

# Survival with Osimertinib plus Chemotherapy in EGFR-Mutated Advanced NSCLC

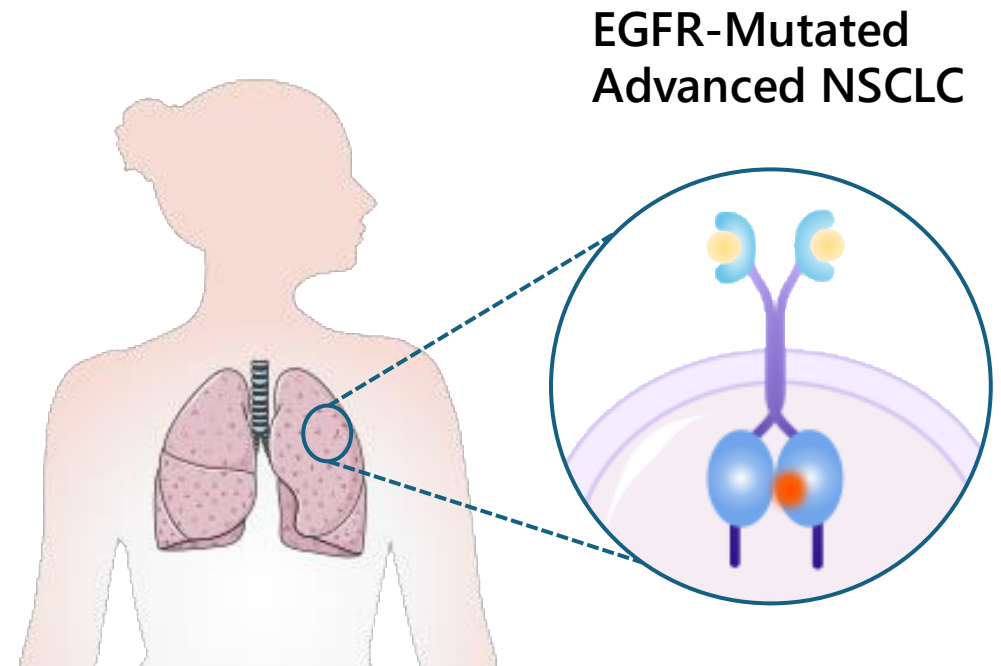
Results from the FLAURA2 Phase III,  
Randomized, International Trial

Jänne PA, et al. N Engl J  
Med. 2026;394(1):27-38.

