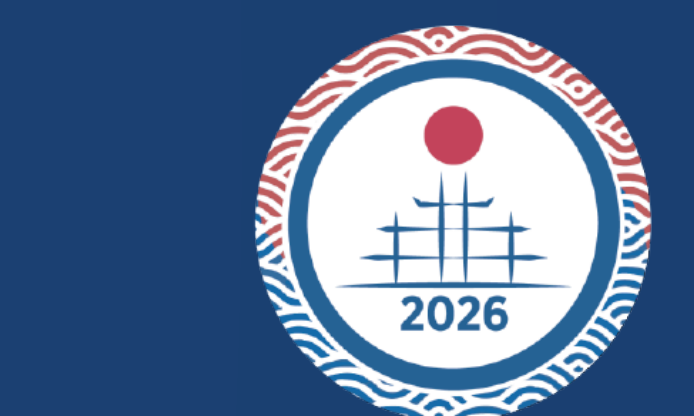




EP12.35: NGS-Based Clinicogenomic Risk Stratification for First-Line EGFR-TKI Selection in EGFR-Mutant NSCLC: A Multicenter Real-World Study

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IASLC 2026 World
Conference on Lung Cancer
SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

WHY THIS STUDY

EGFR-mutant NSCLC is biologically heterogeneous beyond the canonical EGFR driver. Co-occurring alterations may influence treatment response and survival, yet practical clinicogenomic tools for first-line TKI decision-making remain limited.

OBJECTIVE Develop a pragmatic PFS/OS risk model and explore afatinib-osimertinib outcomes across risk strata.

DESIGN & ANALYSIS

1 Cohort

Multicenter retrospective study; advanced EGFR-mutant NSCLC; first-line afatinib or osimertinib.

2 Targeted NGS

EGFR subtype plus TP53, RAS-PI3K-RAF, RTK (MET/ERBB2/FGF), and other alterations.

3 Risk score

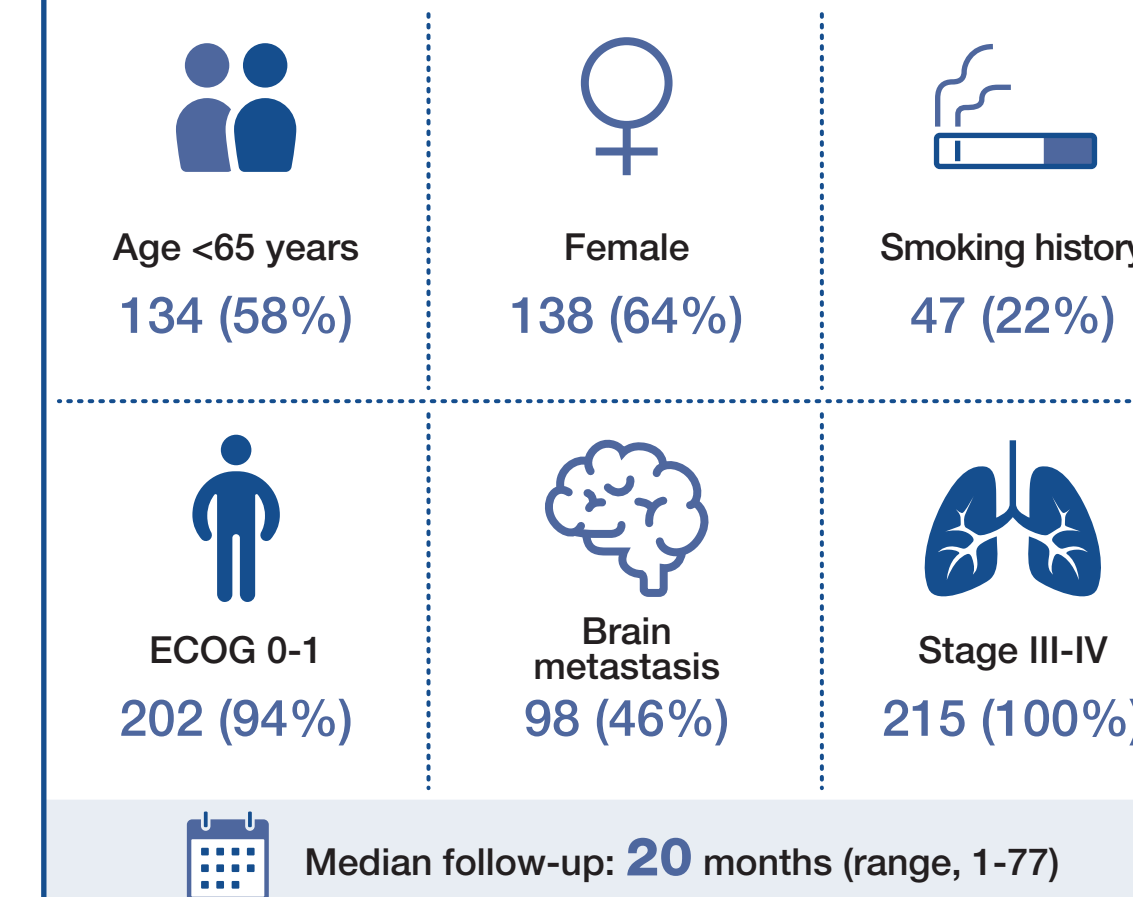
One point each for male sex, PD-L1 $\geq 50\%$, L858R $\pm$ compound mutation, and RTK alteration.

