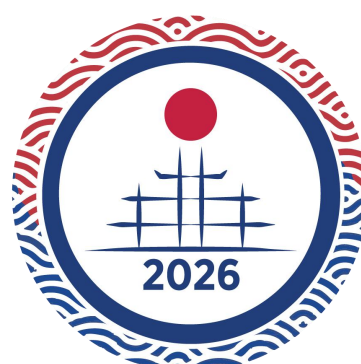




# EP12.04: RET Fusion in Solid Tumors

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## INTRODUCTION

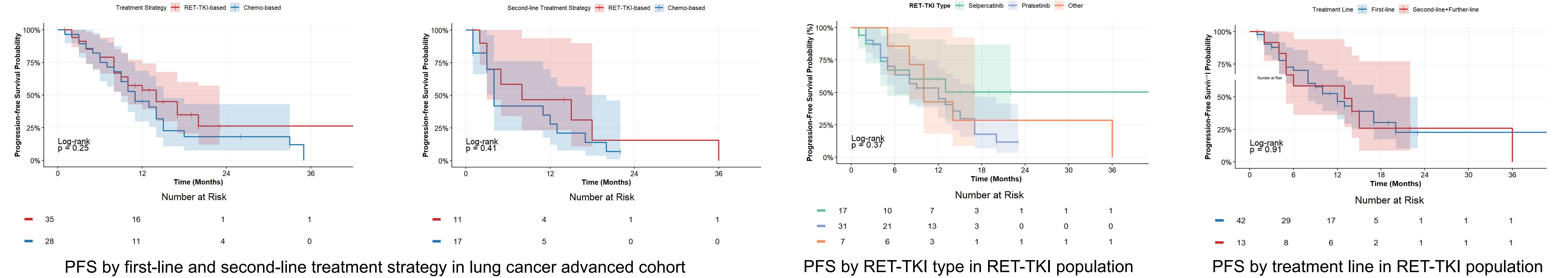
RET activates downstream oncogenic signaling pathways, including RAS/MAPK, PI3K-AKT, and JAK-STAT. RET is an established actionable target in multiple solid tumors. However, the clinicopathological features, treatment patterns, and prognostic implications of patients with RET fusion-positive solid tumors remain poorly characterized<sup>[1, 2]</sup>.

## METHODS

This single-center retrospective cohort study included patients with RET fusion-positive solid tumors who were diagnosed or treated at our institution from August 1, 2016 to May 1, 2025. Demographic, pathological, molecular, treatment, and follow-up data were retrospectively collected. The primary endpoints were PFS or DFS and OS. Kaplan-Meier curves with log-rank tests were used for univariate analysis, Lasso regression for variable selection, and multivariate Cox analysis to identify independent prognostic factors. Safety was assessed according to CTCAE v5.0.

## RESULTS

The study enrolled 160 patients with RET fusion-positive solid tumors. The median age was 58 years (range 20-78); 70.6% of patients were aged <65 years, 56.3% were female, and 73.1% had no smoking history. KIF5B was the most frequent fusion partner (50.5%), while TP53 was the most common co-altered gene (35.3%). Efficacy analysis showed differential mOS across tumor types: with 48 months for patients with lung cancer (n=115), not reached for patients with thyroid cancer (n=21), and 20 months for patients with gastrointestinal tumor (n=9). In the lung cancer subgroup, baseline liver metastasis (HR=6.4, 95%CI: 1.838-22.051, P=0.003), regional lymph node metastasis (HR=5.7, 95%CI: 1.743-18.51, P=0.004), and adrenal metastasis (HR=9.9, 95%CI: 2.845-35.094, P<0.001) emerged as independent risk factors for OS, DFS, and PFS, respectively, while surgery emerged as an independent protective factor for OS (HR=0.15, 95%CI: 0.033-0.662, P=0.012). Among the 56 patients in the early-stage cohort, mDFS was 33 months, and recurrence rates increasing with disease stage. Bone (38.5%) represented the most common recurrence site. Among the 72 patients in the advanced cohort, mPFS was 12 months. Compared to chemotherapy, RET-TKIs were associated with longer mPFS in both first-line (14 vs. 11 months, HR=0.71) and second-line treatment (8 vs. 4 months, HR=0.67). Among 55 patients treated with RET-TKIs, mPFS was 12 months, and significantly shorter mPFS observed in those harboring co-altered driver genes (4 vs. 14 months, P<0.05). No statistically significant differences in mPFS were detected between selpercatinib, pralsetinib, and other RET-TKIs (13 vs. 12 vs. 10 months, P=0.37), nor between first-line and subsequent-line administration (12 vs. 13 months, P=0.91). Patients receiving selpercatinib more frequently experienced edema, rash, and hypertension, while those receiving pralsetinib were more prone to myelosuppression and infections.



## DISCUSSION AND CONCLUSION

RET fusion occur more frequently in younger, female, never-smokers. Survival outcomes vary significantly by cancer type. In lung cancer, baseline liver, lymph node, and adrenal metastases were independent risk factors for survival, while surgery was protective. RET-TKIs exhibited superior efficacy compared with chemotherapy and showed similar efficacy across different agents and treatment lines. Co-occurring driver gene alterations predicted poorer outcomes. RET-TKIs were generally well tolerated with distinct safety profiles.

## REFERENCES & ACKNOWLEDGEMENTS

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2 Tumour-agnostic efficacy and safety of selpercatinib in patients with RET fusion-positive solid tumours other than lung or thyroid tumours (LIBRETTO-001): a phase 1/2, open-label, basket trial [J]. Lancet Oncol, 2022, 23(10): 1261-73.