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LUNG CONNECT

ONCOGENE-ADDICTED NSCLC HIGHLIGHTS FROM ELCC 2026

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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

- **Beamion-Lung1:** Zongertinib shows practice-changing potential as a first-line targeted therapy in *HER2*-mutant NSCLC, with high systemic response rates, durable disease control, and clinically meaningful CNS activity, including responses in patients with untreated or active brain metastases, alongside a manageable safety profile
- **SOHO-01:** Diarrhea with sevabertinib is predictable and manageable with proactive measures, meaning patients can stay on treatment longer without compromising dose intensity
- **IELCART:** In patients with resected stage IA NSCLC, *HER2* mutations occur at a similar frequency to advanced disease but in early-stage disease there was no clear impact on outcomes, suggesting these alterations do not currently inform prognosis or adjuvant treatment decisions
- **OptiTROP-Lung03:** Sacituzumab tirumotecan demonstrates a clinically meaningful overall survival benefit over docetaxel in previously treated *EGFR*-mutant NSCLC, supporting its use as a preferred post-TKI treatment option and reinforcing the growing role of ADCs in this setting

ADC, antibody-drug conjugate; CNS, central nervous system; NSCLC, non-small cell lung cancer

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

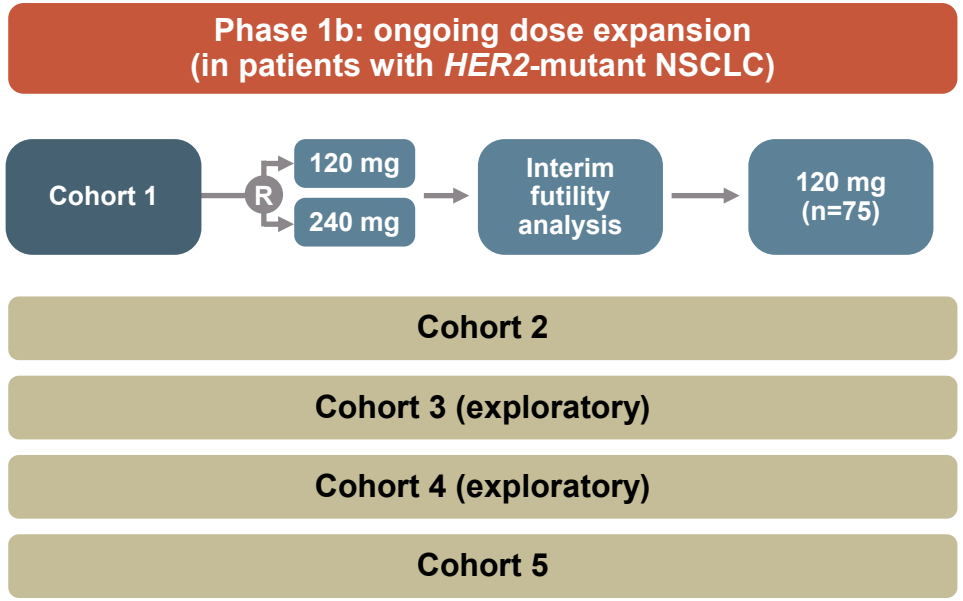
BEAMION LUNG-1: ZONGERTINIB IN TREATMENT-NAÏVE PATIENTS WITH *HER2*-MUTANT NSCLC, INCLUDING THOSE WITH ACTIVE BRAIN METASTASES

Heymach J, et al. Abstract 6MO, ELCC 2026

NSCLC, non-small cell lung cancer

BEAMION LUNG-1: BACKGROUND AND STUDY DESIGN

- **Zongertinib, a novel HER2-specific TKI**, binds selectively and covalently to the HER2 tyrosine kinase domain while sparing wild-type EGFR and limiting EGFR-related adverse events
- **Beamion LUNG-1** is 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 efficacy and safety of zongertinib in **treatment-naïve patients (cohort 2),** and patients with **active brain metastases (cohort 4),** including those with no prior brain radiotherapy were reported at ELCC 2026



Cohort 1: Pre-treated NSCLC[a,b] with a *HER2* TKD mutation

Cohort 2: Treatment-naïve NSCLC with *HER2* TKD mutation

Cohort 3: Pre-treated[a] NSCLC with a non-TKD *HER2* mutation or *HER2* TKD mutation-positive squamous NSCLC

Cohort 4: NSCLC with active brain metastases with *HER2* TKD mutation

Cohort 5: Pre-treated[a] NSCLC with a *HER2* TKD mutation and prior treatment with HER2-directed ADCs

Phase 1b primary endpoint

- ORR by RECIST

Key inclusion criteria

- Patients with *HER2* mutation-positive NSCLC
- Received ≥1 line of platinum-based combination chemotherapy (Cohorts 1,3,5)

NCT04886804; [a] Received ≥1 line of platinum-based combination chemotherapy; [b] excluding patients treated with ADCs

ADC, antibody-drug conjugate; NSCLC, non-small cell lung cancer; ORR, overall response rate; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours; TKD, tyrosine kinase domain; TKI, tyrosine kinase inhibitor