4 Outcomes

Kaplan-Meier and Cox models for PFS/OS; treatment-risk interaction was exploratory.

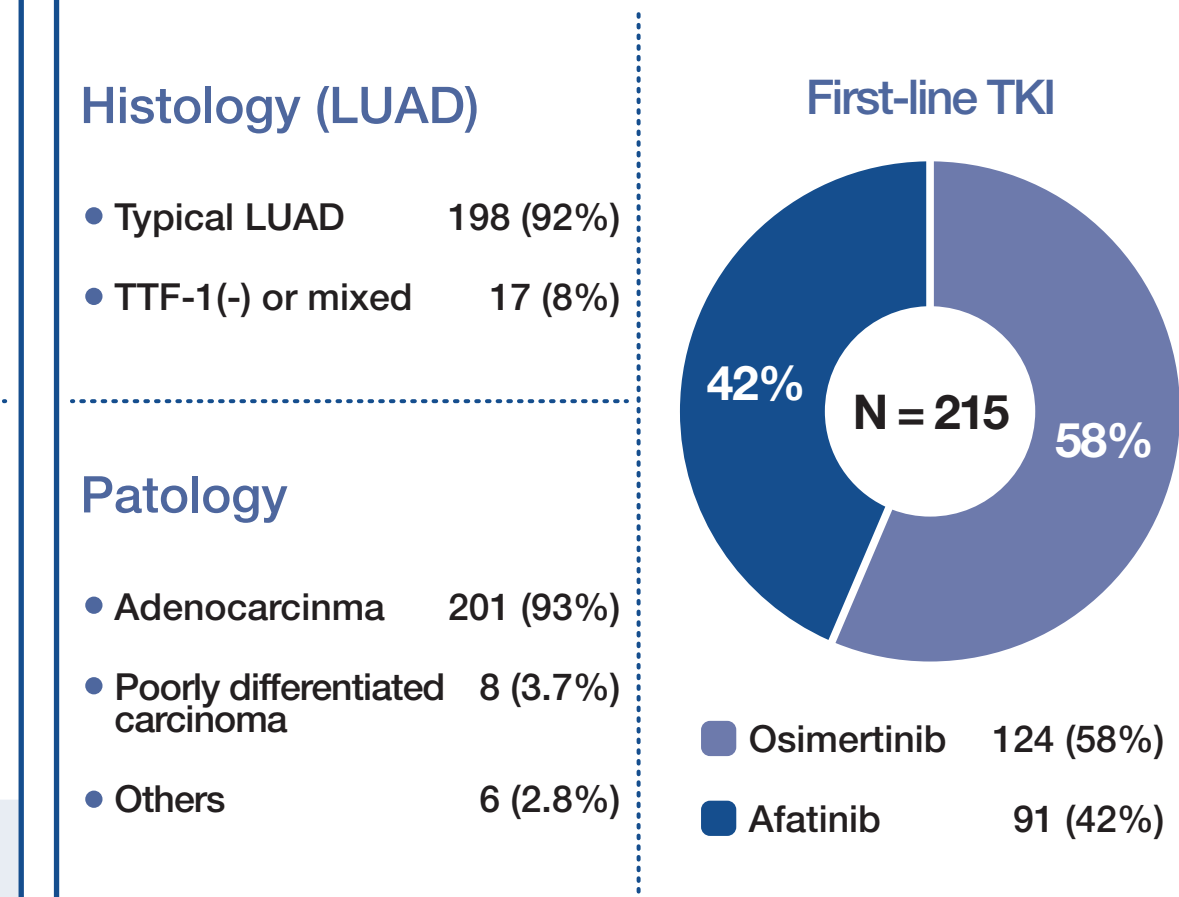
