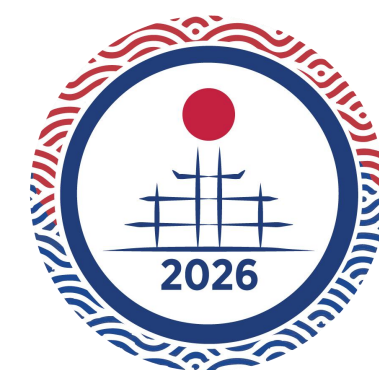




P2.255: Association Between Continued Immunotherapy Beyond Progression and Prognosis in Advanced Non–Small Cell Lung Cancer

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

INTRODUCTION

Immune checkpoint inhibitors (ICIs)—as monotherapy, combined with chemotherapy, or as dual immunotherapy—are the standard first-line treatment for driver-negative NSCLC. However, resistance is inevitable, and optimal post-progression management remains undefined. Continuing immunotherapy beyond progression (TBP) may benefit selected patients through atypical response patterns such as delayed tumor shrinkage, yet clinical trials (e.g., SAPPHIRE) show inconsistent survival advantage. Controversy persists regarding which histological subtypes benefit, and the subgroups most likely to derive benefit remain poorly defined. We evaluated the impact of TBP and identified predictive subgroups in a real-world cohort.

METHODS

Design: Retrospective cohort, Zhejiang Cancer Hospital, Dec 2019 – Feb 2025. Of 3,560 NSCLC patients receiving ICIs, 202 driver-negative NSCLC patients who progressed after first-line ICI (RECIST v1.1) were included (TBP=113; non-TBP=89). STROBE-compliant.

Resistance: Primary = PD ≤6 months after ICI initiation (despite CR/PR); Secondary = PD ≥6 months (Schoenfeld et al., Ann Oncol 2021).

Progression patterns (modified Saal et al., JAMA Oncol 2025): Low-risk = progression confined to existing lesions; Intermediate-risk = new lesions without existing lesion progression; High-risk = existing lesion progression + new lesions. Oligoprogession = limited sites; Systemic progression = widespread.

Endpoints: TTF (ICI initiation to discontinuation for any reason); PFS1 (ICI initiation to first PD); PFS2 (post-progression therapy initiation to second PD); OS (post-progression therapy initiation to death/last follow-up). Cutoff: Feb 27, 2025.

Statistics: χ^2 / t-test / Mann–Whitney U; Kaplan–Meier + log-rank; Cox regression; R v4.4.1.

DISCUSSION AND CONCLUSION

Key findings: TBP benefit is not universal but restricted to well-defined subgroups—oligoprogession, secondary resistance with durable first-line benefit (PFS1 ≥8.2 mo), and low-risk progression patterns—while systemic progression and primary resistance derive no advantage.

Clinical implications: These results support a selective, rather than universal, application of TBP. Patients with oligoprogession or secondary resistance after durable response may retain sensitivity to ICIs, possibly due to sustained antitumor immune activation despite radiographic progression. The modified progression pattern classification provides a practical tool for patient stratification. Conversely, continuing ICIs in systemic progression or primary resistance may delay transition to more effective alternatives and expose patients to unnecessary toxicity.

ICI switching: Switching between PD-1 and PD-L1 inhibitors during TBP did not improve outcomes, consistent with previous small-scale studies, suggesting that changing agents with the same mechanism of action is unlikely to overcome resistance.

Limitations: Retrospective, single-center design (selection bias); limited subgroup sample sizes; lack of biomarker data (PD-L1 dynamics, TMB); heterogeneity in molecular testing platforms.

Conclusion: TBP may prolong survival in carefully selected NSCLC patients. Prospective multicenter trials incorporating molecular and imaging biomarkers are warranted.

REFERENCES & ACKNOWLEDGEMENTS

References

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Acknowledgments

This study was supported by the Natural Scientific Foundation of Zhejiang Province, China (Grant No. LTGY23H160007) and the Zhejiang Provincial Health and Medical Science and Technology Project (2022KY638). The authors thank the Department of Thoracic Oncology, Zhejiang Cancer Hospital, for clinical data support.

Registry of the study

This study was approved by the Ethics Committee of Zhejiang Cancer Hospital (approval number: IRB-2023-378) and the study adhered to the ethical principles of the Declaration of Helsinki.

RESULTS

Overall (N=202): TBP improved OS (21.6 vs. 17.9 mo; p=0.028; HR=0.58, 95% CI 0.38–0.89), but not TTF (p=0.29) or PFS2 (p=0.30).

