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Savolitinib or placebo combined with osimertinib in treatment-naïve advanced NSCLC with EGFR mutation and MET overexpression: Results from the phase 3 SANOVO study

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Background

EGFR-mutant (*EGFR*m) advanced NSCLC patients (pts) with de novo MET overexpression (MET-OE) were observed to have reduced efficacy with first-line *EGFR*-TKI monotherapy (Ma L, et al). Here we report Ph3 SANOVO study (NCT05009836) primary results, evaluating savolitinib (savo, a potent, CNS penetrated METi) + osimertinib (osi) vs. placebo + osi in first-line *EGFR*m and MET-OE advanced NSCLC in China.

Methods

Treatment-naive pts with locally advanced/metastatic NSCLC harboring *EGFR*m (exon 19 del/L858R) and MET-OE (IHC 2+ [H-score ≥220, <90% tumor cells with strong staining] or IHC 3+ [≥90% tumor cells with strong staining]) were randomized 1:1 in a double-blind manner to savo+osi or placebo+osi, stratified by EGFRm type (exon 19 del/L858R), brain metastases (yes/no), and MET-OE level (IHC 2+/3+). Savo/placebo (300 or 200 mg BID, weight-based) and osi (80 mg QD) were dosed until disease progression, intolerable toxicity or death, whichever occurred first. The primary endpoint, investigator (INV)-assessed PFS, was tested hierarchically (MET IHC 3+ first, then ITT if positive). DCO: 31 Jul, 2026.

Results

Of 326 pts randomized (savo+osi, n=162; placebo+osi, n=164), 98 per group had MET IHC 3+ status. Baseline characteristics were generally balanced. Savo+osi significantly prolonged INV-assessed PFS vs. placebo+osi in both MET IHC 3+ (24.8 vs. 11.1 mo; HR 0.45; 95% CI 0.31 to 0.66; P<0.0001) and ITT populations (24.9 vs. 13.8 mo; HR 0.56; 95% CI, 0.43 to 0.74; P<0.0001). Median OS in the ITT population was 44.5 vs. 34.9 mo (HR, 0.48; 95% CI, 0.33 to 0.68) at a median follow-up of 38.7 mo. Median treatment exposure was 22.1 mo with savo+osi vs. 12.9 mo with placebo+osi, while the incidence of AEs leading to discontinuation was 14.8% vs. 4.3%. Safety was consistent with known profiles of this combination.

Conclusions

Savo+osi demonstrated a statistically significant PFS improvement and clinically meaningful OS benefit over osi alone in first-line *EGFR*m and MET-OE advanced NSCLC, with manageable safety and no new safety signals. This dual oral regimen offers a potential new treatment option for this biomarker-defined population.

Clinical trial identification

NCT05009836. First posted date: 2021-08-18.

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Legal entity responsible for the study

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Disclosure

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