DESIGN & ANALYSIS

1 Cohort Snapshot (N=215)



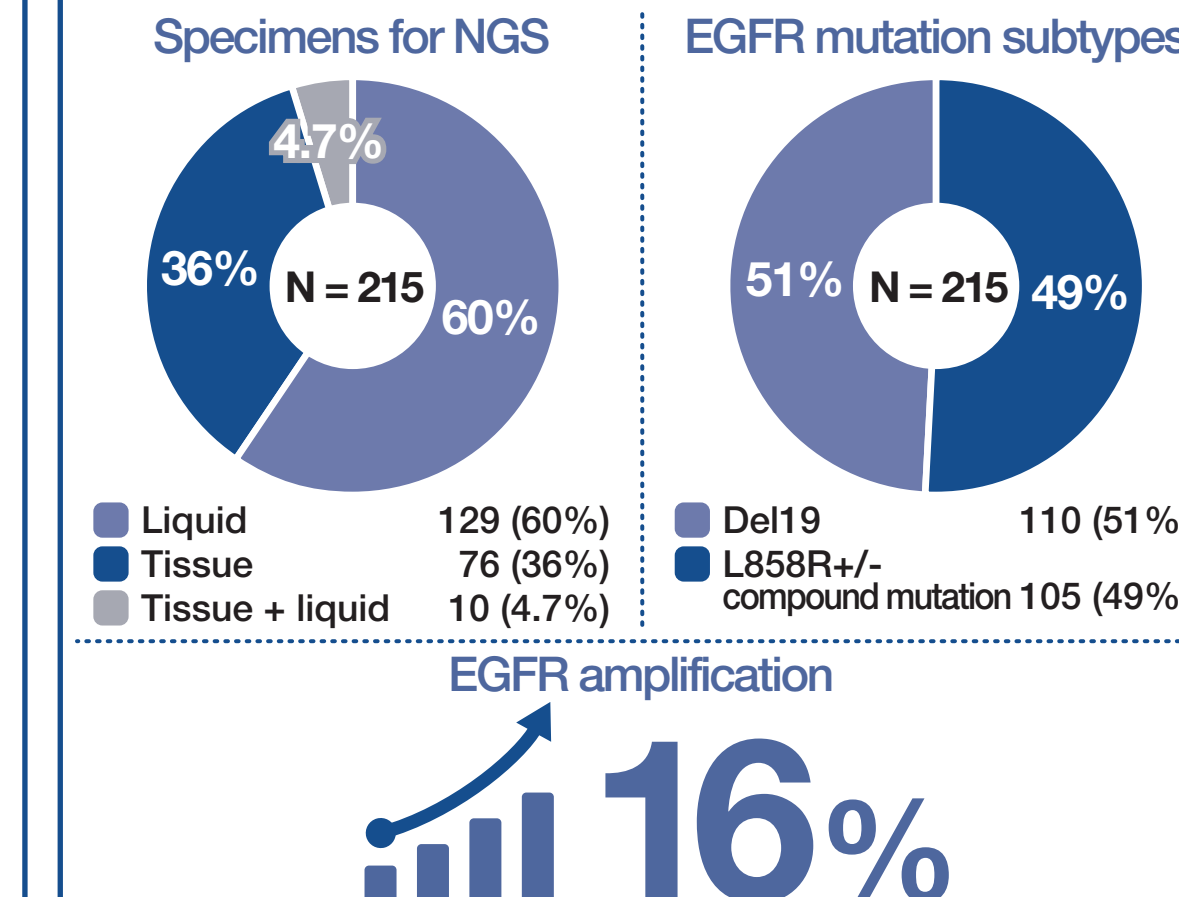
PD-L1 (%)

