

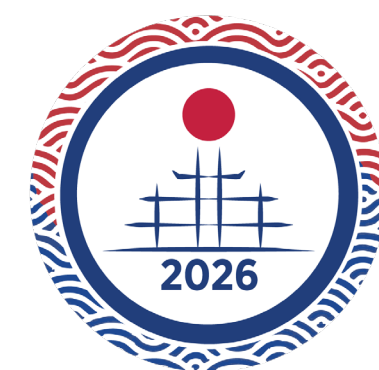


P3.257 First-Line Lazertinib versus Osimertinib in Advanced *EGFR*-Mutant NSCLC: A Real-World Propensity Score–Matched Study

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INTRODUCTION

- Osimertinib and lazertinib improved progression-free survival (PFS) over earlier epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) in advanced *EGFR*-mutant non-small cell lung cancer (NSCLC)¹⁻².
- Lazertinib monotherapy is approved as first-line treatment in South Korea, but only in combination with amivantamab in the United States and Europe.
- Head-to-head evidence is limited to an exploratory MARIPOSA analysis, with, to our knowledge, no real-world comparison to date³⁻⁴.
- Co-occurring genomic alterations were linked to shorter PFS in a prior cohort, but could not detect this association within its osimertinib subgroup (n = 31)⁵.
- We compared real-world PFS between first-line lazertinib and osimertinib monotherapy and explored the impact of co-occurring genomic alterations.

DISCUSSION AND CONCLUSION

➤ Discussion

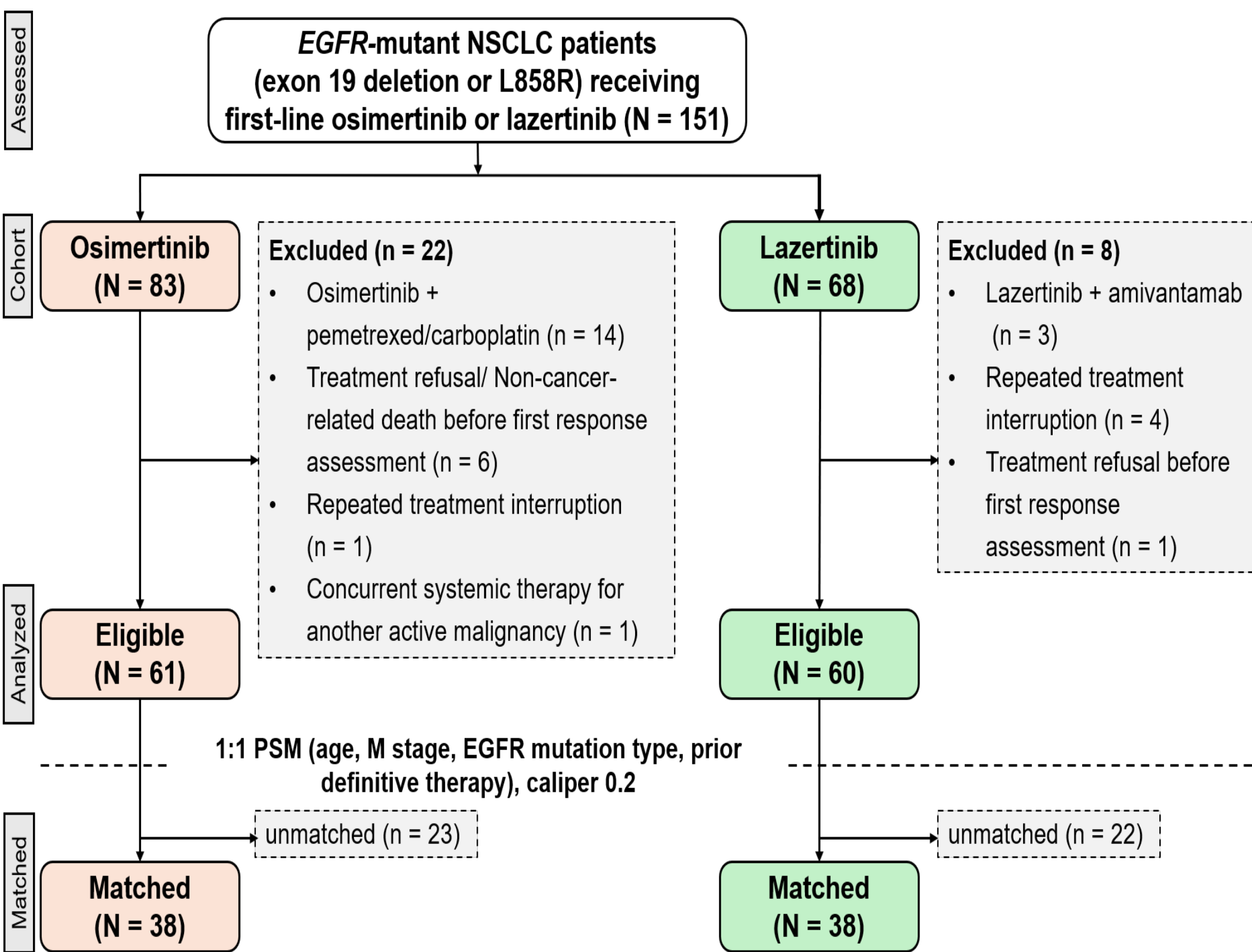
- No significant difference in PFS** was observed between first-line lazertinib and osimertinib monotherapy (**HR 1.00, 95% CI 0.51–1.93**), consistent with the exploratory randomized comparison in MARIPOSA (HR 0.98)⁴. This result was consistent across all adjusted and sensitivity analyses.
- In the baseline NGS/WGS subset (n = 52), a high burden of co-occurring genomic alterations (≥ 3) was associated with shorter PFS, independent of treatment group (HR 5.74, 95% CI 1.94–16.98).

