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Effect of alirocumab on recurrent cardiovascular events after acute coronary syndrome, according to the intensity of background statin treatment

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Background: Statins are a cornerstone of therapy for coronary heart disease. We describe the effects of alirocumab (ALI) in patients (pts) with recent acute coronary syndrome (ACS) and dyslipidaemia per category of statin use.

Methods: ODYSSEY OUTCOMES compared ALI with placebo (PBO) in 18,924 pts with recent ACS and dyslipidaemia despite high-intensity/maximum tolerated statin (atorvastatin 40–80 mg/d or rosuvastatin 20–40 mg/d). Lower doses could be used if there were symptoms, laboratory abnormalities, or contraindications with higher doses. In cases of documented intolerance to ≥2 statins, pts could qualify on no statin treatment. Pts were randomized to ALI (75 mg SC Q2W, with possible uptitration to 150 mg Q2W) or PBO. Median follow-up was 2.8 years. Primary endpoint was major adverse cardiovascular events (MACE: CHD death, nonfatal MI, ischaemic stroke, or unstable angina requiring hospitalization). Pts were categorized by statin therapy at baseline: high intensity (88.8%), low or moderate intensity (8.7%), or no statin use (2.4%). In each category we determined the relative (hazard ratio [HR]) and absolute risk reductions (ARR) for MACE with ALI.

Results: Overall, ALI reduced MACE (HR 0.85, 95% CI 0.78–0.93; P<0.001). HRs were consistent across statin categories (Table). Baseline LDL-C increased across high-intensity, low/moderate-intensity, and no statin categories. Correspondingly, there was a gradient of the risk of MACE in the PBO group across these categories (10.8%, 10.7%, and 26%). With ALI treatment, the mean reduction in LDL-C from baseline to Month 4 increased across the 3 statin categories and correspondingly the ARRs for MACE were 1.3%, 3.2%, and 8.0% (P interaction <.001).

Conclusions: In ODYSSEY OUTCOMES, patients unable to receive high-intensity statin treatment showed greater ARRs with ALI, consistent with higher baseline LDL-C concentration and greater absolute LDL-C reduction. Patients unable to receive high-intensity statin treatment are an important group to consider for treatment with ALI after ACS.

LDL-C values and MACE events

	All patients N=18,924 (100%)		High-intensity statin N=16,811 (88.8%)		Low-/moderate-intensity statin N=1653 (8.7%)		No statin N=460 (2.4%)		Interaction P-value (treatment x statin category)
	PBO (N=9462)	ALI (N=9462)	PBO (N=8431)	ALI (N=8380)	PBO (N=804)	ALI (N=849)	PBO (N=227)	ALI (N=233)	
LDL-C at baseline, mmol/L, mean (SE)*	2.39 (0.01)	2.39 (0.01)	2.35 (0.01)	2.35 (0.01)	2.41 (0.03)	2.43 (0.03)	3.76 (0.08)	3.82 (0.08)	
Change in LDL-C from baseline to Month 4, mmol/L, mean (SE)	0.03 (0.01)	−1.4 (0.01)	0.03 (0.01)	−1.37 (0.01)	0.01 (0.02)	−1.47 (0.02)	−0.004 (0.06)	−2.27 (0.06)	<0.001
MACE, n (%)*	1052 (11.1)	903 (9.5)	907 (10.8)	797 (9.5)	86 (10.7)	64 (7.5)	59 (26.0)	42 (18.0)	
HR (95% CI)	0.85 (0.78–0.93)		0.88 (0.80–0.96)		0.69 (0.50–0.95)		0.65 (0.43–0.96)		0.14
ARR (%) (95% CI)	1.6 (0.7–2.4)		1.3 (0.3–2.2)		3.2 (0.4–5.9)		8.0 (0.4–15.5)		<0.001

*P<0.001 for difference among statin categories.