



P3.249: Comparative Efficacy of Osimertinib and Lazertinib for Stage IV EGFR-Mutant NSCLC in the Second-Line and Beyond: Korean EGFR Registry

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INTRODUCTION

- Osimertinib and lazertinib are both approved third-generation EGFR tyrosine kinase inhibitors (TKIs) for EGFR-mutant NSCLC.
- No head-to-head trial has directly compared their efficacy.
- Real-world comparative data in the second-line and beyond remain limited.

Objective

To compare the real-world efficacy of osimertinib versus lazertinib as ≥2nd-line therapy in patients with stage IV EGFR-mutant NSCLC, using the multicenter Korean EGFR Registry (KER).

METHODS

Data source

Korean EGFR Registry (KER), a multicenter registry across 40 institutions in Korea, including prospective and retrospective cohorts. Data cut-off March 31, 2026.

Population

Stage IV NSCLC with EGFR exon 19 deletion (E19del) or L858R mutation, treated with osimertinib or lazertinib as ≥2nd-line therapy (N = 190).

PFS analyses included patients with evaluable follow-up (n = 145 unweighted; n = 127 after weighting).

Endpoint

Progression-free survival (PFS), from the start of the ≥2nd-line third-generation EGFR TKI.

Statistical analysis

- PFS was estimated by the Kaplan–Meier method and compared using the log-rank test.
- Truncated inverse probability of treatment weighting (IPTW) was applied using 8 covariates: age, sex, histologic subtype, smoking history, EGFR mutational status, ECOG performance status, PD-L1 expression and brain metastasis.
- Institution, pre-specified in the abstract, was dropped from the weighting model: with few patients per site it degraded covariate balance, which improved markedly on its removal.
- Uni- and multivariable Cox models were fitted for PFS.

DISCUSSION AND CONCLUSION

Conclusions

- Osimertinib and lazertinib showed comparable progression-free survival in the ≥2nd-line setting, both unweighted and after IPTW adjustment.

Actionable take-away message

- In the ≥2nd-line setting the two third-generation EGFR TKIs performed similarly in routine practice.
- Treatment selection may therefore be guided by tolerability, dosing convenience, CNS activity and access rather than by an expected difference in efficacy.

REFERENCES & ACKNOWLEDGEMENTS

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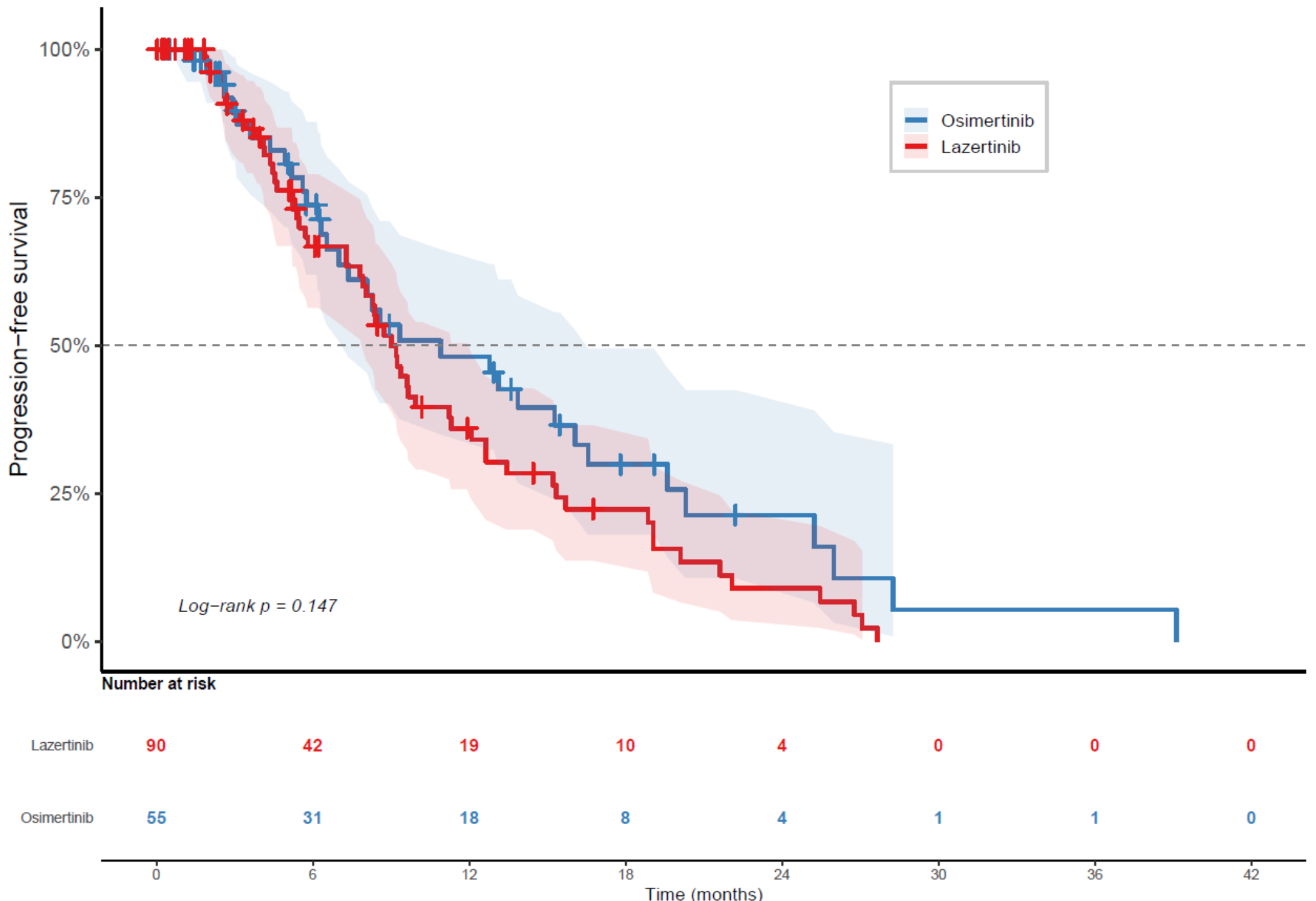
RESULTS