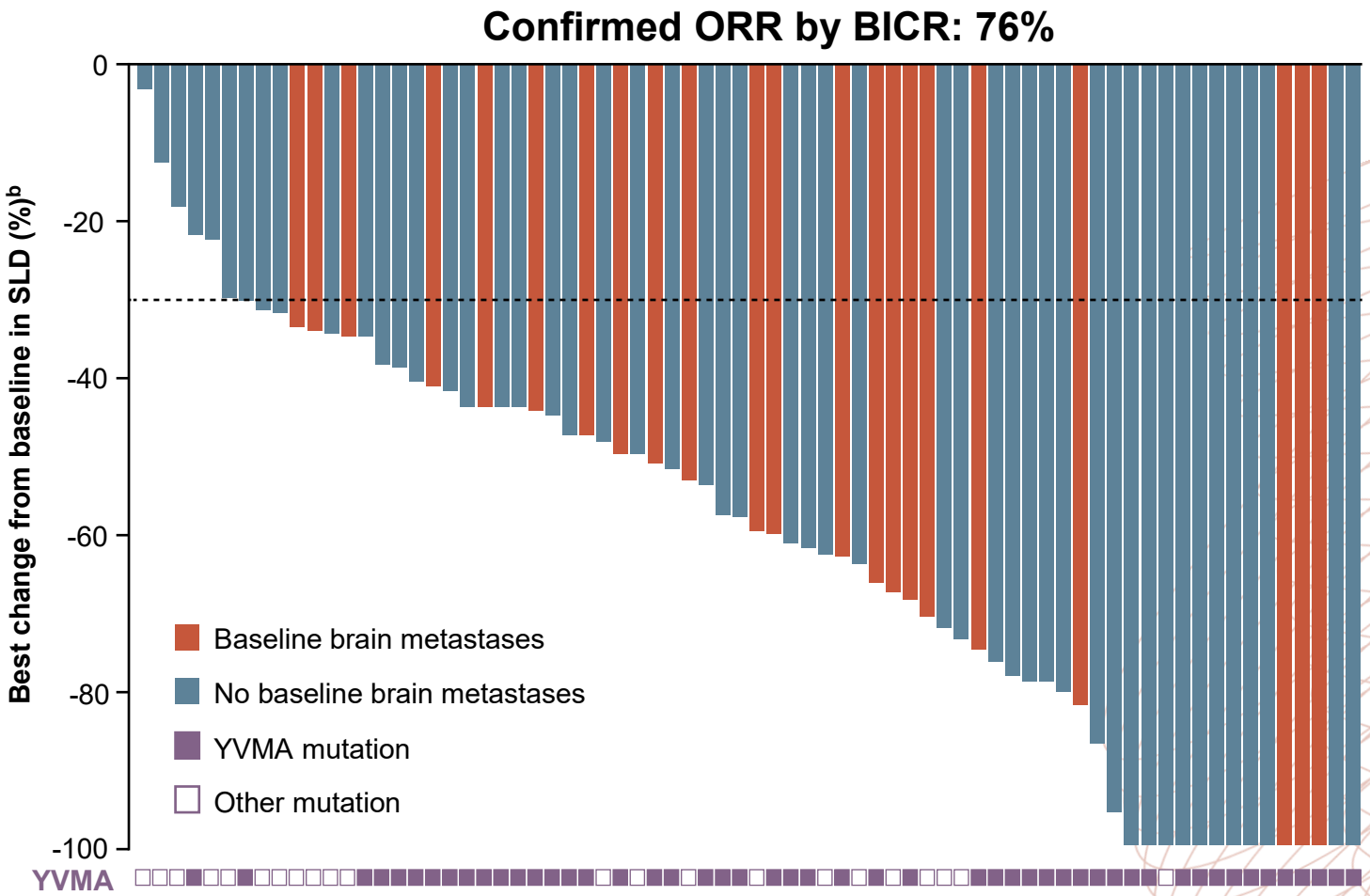
Ruiter G, et al. Abstract PL04.04, WCLC 2024 (oral presentation); Heymach J, et al. Abstract 6MO, ELCC 2026 (oral presentation); Heymach J, et al. N Engl J Med 2025; 392: 2321-33

BEAMION-LUNG-1: ZONGERTINIB IN 1L TREATMENT-NAÏVE PATIENTS

TUMOUR RESPONSE

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)[a]

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



1L zongertinib demonstrated clinical benefit in all patients, irrespective of *HER2* mutation type

[a] PD due to non-target lesion progression; [b] two patients were not evaluable for response (images were not available)

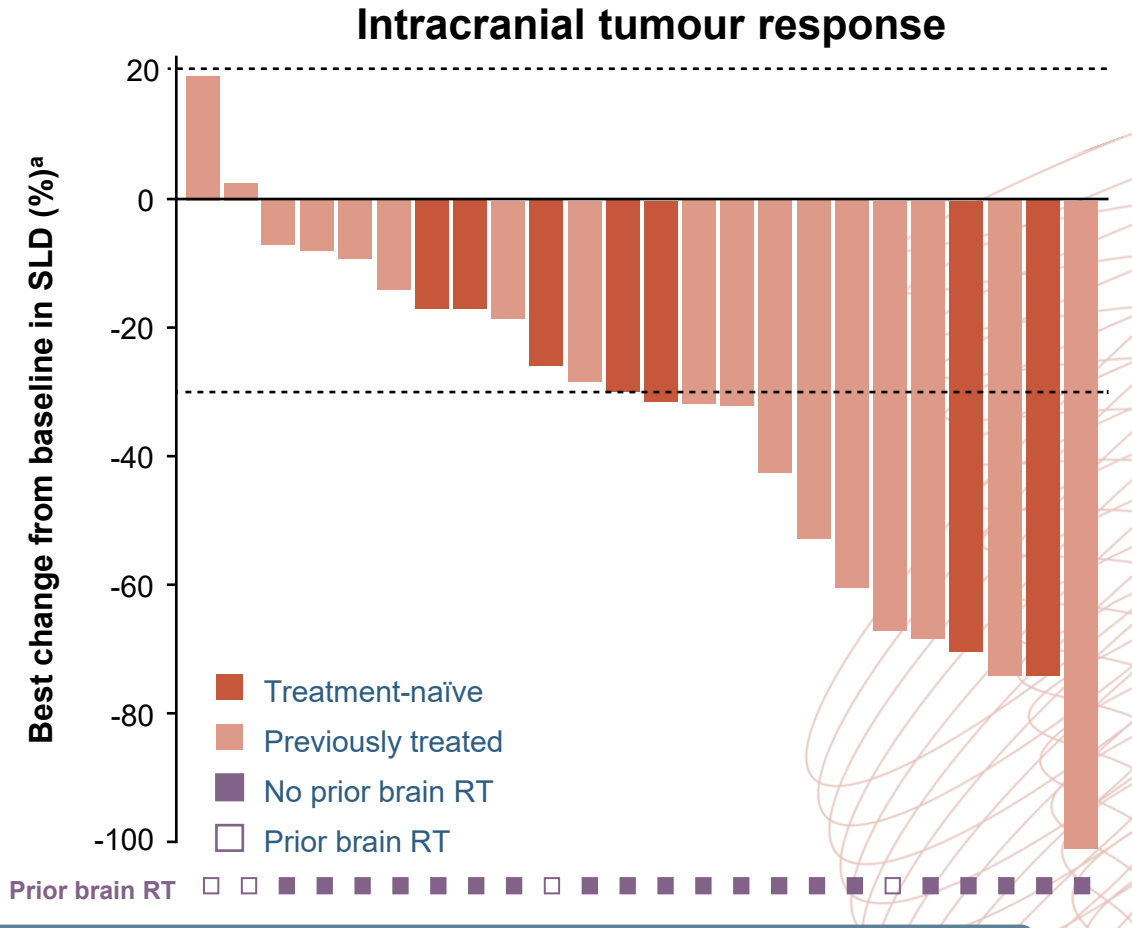
Median follow-up for DoR: 13.8 months (95% CI, 12.4–15.3). Median best percentage change in SLD was -59% (range, -4% to -100%)