Beneficial subgroups: Oligoprogession (TTF 7.4 vs. 4.7 mo, p=0.023; HR=0.57); Secondary resistance with PFS1 ≥8.2 mo (OS 30.9 vs. 18.5 mo, p=0.021; HR=0.26); Low-risk progression (OS 26.0 vs. 18.5 mo, p=0.019; HR=0.46).

No benefit: Systemic progression, primary resistance (OS 14.4 vs. 11.2 mo, p=0.71), and intermediate/high-risk patterns (HR≈1.0).

ICI switching (35/113): No survival difference vs. continuing same agent (p>0.05).

Figure 1

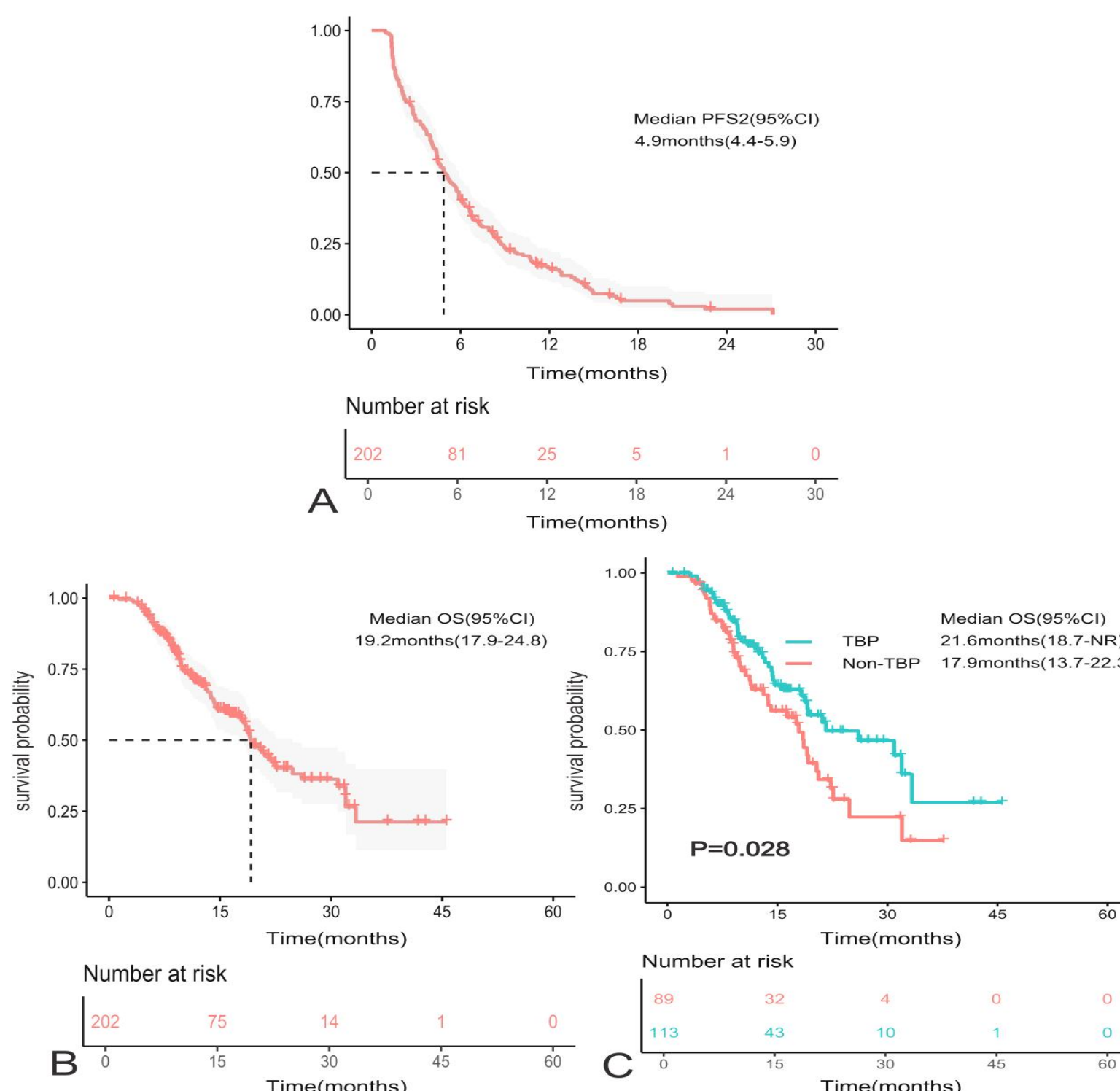


Figure 1: Kaplan–Meier curves of overall survival (OS) and progression-free survival 2 (PFS2) in the total cohort comparing TBP and non-TBP strategies.

