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HER2-MUTATED NSCLC HIGHLIGHTS FROM ASCO 2026

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NSCLC, non-small cell lung cancer

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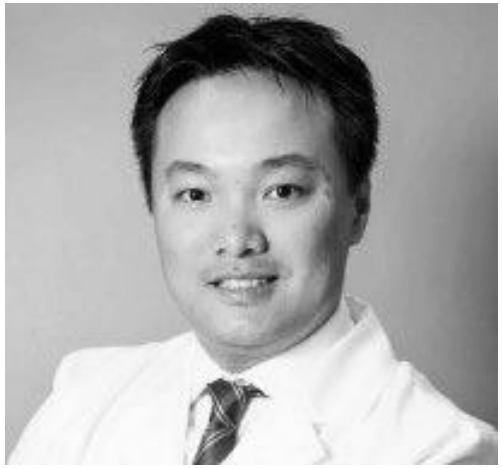

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CLINICAL TAKEAWAYS

- **SOHO-01:** Sevabertinib continues to show robust and durable antitumour activity with a manageable safety profile in *HER2*-mutant NSCLC, supporting its role as an effective targeted therapy in both first-line and previously treated settings
- **PROs from Beamion Lung-1:** first-line zongertinib is associated with early and durable improvements in symptoms and physical functioning, with minimal patient-reported treatment burden, reinforcing its favourable benefit–risk profile in *HER2*-mutant NSCLC
- **Beamion Lung-3:** this ongoing trial will determine whether adjuvant zongertinib can reduce recurrence risk and improve survival after surgery for stage II-IIIB *HER2*-mutant NSCLC, potentially establishing HER2-targeted therapy as a new standard in the adjuvant setting
- **Advancing HER2 Testing:** HER2 testing gaps in NSCLC are primarily institutional and operational, and closing them will be essential to ensuring patients are appropriately identified for biomarker-directed therapies

NSCLC, non-small cell lung cancer; PRO, patient-reported outcome

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

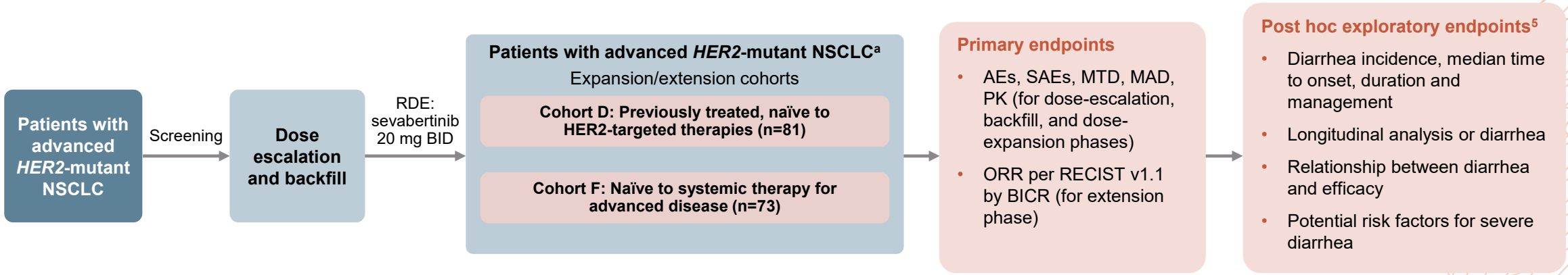
SOHO-01: UPDATED SAFETY AND EFFICACY OF SEVABERTINIB IN PATIENTS WITH ADVANCED *HER2*-MUTANT NSCLC

Loong H, et al. Abstract 8622, ASCO 2026

NSCLC, non-small cell lung cancer

SOHO-01: BACKGROUND AND STUDY DESIGN

- **Sevabertinib** is an oral, **reversible tyrosine kinase inhibitor that potently inhibits HER2 and EGFR** in preclinical models[1,2]
- Sevabertinib demonstrated significant antitumor activity and manageable safety in patients with *HER2*-mutant NSCLC who had **previously received treatment (Cohort D)** or were **treatment-naïve (Cohort F)** in the ongoing, open-label, multicenter, **Phase 1/2 SOHO-01 trial**[3]
- Updated safety and efficacy data from Cohorts D and F was reported at ASCO 2026[4]