Table 1. Baseline characteristics

Characteristic	Overall (N=190)	Osimertinib (n=82)	Lazertinib (n=108)	p
Age, median [IQR]	68 [60–75]	70 [60–77]	68 [60–74]	0.172
Sex, n (%)				0.834
Male	76 (40.0)	34 (41.5)	42 (38.9)	
Female	114 (60.0)	48 (58.5)	66 (61.1)	
Smoking status, n (%)				0.894
Never	120 (63.2)	53 (64.6)	67 (62.0)	
Ever	69 (36.3)	29 (35.4)	40 (37.0)	
ECOG performance status, n (%)				0.140
0–1	168 (88.4)	75 (91.5)	93 (86.1)	
≥2	8 (4.2)	1 (1.2)	7 (6.5)	
Histologic subtype, n (%)				0.029
Adenocarcinoma	186 (97.9)	78 (95.1)	108 (100.0)	
Squamous	3 (1.6)	3 (3.7)	0 (0.0)	
Others	1 (0.5)	1 (1.2)	0 (0.0)	
No. of metastatic organs, n (%)				0.694
<3	128 (67.4)	57 (69.5)	71 (65.7)	
≥3	62 (32.6)	25 (30.5)	37 (34.3)	
Brain metastasis, n (%)				0.295
No	123 (64.7)	57 (69.5)	66 (61.1)	
Yes	67 (35.3)	25 (30.5)	42 (38.9)	
PD-L1 expression, n (%)				0.179
<1%	82 (43.2)	41 (50.0)	41 (38.0)	
1–49%	76 (40.0)	28 (34.1)	48 (44.4)	
≥50%	23 (12.1)	8 (9.8)	15 (13.9)	
EGFR mutation subtype, n (%)				0.247
Exon 19 deletion	115 (60.5)	54 (65.9)	61 (56.5)	
L858R	72 (37.9)	26 (31.7)	46 (42.6)	
Other	3 (1.6)	2 (2.4)	1 (0.9)	
Prior EGFR-TKI generation, n (%)				0.097
1st generation	46 (24.2)	21 (25.6)	25 (23.1)	
2nd generation	133 (70.0)	53 (64.6)	80 (74.1)	
Both 1st and 2nd	11 (5.8)	8 (9.8)	3 (2.8)	

IQR, interquartile range; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed death-ligand 1.