Figure 3

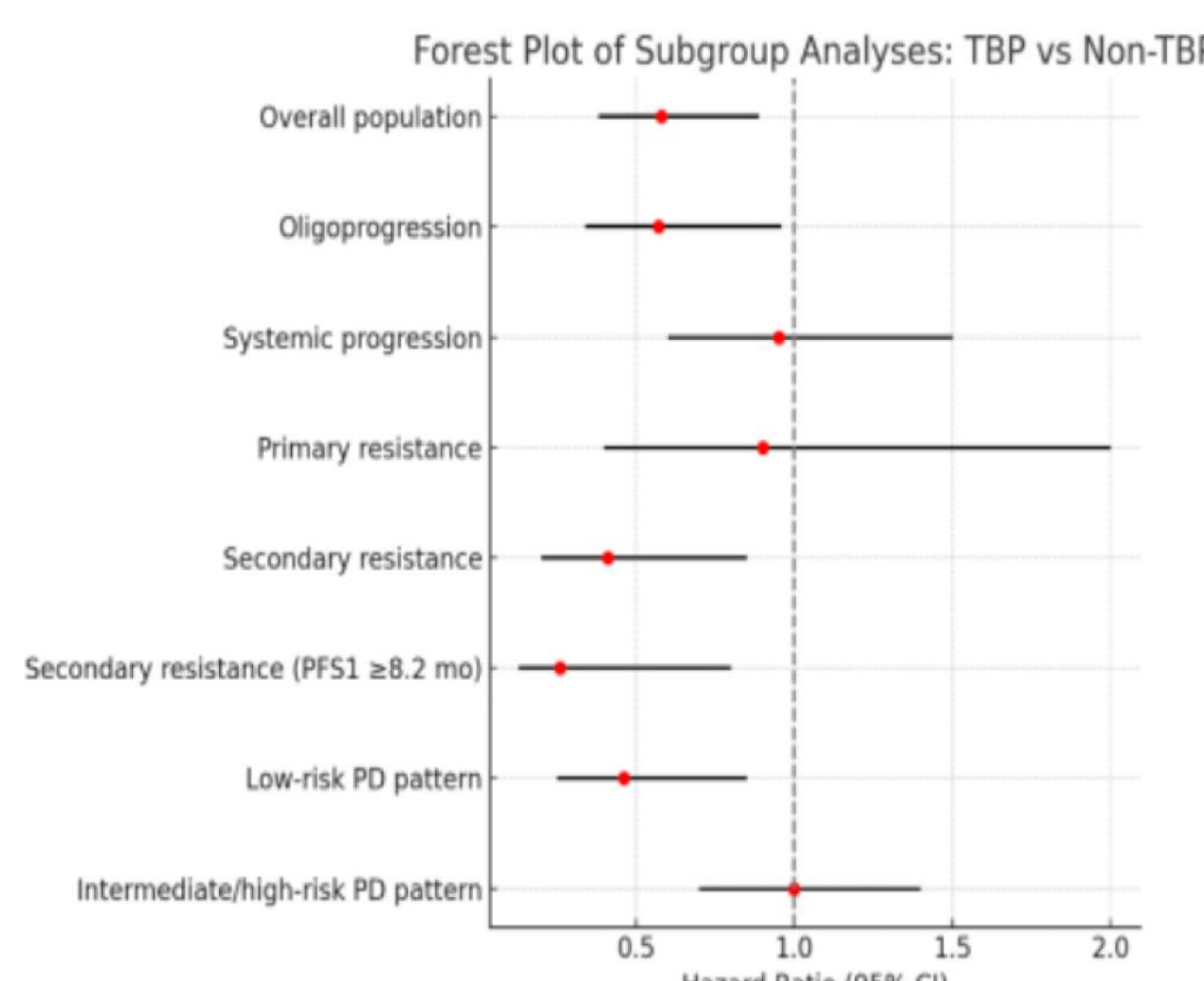


Figure 3 : Hazard ratios (HRs) with 95% confidence intervals (CIs) for overall survival are shown for predefined subgroups comparing TBP with non-TBP. Subgroups include overall population, oligoprogession versus systemic progression, primary versus secondary resistance, secondary resistance stratified by PFS1 duration, and risk classification of progression patterns. Values <1 favor TBP. HRs were estimated by Cox proportional hazards regression.

