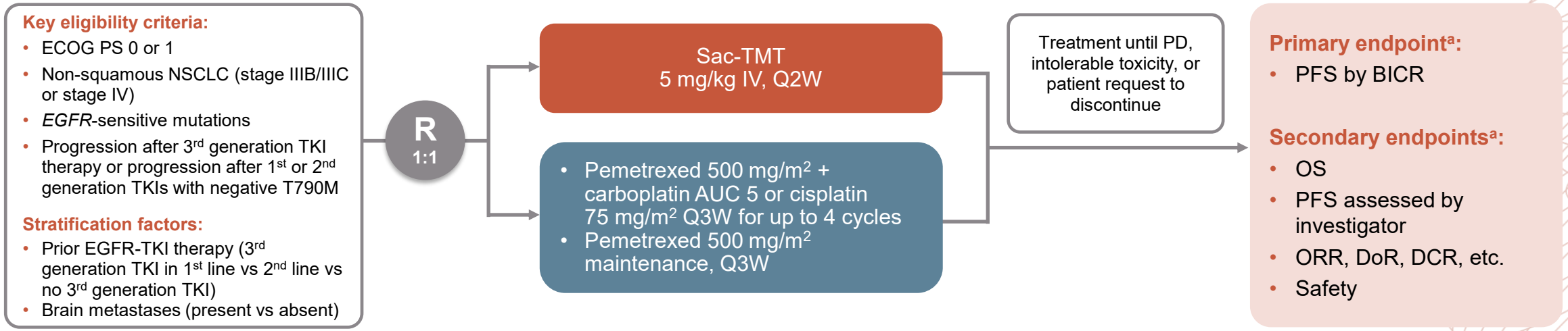
SACITUZUMAB TIRUMOTECAN VS PLATINUM-BASED CHEMOTHERAPY IN *EGFR*-MUTATED NSCLC FOLLOWING PROGRESSION ON EGFR-TKIs: RESULTS FROM THE RANDOMISED, MULTI-CENTRE PHASE 3 OptiTROP-Lung04 STUDY

Zhang L, et al. Abstract LBA5, ESMO 2025

NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

OptiTROP-Lung04: BACKGROUND AND STUDY DESIGN

- *EGFR* mutations are present in ~10-15% of NSCLC patients in the Western population and ~40-50% in the Asian population[1,2]
- Patients with *EGFR*-mutant NSCLC who experience progression after third-generation EGFR TKIs face limited therapeutic options, and outcomes with standard chemotherapy remain poor[3,5]
- Sac-TMT is a TROP2 ADC developed with a novel linker conjugated to a novel topoisomerase I inhibitor which has shown encouraging anti-tumour activity in *EGFR*-mutant NSCLC patients in phase 1/2 trials[3,4]
- The final PFS analysis and preplanned interim OS analysis results from the phase 3 OptiTROP-Lung04 study (NCT05870319) are reported



[a] Tumour response was assessed by RECIST v1.1.

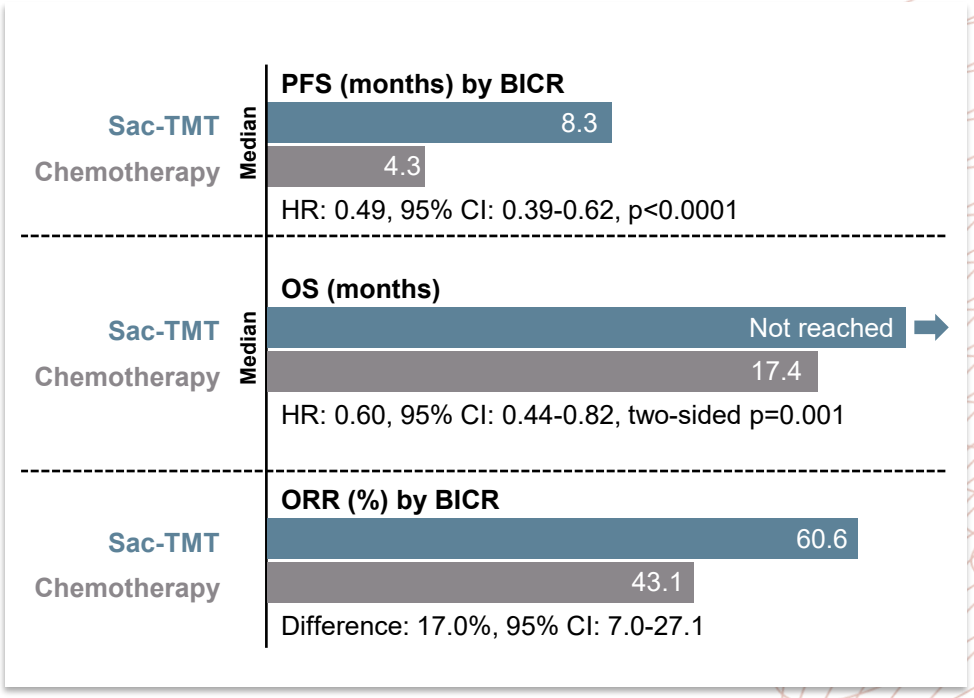
ADC, antibody-drug conjugate; AUC, area under the concentration–time curve; BIRC, blinded independent review committee; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; ex19del, exon 19 deletion; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PBC, platinum-based chemotherapy; PD, progressive disease; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; R, randomisation; sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor

1. Melosky B, et al. Mol Diagn Ther. 2022;26:7-18; 2. Tan AC, Tan DSW. J Clin Oncol. 2022;40:611-25; 3. Zhang L, et al. J Clin Oncol 2025;43(suppl 16). Abstr 8507 (ASCO 2025, oral presentation); 4. Zhao S, et al. Nat Med. 2025; doi: 10.1038/s41591-025-03638-2. Online ahead of print; 5. Zhang L, et al. Abstract LBA5, ESMO 2025. Oral presentation

OptiTROP-Lung04: EFFICACY RESULTS

- A total of 376 patients (median age, 59.5 years; 39.6% male; 79.3% ECOG PS 1; 94.4% prior 3rd generation EGFR TKI) were randomised to the sac-TMT (n=188) or chemotherapy (n=188) groups

	Sac-TMT (n=188)	CT (n=188)
Median PFS[a] (95% CI), months HR (95% CI) p value	8.3 (6.7-9.9) 0.49 (0.39-0.62) <0.0001	4.3 (4.2-5.5)
12-month PFS rate, %, (95% CI)	32.3 (25.5-39.2)	7.9 (4.4-12.8)
Median OS (95% CI), months HR (95% CI) p value	NR (21.5-NE) 0.60 (0.44-0.82) 0.0006	17.4 (15.7-20.4)
Adjusted median OS[a,b] (95% CI), months HR (95% CI) p value	NR (21.5-NE) 0.56 (0.41-0.77) 0.0002	17.2 (15.4-18.9)
ORR[a] (95% CI), %	60.6 (53.3-67.7)	43.1 (35.9-50.5)
Median DoR[a] (95% CI), months	8.3 (6.2-10.0)	4.2 (3.0-4.4)
DCR, % (95% CI)	87.2 (81.6-91.6)	80.3 (73.9-85.7)



- A consistent OS and PFS and benefit of sac-TMT over chemotherapy was observed across all predefined subgroups

Data cutoff: July 6, 2025. p value was presented as one-sided

[a] By BIRC; [b] Censored at the date of initiation of subsequent anti-tumour ADC drug therapy BIRC, blinded independent central review; CI, confidence interval; ADC, antibody-drug conjugate; BICR, blinded independent central review; CI, confidence interval; CT, chemotherapy; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; HR, hazard ratio; NE, not evaluable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor

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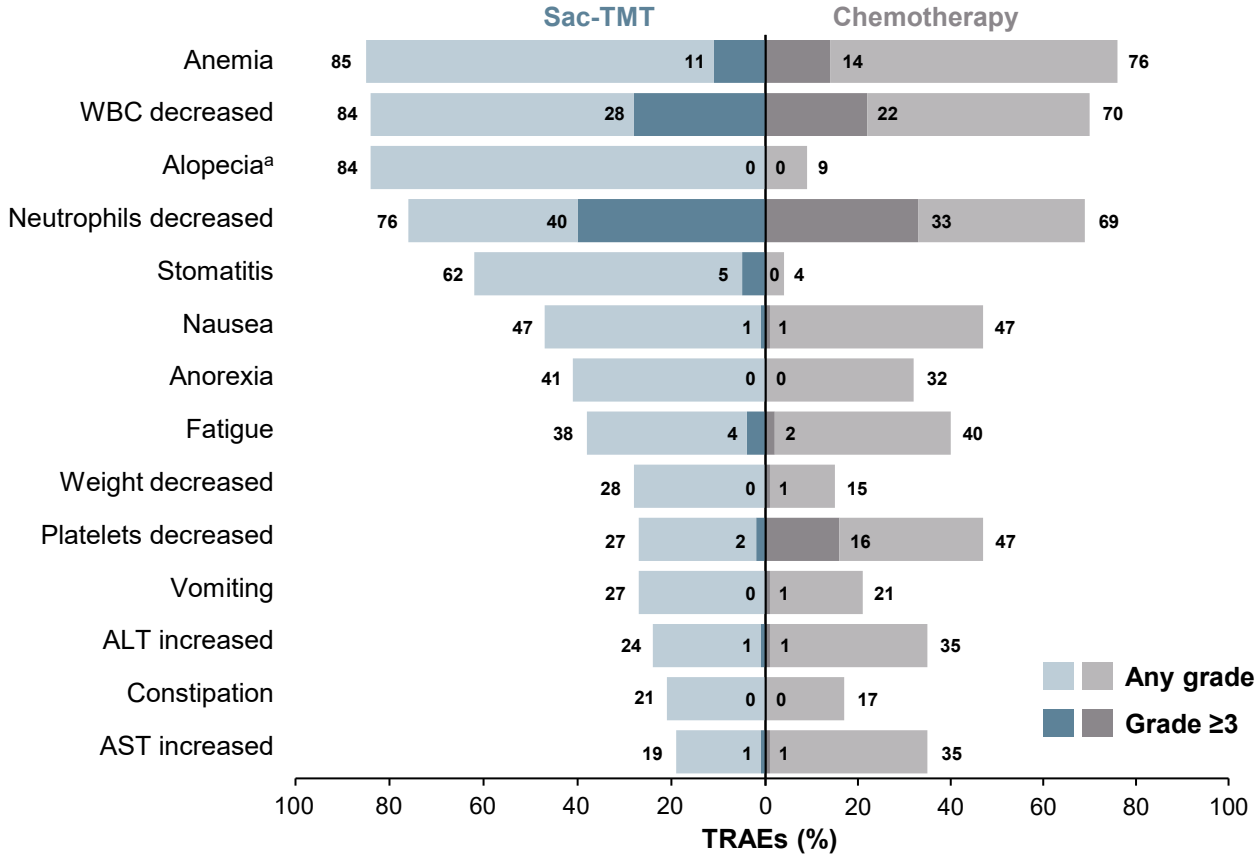
OptiTROP-Lung04: SAFETY RESULTS

TRAEs OF ANY GRADE WITH INCIDENCE ≥20%



- Grade ≥3 TRAEs occurred in 58.0% and 53.8%, and serious TRAEs in 9.0% and 17.6% of patients in the sac-TMT and chemotherapy arms, respectively
- The most common TRAEs for both treatment arms were hematological toxicities
- No drug-related ILD/ pneumonitis occurred in either arm
- Ocular surface toxicity[b] occurred in 9.6% of patients in the sac-TMT group (all grade 1 or 2)

[a] An evaluation of alopecia consistent with hair loss was based on a patient's self-reported experiences included in the Patient-Reported Outcome questionnaires

[b] Ocular surface toxicity: comprising selected PTs from corneal disorder and select relevant PTs from eye disorder system organ class, including dry eye syndrome (n=7), increased lacrimation (n=4), keratitis (n=4), corneal disorder (n=2), blurred vision (n=1), and corneal exfoliation (n=1) in the sac-TMT group, and blurred vision (n=1) in the chemotherapy group. One patient in the sac-TMT group experienced both dry eye syndrome and corneal exfoliation

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ILD, interstitial lung disease; PT, preferred term; sac-TMT, sacituzumab tirumotecan; TRAE, treatment related adverse event; WBC, white blood cell

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OptiTROP-Lung04: SUMMARY

- Sac-TMT demonstrated statistically significant and clinically meaningful improvements in PFS and OS compared to platinum-based chemotherapy
- Sac-TMT had a manageable safety profile, and no unexpected safety signals arose
- There are several ongoing phase 3 studies of sac-TMT monotherapy (NCT06305754, NCT06074588) and in combination with osimertinib in China (NCT06670196) in *EGFR*-mutant NSCLC

Clinical perspective

- The results of OptiTROP-Lung04 support sac-TMT as a promising new treatment option for patients with *EGFR*-mutant NSCLC with EGFR-TKI resistance

NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor

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