

Osimertinib-Chemo Benefit Holds Regardless of Baseline *TP53* Status in *EGFR*⁺ NSCLC

Exploratory analysis, phase 3 FLAURA2 trial (NCT04035486)

Top-Line Finding in *TP53*-Altered Tumors

Progression-Free Survival (PFS)

Osimertinib +
platinum-pemetrexed

21.0
Months

VS

Osimertinib Alone

13.8
Months

HR 0.60 (95% CI, 0.43–0.82)

Overall Survival Rate (OS)

Osimertinib +
platinum-pemetrexed

38.4
Months

VS

Osimertinib Alone

32.4
Months

HR 0.73 (95% CI, 0.53–1.00)

Trial Snapshot



Population

557 patients with previously untreated, locally advanced, or metastatic *EGFR*-mutated NSCLC

1:1

1:1 Comparison

Osimertinib + platinum chemo + pemetrexed vs osimertinib monotherapy



Prior Results

PFS HR 0.62 (0.49–0.79; $P < .001$);
OS HR 0.77 (0.61–0.96; $P = .02$)



Primary End Point

Baseline plasma samples from 353 patients; *TP53* was the most common co-occurring alteration, detected in **67%**

Median Months by Baseline *TP53* status

Subgroup	Osi + plat-pem	Osi alone	HR (95% CI)	
<i>TP53</i> -altered – PFS	21.0	13.8	0.60 (0.43–0.82)	<i>TP53</i> alterations predict shorter PFS and OS – but the combination beats monotherapy in both <i>TP53</i> groups.
<i>TP53</i> -altered – OS	38.4	32.4	0.73 (0.53–1.00)	
<i>TP53</i> wild-type – PFS	27.6	22.3	0.74 (0.42–1.27)	
<i>TP53</i> wild-type – OS	48.3	44.5	0.88 (0.54–1.45)	

EGFR signal bypass alterations:

Osimertinib monotherapy arm only – median months

PFS

With Alteration **13.7** Months VS Without Alteration **16.5** Months

HR 0.78 (0.54–1.13)

OS

With Alteration **29.7** Months VS Without Alteration **39.6** Months

HR 0.66 (0.46–0.95)

Bypass alterations worsened outcomes on osimertinib alone, but that gap largely disappeared with the combination – suggesting it may overcome this resistance mechanism.

Acquired resistance at progression

245 paired samples, combination vs monotherapy

EGFR C797S
5% vs 11%

***RB1* loss/mutation**
1% vs 7%

Any resistance alteration
56% vs 61%

Less resistance with the combination.
No novel resistance mechanisms were identified in either arm.

Why it matters

Findings arrive as adjuvant osimertinib (Tagrisso) is already a recommended option for resected stage IB–IIIA *EGFR*-mutant NSCLC (exon 19 deletion or L858R), with or without chemotherapy. Longer follow-up and MRD dynamics are needed to clarify how TKI- and chemotherapy-based adjuvant strategies fit together.