2 Histology and First-line Treatment



<1
71 (40%)

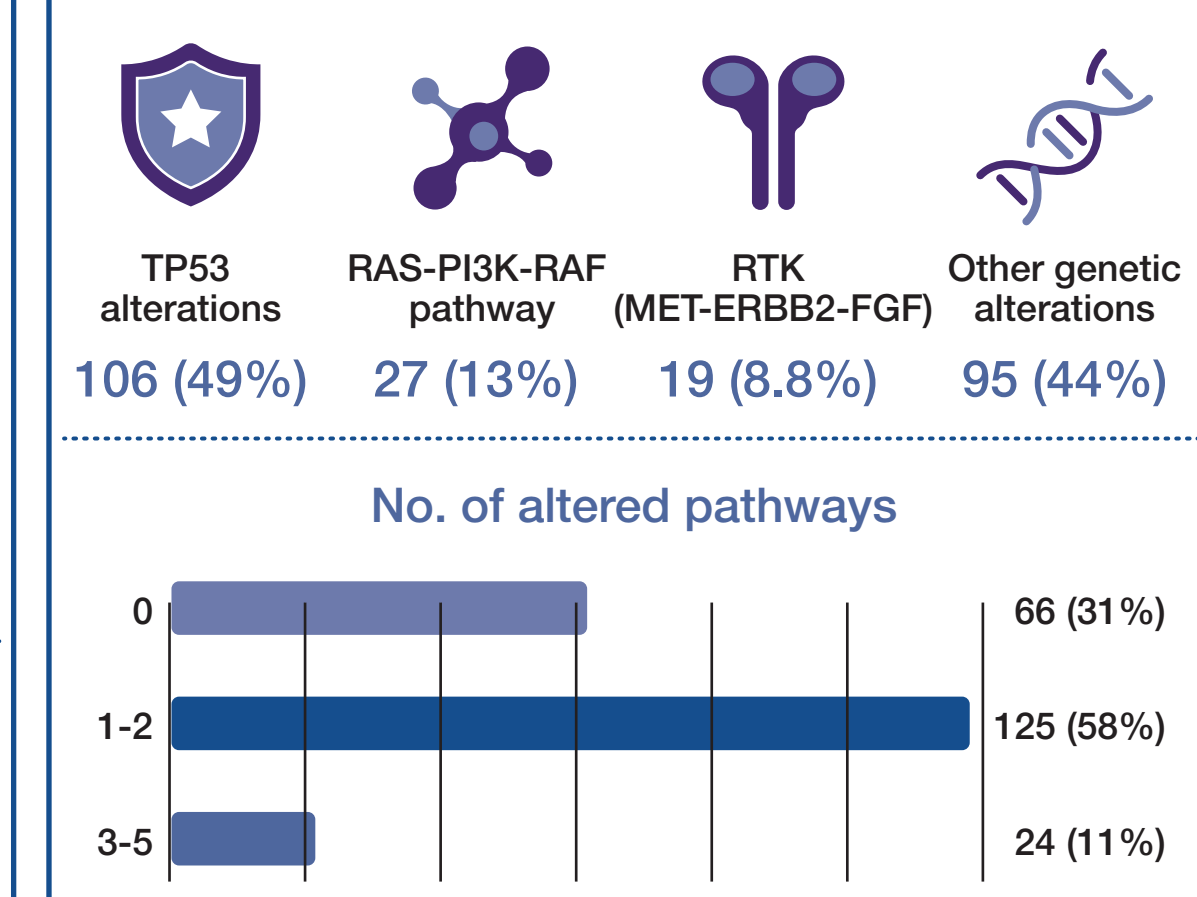
3 NGS and Molecular Profile



1-49
78 (44%)

≥ 50
29 (16%)