1L, first-line; BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease; SLD, sum of lesion diameter

Heymach J, et al. Abstract 6MO, ELCC 2026 (oral presentation)

BEAMION-LUNG-1: ZONGERTINIB IN PATIENTS WITH ACTIVE BRAIN METASTASES

	Cohort 4: Active brain metastases	
Confirmed intracranial response by BICR (RANO-BM)	**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, months 95% CI	6.9 2.9-NE	6.2 2.7-NE
Median PFS, months 95% CI	8.2 4.1-11.3	NE NE



Zongertinib showed intracranial activity in patients with active, untreated brain metastases

[a] Patients who had a baseline assessment and at least one post-baseline assessment (from at least one central reader)

For Cohort 4 (N = 30): median follow-up for DoR: 11.8 months (95% CI, 4.2–NE) and median follow-up for PFS: 9.6 months (95% CI, 6.9–NE)

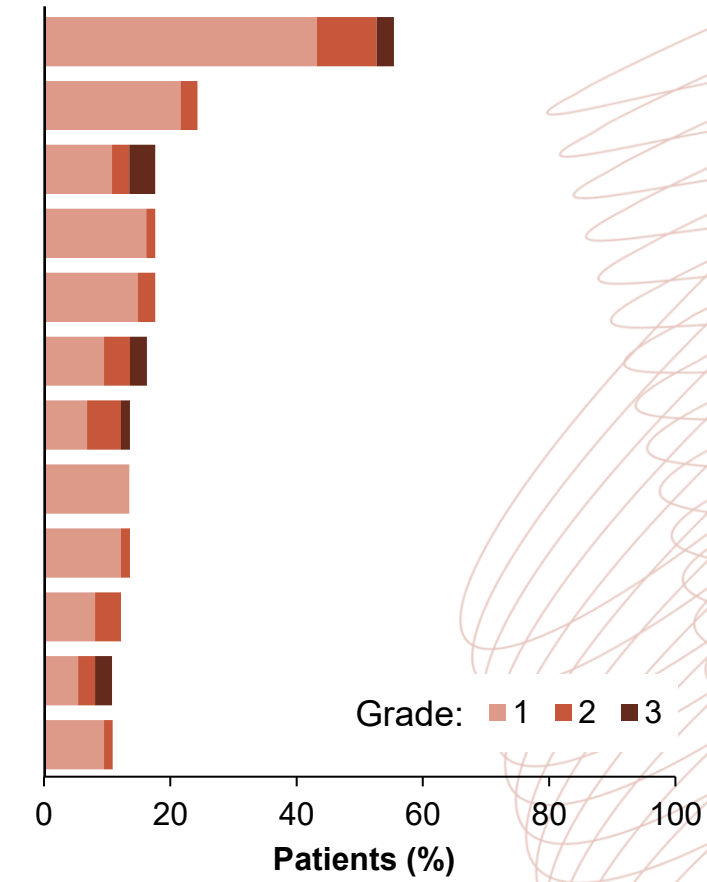
BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; PR, partial response; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; RT, radiotherapy; SD, stable disease; SLD, sum of lesion diameter

Heymach J, et al. Abstract 6MO, ELCC 2026 (oral presentation)

BEAMION-LUNG-1: ZONGERTINIB IN 1L TREATMENT-NAÏVE PATIENTS: SAFETY PROFILE

- Zongertinib had a manageable safety profile in treatment-naïve patients (Cohort 2):
  TRAEs were reported in 67 (91%) patients, with grade ≥3 TRAEs in 14 (19%) patients
  - Most common grade ≥3 TRAE was increased ALT
  - Low rates of grade ≥3 diarrhea and rash
  - AEs leading to dose reduction occurred in 12 (16%) patients
  - AEs leading to discontinuation occurred in 7 (9%) patients

TRAEs, n (%)[a]	All	Grade 3
Diarrhea	41 (55)	2 (3)
Rash[b]	18 (24)	0
Increased ALT	13 (18)	3 (4)
Dysgeusia	13 (18)	0
Nausea	13 (18)	0
Increased AST	12 (16)	2 (3)
Paronychia	10 (14)	1 (1)
Dry skin	10 (14)	0
Pruritus	10 (14)	0
Fatigue	9 (12)	0
Anemia	8 (11)	2 (3)
Stomatitis	8 (11)	0



[a] TRAEs as assessed by the investigator that occurred in ≥10% of patients are shown; [b] grouped term

Median duration of treatment: 14.0 months (range, 0–21.0); two cases (3%) of ILD/pneumonitis were reported (both grade 2); there was one grade 4 TRAE (decreased neutrophil count) and no grade 5 TRAEs

1L, first-line; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ILD, interstitial lung disease; TRAE, treatment-related adverse event

Heymach J, et al. Abstract 6MO, ELCC 2026 (oral presentation)

BEAMION-LUNG-1 : SUMMARY

- In the Beamion-LUNG-1 study, zongertinib demonstrated clinically meaningful benefit in patients with advanced *HER2*-mutant NSCLC, including in patients with active brain metastases, with a manageable safety profile and notably few grade ≥3 TRAEs
  - Given as 1L therapy, the confirmed ORR by BICR was 76%; median PFS and DoR were 14.4 months and 15.2 months, respectively
  - Zongertinib also showed intracranial responses in patients with active brain metastases (47% ORR; RANO-BM), including in those with no prior brain radiotherapy (59% ORR; RANO-BM)

Clinical perspective

In the near term, zongertinib is likely to be considered a frontline option, particularly for patients with brain metastases, pending phase 3 confirmation, with the potential to delay CNS radiotherapy and reshape the HER2 treatment pathway. This could move antibody-drug conjugates such as trastuzumab deruxtecan to later lines of treatment

1L, first-line; BICR, blinded independent central review; CNS, central nervous system; DoR, duration of response; NSCLC, non-small cell lung cancer; ORR, overall response rate; PFS, progression-free survival; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; TRAE, treatment related adverse events

