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MET Overexpression is Associated with Inferior Efficacy in Advanced *ROS1*-Rearranged NSCLC Treated with First-Line Entrectinib

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Introduction

C-ros oncogene 1 (*ROS1*) tyrosine kinase inhibitors (TKIs) have improved the survival outcomes of patients with advanced *ROS1*-rearranged non-small cell lung cancer (NSCLC). However, treatment benefit varies among patients. The impact of MET overexpression on the efficacy of *ROS1* TKIs remains unclear. We investigated whether baseline MET overexpression was associated with the efficacy of first-line entrectinib in advanced *ROS1*-rearranged NSCLC.

Methods

We retrospectively analyzed patients with advanced *ROS1*-rearranged NSCLC who received first-line entrectinib at the Guangdong Provincial People's Hospital from July 2022 to November 2025 (data cutoff March 19, 2026). *ROS1* rearrangement was identified by next-generation sequencing. Baseline MET protein expression levels were assessed by immunohistochemistry (IHC) using the anti-MET (SP44) Rabbit Monoclonal Primary Antibody. MET overexpression was defined as strong staining (+++) in at least 75% of tumor cells. All other cases were classified as MET-negative. Objective response rate (ORR) and progression-free survival (PFS) were assessed.

Conclusion

Baseline MET overexpression was associated with inferior efficacy in advanced *ROS1*-rearranged NSCLC treated with first-line entrectinib. Further investigations are warranted to elucidate the underlying mechanisms and identify potential therapeutic strategies.

Results

A total of 89 *ROS1*-rearranged patients with locally-advanced or metastatic NSCLC were identified during the study period. MET IHC results were available in 49 patients. Among them, 19 (38.8%) patients were MET-positive. For the efficacy analysis, 19 patients with advanced *ROS1*-rearranged NSCLC who received first-line entrectinib were included. Nine patients were MET-positive and ten were MET-negative. The median follow-up was 17.9 months. In the 19 patients, the MET-positive achieved a lower ORR (33.3% vs. 100.0%, $P=0.003$) and shorter PFS (2.9 vs. 14.1 months, $P=0.008$) compared with the MET-negative. In addition, a representative patient-derived organoid (PDO)-guided case suggested potential benefit from combined *ROS1*/*MET* inhibition after progression on first-line entrectinib. The patient achieved an ongoing partial response (PR) at the data cutoff.

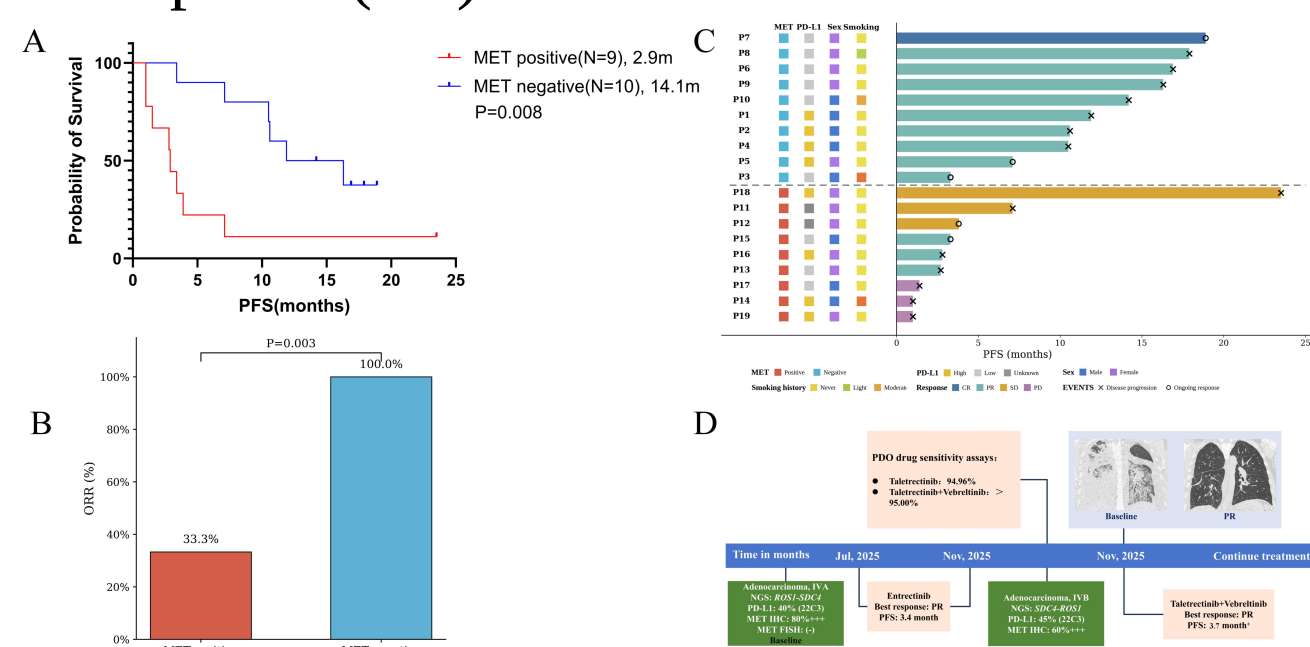


Figure. Clinical outcomes by MET status in 19 patients. (A) Kaplan-Meier analysis of PFS according to MET status. (B) ORR by MET status. (C) Swimmer plot of individual treatment duration, response, and baseline characteristics. (D) Representative case with PDO drug sensitivity. Abbreviations: NSCLC, non-small cell lung cancer; PFS, progression-free survival; ORR, objective response rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; PDO, patient-derived organoid.