[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[3]

AE, adverse event; BICR, blinded independent central review; BID, twice daily; 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

1. Girard N, et al. J Clin Oncol. 2024;42(suppl 17). Abstr LBA8598; 2. Loong HHF, et al. Ann Oncol. 2023;34(Supplement 2):S761-S762; 3. Le X, et al. N Engl J Med. 2025;393:1819-1832; 4. Loong H, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8622 (ASCO 2026, Poster presentation); 5. 7. Girard N, et al. Abstract 18P, ELCC 2026 (poster presentation)

SOHO-01: EFFICACY RESULTS

- Median DoR and PFS were longer in treatment naïve patients (cohort F) than in patients previously treated with systemic therapy (cohort D) in all treated patients, and in treated patients with non-squamous histology and *HER2* TKD or *HER2* YVMA mutations

EFFICACY PER BICR (RECIST V1.1) IN COHORTS D AND F

	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 (95% CI), months	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 (95% CI), months	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 CR or PR (Cohort D, n=54; Cohort F, n=55); [f] Value cannot be estimated

BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; (m)DoR, (median) duration of response; (m)PFS, (median) progression-free survival; NE, not estimable; ORR, objective response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; TKD, tyrosine kinase domain

Loong H, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8622 (ASCO 2026, Poster presentation)

SOHO-01: SAFETY RESULTS

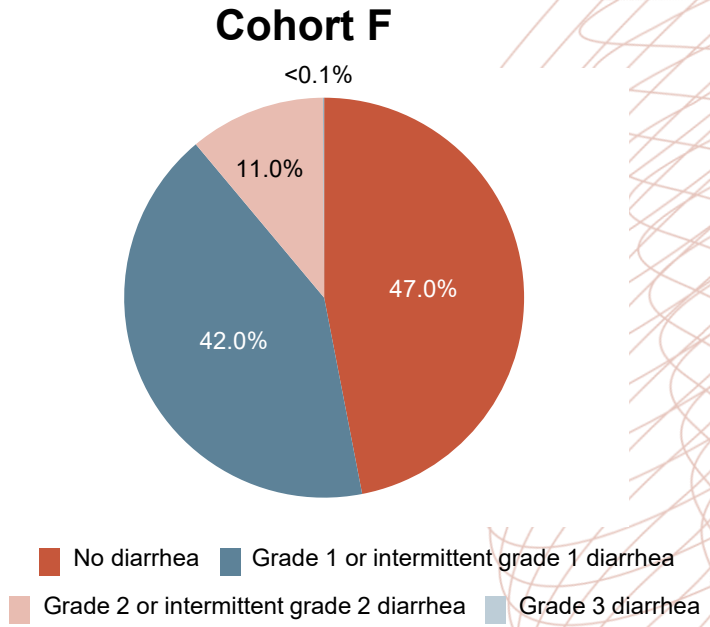
- TEAEs led to dose modifications (delays, interruptions and reductions) in 52% of patients in Cohort D and 55% of patients in Cohort F
- 5% of patients in Cohort D and 3% in Cohort F discontinued treatment due to TEAEs
- No cases of interstitial lung disease or grade 4 diarrhea, discontinuations due to diarrhea, or new safety signals were observed
- In Cohort F the proportions of patient-days with grade 2/3 treatment-emergent diarrhea were 11% and <0.1%, respectively

