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Osimertinib (osi) + savolitinib (savo) vs platinum–pemetrexed (plat–pem) in EGFRm MET-overexpressed (OE) and/or -amplified (AMP) advanced NSCLC post-osi: SAFFRON phase (Ph) 3 primary results

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Background

Targeted treatments (txs) for *EGFR*m MET-OE and/or -AMP advanced NSCLC post-osi are limited. In SAVANNAH (Ph 2, NCT03778229), osi (3rd-gen, irreversible, CNS-active EGFR-TKI) + savo (oral, potent, highly selective, CNS-penetrant MET-TKI) demonstrated high and clinically meaningful response rates in this setting. We report primary results from the global Ph 3 SAFFRON study (NCT05261399), assessing efficacy and safety of osi + savo vs plat–pem in *EGFR*m MET-OE and/or -AMP advanced NSCLC post-osi.

Methods

Eligible pts: ≥18 years, *EGFR*m (Ex19del/L858R and/or T790M), MET-OE and/or -AMP (MET IHC3+ intensity in ≥90% of tumour cells and/or ≥10 *MET* gene copies by FISH) advanced NSCLC, post-1/-2L osi. Pts (randomised 1:1) received osi 80 mg QD + savo 300 mg BID or plat–pem (pem + carboplatin/cisplatin Q3W, 4 cycles, then maintenance pem Q3W) until RECIST 1.1 progression/discontinuation. Primary endpoint: PFS by BICR (RECIST 1.1); secondary/exploratory endpoints: OS, investigator-assessed PFS and safety. DCO: 06 Jul 2026.

Results

Overall, 338 pts were randomised: osi + savo n=171, plat–pem n=167. Osi + savo significantly improved PFS and OS vs plat–pem (PFS HR: 0.55; 95% CI 0.42, 0.72; p<0.001; OS HR: 0.68; 95% CI 0.50, 0.91; p=0.010; table). PFS benefit was consistent in the MET-OE and *MET*-AMP subgroups. All causality tx-emergent AEs (TEAEs): osi + savo 99% (Gr ≥3 64%); plat–pem 97% (Gr ≥3 63%). TEAEs leading to tx discontinuation: osi + savo 14%; plat–pem 8%. Serious TEAEs: osi + savo 41%; plat–pem 28%. Tx-related AEs: osi + savo 93% (Gr ≥3 40%); plat–pem 92% (Gr ≥3 52%).

Conclusions

Osi + savo showed statistically significant and clinically meaningful improvements in PFS and OS vs plat–pem, with a manageable safety profile, in pts with *EGFR*m MET-OE and/or -AMP advanced NSCLC post-osi. These data support osi + savo as an effective, oral, targeted tx for these pts and establish a new global standard of care.Table: LBA6

Efficacy endpoints	Osi + savo (n=171)	Plat–pem (n=167)
Median PFS by BICR, mo (95% CI)	7.6 (5.6, 9.7)	5.4 (4.2, 5.8)

Efficacy endpoints	Osi + savo (n=171)	Plat–pem (n=167)
HR (95% CI); p-value	0.55 (0.42, 0.72); p<0.001	
Median PFS by investigator assessment, mo (95% CI)	7.4 (5.6, 9.7)	4.2 (3.4, 4.5)
HR (95% CI)	0.47 (0.36, 0.61)	
Median OS, mo (95% CI)	17.8 (15.6, 23.7)	12.9 (10.6, 16.8)
HR (95% CI); p-value	0.68 (0.50, 0.91); p=0.010	
Median DoR by BICR, mo (95% CI)	9.7 (7.6, 12.5)	5.7 (4.4, 8.1)

BICR, blinded independent central review; CI, confidence interval; DoR, duration of response; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

Clinical trial identification

NCT05261399.

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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