➤ Conclusion

- In this real-world cohort, no significant difference in PFS was observed between first-line lazertinib and osimertinib monotherapy. Larger studies are needed to confirm their comparative effectiveness.

METHODS

- Retrospective, single-center study included patients with stage IV *EGFR*-mutant NSCLC who received first-line osimertinib or lazertinib monotherapy
- Treatment period: osimertinib (Sep 2019 – Feb 2026); lazertinib (Jul 2023 – Feb 2026)



- ✓ **Primary outcome: Progression-free survival (PFS)**
- ✓ Exploratory analyses
 - Association between co-occurring genomic alterations and PFS
 - Overall survival (OS) was not analyzed owing to data immaturity

REFERENCES & ACKNOWLEDGEMENTS

➤ References

- Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated *EGFR*-mutated advanced non-small-cell lung cancer. *N Engl J Med* 2018;378:113-25.
- Cho BC, Ahn MJ, Kang JH, et al. Lazertinib versus gefitinib as first-line treatment in patients with *EGFR*-mutated advanced non-small-cell lung cancer: results from LASER301. *J Clin Oncol* 2023;41:4208-17.
- Cho BC, Lu S, Felip E, et al. Amivantamab plus lazertinib in previously untreated *EGFR*-mutated advanced NSCLC. *N Engl J Med* 2024;391:1486-98.
- Lee SH, Lu S, Hayashi H, et al. Lazertinib versus osimertinib in previously untreated *EGFR*-mutant advanced NSCLC: A randomized, double-blind, exploratory analysis from MARIPOSA. *J Thorac Oncol* 2025;20:1655-68.
- Heredia D, Mas L, Cardona AF, et al. A high number of co-occurring genomic alterations detected by NGS is associated with worse clinical outcomes in advanced *EGFR*-mutant lung adenocarcinoma: Data from LATAM population. *Lung Cancer* 2022;174:133-40.

