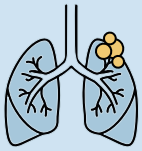
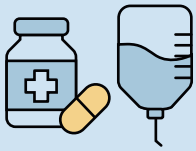
EGFRChannel | OncLive

Osimertinib + Chemotherapy Doubles Progression-Free Survival in High-Risk NSCLC

The Trial: TOP (Phase 3)



Patient Population
Advanced Non–Small Cell Lung Cancer (NSCLC) with concurrent *EGFR* and *TP53* mutations



Treatment Arm
Osimertinib + carboplatin/pemetrexed
(followed by maintenance).

Control Arm:
Osimertinib alone.

The Primary End point: Progression-Free Survival (PFS)

Combination Therapy	34.0 Mos
Osimertinib Alone	15.6 Mos

56% Reduction in the risk of disease progression or death
(HR, 0.44; $P < .001$).

Note: The PFS benefit held strong across all subgroups (age, sex, brain metastases, etc.).

Secondary Efficacy Highlights

Objective Response Rate (ORR)
82.9% (Combo)
vs 71.6% (Monotherapy)

Duration of Response (DOR)
32.7 months (Combo)
vs 15.3 months (Monotherapy)

Interim Overall Survival (OS)
48.4 months (Combo)
vs 36.5 months (Monotherapy)

Safety & Tolerability Trade-offs

Grade ≥3 Treatment-Related Adverse Effects (TRAEs)

Jumped significantly with the combination (62.4%) compared with monotherapy (14.9%).

Key Toxicities

The combination mostly drove hematologic (blood-related) toxicities like anemia and decreased white blood cell/neutrophil counts.

Treatment Discontinuation

TRAEs led to discontinuation in 26.2% of combination patients, versus just 1.4% of monotherapy patients.

The Clinical Bottom Line

"These findings provide key evidence to support a molecular risk–guided, individualized treatment strategy."

Intensifying treatment works exceptionally well for this high-risk *TP53*-mutant population, but careful patient selection is required due to increased toxicities.-Yungpeng Yang, MD.