

Introduction

NSCLC is the leading cause of cancer-related mortality. While combined therapy including savolitinib and osimertinib appears promising, there exists a lack of comprehensive pooled evidence regarding its anti-oncological activity.

Objectives

The objective of this study is to evaluate the efficacy and safety of combined therapy in patients with NSCLC

Methods

A comprehensive literature search was conducted in MEDLINE, the Cochrane Central Register of controlled trials, and ClinicalTrials.gov. Randomized controlled trials and prospective single-arm studies evaluating savolitinib combined with osimertinib were included. A random-effects single-arm meta-analysis of proportions was performed using logit transformation and inverse variance weighting, with restricted maximum likelihood (REML) estimation and Knapp-Hartung adjustment. Results were reported with a 95% CI, and heterogeneity was assessed using the I2 statistic. Sensitivity analysis was conducted using the Freeman-Tukey transformation.

Results

- The primary analysis included 4 post-TKI, MET-selected combination cohorts (SACHI, SAVANNAH, and TATTON Part B; n = 338) from 7 reports of 5 trials after deduplication of overlapping data sets.
- First-line (FLOWERS) and MET-unselected (Yoh) cohorts were analyzed separately. The pooled objective response rate (ORR) was 53.9% (95% CI: 45.1-62.4), disease control rate (DCR) was 85.2% (79.2-89.8), 6-month progression-free survival (PFS) rate was 59.8%, and grade ≥ 3 adverse events occurred in 48.8% of patients.
- ORR estimates were consistent across studies and remained robust across sensitivity and subgroup analyses.

Outcome	Cohorts (k)	Pooled estimate, % (95% CI)	I ²
Objective response rate (primary)	4	53.9 (45.1-62.4)	4.9%
Disease control rate	4	85.2 (79.2-89.8)	0%
Grade ≥3 adverse events (primary)	4	53.1 (42.3-63.5)	56%
6-month PFS rate (landmark; exploratory)	4	59.8 (45.9-72.3)	39.2%
ORR sensitivity (+ TATTON Part D)	5	55.1 (47.4-62.6)	NA
ORR sensitivity (+ MET-unselected)	6	54.5 (47.5-61.3)	NA
Grade ≥3 AEs sensitivity (6 cohorts)	6	48.8 (36.6-61.2)	57%
ORR first-line (FLOWERS; single study)	1	90.5 (69.6-98.8)	NA

Literature Search

PubMed

Cochrane Library

ClinicalTrials.gov

Until April 26, 2026

Study Type : Randomized Controlled Trials

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Patients with Non-Small Cell Lung Cancer (NSCLC)

Savolitinib Plus Osimertinib

Placebo/ Chemotherapy

ORR, DCR, PFS

Pooled Results

Efficacy

Safety

Study

Events

Total

Events per 100 observations

ORR

95% CI

Weight

Random effects model

Prediction interval

Heterogeneity: I² = 4.9%, τ² = 0.0183, p = 0.3686

Study

Events

Total

Events per 100 observations

DCR

95% CI

Weight

Random effects model

Prediction interval

Heterogeneity: I² = 0.0%, τ² = 0, p = 0.5440

Study

Events

Total

Events per 100 observations

Grade ≥3

95% CI

Weight

Random effects model

Prediction interval

Heterogeneity: I² = 57.5%, τ² = 0.0895, p = 0.0383

PRISMA Flow sheet

Identification

Screening

Included

Records identified from: Databases (n = 135) PubMed (n = 103) Cochrane (n = 32) ClinicalTrials.gov (n = 1)

Records removed before screening: Duplicate records removed (n = 8) Records marked as ineligible by automation tools (n = 0) Records removed for other reasons (n = 0)

Records screened (n = 127)

Records excluded** (n = 100)

Reports sought for retrieval (n = 27)

Reports not retrieved (n = 20)

Reports assessed for eligibility (n = 10)

Reports excluded: Irrelevant comparator (n = 3)

Studies included in review (n = 7) 4 Primary Analysis 2 Secondary Analysis 1 Analysed separately

Conclusion

Combined therapy shows encouraging results in selected MET, post-TKI NSCLC. However, reliance on single-arm data warrants further randomized controlled trials.

References

Please scan the QR code for references and author affiliations.