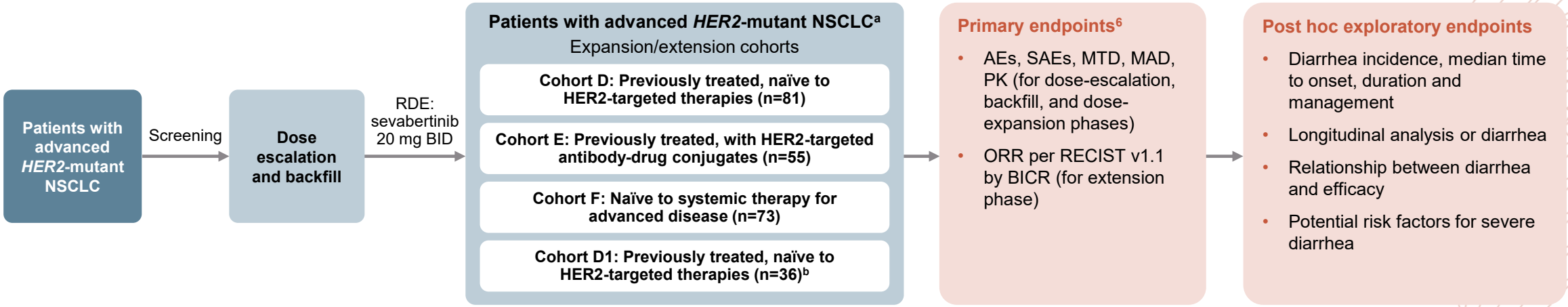
Heymach J, et al. Abstract 6MO, ELCC 2026 (oral presentation)

SOHO-01: CHARACTERISATION AND MANAGEMENT OF SEVABERTINIB-INDUCED DIARRHEA

Girard N, et al. Abstract 18P ELCC 2026

SOHO-01: BACKGROUND AND STUDY DESIGN

- *HER2*-activating mutations have been reported in approximately 2-4% of patients with NSCLC and are associated with poor prognosis[1-5]
- **Sevabertinib** is an oral, **reversible tyrosine kinase inhibitor that potently inhibits HER2 and EGFR** in preclinical models[3,6]
- Encouraging anti-tumour activity and manageable safety were observed in patients with NSCLC harbouring a *HER2*-activating mutation treated with sevabertinib[3,6]
- **Diarrhea is the most common adverse event** associated with HER2 TKI treatment in NSCLC. At ELCC, we saw a report of an exploratory analysis of the phase 1/2 **SOHO-01 trial** (NCT05099172) which aimed to characterise diarrhea in sevabertinib-treated patients, with a focus on **cohorts D and F**[7]



[a]Cohorts not included in this analysis are not shown; [b]Cohort D1 was not included in the extension phase and investigated sevabertinib at 10 mg BID

AE, adverse event; BICR, blinded independent central review; BID, twice daily; ELCC, European Lung Cancer Congress; MAD, maximum administered dose; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; ORR, objective response rate; PK, pharmacokinetics; RDE, recommended dose for expansion; RECIST, Response Evaluation Criteria in Solid Tumours; SAE, serious adverse event; 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. Le X, et al. N Engl J Med. 2025;393:1819-1832; 5. Ren S, et al. ESMO Open. 2022;7:100395; 6. Loong HHF, et al. Ann Oncol. 2023;34(Supplement 2):S761-S762; 7. Girard N, et al. Abstract 18P, ELCC 2026 (poster presentation);

SOHO-01: EXPLORATORY ANALYSIS RESULTS

MOST COMMON TEAEs OCCURRING IN >25% OF PATIENTS IN COHORTS D AND F

n (%)	Cohort D (N=81)			Cohort F (N=73)		
	Any grade	Grade 1 or 2	Grade 3	Any grade	Grade 1 or 2	Grade 3
Diarrhea	70 (86)	51 (63)	19 (23)	64 (88)	60 (82)	4 (5)
Rash	43 (53)	42 (52)	1 (1)	43 (59)	43 (59)	0
Paronychia	24 (30)	24 (30)	0	19 (26)	19 (26)	0
Stomatitis	15 (19)	14 (17)	1 (1)	20 (27)	20 (27)	0
Anemia	23 (28)	21 (26)	2 (2)	24 (33)	21 (29)	3 (4)
Hypokalemia[a]	22 (27)	12 (15)	9 (11)	19 (26)	13 (18)	6 (8)
Nausea	20 (25)	18 (22)	2 (2)	11 (15)	9 (12)	2 (3)
Decreased weight	21 (26)	20 (25)	1 (1)	13 (18)	13 (18)	0

[a] One grade 4 TEAE was reported in Cohort D

- There were no reports of grade 4 diarrhea or discontinuations due to diarrhea

TEAE, treatment-emergent adverse event

Girard N, et al. Abstract 18P, ELCC 2026 (poster presentation)

SOHO-01: EXPLORATORY ANALYSIS RESULTS

CHARACTERISATION AND MANAGEMENT OF TREATMENT-EMERGENT DIARRHEA

	Cohort D (N=81)	Cohort F (N=73)
No diarrhea, n (%)	11 (14)	9 (12)
Treatment-emergent diarrhea (worst toxicity grade), n (%)	70 (86)	64 (88)
Grade 1	21 (26)	36 (49)
Grade 2	30 (37)	24 (33)
Grade 3	19 (23)	4 (5)
Grade 4	0	0
Onset at grade 3, n (%)	2 (2)	0
Action taken due to diarrhea, n (%)	70 (86)	64 (88)
Dose not changed	69 (85)	60 (82)
Dose interruptions or delays	12 (15)	3 (4)
Dose reductions[a]	10 (12)	6 (8)
Discontinuation	0	0
Loperamide use, n (%)	56 (69)	39 (53)
Loperamide started ≤24 hours after first diarrhea event of any grade	30 (37)	13 (18)
Characteristics of grade 3 diarrhea events		
Patients with >1 episode, n (%)	3 (4)	0
Median episodes per patient (IQR)	1 (1-1)	1 (1-1)
Median duration of episodes (IQR), days	4 (2-11)	2 (2-2)
Median time to first episode (IQR), days	39 (15-123)	29 (14-50)
Median cumulative duration (IQR), days	6 (3-14)	2 (2-2)

- Patients with grade 3 diarrhea had a median of 1 episode with a median duration of 2-4 days
- Loperamide use was not mandated and was reported in 69% (Cohort D) and 53% (Cohort F) of patients

