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ALIROCUMAB EFFICACY AND SAFETY IN PATIENTS WITH HYPERCHOLESTEROLEMIA AND WITH OR WITHOUT CLINICAL ATHEROSCLEROTIC CARDIOVASCULAR DISEASE: POOLED ANALYSIS OF 10 ODYSSEY RANDOMIZED TRIALS

Moderated Poster Contributions
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Background: The alirocumab (ALI) ODYSSEY clinical trial program recruited patients with hypercholesterolemia, ~70% of whom had atherosclerotic cardiovascular disease (ASCVD) and were at very high ASCVD risk. This analysis evaluated the lipid-lowering efficacy and safety of ALI among patients with or without clinical ASCVD.

Methods: The dataset originated from 4,983 patients with hypercholesterolemia randomized in 10 Phase 3 trials. Data were grouped into 4 pools based on ALI dose and control (placebo, Pools 1+2; ezetimibe, Pools 3+4) (Table). Patients in Pools 1–3 received background statins, which were at maximally tolerated dose in most patients (85%); patients in Pool 4 did not receive statins.

Results: LDL-C % reductions from baseline and goal achievement at Week 24 were comparable in patients with or without clinical ASCVD in placebo-controlled trials (Table). LDL-C goal achievement was consistent in ALI-treated patients in ezetimibe-controlled trials. Treatment emergent adverse event (TEAE) rates and discontinuations due to TEAEs with ALI were similar to controls regardless of clinical ASCVD status (Table).

Conclusions: Compared with controls, ALI administration substantially reduced LDL-C levels, allowed greater LDL-C goal achievement, and was generally well tolerated in both patients with and without clinical ASCVD.

Table: Efficacy and safety summary in patients with and without clinical ASCVD, according to treatment pool

		Control group		Alirocumab group		
		Cinical ASCVD (No/Yes)		Cinical ASCVD (No/Yes)		
		No	Yes	No	Yes	
Baseline LDL-C mg/dL, mean (SD) - randomized population						
POOL 1: ALI 150 mg Q2W vs PBO		131.3 (45.0)	123.5 (44.2)	141.1 (56.6)	121.0 (40.6)	
POOL 2: ALI 75/150 mg Q2W vs PBO		143.3 (41.6)	120.4 (45.7)	144.6 (48.5)	117.3 (42.9)	
POOL 3: ALI 75/150 mg Q2W vs EZE		115.6 (40.6)	102.3 (34.6)	117.8 (34.7)	108.0 (35.5)	
POOL 4: ALI 75/150 mg Q2W vs EZE		180.0 (67.7)	171.6 (62.4)	175.2 (73.5)	178.8 (53.7)	
% LDL-C change from baseline at Week 24, LS mean (SE) - ITT population						**Interaction P-value**
POOL 1: ALI 150 mg Q2W vs PBO		2.6 (2.1) n=188	-0.1 (1.2) n=627	-55.7 (1.5) n=393	-61.9 (0.8) n=1208	0.2493
POOL 2: ALI 75/150 mg Q2W vs PBO		6.7 (2.3) n=151	2.2 (2.0) n=199	-46.6 (1.7) n=299	-50.0 (1.4) n=394	0.7502
POOL 3: ALI 75/150 mg Q2W vs EZE		-18.8 (3.9) n=88	-19.2 (1.9) n=348	-38.4 (3.8) n=98	-50.9 (1.5) n=571	0.0340
POOL 4: ALI 75/150 mg Q2W vs EZE		-15.3 (2.2) n=121	-13.5 (3.5) n=52	-42.1 (2.3) n=113	-51.7 (3.1) n=65	0.0352
% patients reaching risk-based LDL-C goals at Week 24[†] - ITT population						**Interaction P-value**
POOL 1: ALI 150 mg Q2W vs PBO		9.0%	8.2%	73.9%	80.6%	0.7143
POOL 2: ALI 75/150 mg Q2W vs PBO		8.0%	5.2%	79.2%	72.1%	0.9130
POOL 3: ALI 75/150 mg Q2W vs EZE		62.7%	49.8%	77.4%	78.2%	0.0446
POOL 4: ALI 75/150 mg Q2W vs EZE		6.0%	2.2%	40.9%	38.7%	0.3652
% patients with TEAEs, SAEs and TEAEs leading to discontinuation						
TEAEs	PBO-controlled pools	83.2%	80.5%	78.1%	80.6%	
	EZE-controlled pools	68.2%	76.9%	69.2%	78.3%	
SAEs	PBO-controlled pools	10%	20.1%	9%	19.9%	
	EZE-controlled pools	2.8%	19.7%	4.2%	21.2%	
TEAEs leading to discontinuation	PBO-controlled pools	4.4%	6.2%	5.2%	6.7%	
	EZE-controlled pools	9.5%	11.3%	12.1%	8.9%	

Pool 1: LONG TERM and HIGH FH; Pool 2: COMBO I, FH I and FH II; Pool 3: COMBO II, OPTIONS I, OPTIONS II; Pool 4: MONO and ALTERNATIVE. Interaction *P*-value compares the difference in the endpoint (ALI vs control) for subgroups with/without clinical ASCVD.
Pools 1-3 were conducted with background statins; Pool 4 was conducted without background statins.
Risk-based goals of LDL-C <70 mg/dL for patients with clinical ASCVD (as defined by CHD, ischemic stroke, or PAD) and <100 mg/dL for those without clinical ASCVD.
ALI, alirocumab; ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; EZE, ezetimibe; ITT, intention-to-treat (analysis including all lipid values regardless of adherence to treatment); LDL-C, low-density lipoprotein; PAD, peripheral artery disease; PBO, placebo; SAE, serious adverse event; SD, standard deviation; SE, standard error, TEAE, treatment-emergent adverse event.