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FLAURA2: Analysis of on-treatment plasma EGFRm dynamics and associated clinical outcomes in patients (pts) with EGFRm advanced NSCLC treated with first-line (1L) osimertinib (osi) ± platinum–pemetrexed (plat–pem)

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Background

In the phase III FLAURA2 trial (NCT04035486), 1L osi + plat–pem led to significantly improved PFS and OS vs osi mono in pts with EGFRm advanced NSCLC. In our previous analysis, EGFRm clearance at Week (Wk) 3 and 6 was prognostic, but not predictive of a PFS benefit with osi + plat–pem vs osi mono. We report exploratory analyses of PFS and OS by plasma EGFRm clearance at Wks 1, 2, 3 and 6 to understand if EGFRm clearance rates differ between treatment arms, and to evaluate the use of early EGFRm circulating tumour DNA (ctDNA) dynamics for identifying pts most likely to benefit from osi + plat–pem.

Methods

Pts with untreated EGFRm (Ex19del or L858R) advanced NSCLC were randomised 1:1 to receive either osi (80 mg QD) + plat–pem (Q3W; 4 cycles) followed by osi (QD) + pem (Q3W), or osi (QD) mono, until PD or discontinuation. BL and Wks 1, 2, 3 and 6 plasma EGFRm were analysed by ddPCR (Biodesix). Clearance was defined as undetected EGFRm ctDNA post-treatment start, where it was detected at BL. Association between clearance and PFS (by investigator assessment; DCO: 03 April 2023) and OS (DCO: 12 June 2025) was examined.

Results

Among pts with evaluable BL and Wk 1, 2, 3 and 6 plasma ddPCR results, the rate of clearance was 38%, 64%, 81%, and 88%, in the osi + plat–pem arm, respectively, and 42%, 64%, 71%, and 89%, in the osi mono arm, respectively. A consistent PFS and OS benefit was seen with osi + plat–pem vs osi mono, irrespective of clearance status (Table).

Conclusions

On-treatment EGFRm clearance was prognostic, but not predictive of PFS or OS benefit with osi + plat–pem at all timepoints; efficacy of osi + plat–pem was superior to osi mono regardless of clearance status. Clearance rates were comparable across treatment arms and timepoints. Studies using ultra-sensitive multi-marker ctDNA assays are planned to investigate early ctDNA dynamics as a predictive biomarker.
Table: 2719R0

Timepoint, Week	EGFRm clearance (Y/N)	Osi + plat–pem, n (%)	Osi mono, n (%)	Osi + plat–pem vs osi mono PFS HR (95% CI)	Osi + plat–pem vs osi mono OS HR (95% CI)
1	Y	39 (38)	55 (42)	0.56 (0.31, 1.03)	0.79 (0.45, 1.37)

Timepoint, Week	EGFRm clearance (Y/N)	Osi + plat–pem, n (%)	Osi mono, n (%)	Osi + plat–pem vs osi mono PFS HR (95% CI)	Osi + plat–pem vs osi mono OS HR (95% CI)
N	65 (63)	76 (58)	0.52 (0.34, 0.81)	0.69 (0.47, 1.02)	
2	Y	72 (64)	85 (64)	0.52 (0.34, 0.81)	0.69 (0.46, 1.03)
N	41 (36)	48 (36)	0.56 (0.33, 0.96)	0.78 (0.48, 1.26)	
3	Y	88 (81)	100 (71)	0.50 (0.34, 0.75)	0.84 (0.58, 1.21)
N	21 (19)	40 (29)	0.59 (0.30, 1.16)	0.65 (0.36, 1.20)	
6	Y	92 (88)	122 (89)	0.52 (0.36, 0.76)	0.73 (0.52, 1.04)
N	13 (12)	15 (11)	0.40 (0.16, 0.97)	0.50 (0.22, 1.13)	

CI, confidence interval; HR, hazard ratio; N, no; Y, yes.

Clinical trial identification

NCT04035486.

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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