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Final OS analysis of sacituzumab tirumotecan (sac-TMT) versus platinum-based chemotherapy in EGFR-mutated non-small cell lung cancer (NSCLC) after progression on EGFR-TKI: Phase III OptiTROP-Lung04 study

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Background

Sac-TMT is a TROP2-directed ADC with a unique bifunctional linker and a belotecan-derivative topoisomerase I inhibitor payload. In phase III OptiTROP-Lung04, sac-TMT significantly improved PFS and OS versus platinum-based chemotherapy in patients (pts) with EGFRm NSCLC after progression on EGFR-TKI at the prespecified interim OS analysis (*Fang et al. NEJM 2025*). Here, we report the prespecified final OS analysis with extended follow-up.

Methods

Eligible pts with locally advanced or metastatic EGFRm NSCLC who had progressed on EGFR-TKI therapy were randomized (1:1) to receive sac-TMT monotherapy (5 mg/kg Q2W) or pemetrexed plus platinum, followed by maintenance pemetrexed. OS was a key secondary endpoint. OS was adjusted for subsequent ADC therapy in the chemotherapy group using the rank-preserving structural failure time (RPSFT) model.

Results

A total of 376 pts were randomly assigned (188/group). As of 06 August, 2026, median follow-up was 32.3 months (mo). The statistically significant OS benefit observed at the prespecified interim analysis was sustained in the final analysis. Median OS was 25.9 mo (95% CI: 22.2-27.5) with sac-TMT vs 17.4 mo (95% CI: 15.7-20.3) with chemotherapy (HR 0.69, 95% CI: 0.54-0.89; nominal one-sided p=0.0021). The 24-mo and 30-mo OS rates were 54.1% vs 37.2% and 40.5% vs 28.4%, respectively. Subsequent ADC therapy was received by 22.6% of pts in the chemotherapy group. After RPSFT analysis adjusted for subsequent ADC therapy, median OS was 25.9 vs 16.6 mo (HR 0.57, 95% CI: 0.42-0.75). No new safety signals emerged with extended follow-up.

Conclusions

With an extended follow-up of 32.3 mo, sac-TMT continues to demonstrate clinically meaningful and sustained OS benefit compared with platinum-based chemotherapy in advanced EGFRm NSCLC after progression on EGFR-TKI therapy, including after adjustment for subsequent ADC therapy. These findings further support sac-TMT as an effective treatment option in this patient population.

Clinical trial identification

NCT05870319; first posted on May 23, 2023.

Legal entity responsible for the study

Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China.

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Disclosure

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