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FLAURA2: Exploratory overall survival (OS) analysis in patients (pts) with poorer prognostic factors treated with osimertinib (osi) ± platinum-pemetrexed chemotherapy (CTx) as first-line (1L) treatment (tx) for EGFR-mutated (EGFRm) advanced NSCLC

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Background

In the planned final OS analysis of FLAURA2 (phase III; NCT04035486), 1L osi (a 3rd-generation, CNS-active EGFR-TKI) + CTx demonstrated a statistically significant, clinically meaningful improvement in OS vs osi mono in pts with EGFRm advanced NSCLC (HR: 0.77; 95% CI 0.61, 0.96; p=0.02). A survival benefit favouring osi + CTx vs osi mono was consistently observed across predefined subgroups. Prior studies in EGFRm NSCLC have identified baseline factors associated with poorer prognosis, such as CNS metastases (mets), L858R mutation, detected (det) plasma EGFRm and altered TP53. We report OS analyses from FLAURA2 based on baseline prognostic factors.

Methods

The study design was presented previously (Planchard, et al. N Engl J Med 2023;389:1935–48). Baseline CNS scans (CT/MRI) were required. Tissue EGFRm type was tested via central or locally approved assays. Plasma EGFRm status was assessed via droplet digital PCR (Biosesix). Tissue TP53 was assessed via FoundationOne CDx test (Foundation Medicine). Subgroup OS was analysed via an unstratified Cox proportional hazards model.

Results

Overall, 557 pts were randomised to osi + CTx (n=279) or osi mono (n=278). The proportion of pts in each prognostic subgroup was generally similar across tx arms (Table). HRs for OS favoured osi + CTx vs osi mono across each prognostic subgroup and were consistent with the HR for the overall population (0.77). Median OS (mOS) was not reached (NR) for several subgroups; however, mOS was longer with osi + CTx vs osi mono in subgroups with poorer baseline prognostic factors (i.e. CNS mets, L858R mutation, det plasma EGFRm, or altered TP53). Further analyses will be presented.

Conclusions

A survival benefit favouring osi + CTx vs osi mono was consistently observed across each prognostic subgroup evaluated, reinforcing osi + CTx as a 1L standard of care in this setting. Table: LBA77

	Osi + CTx		Osi mono		HR (95% CI)
	Events/pts, n	mOS, mo (95% CI)	Events/pts, n	mOS, mo (95% CI)	
Baseline CNS mets					
Yes	71/116	40.9 (35.2, 46.6)	79/110	29.7 (25.6, 35.8)	0.72 (0.52, 0.99)
No	73/163	NR (45.0, NC)	92/168	43.9 (37.8, 53.3)	0.77 (0.57, 1.05)
EGFRm					
L858R	66/106	38.1 (33.4, 42.0)	74/107	32.4 (28.0, 37.6)	0.76 (0.55, 1.07)
Ex19del	78/172	NR (47.2, NC)	95/169	43.0 (35.7, 51.9)	0.76 (0.56, 1.02)
Plasma EGFRm					
Det	88/148	38.4 (33.2, 46.6)	114/161	32.5 (28.8, 35.8)	0.79 (0.60, 1.03)
Undet	24/65	NR (50.8, NC)	21/48	NR (46.0, NC)	0.79 (0.44, 1.44)
Tissue TP53					
Altered	22/46	51.1 (35.0, NC)	25/40	43.1 (34.0, 50.1)	0.71 (0.40, 1.27)
Wild type	11/33	NR (46.6, NC)	14/34	NR (41.3, NC)	0.70 (0.32, 1.54)

NC, not calculable

Clinical trial identification

NCT04035486, 29 July 2019.

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Disclosure

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