MOST COMMON DRUG-RELATED AEs OCCURRING IN >20% OF PATIENTS IN COHORT D OR F

N (%)[a]	Cohort D (n=81)		Cohort F (N=73)	
	All grade	Grade 3	All grade	Grade 3
Diarrhea	70 (86)	19 (23)	62 (85)	4 (5)
Rash	42 (52)	1 (1)	41 (56)	0
Paronychia	23 (28)	1 (1)	20 (27)	1 (1)
Stomatitis	15 (19)	1 (1)	20 (27)	0
Anemia	15 (19)	1 (1)	19 (26)	1 (1)
Nausea	17 (21)	2 (2)	8 (11)	2 (3)

[a] Shown are drug-related AEs of any grade that occurred in >20% of patients from cohort D or F. Relatedness of AEs to treatment was assessed by the investigator. Drug-related AEs were graded by the investigator based on CTCAE v5.0

PROPORTION OF PATIENT-DAYS WITH DIARRHEA



AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; TEAE, treatment-emergent adverse event

Loong H, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8622 (ASCO 2026, Poster presentation)

SOHO-01: SUMMARY

- Sevabertinib demonstrated robust and consistent efficacy across treatment settings, with high response rates and prolonged PFS, particularly in treatment-naïve patients
- Responses were higher in patients with non-squamous histology and *HER2* TKD mutations, reaching an ORR of 78% in pre-treated patients with *HER2*-activating YVMA mutations
- The safety profile was manageable and consistent with the TKI class, with low-grade diarrhea being the most frequently reported TRAE
  - Low rates of grade 3 diarrhea events in the first-line setting and no grade 4 events or discontinuations due to diarrhea

Clinical perspective

- These data support a favourable benefit:risk profile and further development of sevabertinib in earlier lines of therapy for *HER2*-mutant NSCLC

NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; TKD, tyrosine kinase domain; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse events

Loong H, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8622 (ASCO 2026, Poster presentation)

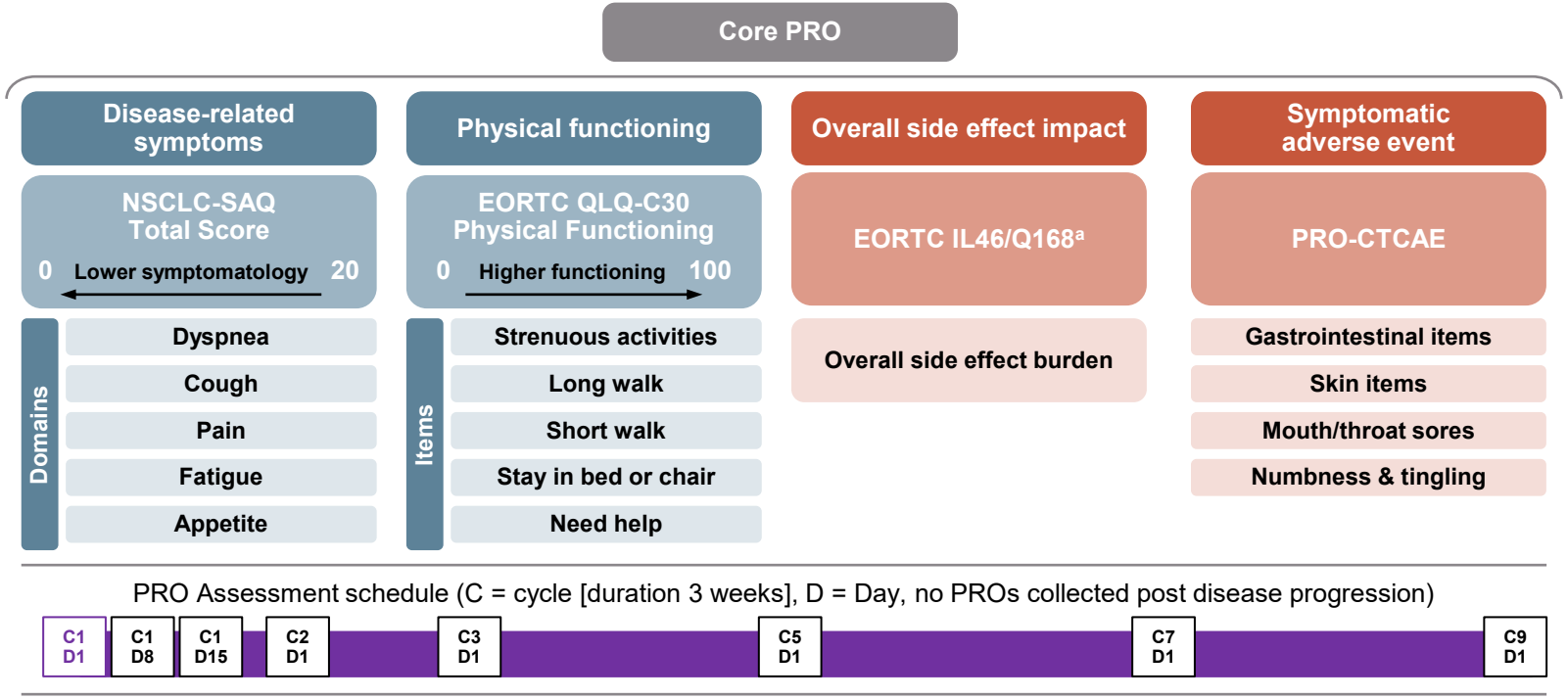
PRO RESULTS FROM THE BEAMION LUNG-1 TRIAL IN TREATMENT-NAÏVE PATIENTS WITH *HER2*-MUTANT ADVANCED NSCLC

