

ACC 2022 - full vupanorsen data shed light on Pfizer's split



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Ionis's anti-ANGPTL3 antisense vupanorsen already looked dead in the water after Pfizer abandoned it in January after [ostensibly positive topline results last year](#). Now full data from the phase 2b Translate Timi 70 dose-ranging trial, presented at ACC yesterday, show why the big pharma walked away. While the study met its primary endpoint, non-HDL cholesterol lowering at week 24, even the most effective dose of vupanorsen produced an unimpressive 28% placebo-adjusted reduction. LDL cholesterol lowering was even more lacklustre, and a cross-trial comparison against Regeneron's approved ANGPTL3 inhibitor Evkeeza and marketed anti-PCSK9 products show just how uncompetitive vupanorsen looks. It is worth noting that the Elipse study of Evkeeza only included patients with homozygous familial hypercholesterolaemia, the most serious form of FH, while Translate Timi 70 enrolled a broad dyslipidaemia population. But vupanorsen has also been hit by previously disclosed liver toxicity concerns, and ACC heard that 39% of patients in the highest dose, 160mg every two weeks, had ALT or AST increases over three-times the upper limit of normal. Other groups involved in ANGPTL3 include Arrowhead, Lilly/Novo Nordisk - via Dicerna - and Verve Therapeutics. They will hope that these issues are unique to vupanorsen.

How vupanorsen stacks up against approved cholesterol lowerers

Product/project	Company	Description	Non-HDL lowering	LDL lowering
Vupanorsen	Ionis	SC anti-ANGPTL3 antisense	28%*	16%*
Evkeeza	Regeneron	IV anti-ANGPTL3 MAb	52%**	49%**
Leqvio (inclisiran)	Novartis	SC anti-PCSK9 RNAi	44-47% [^]	50-52% [^]
Repatha	Amgen	SC anti-PCSK9 MAb	46% ^{^^}	55% ^{^^}
Praluent	Sanofi/Regeneron	SC anti-PCSK9 MAb	50% [~]	58% [~]

*All on top of background statins; all data placebo-adjusted; SC=subcutaneous; IV=intravenous; *best result from dose-ranging [Translate Timi 70](#); **[Elipse-HoFH](#) (homozygous familial hypercholesterolemia pts only); [^][Orion-10](#) & [11](#); ^{^^}[Descartes](#); [~][Odyssey Long Term](#). Source: product labels & ACC 2022.*

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