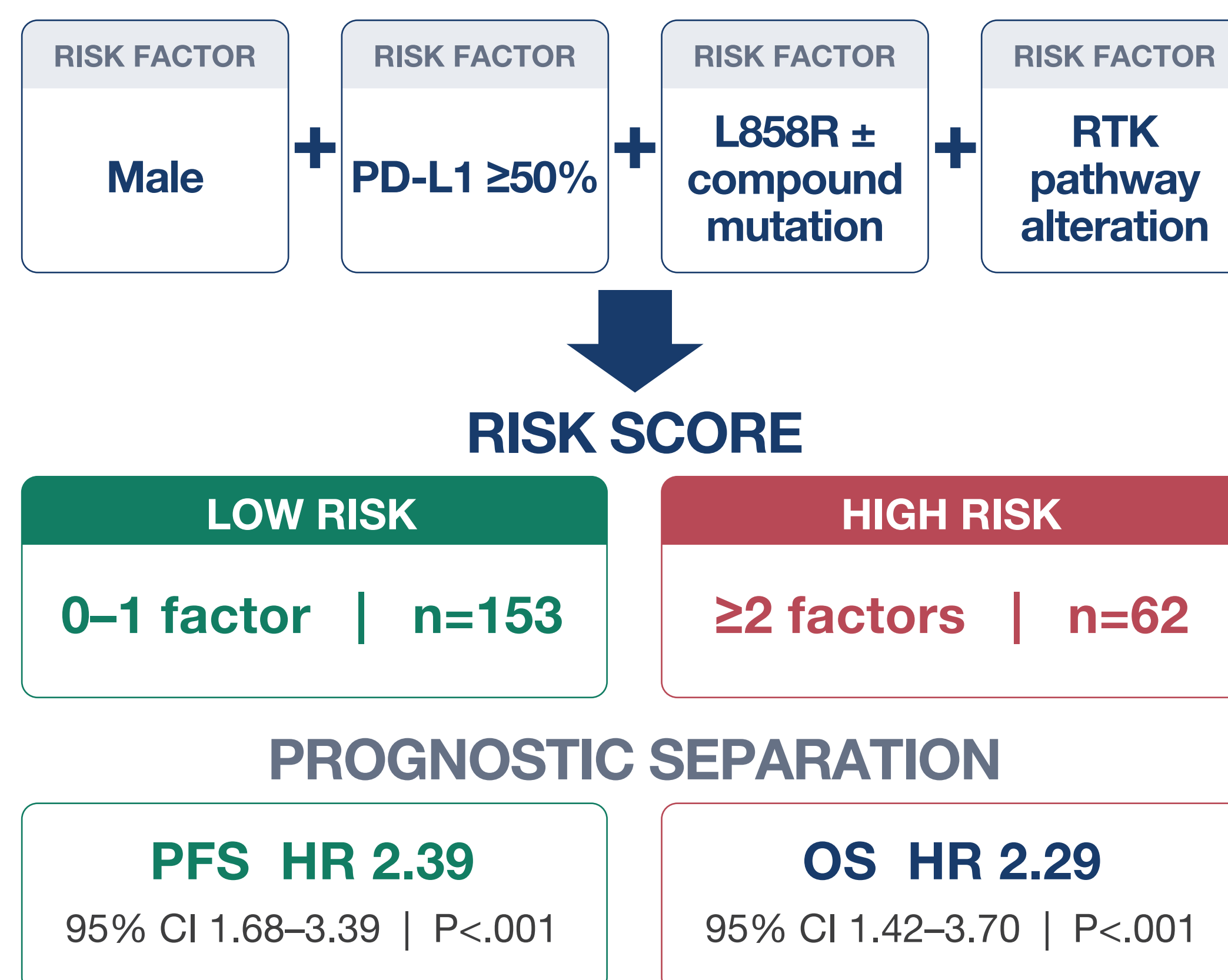
4 Concomitant Alterations



Unknown
37

RESULTS

Figure 1. Construction and prognostic performance of the clinicogenomic risk model.



High-risk disease was associated with more than a two-fold increase in progression and mortality risk.

