Targeting Brain Metastases: Intracranial Activity of Zongertinib in *HER2 (ERBB2)*-Mutant NSCLC

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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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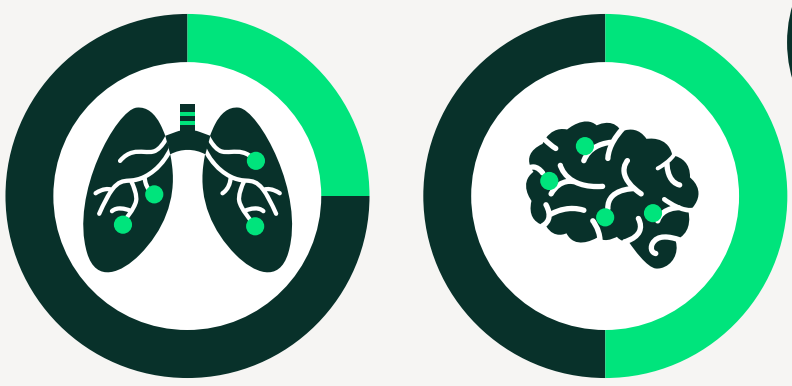
Unmet need for treatments with intracranial activity for *HER2 (ERBB2)*-mutant NSCLC

25% of patients with *HER2*-mutant NSCLC present with BM at diagnosis.[1,2]

50% develop BM during disease course.[1,2]



Does zongertinib show meaningful intracranial activity?

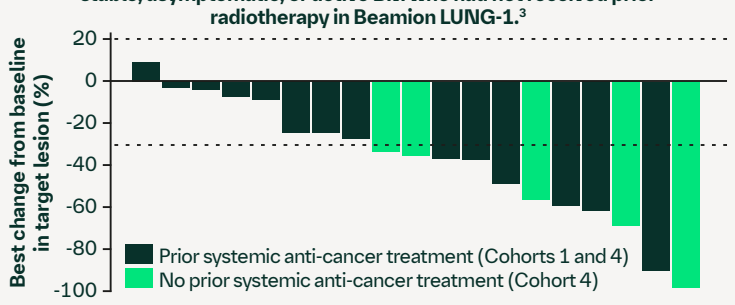
Zongertinib provides intracranial response without prior brain radiotherapy

95% (18/19) of evaluable patients showed reduction in brain lesion size from baseline*[,3]

44% ORR[3]

8.1-month median PFS[3]

Confirmed intracranial response by RANO-BM in patients (n=41) with stable, asymptomatic, or active BM who had not received prior radiotherapy in Beamion LUNG-1.[3]



*Patients with BM at baseline, evaluable by RANO-BM as assessed by the investigator, in Beamion LUNG-1.

Pooled analysis of 41 patients in Cohorts 1 and 4. Responses were observed in both previously treated and treatment-naive patients.

Does zongertinib show intracranial activity in the broader patient population with BM?

Zongertinib demonstrated intracranial efficacy across patients with stable, asymptomatic or active BM (n=58).‡,[3]

41% intracranial ORR (RANO-BM)

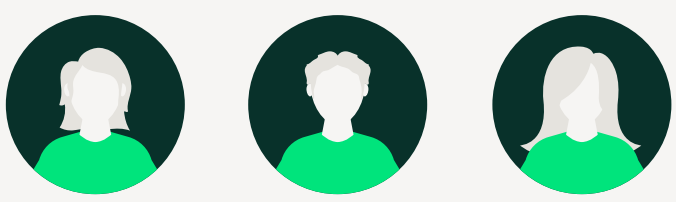
83% DCR

8.2-month median PFS

‡Included patients with and without prior brain radiotherapy.

Does zongertinib also provide systemic responses in patients with BM?

Zongertinib demonstrated similar systemic activity in patients with and without BM at baseline.§,[3]



77% ORR in patients without BM (n=47)

64% ORR in patients with stable, asymptomatic BM (n=28)

63% ORR in patients with active BM (n=30)

§Confirmed systemic response by RECIST v1.1.

What about the tolerability of zongertinib in patients with BM?

Manageable safety profile in patients with stable, asymptomatic brain metastases (n=28)

Most treatment-related AEs were low grade.[3]

Common AEs: diarrhea 64% (G ≥3: 4%), rash 25% (G ≥3: 0%), and neutrophil count decreased 25% (G ≥3: 4%).[3]

Similar safety profile in patients with and without BM.[3,4]

Conclusion

Zongertinib demonstrated clinically meaningful intracranial responses in patients with stable, asymptomatic, or active BM.[3]

Systemic efficacy and safety were consistent regardless of BM status at baseline.[3,4]

References:

1. Offin M et al. Cancer. 2019;125(24):4380-7.
2. Zhang Q et al. Lung Cancer. 2025;205:108616.
3. Ruiter G et al. Abstract No. PT2.12.03. WCLC, September 6-9, 2025.
4. Heymach JV et al. N Engl J Med. 2025;392(23):2321-33.

Abbreviations:

AE: adverse event; BM: brain metastasis; DCR: disease control rate; G: grade; NSCLC: non-small cell lung cancer; ORR: objective response rate; PFS: progression-free survival; RANO-BM: Response Assessment in Neuro-Oncology Brain Metastases; RECIST v1.1: Response Evaluation Criteria in Solid Tumours version 1.1.