Slide Deck Developed By  
Gorana Jendrisek, PhD

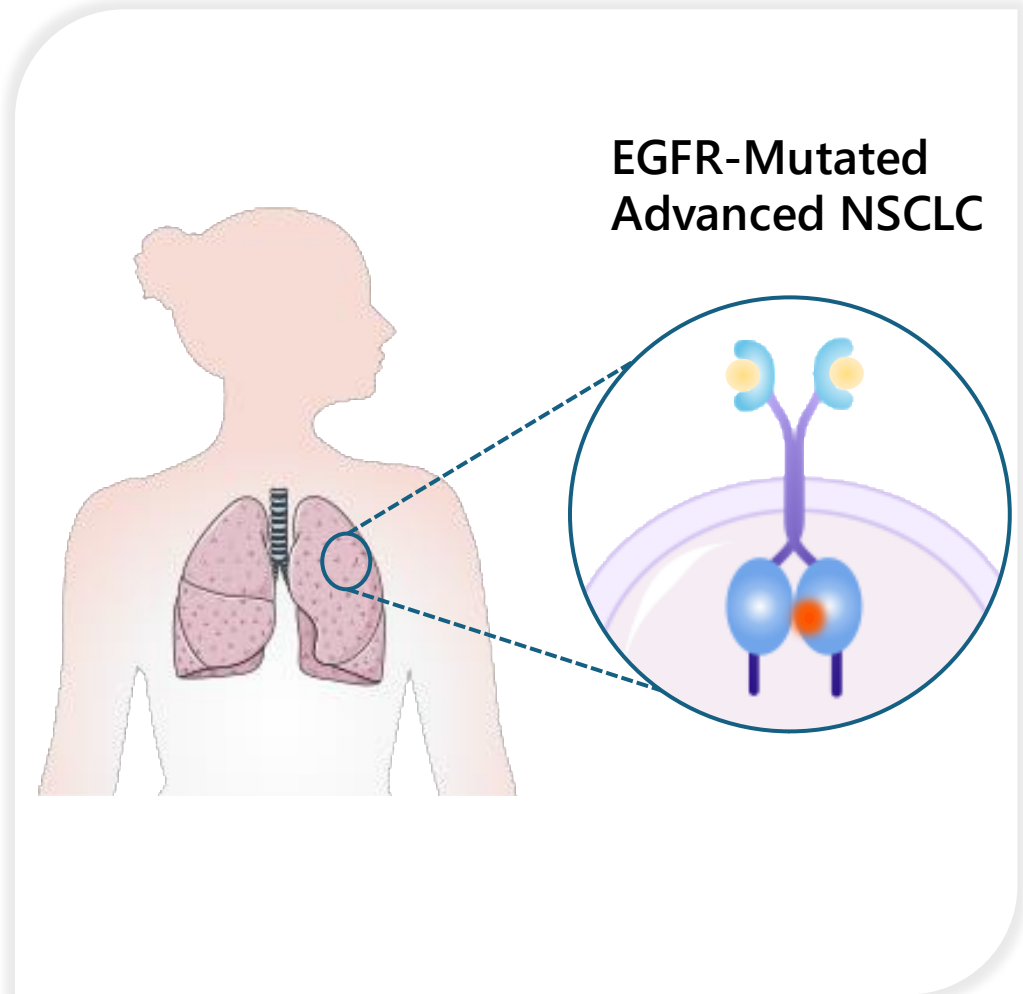
Disclaimer: This slide deck was created solely as an independent  
mock portfolio deck created from published data for  
demonstration purposes only.

Not affiliated with AstraZeneca or NEJM.



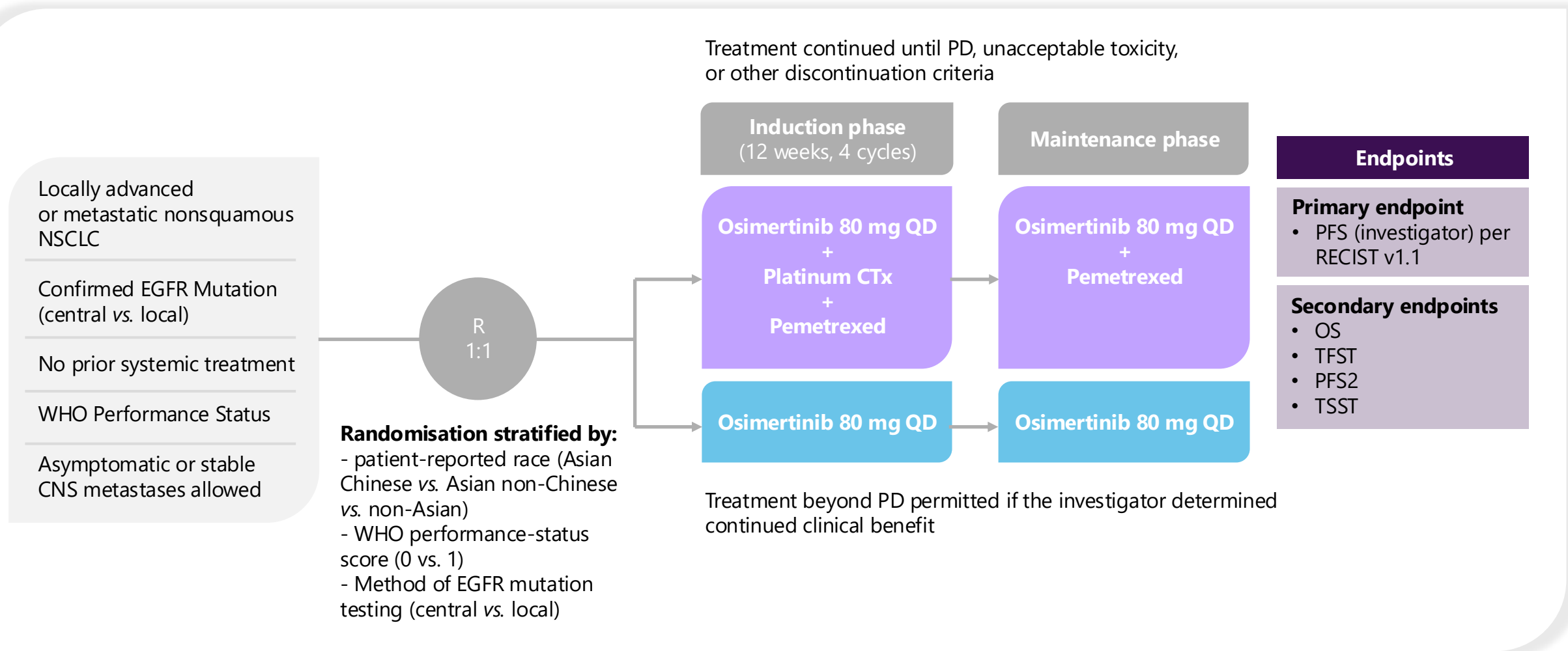
# Background: EGFR-Mutated Advanced NSCLC