Sabari JK, et al. Abstract 8616, ASCO 2026

NSCLC, non-small cell lung cancer

BEAMION LUNG-1 (PRO): 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[1] and limiting EGFR-related adverse events[2]
- **Beamion LUNG-1** is a phase 1b, ongoing dose-expansion study of zongertinib as monotherapy in patients with advanced/metastatic *HER2*-mutant NSCLC with or without prior treatment.[3] Patient reported outcomes were reported from **treatment-naïve patients (cohort 2)** from the study[4]



[a] IL46/Q168: EORTC item library question (assessing overall treatment-related side-effect burden)

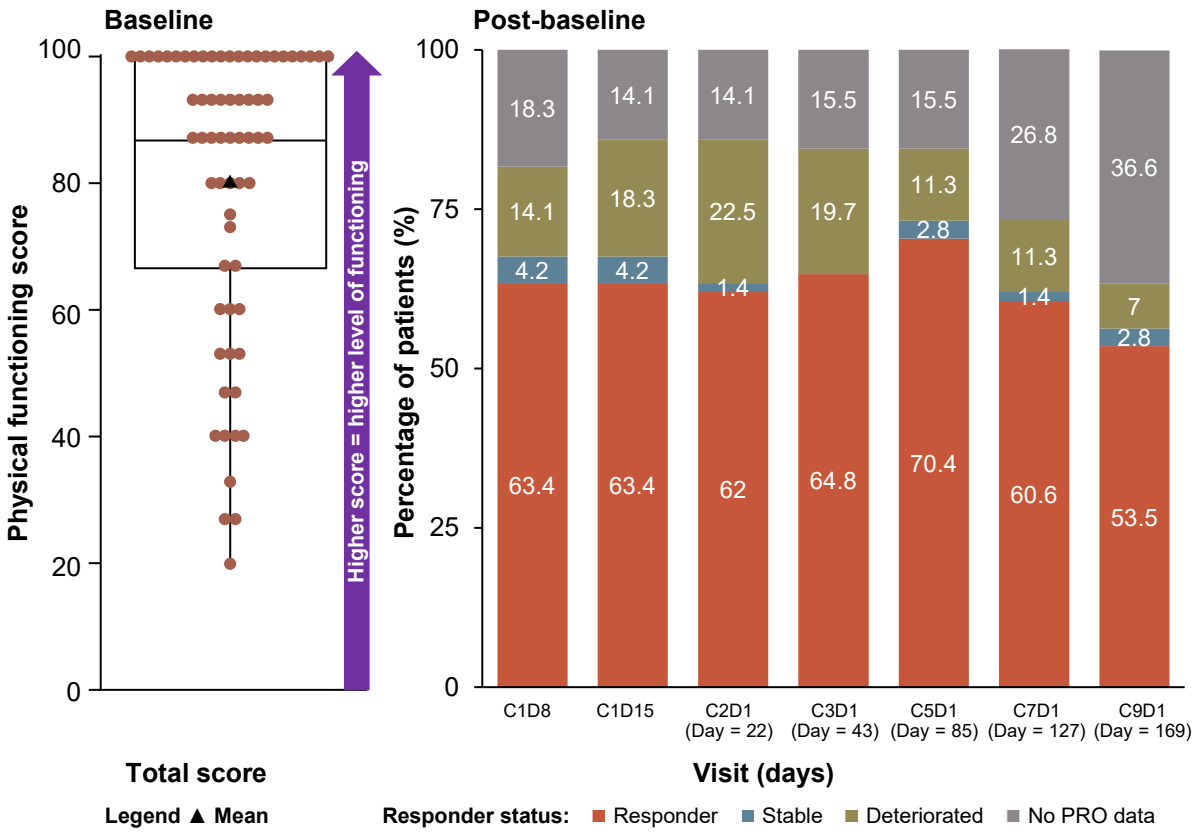
CTCAE, Common Terminology Criteria for Adverse Events; EORTC, European Organisation for Research and Treatment of Cancer; NSCLC, non-small cell lung cancer; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire-Core 30; SAQ, Symptom Assessment Questionnaire; TKI, tyrosine kinase inhibitor

