PRO Results From the Beamion LUNG-1 Trial in Treatment-Naïve Patients With *HER2*-Mutant Advanced NSCLC

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Introduction

- *HER2* mutations occur in approximately 2–4% of NSCLC cases and are associated with highly aggressive disease, a poor prognosis, and a high incidence of brain metastases[1]
- Zongertinib is an orally administered, irreversible TKI that selectively inhibits HER2 while sparing wild-type EGFR, thereby minimizing associated toxicities[2]
- Zongertinib received accelerated approval in the United States for patients with unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC) whose tumors have *HER2* (*ERBB2*) tyrosine kinase domain activating mutations[3,4]
- Beamion LUNG-1 (NCT04886804) Phase Ib is an ongoing dose-expansion study of zongertinib as a monotherapy in patients with advanced or metastatic *HER2*-mutant NSCLC with or without prior treatment; Cohort 2 includes first-line patients with non-squamous NSCLC and a *HER2* TKD mutation[5]
  - Clinically meaningful efficacy has been previously reported for this cohort: confirmed objective response, 76%; median duration of response, 15.2 months; and median progression-free survival, 14.4 months[6]
- The trial utilizes PROs assessing disease-related symptoms, symptomatic adverse events, overall side effect impact, and physical functioning, as recommended in FDA guidance, to explore the experience of patients taking zongertinib[7]

EGFR epidermal growth factor receptor; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; NSCLC, non–small cell lung cancer; PROs, patient-reported outcomes; TKD, tyrosine kinase domain; TKI, tyrosine kinase inhibitor

Methods

- PRO data from Beamion LUNG-1 Phase Ib dose expansion; Cohort 2 zongertinib 120 mg QD as first-line therapy (database lock: March 26, 2025)
- PROs utilized are outlined in Figure 1

Statistical analysis

- Descriptive summaries of patient demographics, PRO available data rates, patient disposition, and all domain and item level responses

NSCLC-Symptom Assessment Questionnaire (NSCLC-SAQ) total score and EORTC QLQ-C30 physical functioning analysis

- Responder analysis was conducted utilizing responder definition:
  - Patients experiencing a MWPC meeting published improvement thresholds (Table 1), or
  - Patients with low levels of baseline symptomatology/high functioning experiencing either no change or an improvement from baseline (i.e., no change or improvement from baseline NSCLC-SAQ total score ≤2.5/baseline EORTC QLQ-C30 physical functioning score ≥83)
- Patients not meeting the responder criteria classified as stable or deteriorated using MWPC thresholds
- Mean change from baseline scores analyzed longitudinally using MMRM

Figure 1. PROs, including assessment schedule, utilized in Beamion LUNG-1

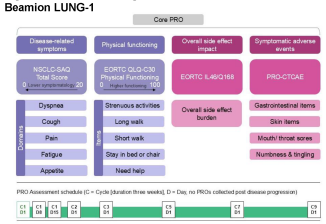


Table 1. Published meaningful within-patient change thresholds

PRO	Meaningful within-patient change threshold	
	Improvement	Deterioration
NSCLC-SAQ total score[8]	-2.5	2
EORTC QLQ-C30 physical functioning[†9]	6.7	-6.7

[†]Taken as the minimal possible change

IL46/Q16B, Item Library 46/Question 16B; EORTC, European Organisation for Research and Treatment of Cancer; MMRM, mixed model for repeated measures; MWPC, meaningful within-patient change; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; QD, once daily; QLQ-C30, Quality of Life Questionnaire-Core 30

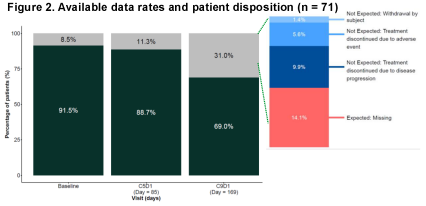
Results: Patients

- 71 patients with expected PRO data, Cohort 2, zongertinib 120mg QD
- Demographics: 49.3% female, 50.7% male; 48.4% Asian, 50% White; age groups: 43.7% 18–65 years, 39.4% 65–75 years, 16.9% ≥75 years; 62.9% never smoked tobacco

PRO completion and patient disposition (Figure 2)

- High levels of PRO completion
- Available data rates: 87%+ up to Cycle 5, 69% at Cycle 9
- Missing data due to design, 14.1% of missing PRO data at Cycle 9 was expected

Figure 2. Available data rates and patient disposition (n = 71)



C5D1, Cycle 5 Day 1; C9D1, Cycle 9 Day 1

Key Findings and Conclusions

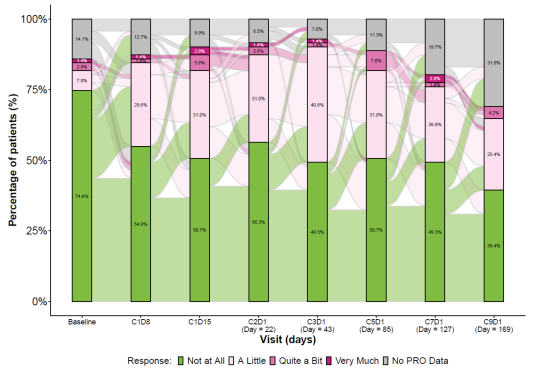
- High proportions of patients reported experiencing a meaningful improvement of NSCLC-related symptoms, or sustained low symptom burden, with meaningfully improved or preserved physical functioning while receiving first-line zongertinib 120 mg QD for advanced *HER2*-mutant NSCLC
- Benefits emerged rapidly (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