[a] Dose was not re-escalated after reduction for toxicity

IQR, interquartile range

Girard N, et al. Abstract 18P, ELCC 2026 (poster presentation)

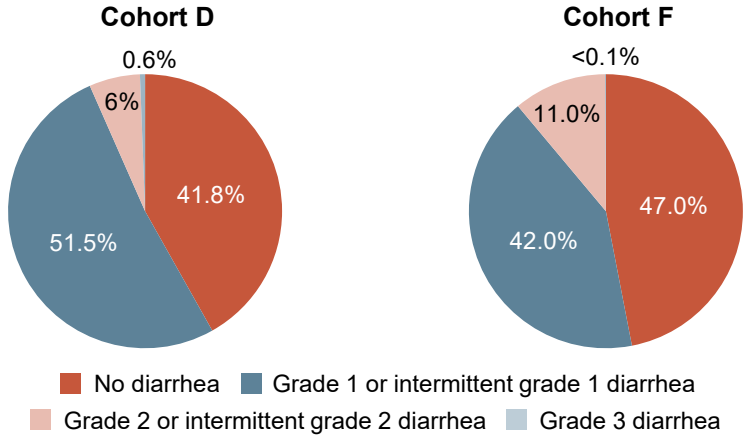
SOHO-01 EXPLORATORY ANALYSIS RESULTS

RESPONSE PER BICR (RECIST V1.1) BY PRESENCE OF GRADE ≥2 DIARRHEA

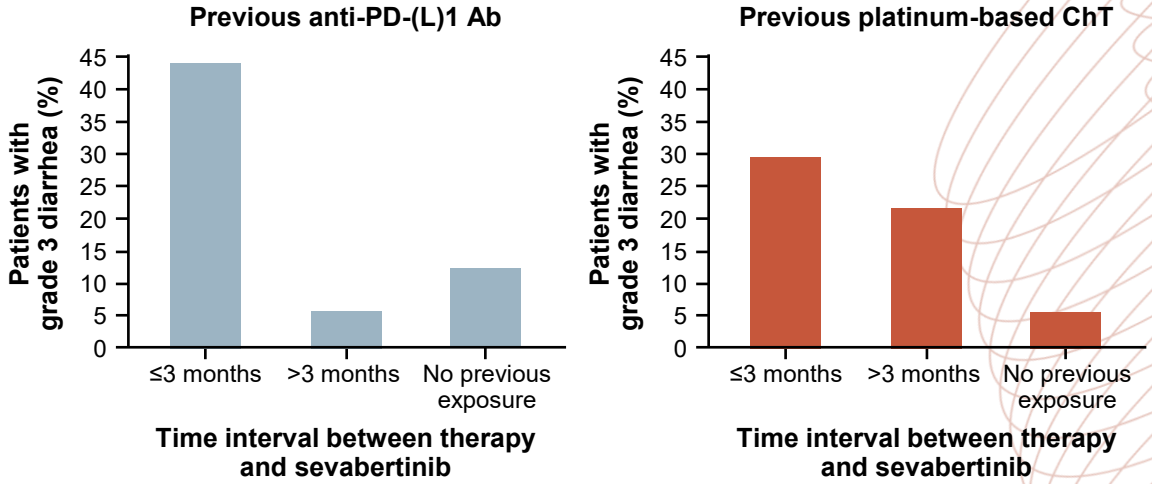
- In Cohorts D and F, efficacy was generally similar among patients who did or did not experience grade ≥2 diarrhea

	Cohort D (N=81)		Cohort F (N=73)	
	Grade ≥2 diarrhea (N=49)	No grade ≥2 diarrhea (N=32)	Grade ≥2 diarrhea (N=28)	No grade ≥2 diarrhea (N=45)
ORR, n (%)	34 (69)	20 (63)	20 (71)	33 (73)
Median DoR (min, max), months[a]	7 (2, 30)	6 (1, 15)	9 (2, 13)	7 (1, 13)
Median PFS (min, max), months	8 (1, 31)	5 (0, 16)	9 (0, 15)	8 (0, 15)

PROPORTION OF PATIENT-DAYS WITH DIARRHEA



DIARRHEA FREQUENCY BY TIMING OF PRIOR THERAPY[b]



[a] Based on patients with an objective response; [b] in cohorts D, E, F and D1

Ab, antibody; BICR, blinded independent central review; ChT, chemotherapy; DoR, duration of response; max, maximum; min, minimum; ORR, objective response rate; PD-(L)1: programmed cell death-1/programmed death-ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours

Girard N, et al. Abstract 18P, ELCC 2026 (poster presentation)

SOHO-01: SUMMARY

- This exploratory analysis indicates that despite the high incidence of any grade and grade 3 diarrhea, events were short and effectively managed without compromising sevabertinib efficacy:
  - In cases of severe diarrhea, episodes were generally not sustained or recurrent and were effectively managed with loperamide use and dose interruptions, delays, and/or reductions
  - Higher sevabertinib exposure was associated with a higher risk of severe diarrhea
  - Overall response rates were similar across cohorts irrespective of diarrhea occurrence
  - Timing of previous PD-(L)1 therapy and platinum-based chemotherapy may affect the risk of diarrhea

Clinical perspective

- This exploratory analysis provides reassurance that the diarrhea experienced during treatment with sevabertinib **can be effectively managed with timely supportive measures**, supporting the **sustained use of emerging HER2-targeted TKIs** in routine care

PD-(L)1: programmed cell death-1/programmed death-ligand 1; TKI, tyrosine kinase inhibitor

Girard N, et al. Abstract 18P, ELCC 2026 (poster presentation)

IELCART: CLINICAL OUTCOMES IN PATIENTS WITH EARLY-STAGE *HER2*-MUTATED NSCLC: A PROSPECTIVE COHORT STUDY

Gros L, et al. Abstract 239P, ELCC 2026

NSCLC, non-small cell lung cancer

IELCART: BACKGROUND AND STUDY DESIGN

- HER2-directed therapies have shown promising activity in advanced stage NSCLC[1,2], but the clinical and prognostic significance of *HER2* mutations in early-stage resected NSCLC remains poorly defined[3]
- This study aimed to characterise the clinicopathologic features and postoperative outcomes of patients with early stage *HER2*-mutated NSCLC[3]
- Data was analysed from the Initiative for Early Lung Cancer Research for Treatment (IELCART) study, a multi-institutional cohort initiated in 2016[3]

