EGFRChannel | OncLive

Sequential Erlotinib + Ramucirumab Before Osimertinib Does Not Improve Outcomes in EGFR L858R–Mutant NSCLC

Phase 3 REVOL858R/WJOG14420L Trial | Presented at 2026 ASCO Annual Meeting

Reason for Study

- **Osimertinib** (Tagrisso) is the frontline standard of care for *EGFR*-mutant NSCLC
- But **L858R mutation patients fare worse** than exon 19 deletion patients on osimertinib
- **Hypothesis: Could adding erlotinib + ramucirumab before osimertinib improve outcomes?**

Trial Design

Phase 3 WU-KONG28

Arm A	Arm B
Erlotinib + Ramucirumab (150 mg/day) (10 mg/kg Q2W)	**Osimertinib alone** (80 mg/day)

Primary End point: *Time to Failure of Strategy (TFS)*

Element	Detail
Phase	Phase 3, open-label, randomized
Patients	232 enrolled
Mutation	EGFR L858R only
Setting	Untreated advanced/recurrent NSCLC
Randomization	1:1

Patients Profile

n = 232

Baseline Characteristics

- **73** Median Age
- **62%** Female
- **73%** Stage IIIB–IV
- **29%** Brain Metastases
- **35%** were smokers

Primary End point Time to Failure of Strategy (TFS)

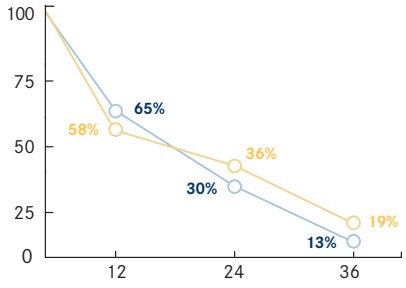
Median TFS

Combo	Osimertinib
16.6 Months	14.8 Months

HR = 0.65 • (*P* = .0008)

No statistically significant difference

Landmark Rates



Progression-Free Survival (PFS)

Median PFS has **virtually identical outcomes**

Combo

14.9 Months

Osimertinib

14.8 Months

Overall Survival (OS)

Numerically favored **osimertinib alone** (not statistically significant)

Combo

38.4 Months

Osimertinib

44.0 Months

Safety Comparison

Adverse Event	Combo (Gr 3/4)	Osimertinib (Gr 3/4)
Any grade 3+ AE	72%	44%
Treatment discontinuation due to AE	36%	21%
Hypertension	17%	0%
Acneiform rash	19%	1%
ILD/Pneumonitis (Gr 1+)	2%	10%

Combination = significantly more toxicity

Osimertinib alone had more ILD, but far less overall high-grade toxicity

REVOL858R/WJOG14420L Primary Analysis

Sequential erlotinib + ramucirumab followed by osimertinib did not improve TFS, PFS, or OS compared with osimertinib alone in EGFR L858R–mutant NSCLC—and comes with substantially higher toxicity.

EGFR L858R remains an unmet clinical need. Longer follow-up is ongoing.

Source: Caroline Seymour, Sequential Erlotinib Plus Ramucirumab Prior to Osimertinib Fails to Improve Outcomes in EGFR L858R–Mutant NSCLC