

Zongertinib in Previously Treated *HER2*-Mutant NSCLC: Diarrhea Characterization and Management

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Zongertinib is a tyrosine kinase inhibitor (TKI) that selectively inhibits *HER2* (*ERBB2*). This orally administered, targeted therapy was approved as HERNEXEOS® (zongertinib tablets) under the FDA's Accelerated Approval Program, after securing Priority Review as well as Breakthrough Therapy and Fast Track designations. Please see full [Prescribing Information](#) for HERNEXEOS.

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ZONGERTINIB: *HER2*-SELECTIVE TKI FOR ADVANCED *HER2* (*ERBB2*)-MUTANT NSCLC

MOA^{1,2}



Zongertinib is an oral, irreversible TKI that selectively inhibits *HER2* while sparing wild-type *EGFR*, limiting *EGFR*-associated toxicities

Efficacy in Phase Ib Beamion LUNG-1^{2,*}



71% ORR
14.1 mo mDOR
12.4 mPFS

Safety²



Diarrhea was the most common, clinically relevant AE, but it was typically early onset, low grade, and manageable

*Dose-expansion study (120 mg orally, once daily) in previously treated adults with advanced/metastatic *HER2* (*ERBB2*) TKD-mutant NSCLC (N=75).

KEY LEARNINGS

- ✓ Diarrhea events with zongertinib were of early onset (within 1–2 weeks) and typically low grade (majority Grade 1 or 2)³
- ✓ Diarrhea events did not lead to treatment discontinuations and typically did not recur³
- ✓ Treatment modifications were infrequent and are manageable in clinical practice through education and awareness for patients^{3,4}

SUPPORT CHECKLIST

Educate patients at the start of therapy

- ✓ When diarrhea occurs, it is usually mild (57.3% Grade 1 or 2)^{2,3}
- ✓ Most likely to occur within the first 2 weeks (64% within the first 1–2 weeks)^{2,3}
- ✓ Encourage early reporting of new or worsening diarrhea⁴

Monitor and act promptly

- ✓ Initiate anti-diarrheal therapy as needed⁴
- ✓ Follow PI guidance on management of new or persisting diarrhea of Grade ≥ 2 ⁴

DIARRHEA EVENTS WERE EARLY ONSET AND MANAGEABLE

75 total patients

Previously treated adults with advanced/metastatic *HER2* (*ERBB2*) TKD-mutant NSCLC who received 120 mg zongertinib orally once daily in Phase Ib Beamion LUNG-1³

44 patients with diarrhea (58.7%)

Any grade, typically early onset and low grade³

25 patients (56.8%) received supportive care³

18 patients received loperamide, while 7 received other therapies³

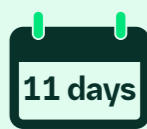
Zero discontinuations

One dose interruption³
Zero dose reductions³

Diarrhea events were of early onset and showed limited recurrence³

64%

of events occurred within the first 1–2 weeks of treatment



11 days

median time to first onset

81.8%

(36 of 44) had only one or two events

18.2%

(8 of 44) had recurrent events (≥ 3 episodes)

Grade distribution among 44 of 75 patients who experienced diarrhea³

45.3%
(n=33)

Grade 1

12.0%
(n=10)

Grade 2

1.3%
(n=1)

Grade 3

0%
(n=0)

Grade 4

1

8 patients with a single event



3 days median duration



The event resolved after a brief dose interruption and supportive care

References

1. Wilding B et al. Cancer Discov. 2025;15(1):119-38.
2. Heymach JV et al.; Beamion LUNG-1 Investigators. N Engl J Med. 2025;392(23):2321-33.
3. Irwin C et al. Poster 19264. ONS Congress, May 13-17, 2026.
4. FDA. 2026. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/219042s001lbl.pdf. Last accessed: March 26, 2026.

Abbreviations

AE: adverse event; *EGFR*: epidermal growth factor receptor; *HER2*: human epidermal growth factor receptor 2; mDOR: median duration of response; mo: months; MOA: mechanism of action; mPFS: median progression-free survival; NSCLC: non-small cell lung cancer; ORR: objective response rate; PI: prescribing information; TKD: tyrosine kinase domain; TKI: tyrosine kinase inhibitor.