- Osimertinib monotherapy is a **preferred first-line treatment** for patients with EGFR-mutated advanced NSCLC
- Osimertinib is a third-generation, CNS-active, irreversible, oral EGFR-TKI that **selectively targets** both EGFR-TKI-sensitizing and T790M resistance mutations
- Evidence from previous trials with first-generation EGFR-TKIs (gefitinib) suggested that **adding chemotherapy with a platinum-based agent and pemetrexed** could extend survival benefits compared to TKI therapy alone
- The addition of a platinum-based agent and pemetrexed to osimertinib **was hypothesized to extend the benefit** provided by osimertinib alone



# FLAURA2 Phase III Study Design

International, open-label, randomized trial



**Notes:** 1. World Health Organization performance-status score of 0 or 1 (scores range from 0 to 5, with higher scores indicating greater disability). 2. CNS metastases at baseline were determined by investigator assessment. 3. The primary endpoint of PFS was assessed by the investigator per RECIST v1.1. 4. Chemotherapy consisted of pemetrexed (500 mg/m<sup>2</sup>) plus cisplatin (75 mg/m<sup>2</sup>) or carboplatin (area under the concentration-time curve of 5 mg per milliliter per minute). **References:** 1. Planchard D, et al. *N Engl J Med.* 2023;389(21):1935-1948. 2. Jänne PA, et al. *N Engl J Med.* 2026;394(1):27-38. **Abbreviations:** CNS = central nervous system; CTx = chemotherapy; EGFR = epidermal growth factor receptor; NSCLC = non-small-cell lung cancer; OS = overall survival; PD = progressive disease; PFS = progression-free survival; PFS2 = second progression-free survival; QD = once daily; R = randomisation; RECIST = Response Evaluation Criteria in Solid Tumors; TFST = time to first subsequent therapy; TSST = time to second subsequent therapy; WHO = World Health Organization.

# FLAURA2 - Baseline features

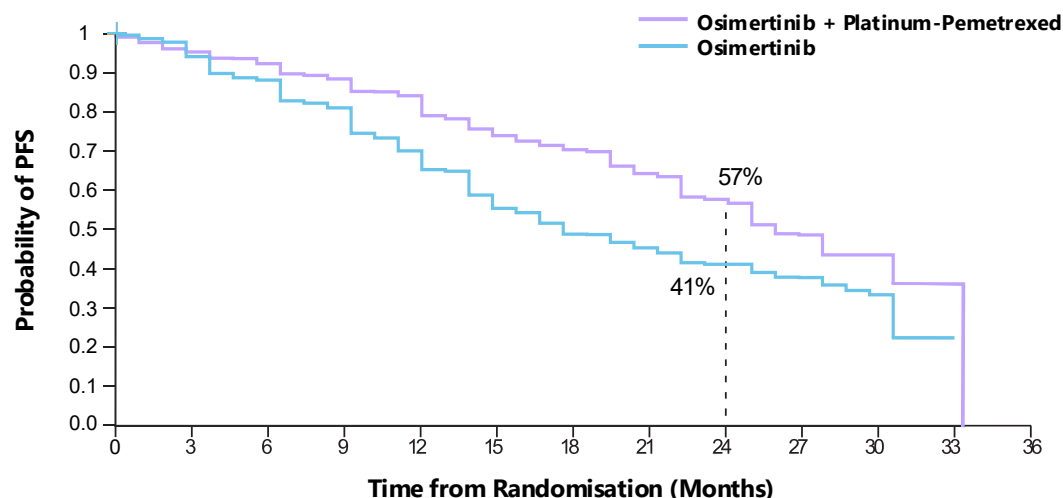
Demographics and baseline characteristics were generally well balanced

