

Esmo 2020 - Pfizer's next-gen lung cancer drug impresses



Amy Brown

Alk-positive non-small cell lung cancer is a small niche well endowed with targeted options, so a prime spot at Esmo's presidential session for the first-line Crown study of Pfizer's Lorbrena heralded impressive results. These did not disappoint, and response rates look competitive, particularly on intracranial tumours, where time to progression yielded an astonishing 0.07 hazard ratio. With median PFS not estimable Alecensa remains the one to beat on this measure; the Roche drug has been shown to extend progression by up to three years in some cases, according to Dr Christine Lovly, who discussed Crown for Esmo. Dr Lovly also highlighted Lorbrena's toxicity profile, which uniquely among these kinase inhibitors includes elevated lipids and neurocognitive disturbances. Dr Benjamin Solomon, lead investigator of Crown, said Lorbrena had been designed to be highly brain-penetrant, which might explain these CNS effects, which ranged from mood changes to attention impairment. Oncologists will not be used to such side effects, which could put the drug at a disadvantage when it comes to deciding which to use first line. Sequencing these agents looks set to remain an open question until additional biomarkers can be found to predict response, or further head-to-head trials are done.

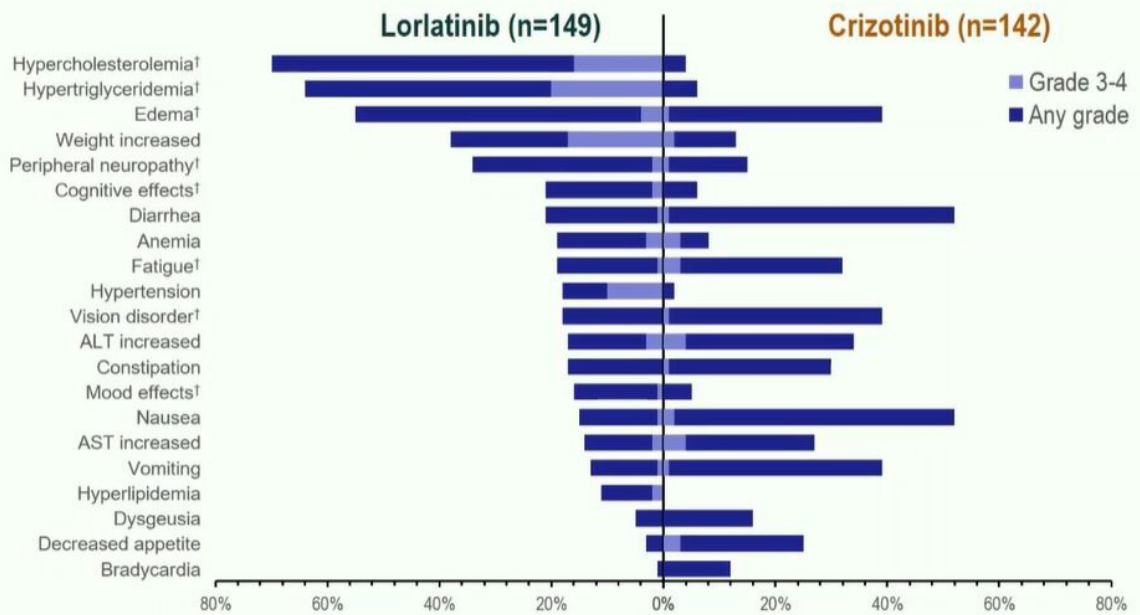
Cross-trial comparison of first-line studies of Alk inhibitors

	Crown (n=296)		Alex (n=303)		Alta-1L (n=275)		Exalt-3 (n=290)	
	Lorbrena (Pfizer)	Xalkori (Pfizer)	Alecensa (Roche)	Xalkori (Pfizer)	Alunbrig (Takeda)	Xalkori (Pfizer)	Ensartinib (Xcovery)	Xalkori (Pfizer)
Median PFS (months)	NR	9.3	25.7	10.4	NR	9.8	25.8	12.7
	HR: 0.28		HR: 0.50		HR: 0.49		HR: 0.51	
ORR (%)	76	58	83	76	71	60	75	67
Intracranial response (%)	82	23	81	50	78	29	64	21

NR: Not reached. Source: Dr Christine Lovly and Esmo.

Side effects of Lorbrena and Xalkori in the Crown study

All Causality Adverse Events with $\geq 10\%$ Difference in Frequency



†Cluster term
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

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