Figure 2A. Progression-free survival according to first-line TKI within clinicogenomic risk strata (low risk: 0-1 factor)

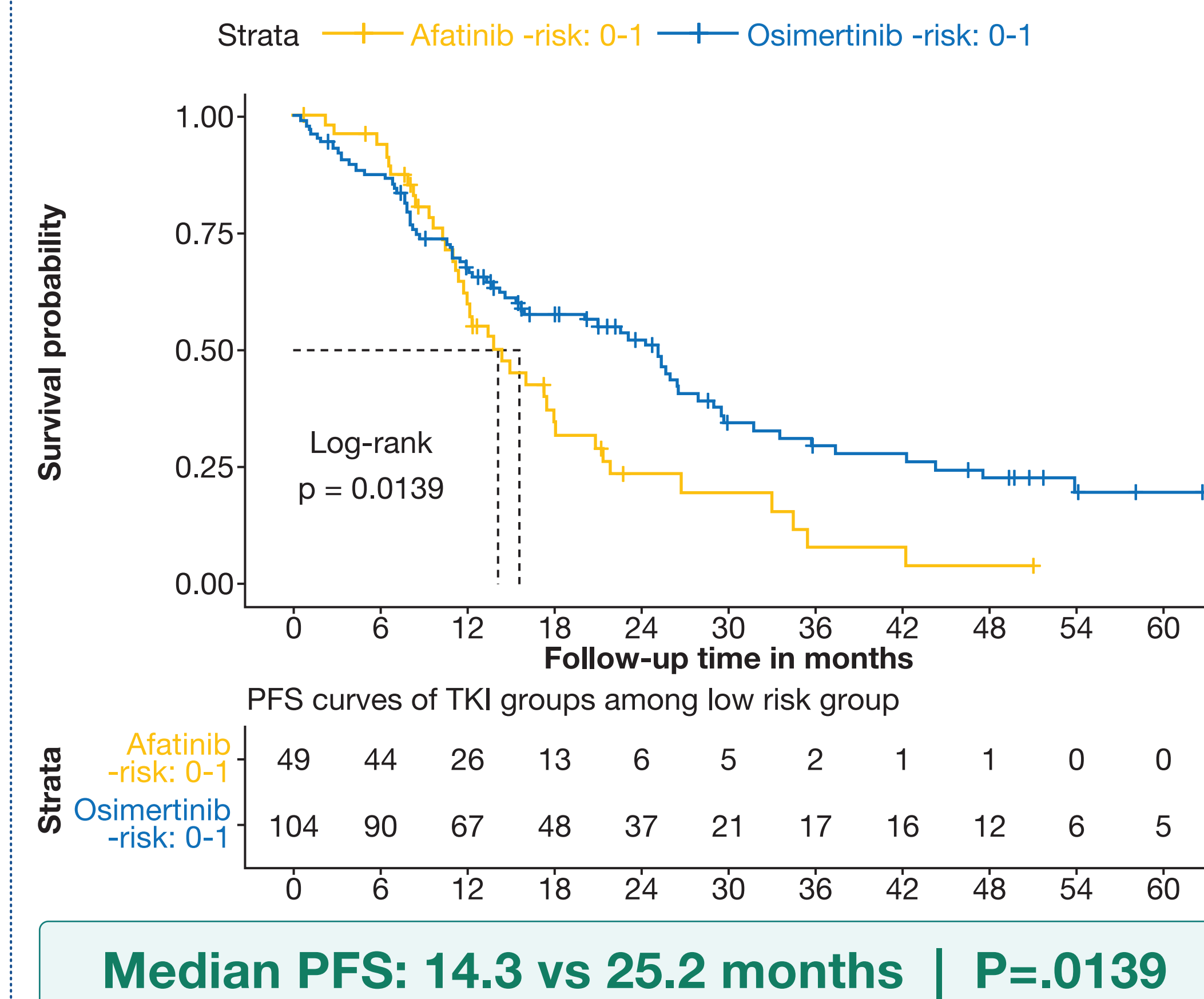


Figure 2B. Progression-free survival according to first-line TKI within clinicogenomic risk strata (high risk: ≥ 2 factors)