1. Heymach JV, et al. Clin Lung Cancer. 2023;24:e65-e68; 2. Wilding B, et al. Cancer Discov. 2024;15:119-138; 3. Heymach JV, et al. N Engl J Med. 2025;392:2321-33; 4. Sabari JK, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8616 (ASCO 2026, Poster presentation)

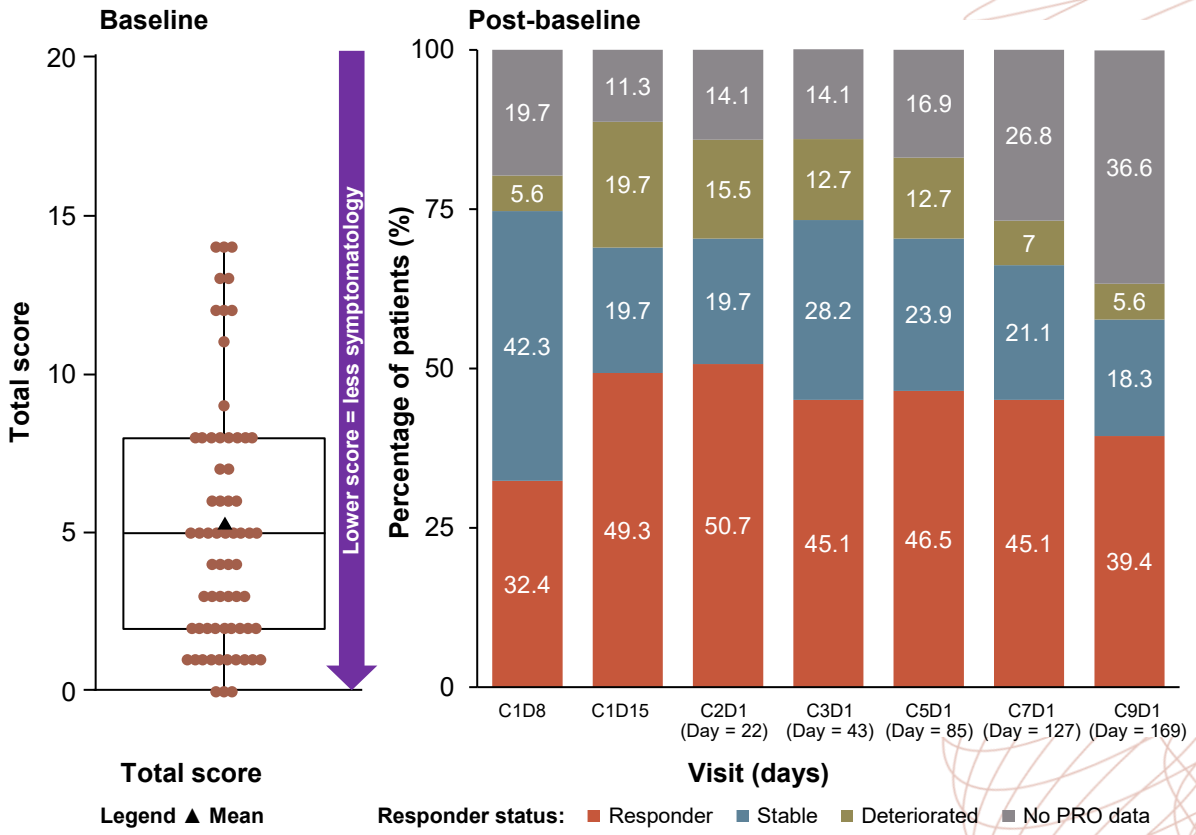
BEAMION LUNG-1 (PRO): EFFICACY RESULTS

BASELINE SUMMARY AND RESPONDER ANALYSIS (N=71)

EORTC QLQ-C30 Physical Functioning



NSCLC-SAQ Total Score



C, Cycle; D, Day; EORTC, European Organisation for Research and Treatment of Cancer; NSCLC, non-small cell lung cancer; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire-Core 30; SAQ, Symptom Assessment Questionnaire

Sabari JK, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8616 (ASCO 2026, Poster presentation)

BEAMION LUNG-1 (PRO): SAFETY RESULTS

EORTC IL46/Q168[a]: Extent troubled with side effects of treatment:

- There was low side effect burden; at any post-baseline timepoint a maximum of 8.4% of patients [n=6] reported being troubled with side-effects of treatment ‘Quite a bit’ or ‘Very much’
- Vast majority reported being ‘Not at all/A little’ troubled

PRO-CTCAE: Patient reported symptomatic AEs:

- Very little symptomology for most symptoms (~78% ‘None’/’Never’/’Not at All’ at cycle 5, 1.4% (n=1) reporting either of the two worst responses
- **Diarrhea frequency:**