IELCART study
Prospective Multi-institutional Cohort
(Since 2016)[3]

Study Population

- Underwent surgical resection for clinical stage IA NSCLC (<30 mm; cT1a–cN0M0)
- Subsequent pathologic confirmation of stage IA
- Only with genomic profiling data available

Genomic Profiling

- HER2-mutated tumours were defined by ***HER2* exon 20 insertions** detected by NGS

Clinical Variables and Outcomes

- Clinical, radiologic, pathologic and surgical variables collected

c/p, clinical/pathologic; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; TNM, tumour-node-metastasis staging system

1. Heymach JV, et al. N Engl J Med. 2025;392:2321-33; 2. Le X, et al. N Engl J Med. 2025;393:1819-1832;
3. Gros L, et al. Abstract 239P, ELCC 2026 (poster presentation)

IELCART: BASELINE CHARACTERISTICS

Characteristics	Overall N=350	*HER2* N=16	Non-*HER2* N=334	p value
Median age (IQR), years	70 (63-77)	69 (60-77)	71 (63-77)	0.6
Sex, n (%)				0.4
Female	204 (58)	11 (69)	193 (58)	
Male	146 (42)	5 (31)	141 (42)	
Median BMI (IQR), kg/m^2	25.7 (22.7-29.5)	25.8 (22.8-33.4)	25.7 (22.7-29.5)	0.6
Race, n (%)				0.5
African American	45 (13)	1 (6.3)	44 (13)	
Asian	45 (13)	2 (13)	43 (13)	
Others	31 (8.9)	3 (19)	28 (8.4)	
White	229 (65)	10 (63)	219 (66)	
Ethnicity, n (%)				0.7
Hispanic or Latino	44 (13)	1 (6.3)	43 (13)	
Not Hispanic or Latino	306 (87)	15 (94)	291 (87)	
Smoking status, n (%)				0.030
Current	35 (10)	1 (6.3)	34 (10)	
Former	223 (64)	6 (38)	217 (65)	
Never	92 (26)	9 (56)	83 (25)	
Median pack-years among smokers (IQR)	28 (13-45)	13 (3-46)	29 (13-45)	0.2
Cardiac disease	44 (13)	0 (0)	44 (13)	0.2
Hypertension	162 (46)	5 (31)	157 (47)	0.2
COPD	64 (18)	1 (6.3)	63 (19)	0.3
Diabetes	55 (16)	2 (13)	53 (16)	>0.9
Family history of lung cancer	62 (18)	3 (19)	59 (18)	>0.9

- Among 350 patients with genomic profiling, **16 (4.6%) harboured *HER2* ex20 mutations**
- **Median age was 69 years**; most patients were **female (69%), white (63%)**, and **non-Hispanic (94%)**
- Over half were **never-smokers (56%)**
- Three patients (19%) with *HER2*m had a family history of lung cancer

Ex20, exon 20; COPD, chronic obstructive pulmonary diseases; HERm, HER2 mutation; IQR, interquartile range

Gros L, et al. Abstract 239P, ELCC 2026 (poster presentation)

IELCART: RESULTS

POST-OPERATIVE HOSPITAL OUTCOMES – *HER2*m PATIENTS

- Surgical management included **lobectomy (31%)** and **sublobar resection (69%)**
- Median hospital stay was 3.5 days; one patient required ICU admission, and no 30-day readmissions occurred
- After a median follow-up of **71 months**, **one patient developed recurrence and died**

n (%)[a]	Overall N=350	*HER2* N=16	Non-*HER2* N=334	p value[b]
Median length of stay (Q1, Q3), days	3.00 (2.00, 4.00)	3.50 (3.00, 5.00)	3.00 (2.00, 4.00)	0.4
ICU care	4 (1.1)	1 (6.3)	3 (0.9)	0.2
Postoperative complications	89 (25)	4 (25)	85 (25)	>0.9
Pulmonary complications	20 (5.7)	1 (6.3)	19 (5.7)	>0.9
30-day readmission after surgery	10 (2.9)	0 (0)	10 (3.0)	>0.9

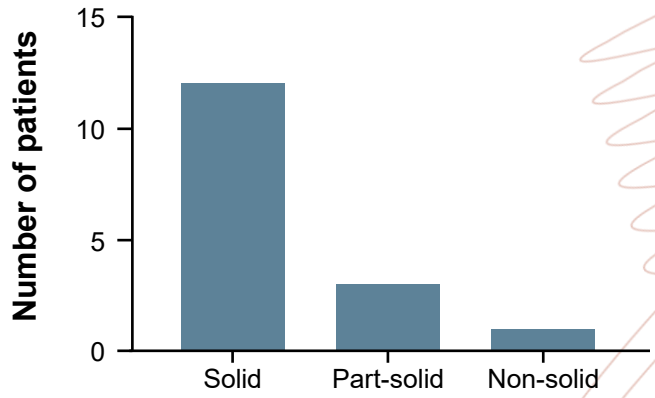
[a] Unless otherwise stated

[b] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

*HER2*m, HER2-mutant; ICU, intensive care unit; Q1, quarter 1; Q3, quarter 3

Gros L, et al. Abstract 239P, ELCC 2026 (poster presentation)

RADIOLOGIC NODULE TYPE - *HER2*m PATIENTS



- Radiologically, tumours were predominantly **solid nodules (75%)**, with a median size of **15 mm**
- All tumours were **adenocarcinomas**

IELCART: SUMMARY

- In this prospective cohort of stage IA NSCLC, *HER2* mutations occurred at frequencies similar to those in advanced disease and were more frequent among never-smokers
- Despite their adverse prognostic role in advanced NSCLC, no inferior surgical or survival outcomes were observed, supporting curative-intent surgery in early-stage *HER2*-mutated NSCLC
- Larger studies are needed to better define recurrence risk and molecular predictors of outcome

Clinical perspective

- *HER2* mutations can be identified in early-stage NSCLC at a similar frequency to advanced disease, but:
  - Prognostic relevance remains unclear
  - No role yet in guiding adjuvant therapy
- Clinical trials are needed to evaluate HER2-directed therapy in the adjuvant setting for these patients

NSCLC, non-small cell lung cancer

Gros L, et al. Abstract 239P, ELCC 2026 (poster presentation)