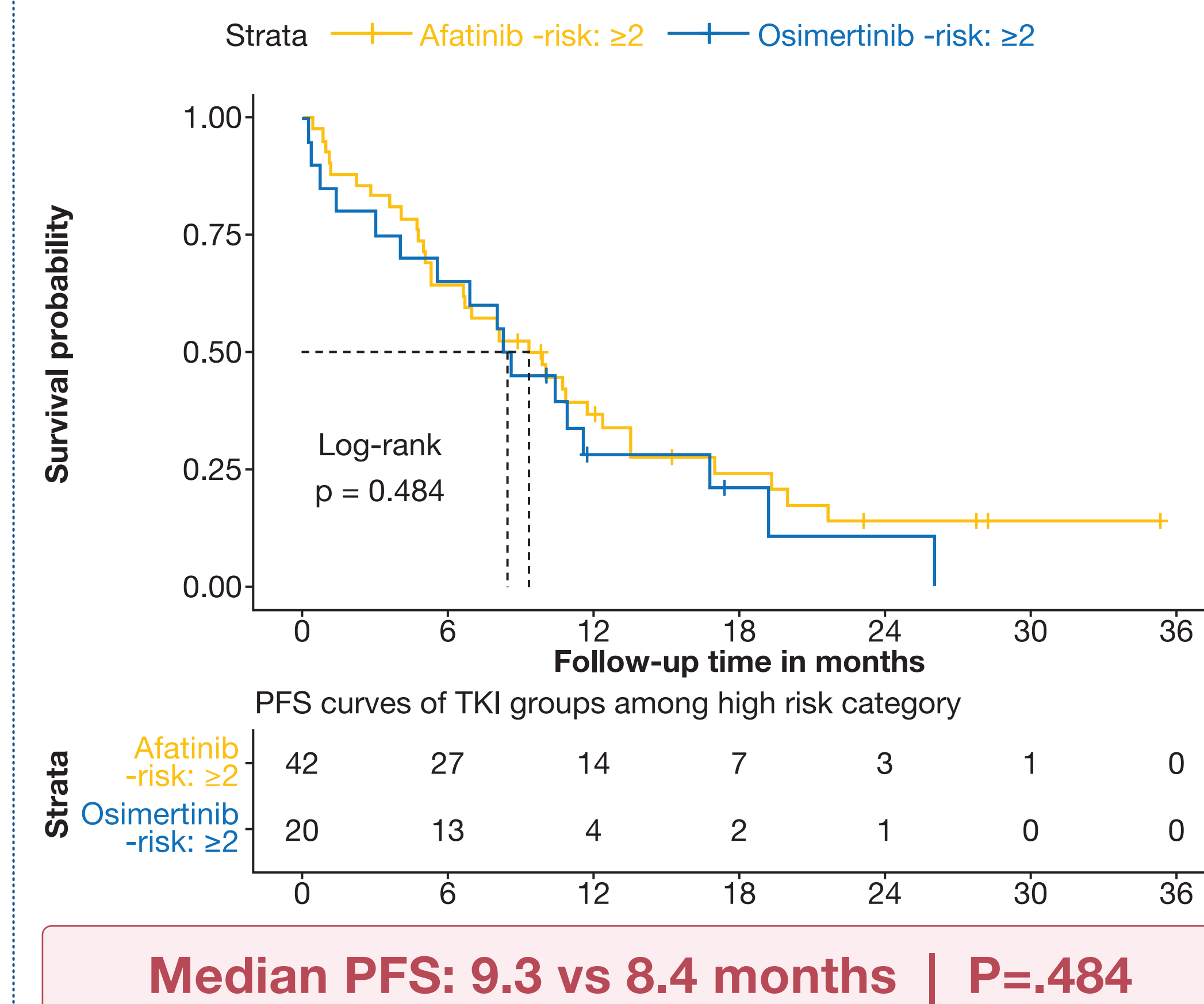
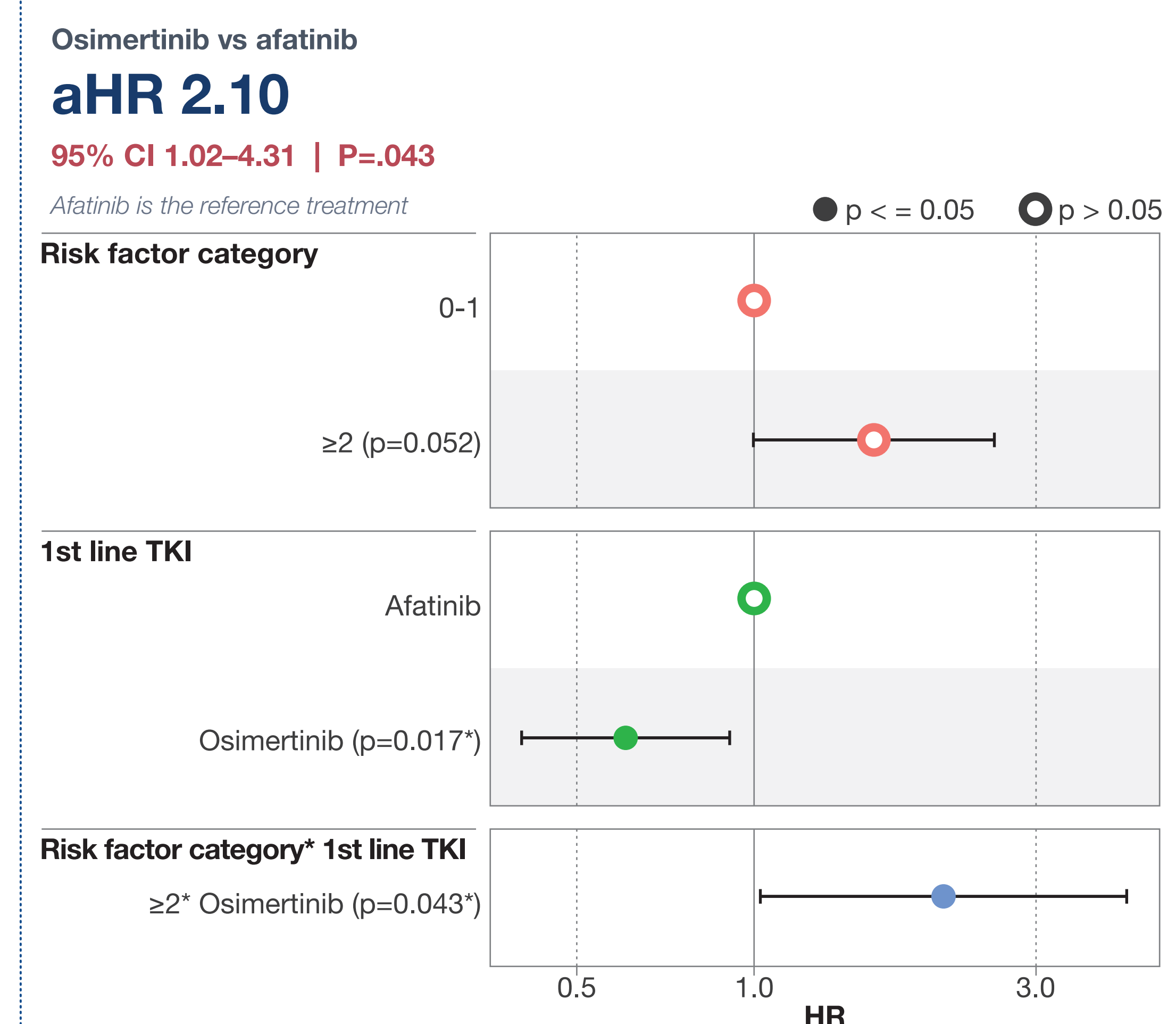


Figure 3. Adjusted PFS treatment contrast in the high-risk group.



INTERPRETATION & LIMITATIONS

- Retrospective, nonrandomized treatment allocation.
- Marked imbalance in EGFR subtype between TKI groups.
- Only 20 high-risk patients received osimertinib.
- The risk model requires independent prospective validation.

CONCLUSIONS

Osimertinib was associated with longer PFS in low-risk patients. In contrast, high-risk patients had a median PFS of less than 10 months with either TKI, and no significant unadjusted treatment difference was observed. The adjusted signal favoring afatinib in the high-risk group should therefore be regarded as hypothesis-generating rather than definitive evidence for drug-specific selection. These findings support prospective validation of NGS-informed, risk-adapted front-line treatment strategies rather than immediate application of the score as a definitive rule for selecting afatinib versus osimertinib.

KEY REFERENCES

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ACKNOWLEDGEMENTS

We thank the investigators and data teams at the three participating centers. We also thank Nova Journal Experts for editorial and graphic assistance.

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No AI tool was used to generate or alter study data or perform the statistical analyses.