Figure 2

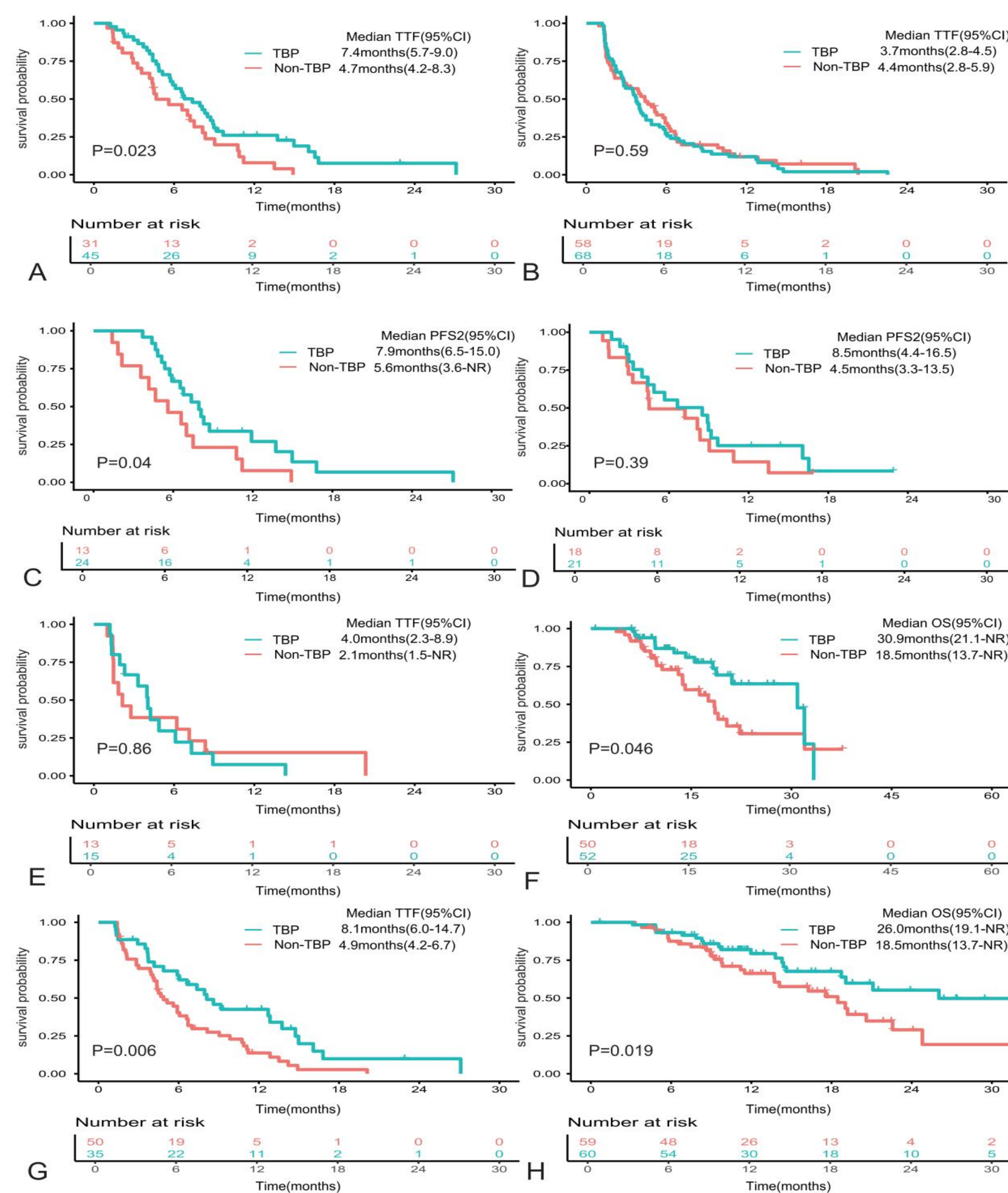


Figure 2: Subgroup Kaplan–Meier curves. (A) TTF of the TBP and Non-TBP groups in oligoprogession cohort; (B) TTF of the TBP and Non-TBP groups in systemic progression cohort; (C) PFS2 of the TBP and Non-TBP groups in oligoprogession cohort with a prior history of radiotherapy; (D) PFS2 of the TBP and Non-TBP groups in oligoprogession cohort without a prior history of radiotherapy; (E) TTF of the TBP and Non-TBP groups in primary resistance cohort; (F) OS of the TBP and Non-TBP groups in secondary resistance cohort; (G) TTF of the TBP and Non-TBP groups in secondary resistance cohort of PFS1≥8.2months; (H)OS of the TBP and Non-TBP groups in low-risk PD cohort; CI, confidence interval; TBP,continuing immunotherapy beyond progression;