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SAFFRON Data Reveal New Global SOC in *EGFR*+ NSCLC With MET Overexpression and/or Amplification After Osimertinib

Phase 3 SAFFRON primary results | 2026 ESMO Congress | Published in the *New England Journal of Medicine*

Top-Line Finding

45% reduction in risk of progression or death

Median PFS by BICR:

Osimertinib + savolitinib		Platinum/Pemetrexed
7.6 Months	VS	5.4 Months

HR, 0.55 (95% CI, 0.42-0.72); P < .001

Efficacy

Finding	Osimertinib + Savolitinib	Platinum/ Pemetrexed
12-month PFS rate	36%	10%
Median OS	17.8 months	12.9 months
12-month OS rate	70%	53%

OS: HR, 0.68 (95% CI, 0.50-0.91); *P* = .010

Trial Snapshot

Design
Global, randomized 1:1, phase 3; 338 patients from 25 countries

Primary End Point
PFS by BICR

Population
Advanced *EGFR*-mutated NSCLC progressing on osimertinib, with centrally confirmed MET overexpression and/or amplification

Arms
Osimertinib 80 mg QD + savolitinib 300 mg BID (n = 171) vs platinum/ pemetrexed (n = 167)

Response Outcomes

End Point	Osimertinib + Savolitinib	Platinum/ Pemetrexed
Confirmed ORR (BICR)	51%	27%
Median DOR	9.7 months	5.7 months
DCR	85%	65%

Takeaway: Nearly double the response rate, with responses lasting 4 months longer.

PFS by Subgroup

Subgroup	n (Combo / Chemo)	Median PFS (Combo vs Chemo)	HR (95% CI)
MET overexpressed	171/167	8.5 vs 5.6 months	0.51 (0.37-0.71)
MET amplified*	124/118	7.6 vs 4.2 months	0.48 (0.35-0.66)
Baseline brain metastases	129/116	NR	0.50 (0.31-0.82)
IHC overexpression + FISH amplification	53/51	NR	0.39 (0.26-0.59)

Takeaway: PFS benefit held across all prespecified subgroups, including brain metastases.

SAFETY

Grade ≥3 treatment-related AEs were less frequent with the combination (40% vs 52%). Most common AE with the combination: peripheral edema (49%); with chemotherapy: anemia (54%).

Why It Matters

- Presenting author Shun Lu, MD, PhD, called the combination a new global standard of care for this population.
- An NDA for savolitinib plus osimertinib was submitted to the FDA in September 2026.
- The combination is already approved in China for *EGFR*-mutated, MET-amplified nonsquamous NSCLC after EGFR TKI progression (phase 3 SACHI).

Lu S, Girard N, Okuma Y, et al. SAFFRON phase III primary results. Presented at: 2026 ESMO Congress; October 23-27, 2026; Madrid, Spain. Abstract LBA6.

*Not formally tested.