	Osimertinib + Platinum-Pemetrexed (N = 279)	Osimertinib (N = 278)
Median age (range), yr	61 (26–83)	62 (30–85)
Female, no. (%)	173 (62)	169 (61)
Race, no. (%) Asian / Non-Asian	179 (64) / 100 (36)	176 (63) / 102 (37)
WHO performance-status score, no. (%) 0 / 1	104 (37) / 174 (62)	102 (37) / 176 (63)
Histologic characteristics, no. (%) Adenocarcinoma	275 (99)	275 (99)
Smoking status, no. (%) Never smoker	185 (66)	181 (65)
EGFR mutation, no. (%) Ex19del / L858R	169 (61) / 106 (38)	168 (60) / 107 (38)
CNS metastases at baseline, no. (%)	116 (42)	110 (40)

**Notes:** **1.** World Health Organization performance-status score of 0 or 1 (scores range from 0 to 5, with higher scores indicating greater disability). **2.** One patient in the combination group was recorded as having a WHO performance-status score of 2 at baseline (a protocol deviation). **3.** CNS metastases at baseline were determined by investigator assessment. **References:** **1.** Planchard D, et al. *N Engl J Med.* 2023;389(21):1935-1948.; **2.** CADTH Reimbursement Review: Osimertinib (Tagrisso); **3.** Jänne PA, et al. *N Engl J Med.* 2026;394(1):27-38. **Abbreviations:** CNS = central nervous system; EGFR = epidermal growth factor receptor; Ex19del = exon 19 deletion; L858R = leucine-to-arginine substitution at conformational position 858; no. = number; WHO = World Health Organization.

# FLAURA2 - Primary endpoint: investigator-assessed PFS

Statistically Significant PFS Benefit with Osimertinib + Platinum-Pemetrexed



No. at Risk

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36
Osimertinib + Platinum-Pemetrexed	279	254	241	225	207	187	165	133	84	42	21	3	0
Osimertinib	278	246	227	203	17	148	119	94	67	48	21	1	0

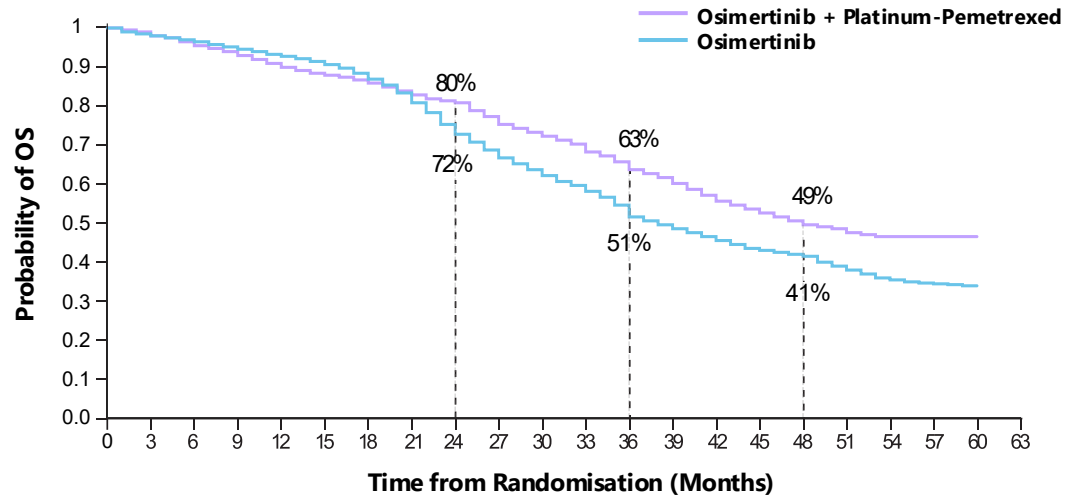
	Osimertinib + Platinum-Pemetrexed	Osimertinib
Events, no. (%)	120 (43)	166 (60)
Median PFS (95% CI), months	<b>25.5</b> (24.7–NC)	<b>16.7</b> (14.1–21.3)
Hazard Ratio (95% CI)	<b>0.62</b> (95% CI, 0.49–0.79) <i>P</i> < 0.001	