Figure 1. Unadjusted progression-free survival

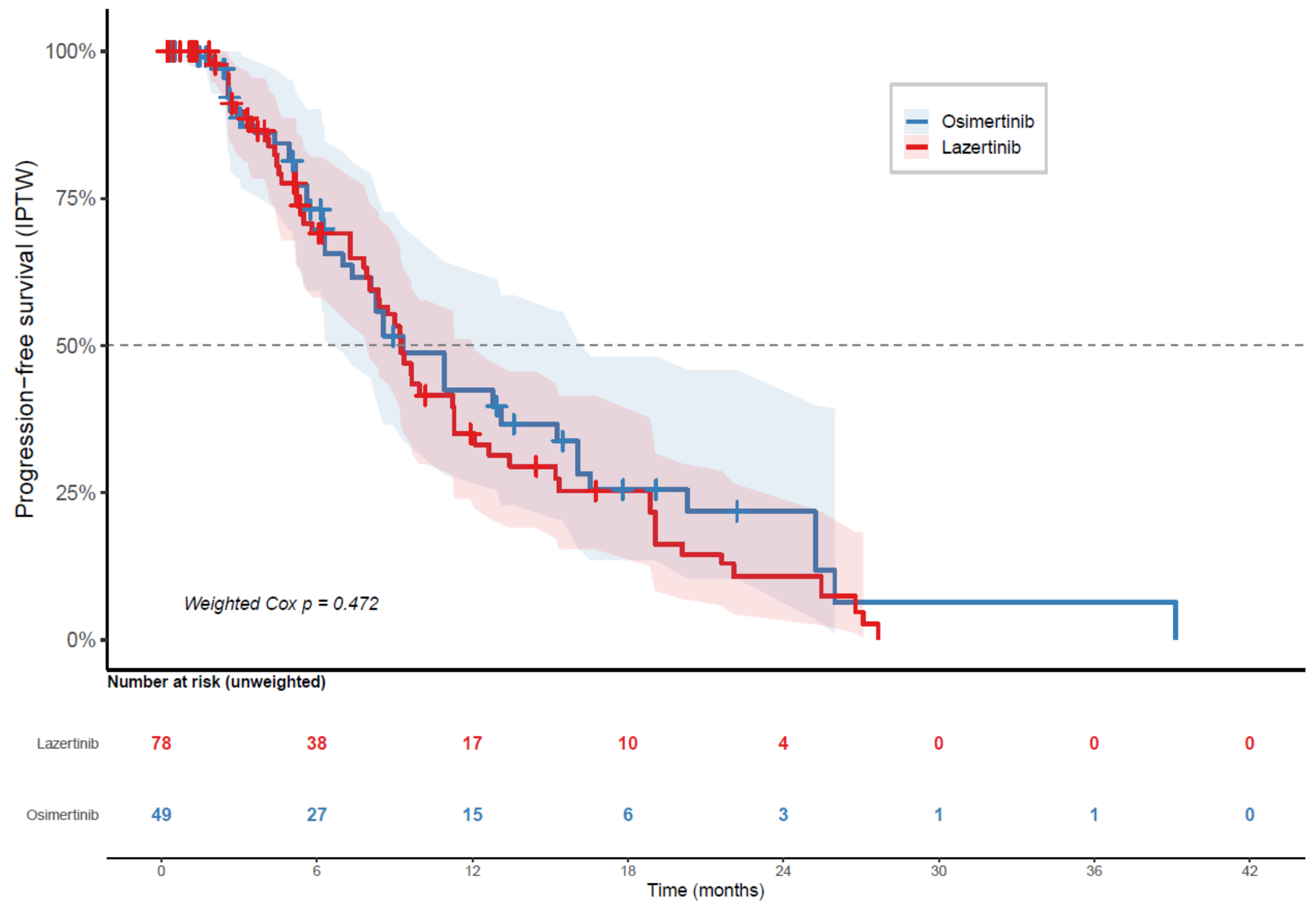


Unweighted Kaplan–Meier estimates (n = 145); HR 1.379 (95% CI 0.894–2.128), log-rank p = 0.147.



- 190 patients received a third-generation EGFR TKI as ≥2nd-line therapy (osimertinib n = 82; lazertinib n = 108).
- IPTW adjustment without institution achieved good covariate balance between groups.
- Dose modification was more frequent with lazertinib than with osimertinib (57.4% vs 19.5%; p < 0.001).

Figure 2. IPTW-adjusted progression-free survival



Weighted Kaplan–Meier estimates (n = 127); weighted HR 1.189 (95% CI 0.742–1.904), p = 0.472. Numbers at risk are unweighted.

Table 2. Progression-free survival

Progression-free survival	Osimertinib months (95% CI)	Lazertinib months (95% CI)
Median PFS, unweighted	10.9 (7.4–16.6)	9.0 (7.9–12.1)
Median PFS, IPTW-weighted	9.3 (7.0–16.6)	9.2 (7.9–12.1)
Univariable HR 1.38 (95% CI 0.89–2.13); p = 0.146		
Multivariable HR 1.32 (95% CI 0.80–2.17); p = 0.274		
PFS events, %	61.8	64.4
Median follow-up, months	20.2	20.7

Cox models for PFS; hazard ratios are for lazertinib versus osimertinib (reference). The multivariable model was adjusted for sex, smoking history, histologic subtype, EGFR mutation subtype, brain metastasis and PD-L1 expression.