Artificial Intelligence (AI) Use Disclaimer

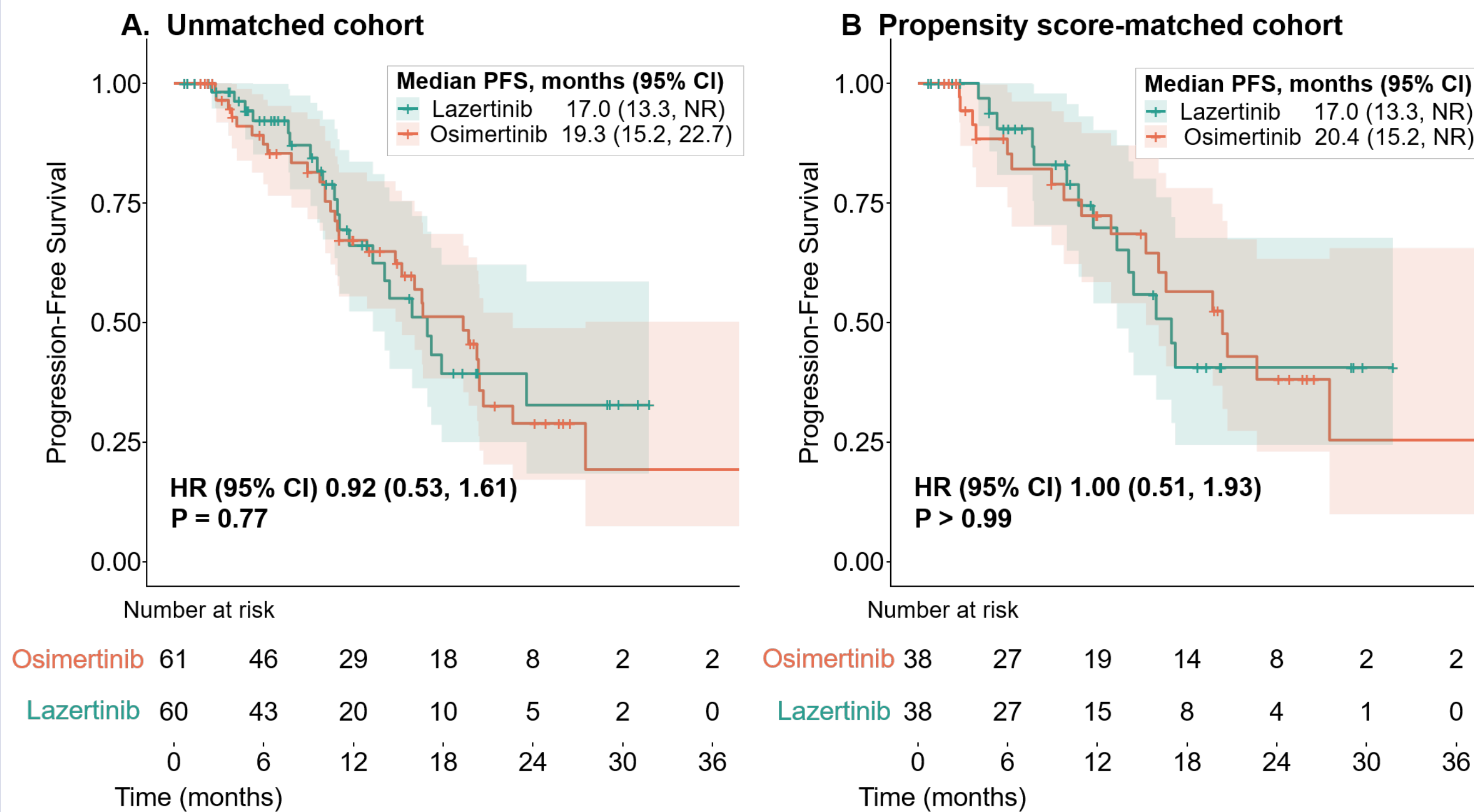
Claude (Opus 5, Anthropic) was used to review the English language and grammar of the poster text. No AI-generated content was used for the scientific content or medical interpretation.