  - 33.8–49.3% ‘Never’ post baseline (64.8% at baseline)
  - Most patients with symptoms reported ‘Rarely’/’Occasionally’
  - Maximum 15.5% (n=11) ‘Frequently’/’Almost Constantly’ at any one timepoint
- **Skin-related AEs:**
  - 50% and 60% of patients reported ‘None’ for skin dryness and itching severity at any timepoint, maximum of 5.2% (n=4) ‘Severe’/’Very Severe’
- Patient-reported symptomatic AEs in line with the known safety profile of zongertinib

[a] IL46/Q168: EORTC item library question (assessing overall treatment-related side-effect burden)

AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; EORTC, European Organisation for Research and Treatment of Cancer; PRO, patient-reported outcome

Sabari JK, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8616 (ASCO 2026, Poster presentation)

BEAMION LUNG-1 (PRO): SUMMARY

- High proportions of patients reported experiencing a meaningful improvement of NSCLC-related symptoms, or sustained low symptom burden, with meaningfully improved or preserved physical functioning while receiving first-line zongertinib for advanced *HER2*-mutant NSCLC
- Benefits emerged rapidly (within 1 week of treatment) and were maintained throughout PRO follow-up
- Zongertinib was well tolerated, with patients reporting being minimally troubled by side effects of their treatment and low rates of patient reported symptomatic adverse events

