

Safety of Zongertinib Following Immune Checkpoint Inhibitors in *HER2*-Mutant Advanced NSCLC: Beamion LUNG-1 Cohort 1

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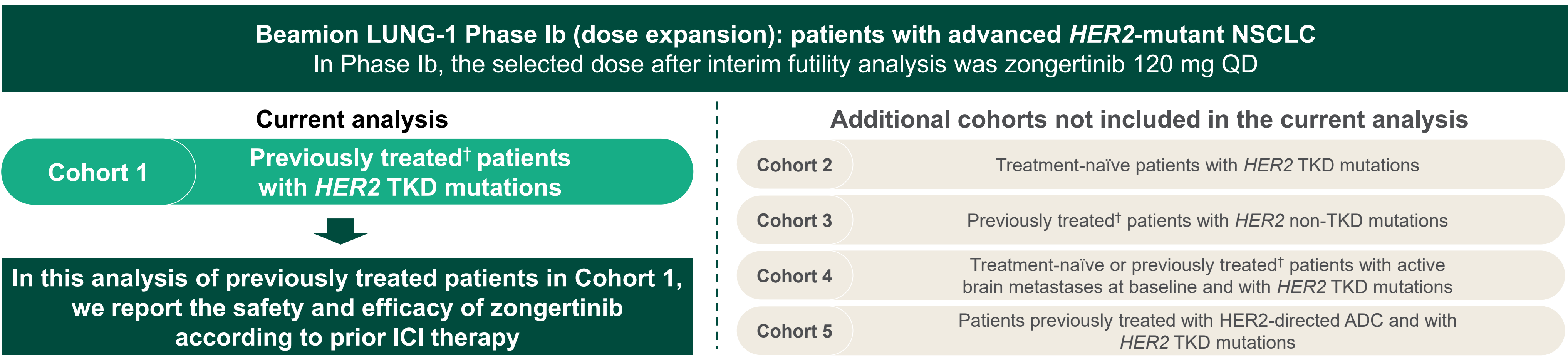
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Introduction

- Zongertinib is an orally administered, irreversible TKI that selectively inhibits HER2 while sparing wild-type EGFR, thereby minimizing associated toxicities^{1,2}
- In routine clinical practice, many patients with advanced NSCLC receive ICIs before targeted therapy, making the safety of zongertinib following prior ICI exposure a clinically important consideration
- Here, we evaluated the safety and efficacy of zongertinib in patients with previously treated *HER2*-mutant advanced/metastatic NSCLC from Cohort 1 of the Beamion LUNG-1 study, stratified by prior ICI exposure (no prior ICI, prior ICI ≤90 days, or prior ICI >90 days)

EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

Methods



[†]Excluding those previously treated with a *HER2*-directed ADC. ADC, antibody–drug conjugate; QD, once daily; TKD, tyrosine kinase domain

Patients

In Cohort 1 (data cut-off November 29, 2024), 56 of 75 (75%) patients had received prior ICI therapy*			
	No prior ICI therapy n=18	Prior ICI therapy ≤90 days n=35	Prior ICI therapy >90 days n=21
Median age, years (range)	59 (32–73)	61 (30–80)	70 (32–80)
Female, n (%)	14 (78)	22 (63)	14 (67)
Race, n (%)[§]			
Asian	9 (50)	17 (49)	14 (67)
White	8 (44)	10 (29)	5 (24)
ECOG PS, n (%)			
0	6 (33)	13 (37)	8 (38)
1	12 (67)	22 (63)	13 (62)
Tobacco use, n (%)			
Never	11 (61)	23 (66)	14 (67)
Current	1 (6)	1 (3)	0
Former	6 (33)	11 (31)	7 (33)

*One patient (55-year-old White female, never-smoker, ECOG PS 0) had received prior ICI therapy at an unknown date; [§]missing due to legal requirements: no prior ICI therapy, n=1; prior ICI therapy ≤90 days, n=8; prior ICI therapy >90 days, n=2. ECOG PS, Eastern Cooperative Oncology Group performance status