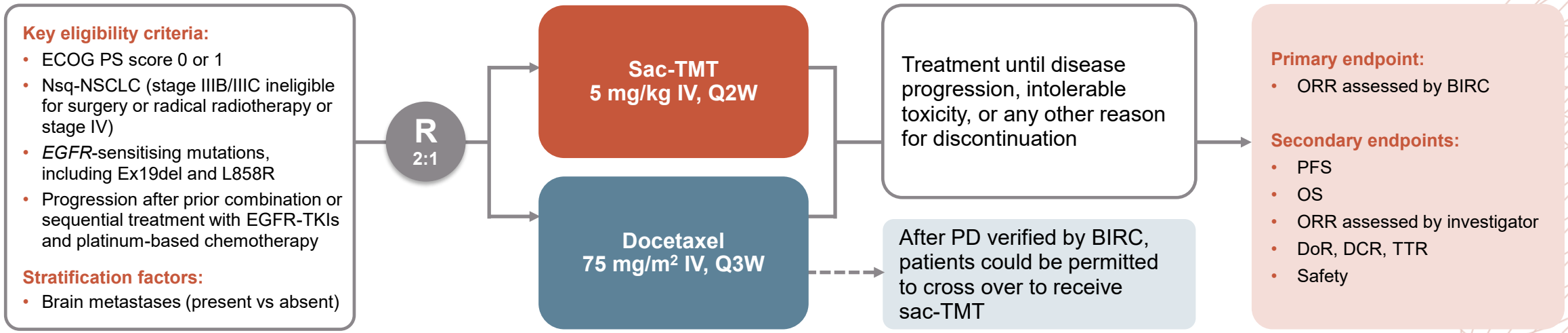
OptiTROP-Lung03: SACITUZUMAB TIRUMOTECAN IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED *EGFR*-MUTATED NSCLC: FINAL OS ANALYSIS FROM THE RANDOMISED STUDY

Yang Y, et al. Abstract LBA4, ELCC 2026

NSCLC, non-small cell lung cancer

OptiTROP-Lung03: BACKGROUND AND STUDY DESIGN

- *EGFR* mutations are present in ~10-15% of NSCLC patients in the Western population and ~50% in the Asian population[1,2]
- Sac-TMT, a novel TROP2 ADC developed to conjugate a belotecan-derivative topoisomerase I inhibitor, has shown encouraging antitumour activity in *EGFR*m NSCLC patients in phase 1/2 trials[3,4]
- OptiTROP-Lung03 (NCT05631262), previously demonstrated statistically significant PFS and OS benefits with sac-TMT vs docetaxel in previously treated *EGFR*-mutant NSCLC[3,5]
- Updated results were presented at ELCC 2026[6]



ADC, antibody-drug conjugate; BIRC, blinded independent review committee; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; ELCC, European Lung Cancer Congress; Ex19del, exon 19 deletion; IV, intravenous; (Nsq-)NSCLC, non-squamous non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q2/3W, every 2 or 3 weeks; R, randomisation; sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor; TTR, time to response

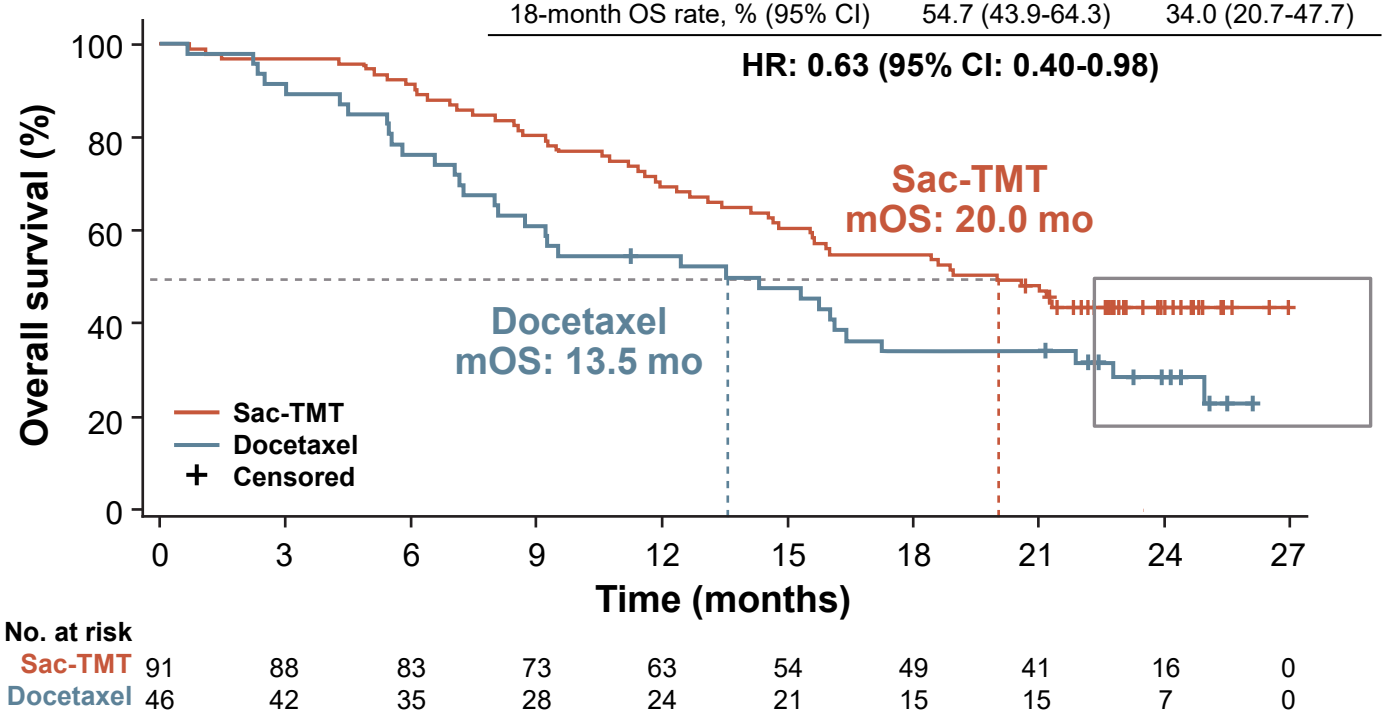
1. Melosky B, et al. Mol Diagn Ther. 2022;26(1):7-18; 2. Tan AC and Tan DSW. J Clin Oncol. 2022;40:611-25; 3. Zhang L, et al. J Clin Oncol. 2025;43(suppl 16). Abstr 8507 (ASCO 2025, oral presentation); 4. Zhao S, et al. Nat Med. 2025;31:1976-1986; 5. Fang W, et al. BMJ. 2025;389:e085680; 6. Yang Y, et al. Abstract LBA4, ELCC 2026 (oral presentation)