Clinical perspective

First-line zongertinib is associated with early and durable improvements in symptoms and physical functioning, with minimal patient-reported treatment burden, reinforcing its favourable benefit–risk profile in *HER2*-mutant NSCLC

NSCLC, non-small cell lung cancer; PRO, patient reported outcomes

Sabari JK, et al. J Clin Oncol. 2026;44(suppl 16). Abstr 8616 (ASCO 2026, Poster presentation)

BEAMION LUNG-3: ZONGERTINIB IN RESECTABLE *HER2*-MUTANT NSCLC

Cummings A, et al. Abstract TPS8129, ASCO 2026

NSCLC, non-small cell lung cancer

BEAMION LUNG-3: 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[1] and limiting EGFR-related adverse events.[2] Based on the findings of the recent Beamion LUNG-1 study,[3] zongertinib was granted accelerated approval by the FDA for patients with advanced *HER2*-mutant NSCLC[4]
- **Beamion LUNG-3 (NCT07195695)[5]** is a global, open-label, randomised, controlled, parallel-group, multicentre, multiregional, phase 3 trial investigating the efficacy and safety of adjuvant zongertinib compared with physician's choice standard of care in patients with resectable, Stage II-IIIB *HER2*-mutant NSCLC. The trial is ongoing at ~200 sites in 32 countries

Eligibility:

N≈400

- Histologically confirmed, primary, non-squamous, NSCLC (Stage II-IIIB) with a *HER2* mutation
- ECOG PS 0 or 1

Patients must have undergone **complete resection**, plus either:

- 3-4 cycles of neoadjuvant pt-CT and immunotherapy
- 4 cycles of adjuvant pt-CT

R 1:1

Stratified by:

- Stage
- Prior therapy
- Physician's choice standard of care

Treatment

Zongertinib
Orally administered;
120 mg once daily; ≤3 years[a]
N≈200

Physician's choice of standard of care
Observation or immunotherapy; ≤1 year[a]
N≈200

Primary endpoint:

- DFS by INV

Secondary endpoints:

- OS
- Grade ≥3 trial-related AEs

Exploratory endpoints:

- Time to subsequent treatment from recurrence
- Type of subsequent treatment
- Type of recurrence
- Biomarker status (tumour/blood)
- PK
- PRO

- Zongertinib self-administered in 6-week cycles in Cycles 1-10 and 12-week cycles in Cycles 11-18
- Physician's SoC determined by prior treatment:
  - Prior adjuvant Pt-CT + IO – observation or same IO as previously received (NIVO, pembro or durva)
  - Prior adjuvant Pt-CT – observation or IO (pembro /atezolizumab)

[a]Or until tumour recurrence, undue toxicity, or any other protocol-defined stopping criterion

AE, adverse event; DFS, disease-free survival; durva, durvalumab; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, Food and Drug Administration; INV, investigator assessment; IO, immunotherapy; NIVO, nivolumab; NSCLC, non-small cell lung cancer; OS, overall survival; pembro, pembrolizumab; PK, pharmacokinetics; PRO, patient-reported outcome; Pt-CT, platinum-based chemotherapy; R, randomisation; SoC, standard of care; TKI, tyrosine kinase inhibitor

1. Heymach JV, et al. Clin Lung Cancer. 2023;24:e65-e68; 2. Wilding B, et al. Cancer Discov. 2024;15:119-138; 3. Heymach JV, et al. N Engl J Med. 2025;392:2321-33; 4. US FDA. FDA grants accelerated approval to zongertinib for non-squamous NSCLC with HER2 TKD activating mutations. Available here (accessed June 3, 2026). 5. Cummings A, et al. J Clin Oncol. 2026;44(suppl 16). Abstr TPS8129 (ASCO 2026, Poster presentation)

ADVANCING HER2 TESTING AND EVIDENCE-BASED TREATMENT IN NSCLC: A QUALITY IMPROVEMENT INITIATIVE ACROSS ACADEMIC AND COMMUNITY SETTINGS