BICR-assessed PFS findings were **consistent** with the primary analysis

All observed HR point estimates **avored** osimertinib + platinum-pemetrexed

**Notes:** **1.** PFS was assessed by the investigator according to RECIST v1.1. **2.** Hazard ratios are based on a Cox proportional-hazards model; a hazard ratio < 1.0 favors the osimertinib+ chemotherapy arm. **3.** Median follow-up for the primary analysis was 19.5 months for the osimertinib plus chemotherapy and 16.5 months for the osimertinib group. **4.** P-value was calculated using a log-rank test stratified by race, performance status, and tissue testing method. **5.** Data visualizations generated in Python for illustrative purposes; source data from Planchard D, et al. 2023. **References:** Planchard D, et al. N Engl J Med. 2023;389(21):1935-1948. **Abbreviations:** BICR = blinded independent centralised review; CI = confidence interval; HR = hazard ratio; NC = not calculable; No. = number; PFS = progression-free survival.

# FLAURA2 - OS



## No. at Risk

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
Osimertinib + Platinum-Pemetrexed	279	267	258	253	245	240	236	226	218	202	196	183	170	158	143	123	105	71	36	16	1	0
Osimertinib	278	267	260	257	252	245	229	214	195	180	165	152	137	131	118	103	93	61	38	16	1	0

	Osimertinib + Platinum-Pemetrexed	Osimertinib
Events, no. (%)	144 (52)	171 (62)
Median OS (95% CI), months	<b>47.5</b> (41.0–NC)	<b>37.6</b> (33.2–43.2)
Hazard Ratio (95% CI)	<b>0.77</b> (95% CI, 0.61–0.96) <i>P</i> =0.02	

Median OS difference: **9.9 months**

# FLAURA2 - Overall safety summary and adverse effects

AEs, no. (%)	Osimertinib + Platinum-Pemetrexed	Osimertinib
Any AE	276 (100)	269 (98)
Grade $\geq 3$ AEs	193 (70)	94 (34)
Serious AEs	126 (46)	75 (27)
AEs leading to discontinuation of osimertinib	34 (12)	20 (7)
AEs leading to death	22 (8)	10 (4)

**Median duration of exposure** was longer with osimertinib + platinum-pemetrexed than with osimertinib monotherapy (**30.5** vs. **21.2** months)

**Grade  $\geq 3$  AEs** and **serious AEs** were more frequent with combination therapy than with osimertinib monotherapy (70% vs. 34% and 46% vs. 27%, respectively)

The higher incidence of grade  $\geq 3$  AEs was largely attributable to expected chemotherapy-related hematologic toxicities

**Discontinuation of osimertinib** due to AEs remained low in both groups, although numerically higher with combination therapy (12% vs. 7%)

# FLAURA2 - Conclusions

- In FLAURA2, first-line osimertinib + platinum-pemetrexed **improved PFS** at the primary analysis and **improved OS** at the planned final analysis versus osimertinib monotherapy
- A general trend **favoring** combination therapy was observed across prespecified subgroups; subgroup analyses were descriptive
- Combination therapy was **associated with more grade  $\geq 3$  and serious adverse events**, largely expected chemotherapy-related hematologic toxicities
- These results support consideration of osimertinib + platinum-pemetrexed as a first-line option for selected patients with EGFR-mutated advanced NSCLC

Combination therapy improved OS, with increased toxicity largely driven by expected chemotherapy-related hematologic events.