OptiTROP-Lung03: EFFICACY RESULTS

OVERALL SURVIVAL

	Sac-TMT (N=91)	Docetaxel (N=46)
OS events, n (%)	51 (56.0)	33 (71.7)
Median OS (95% CI), months	**20.0** (14.8-NE)	**13.5** (8.0-17.2)
18-month OS rate, % (95% CI)	54.7 (43.9-64.3)	34.0 (20.7-47.7)

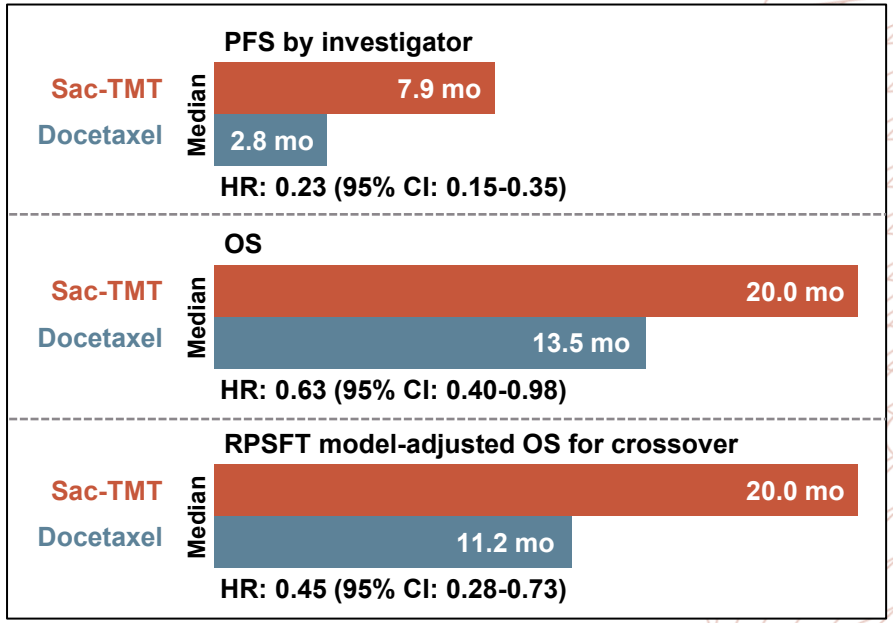
HR: 0.63 (95% CI: 0.40-0.98)



No. at risk

Sac-TMT	91	88	83	73	63	54	49	41	16	0
Docetaxel	46	42	35	28	24	21	15	15	7	0

EFFICACY ENDPOINTS



Data cut-off: 11 December 2025 (23.8 months follow-up)

CI, confidence interval; HR, hazard ratio; mo, months; NE, not estimable; (m)OS, (median) overall survival; PFS, progression-free survival; RPSFT, rank preserving structural failure time model; sac-TMT, sacituzumab tirumotecan

Yang Y, et al. Abstract LBA4, ELCC 2026 (oral presentation)

OptiTROP-Lung03: SAFETY RESULTS

SAFETY SUMMARY AND COMMON TRAEs (≥30%[a])

Safety-related variables, n (%)	Sac-TMT 5 mg/kg (N=91)		Docetaxel 75 mg/kg² (N=46)	
TRAEs	89 (97.8)		45 (97.8)	
Grade ≥3 TRAEs	55 (60.4)		34 (73.9)	
Serious TRAEs	19 (20.9)		19 (41.3)	
TRAEs leading to dose reduction	39 (42.9)		20 (43.5)	
TRAEs leading to dose interruption	42 (46.2)		14 (30.4)	
TRAE preferred term	All grades	Grade ≥3	All grades	Grade ≥3
Anemia	74 (81.3)	12 (13.2)	31 (67.4)	2 (4.3)
WBC count decreased	68 (74.7)	25 (27.5)	29 (63.0)	24 (52.2)
Neutrophil count decreased	62 (68.1)	40 (44.0)	27 (58.7)	27 (58.7)
Stomatitis	60 (65.9)	17 (18.7)	4 (8.7)	1 (2.2)
Alopecia	44 (48.4)	0	23 (50.0)	0
Platelet count decreased	33 (36.3)	5 (5.5)	9 (19.6)	0
Asthenia	26 (28.6)	0	15 (32.6)	2 (4.3)

- **Median duration of exposure**
  - Sac-TMT: 7.1 months (range: 0.5, 25.0)
  - Docetaxel: 2.8 months (range: 0.7, 13.1)
- Despite more than double the median duration of treatment in the sac-TMT group, the incidences of grade ≥3 and serious TRAEs were much lower with sac-TMT than with docetaxel
- The most common TRAEs for both sac-TMT and docetaxel were hematologic toxicities
  - Febrile neutropenia: none in the sac-TMT group and 19.6% of patients in the docetaxel group
- ILD/pneumonitis were reported as 2.2% in both groups
- No TRAEs led to treatment discontinuation or death in the sac-TMT group

[a] Incidence ≥30% in either group

Data cut-off: 11 December 2025 (23.8 months follow-up)

ILD, interstitial lung disease; sac-TMT, sacituzumab tirumotecan; TRAE, treatment-related adverse event; WBC, white blood cell

Yang Y, et al. Abstract LBA4, ELCC 2026 (oral presentation)

OptiTROP-Lung03: SUMMARY

- Sac-TMT continues to demonstrate clinically meaningful and significant improvements in PFS and OS compared to docetaxel, with a manageable safety profile in patients with previously treated advanced *EGFR*m NSCLC. These results underscore sac-TMT as a promising new treatment option for this population

Clinical perspective

- Sacituzumab tirumotecan is poised to become a **new standard of care after EGFR TKI failure**, replacing docetaxel and reinforcing **ADCs as a key pillar in the treatment sequence** for *EGFR*-mutant NSCLC

ADC, antibody-drug conjugate; EGFRm, EGFR mutation; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; sac-TMT, sacituzumab tirumotecan; TKI, tyrosine kinase inhibitor

Yang Y, et al. Abstract LBA4, ELCC 2026 (oral presentation)

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