Efficacy

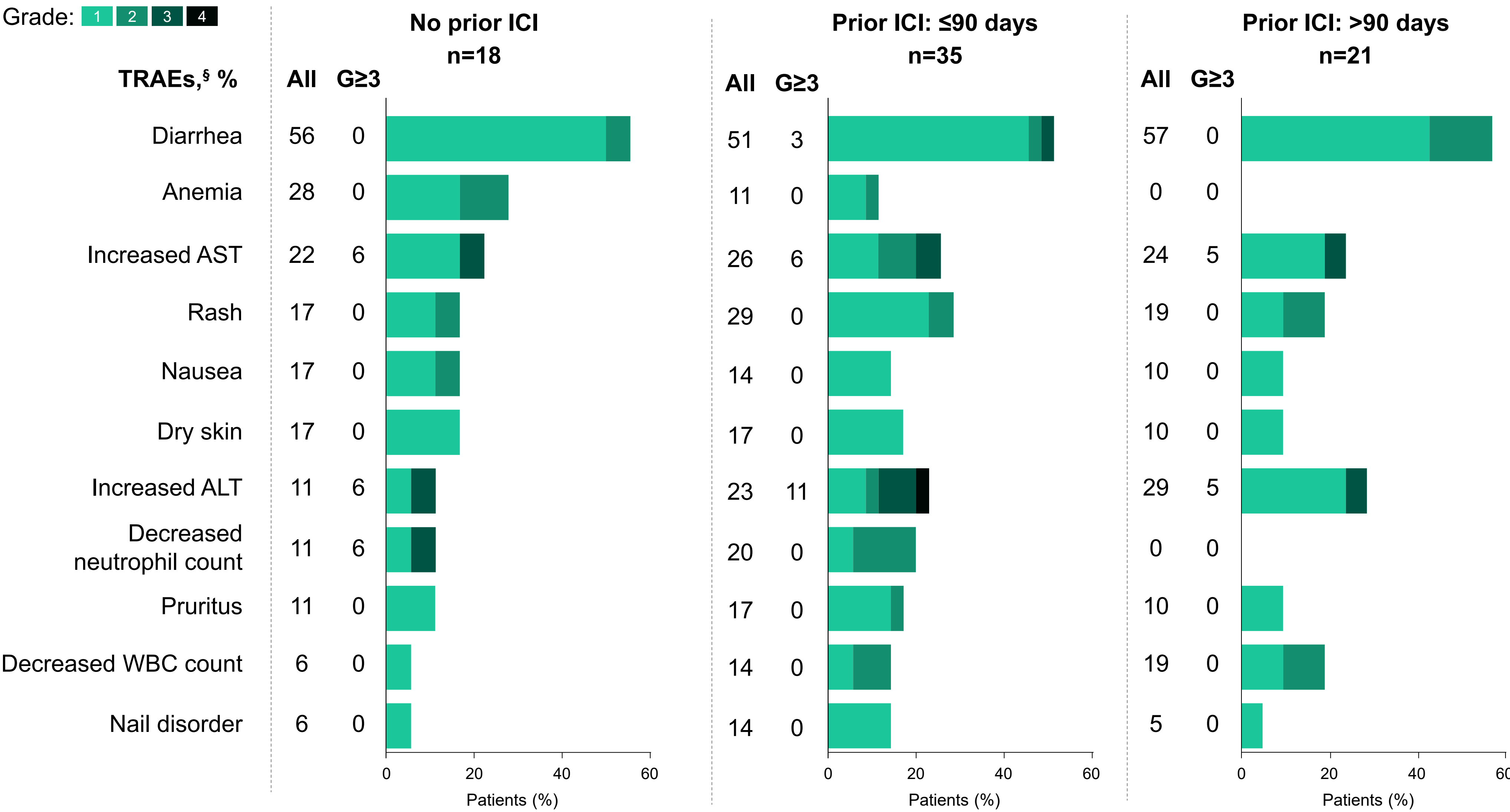
- ORR was 72%, 69%, and 71% in patients with no prior ICI therapy, prior ICI therapy ≤90 days, and prior ICI therapy >90 days, respectively
- DCR was 89%, 100%, and 95% in patients with no prior ICI therapy, prior ICI therapy ≤90 days, and prior ICI therapy >90 days, respectively

ORR, objective response rate; DCR, disease control rate

Plain Language Summary

- Zongertinib, a new drug that targets HER2, has shown strong activity with a manageable safety profile in people living with advanced *HER2*-mutant NSCLC
- As many people receive immunotherapy before targeted treatments such as zongertinib, it is important to understand whether zongertinib can be used safely afterwards
- In this analysis, zongertinib demonstrated a manageable safety profile in people living with previously treated *HER2*-mutant NSCLC, regardless of prior immunotherapy

Safety



	No prior ICI therapy n=18			Prior ICI therapy ≤90 days n=35			Prior ICI therapy >90 days n=21		
TRAEs,[§] n (%)	G1	G2	G≥3	G1	G2	G≥3	G1	G2	G≥3
Diarrhea	9 (50)	1 (6)	0	16 (46)	1 (3)	1 (3)	9 (43)	3 (14)	0
Anemia	3 (17)	2 (11)	0	3 (9)	1 (3)	0	0	0	0
Increased AST	3 (17)	0	1 (6)	4 (11)	3 (9)	2 (6)	4 (19)	0	1 (5)
Rash	2 (11)	1 (6)	0	8 (23)	2 (6)	0	2 (10)	2 (10)	0
Nausea	2 (11)	1 (6)	0	5 (14)	0	0	2 (10)	0	0
Dry skin	3 (17)	0	0	6 (17)	0	0	2 (10)	0	0
Increased ALT	1 (6)	0	1 (6)	3 (9)	1 (3)	4 (11)	5 (24)	0	1 (5)
Decreased neutrophil count	1 (6)	0	1 (6)	2 (6)	5 (14)	0	0	0	0
Pruritus	2 (11)	0	0	5 (14)	1 (3)	0	2 (10)	0	0
Decreased WBC count	1 (6)	0	0	2 (6)	3 (9)	0	2 (10)	2 (10)	0
Nail disorder	1 (6)	0	0	5 (14)	0	0	1 (5)	0	0

- Dose reductions were infrequent, occurring in 2 patients without prior ICI exposure, 1 patient with prior ICI ≤90 days, and 2 patients with prior ICI >90 days
- Discontinuations occurred in 2 patients with prior ICI ≤90 days: 1 patient due to increased AST, increased ALT, increased blood alkaline phosphatase, and increased gamma-glutamyltransferase, and 1 patient due to pyrexia. No discontinuations occurred in the other subgroups

[§]TRAEs were assessed by the investigator; those reported in ≥10% of the overall Cohort 1 population are reported. The one patient with unknown time of prior ICI experienced grade 1 diarrhea, nausea, nail disorder, dyspepsia, increased lipase, and abdominal pain. ALT, alanine aminotransferase; AST, aspartate aminotransferase; G, grade; TRAE, treatment-related adverse event; WBC, white blood cell

Key Findings and Conclusions

- Adverse event patterns with zongertinib appeared generally consistent irrespective of the timing of prior ICI treatment
- No clinically meaningful safety signal suggesting a need to delay zongertinib initiation after prior ICI was observed in this analysis

References

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