McKinnon KE, et al. Abstract e23309, ASCO 2026

NSCLC, non-small cell lung cancer

HER2 TESTING QI INITIATIVE: BACKGROUND AND STUDY DESIGN

Treatment recommendations for biomarker-directed therapy in advanced NSCLC are rapidly evolving, with current clinical guidelines recommending assessment of both HER2 overexpression and *HER2* gene mutations

However, integrating HER2 testing into practice remains a significant challenge

A data-driven quality improvement initiative was implemented to evaluate current practices and identify opportunities to optimise HER2 testing and evidence-based care

NSCLC, non-small cell lung cancer; QI, quality improvement

McKinnon KE, et al. J Clin Oncol. 2026;44(suppl 16). Abstr e23309 (ASCO 2026, e-publication)

HER2 TESTING QI INITIATIVE: METHODS

Surveys at academic centres

- Surveys (n=65) and baseline chart audits (n=75) completed between August–October 2025 by HCPs at two academic cancer centers
- **GOAL:** Development of action plans to address gaps, *including integrating a HER2 testing resource into practice*

Nationwide survey of community HCPs

- Survey of community HCPs conducted in parallel (n=72)
- **GOAL:** To evaluate real-world practice patterns and benchmark community care against academic centres

HCP, healthcare professional; QI, quality improvement

McKinnon KE, et al. J Clin Oncol. 2026;44(suppl 16). Abstr e23309 (ASCO 2026, e-publication)

HER2 TESTING QI INITIATIVE: RESULTS FROM HCP SURVEYS

	aHCPs (%)	cHCPs (%)
ROUTINE ASSESSMENT		
Assessment of *HER2* mutations for every patient	29	18
Assessment of HER2 OE for every patient	31	18
BARRIER TO HER2 OE TESTING		
Executing the ordering for the test	42	32
Limited access to testing facilities/equipment	31	39
Communication and/or coordination between Onc and Path	34	32
KEY STRATEGIES IDENTIFIED FOR IMPROVING HER2 OE TESTING		
Institutional support for reflex testing	65	49
Better EHR integration with pathology	57	53
Integrating training or education sessions	20	42
REPORTED OPPORTUNITIES TO IMPROVE ONC-PATH COLLABORATION		
Sharing EHR	42	51
Reflex testing protocols	37	47
Dedicated liaison or navigators	39	28

- Chart audits revealed HER2 testing was ordered on pathology requisition in 51% of cases
- Among tested patients, 82% received NGS testing for mutations – only 13% received testing by IHC for OE

Academic audit-feedback sessions resulted in action plans focused on:

- ✓ standardising HER2 testing protocols
- ✓ enhancing multidisciplinary communication
- ✓ securing leadership support for integrated testing workflows

EHR, electronic health records; IHC, immunohistochemistry; NGS, next generation sequencing; OE, overexpression; Onc, oncologist; Path, pathologist; QI, quality improvement

McKinnon KE, et al. J Clin Oncol. 2026;44(suppl 16). Abstr e23309 (ASCO 2026, e-publication)

HER2 TESTING QI INITIATIVE: SUMMARY

- Significant gaps exist in HER2 testing in academic and community oncology settings
- Targeted quality improvement interventions addressing workflow inefficiencies, multidisciplinary coordination, and institutional infrastructure may improve implementation of comprehensive HER2 testing and delivery of evidence-based care for patients with advanced NSCLC

Clinical perspective

- It is important to perform next generation sequencing (NGS) on NSCLC patients regardless of stage of disease to identify patients who may benefit from targeted therapies
- HER2 testing gaps in NSCLC are primarily institutional and operational, and closing them will be essential to ensuring patients are appropriately identified for biomarker-directed therapies

NSCLC, non-small cell lung cancer; QI, quality improvement

McKinnon KE, et al. J Clin Oncol. 2026;44(suppl 16). Abstr e23309 (ASCO 2026, e-publication)

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