Results: Overall Side Effect Impact and Symptomatic Adverse Events

EORTC IL46/Q168 extent troubled with side effects of treatment (Figure 3)

- Very few patients reported being 'Quite a Bit' or 'Very Much' troubled
- Vast majority reported being 'Not at All'/'A Little' troubled

Figure 3. Extent troubled with side effects of treatment (n = 71)



PRO-CTCAE patient reported symptomatic AEs

- Very little symptomatology for most symptoms (~78% 'None'/'Never'/'Not at All' at Cycle 5, 1.4% [1 patient] reporting either of the two worst responses)
- **Diarrhea frequency**:
  - 33.8% to 49.3% 'Never' post-baseline (64.8% at baseline)
  - Most patients with symptoms reported 'Rarely'/'Occasionally'
  - Maximum 15.5% (11 patients) 'Frequently'/'Almost Constantly' at any one timepoint
- 50% and 60% of patients reported 'None' for skin dryness and itching severity at any timepoint, maximum of 5.2% (4 patients) 'Severe'/'Very Severe'
- Patient-reported symptomatic AEs assessed by PRO-CTCAE in line with the known safety profile of zongertinib

AE, adverse event

Results: Disease-Related Symptoms and Physical Functioning

NSCLC-SAQ

Total symptom score (Figure 4):

Baseline

- 4.2% (3 patients) with best possible score of 0
- 26.8% (19 patients) reported 0≤ score ≤2.5

Change from baseline

- 32.4% responders at first post-baseline assessment (MWPC or maintained/improved from a baseline score of ≤2.5)
- Peak of 50.7% responders at Cycle 2
- Few patients experienced a deterioration (5.6% to 19.7%, 4 to 14 patients)
- Rapid improvement also evident in mean change from baseline over time

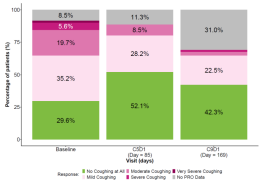
Figure 4. Baseline summary and responder analysis of NSCLC-SAQ total score (n = 71)



Cough (Figure 5):

- 10%+ increase reporting 'No Coughing at All' compared to baseline
- Patients with moderate/severe/very severe cough symptoms at baseline showed improvement

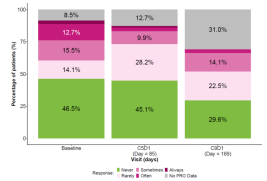
Figure 5. Rating of cough at its worst over the last 7 days (n = 71)



Dyspnea (Figure 6):

- 73% 'Never'/'Rarely' short of breath at Cycle 5, 52% at Cycle 9 (baseline 61%)

Figure 6. Frequency of feeling short of breath during usual activities over the last 7 days (n = 71)



EORTC QLQ-C30 Physical Functioning (Figure 7)

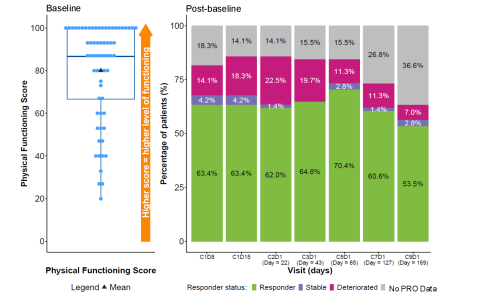
Baseline

- 31% (22 patients) with best possible score of 100

Change from baseline

- Consistent high percentage of responders from first post-baseline assessment (MWPC or maintained/improved from a baseline score ≥83)
- Peak of 70.4% responders at Cycle 5
- 7% to 22.5% (5 to 16 patients) experienced a deterioration at any timepoint
- Conclusions reflected in mean change from baseline over time analysis

Figure 7. Baseline summary and responder analysis of EORTC QLQ-C30 physical functioning (n = 71)



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This study is funded by Boehringer Ingelheim. The authors meet the criteria for authorship as recommended by the International Committee of Medical Journal Editors. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version. The authors did not receive payment related to the development of the poster. Editorial support for this encore poster (in the form of poster layout and formatting) was provided by Jen-Marié Grové, MMedSc, of Nucleus Global, an Inizio company, and funded by Boehringer Ingelheim Pharmaceuticals, Inc (BIPI). BIPI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations

Joshua K. Sabari reports consulting or advisory roles with AstraZeneca, Pfizer, Regeneron, Medscape, Takeda, Janssen, Genetech/Roche, Mirati Therapeutics, Abbvie, Loxo/Lilly, and Sanofi; and institutional consulting or advisory roles with Janssen, Loxo/Lilly, Mirati Therapeutics, and Regeneron

Presented at the Network for Collaborative Oncology Development & Advancement (NCODA) International Fall Summit, Orlando, FL, USA, October 28–30, 2026

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Originally presented at the American Society of Clinical Oncology (ASCO) meeting, Chicago, IL, USA, May 29–June 2, 2026

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