RESULTS

Baseline characteristics before and after propensity score matching

Variable	Before matching			After matching		
	Lazertinib (n=60)	Osimertinib (n=61)	SMD	Lazertinib (n=38)	Osimertinib (n=38)	SMD
Age ≥65, n (%)	45 (75.0)	35 (57.4)	0.379	27 (71.1)	23 (60.5)	0.223
Male, n (%)	28 (46.7)	22 (36.1)	0.217	19 (50.0)	15 (39.5)	0.213
Ever smoker, n (%)	27 (45.0)	24 (39.3)	0.115	15 (39.5)	13 (34.2)	0.109
Prior definitive therapy, n (%)	17 (28.3)	9 (14.8)	0.335	9 (23.7)	9 (23.7)	0.000
Brain metastasis, n (%)	29 (48.3)	26 (42.6)	0.115	18 (47.4)	16 (42.1)	0.106
Bone metastasis, n (%)	28 (46.7)	27 (44.3)	0.048	18 (47.4)	14 (36.8)	0.214
Liver metastasis, n (%)	8 (13.3)	7 (11.5)	0.056	6 (15.8)	5 (13.2)	0.075
M stage, n (%)	M1a 20 (33.3) M1b 9 (15.0) M1c 31 (51.7)	18 (29.5) 9 (14.8) 34 (55.7)	0.088	12 (31.6) 5 (13.2) 21 (55.3)	13 (34.2) 6 (15.8) 19 (50.0)	0.110
EGFR mutation type, n (%)	E19del 23 (38.3) L858R 37 (61.7)	45 (73.8) 16 (26.2)	0.764	21 (55.3) 17 (44.7)	22 (57.9) 16 (42.1)	0.053

PFS in the unmatched and propensity score–matched cohorts.



Consistency of PFS estimates across analytic approaches

Analysis	HR (95% CI)	P value
Unmatched cohort (n = 121)		
Unadjusted	0.92 (0.53-1.61)	0.77
Multivariable-adjusted*	0.98 (0.53-1.79)	0.95
+ Calendar-year adjusted	1.05 (0.58-1.91)	0.86
PS-matched cohort (n = 76)		
Unadjusted	1.00 (0.51-1.93)	0.99
Multivariable-adjusted**	0.93 (0.47-1.86)	0.84
+ Calendar-year adjusted	1.35 (0.68-2.72)	0.39
Concurrent-period analysis (n = 98)		
Adjusted**	1.27 (0.61-2.65)	0.52

*Adjusted for M stage, brain and bone metastases, prior definitive therapy, and EGFR mutation type.

**Adjusted for M stage, brain and bone metastases; covariates were prespecified by clinical relevance and baseline imbalance and limited by the number of events.

• Concurrent-period analysis: patients starting treatment on or after July 2023, the date of the first lazertinib administration in this cohort.

Co-occurring genomic alterations in patients with available baseline NGS or WGS data by treatment group

Alteration	Overall* (n=52)	Lazertinib (n=26)	Osimertinib (n=26)
TP53, n (%)	33 (63.5)	18 (69.2)	15 (57.7)
EGFR amplification, n (%)	16 (30.8)	7 (26.9)	9 (34.6)
CDKN2A deletion, n (%)	10 (19.2)	5 (19.2)	5 (19.2)
CDKN2B deletion, n (%)	6 (11.5)	2 (7.7)	4 (15.4)
PIK3CA, n (%)	6 (11.5)	3 (11.5)	3 (11.5)
RB1, n (%)	4 (7.7)	2 (7.7)	2 (7.7)
CCND1 amplification, n (%)	3 (5.8)	0 (0)	3 (11.5)
MET amplification, n (%)	3 (5.8)	1 (3.8)	2 (7.7)
MYC amplification, n (%)	3 (5.8)	3 (11.5)	0 (0)
CDK6 amplification, n (%)	2 (3.8)	1 (3.8)	1 (3.8)
Other rare alterations**, n (%)	16 (30.8)	12 (46.2)	4 (15.4)

*Among patients with available baseline NGS or WGS data

**Other rare alterations were defined as alterations observed in fewer than 2 patients. NGS, next-generation sequencing; WGS, whole-genome sequencing.

PFS according to co-occurring genomic alterations (≥ 3 vs. < 3) in patients with available baseline NGS/WGS data

