



Primary Tumor Resection After ROS1-TKI Therapy in Advanced ROS1-Positive NSCLC



Lingqiang Jiang^{1,3}, Zhihao Lin², Jin Kang³, Wenzhao Zhong^{1,3}

¹Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, ²Department of Pathology, Guangdong Provincial People's Hospital, ³Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital

Correspondence: syzhongwenzhao@scut.edu.cn

INTRODUCTION

Although ROS1 tyrosine kinase inhibitors (TKIs) yield robust clinical responses in advanced ROS1-rearranged non-small cell lung cancer (NSCLC), acquired resistance and progression from residual disease remain inevitable. Furthermore, whether primary tumor resection in the context of ROS1-TKI therapy can translate into long-term survival benefits while maintaining an acceptable safety profile remains unclear.

METHODS

In this retrospective cohort study, 128 patients with ROS1-positive NSCLC were included. Survival associated with primary tumor resection after ROS1-TKI therapy was evaluated using a 6-month conditional restriction, propensity score matching, and time-dependent Cox models, together with analyses of perioperative outcomes, pathological response, and exploratory multiomic features.

DISCUSSION AND CONCLUSION

Primary tumor resection after ROS1-TKI therapy was feasible and associated with favorable survival in selected patients with advanced ROS1-positive NSCLC. The OS association remained more consistent after accounting for surgical timing, whereas the PFS association was attenuated. These results suggest that consolidative surgery may have a role in selected patients achieving sustained disease control with ROS1-TKI therapy. Prospective studies are needed to define the population most likely to benefit.

REFERENCES

- [1]. Shaw AT, Ou SHI, Bang YJ, et al. Crizotinib in ROS1-rearranged non-small-cell lung cancer. *N Engl J Med*. 2014;371(21):1963-1971.
 - [2]. Shaw AT, Riely GJ, Bang YJ, et al. Crizotinib in ROS1-rearranged advanced non-small-cell lung cancer (NSCLC): updated results, including overall survival, from PROFILE 1001. *Ann Oncol*. 2019;30(7):1121-1126.
 - [3]. Drilon A, Siena S, Dziadziuszko R, et al. Entrectinib in ROS1 fusion-positive non-small-cell lung cancer: integrated analysis of three phase 1-2 trials. *Lancet Oncol*.
 - [4]. Drilon A, Jenkins C, Iyer S, Schoenfeld A, Keddy C, Davare MA. ROS1-dependent cancers — biology, diagnostics and therapeutics. *Nat Rev Clin Oncol*. 2021;18(1):35-55.
 - [5]. Gomez DR, Tang C, Zhang J, et al. Local consolidative therapy vs. Maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer: long-term results of a multi-institutional, phase II, randomized study. *J Clin Oncol*. 2019;37(18):1558-1565.
 - [6]. Lee EH, Kim MH, Kang DH, et al. Clinical impact of local consolidative therapy in EGFR-mutant metastatic NSCLC: a propensity-matched multicenter analysis. *Lung Cancer*. 2026;217:109423.
- AI Use Disclosure: Generative AI was used solely for language editing and did not contribute to study design, data analysis, or scientific interpretation.

RESULTS

After matching, 19 patients were included in each group. Median PFS was 35.2 versus 15.6 months and median OS was not reached versus 52.1 months in the surgery and non-surgery groups, respectively (log-rank P=0.014 for both). Multivariable Cox analysis showed that primary tumor resection was associated with lower hazards of progression or death (aHR, 0.35; 95% CI, 0.15–0.83; P=0.017) and death (aHR, 0.18; 95% CI, 0.04–0.89; P=0.036). In multivariable time-dependent Cox analysis, the association with OS remained significant (aHR, 0.22; P=0.037), whereas the association with PFS was attenuated (aHR, 0.62; P=0.230). Perioperative outcomes after TKI therapy were comparable with those of upfront surgery. Among 28 pathologically evaluable patients, MPR and pCR rates were 46.4% and 14.3%, respectively. Exploratory single-cell and spatial transcriptomic analyses associated favorable pathological response with greater effector T-cell infiltration and less prominent myofibroblast-endothelial spatial barriers.

