Effect of Alirocumab on Lipoprotein(a) Over ≥1.5 Years (from the Phase 3 ODYSSEY Program)

Daniel Gaudet, MD, PhD[a,*], Gerald F. Watts, DSc, MD, PhD[b], Jennifer G. Robinson, MD[c], Pascal Minini, PhD[d], William J. Sasiela, PhD[e], Jay Edelberg, MD, PhD[f], Michael J. Louie, MD[e], and Frederick J. Raal, PhD[g]

Elevated lipoprotein(a) [Lp(a)] is independently associated with increased cardiovascular risk. However, treatment options for elevated Lp(a) are limited. Alirocumab, a monoclonal antibody to proprotein convertase subtilisin/kexin type 9, reduced low-density lipoprotein cholesterol (LDL-C) by up to 62% from baseline in phase 3 studies, with adverse event rates similar between alirocumab and controls. We evaluated the effect of alirocumab on serum Lp(a) using pooled data from the phase 3 ODYSSEY program: 4,915 patients with hypercholesterolemia from 10 phase 3 studies were included. Eight studies evaluated alirocumab 75 mg every 2 weeks (Q2W), with possible increase to 150 mg Q2W at week 12 depending on LDL-C at week 8 (75/150 mg Q2W); the other 2 studies evaluated alirocumab 150-mg Q2W from the outset. Comparators were placebo or ezetimibe. Eight studies were conducted on a background of statins, and 2 studies were carried out with no statins. Alirocumab was associated with significant reductions in Lp(a), regardless of starting dose and use of concomitant statins. At week 24, reductions from baseline were 23% to 27% with alirocumab 75/150-mg Q2W and 29% with alirocumab 150-mg Q2W (all comparisons $p < 0.0001$ vs controls). Reductions were sustained over 78 to 104 weeks. Lp(a) reductions with alirocumab were independent of race, gender, presence of familial hypercholesterolemia, baseline Lp(a), and LDL-C concentrations, or use of statins. In conclusion, in addition to marked reduction in LDL-C, alirocumab leads to a significant and sustained lowering of Lp(a). **(Am J Cardiol 2017;119:40−46)**

Alirocumab, a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 (PCSK9), reduced low-density lipoprotein cholesterol (LDL-C) levels from baseline to 24 weeks by up to 62% versus controls in 10 phase 3 studies involving mainly patients at high cardiovascular (CV) risk, including those with previous CV events and those with heterozygous familial hypercholesterolemia (HeFH).[1−9] Previously, a pooled analysis of 3 alirocumab phase 2 studies reported median reductions in lipoprotein (a) [Lp(a)] of 30% after 8 to 12 weeks of treatment.[10] In individual phase 3 studies, alirocumab reduced Lp(a) by an average of 25% to 30% from baseline to week 24 in patients with HeFH and in non-FH patients.[4,8] The aim of the present analysis was to evaluate the maintenance of the Lp(a)-lowering effect with alirocumab over 24 to 104 weeks in a pooled analysis of 10 phase 3 studies (n = 4,915). Potential heterogeneity of treatment effect according to HeFH status and other baseline characteristics were also examined.

Methods

Data from 10 randomized, double-blind, phase 3, controlled trials were included in this analysis. Efficacy data were pooled into 4 groups according to alirocumab dose, comparator, and concomitant statin use (Figure 1). Two studies used an alirocumab dose of 150 mg every 2 weeks (Q2W). The other 8 studies started with alirocumab 75-mg Q2W that was increased to 150-mg Q2W at week 12 depending on achieved LDL-C at week 8 (indicated in the text as 75/150-mg Q2W). Comparators were placebo or ezetimibe. In 8 studies, patients received concomitant statin (with or without other lipid-lowering therapy). The statin was at maximally tolerated dose in 6 studies (atorvastatin 40 to 80 mg, rosuvastatin 20 to 40 mg, or simvastatin 80 mg daily, unless an investigator-approved reason was given for using a lower dose). All study protocols were approved by the relevant institutional review boards or independent ethics committees, and all patients provided written informed consent.

[a]Department of Medicine, ECOGENE-21 Clinical and Translational Research Center and Lipidology Unit, Université de Montréal, Chicoutimi, Quebec, Canada; [b]Lipid Disorders Clinic, Centre for Cardiovascular Medicine, Royal Perth Hospital, School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia; [c]University of Iowa, Iowa City, Iowa; [d]Biostatistics and Programming, Sanofi, Chilly-Mazarin, France; [e]Regeneron Pharmaceuticals, Inc., Tarrytown, New York; [f]Sanofi, Bridgewater, New Jersey; and [g]Faculty of Health Sciences, University of Witwatersrand, Johannesburg, South Africa. Manuscript received July 28, 2016; revised manuscript received and accepted September 7, 2016.

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See page 45 for disclosure information.

*Corresponding author: Tel: (418) 541-1077; fax: (418) 541-1139.
E-mail address: daniel.gaudet@umontreal.ca (D. Gaudet).

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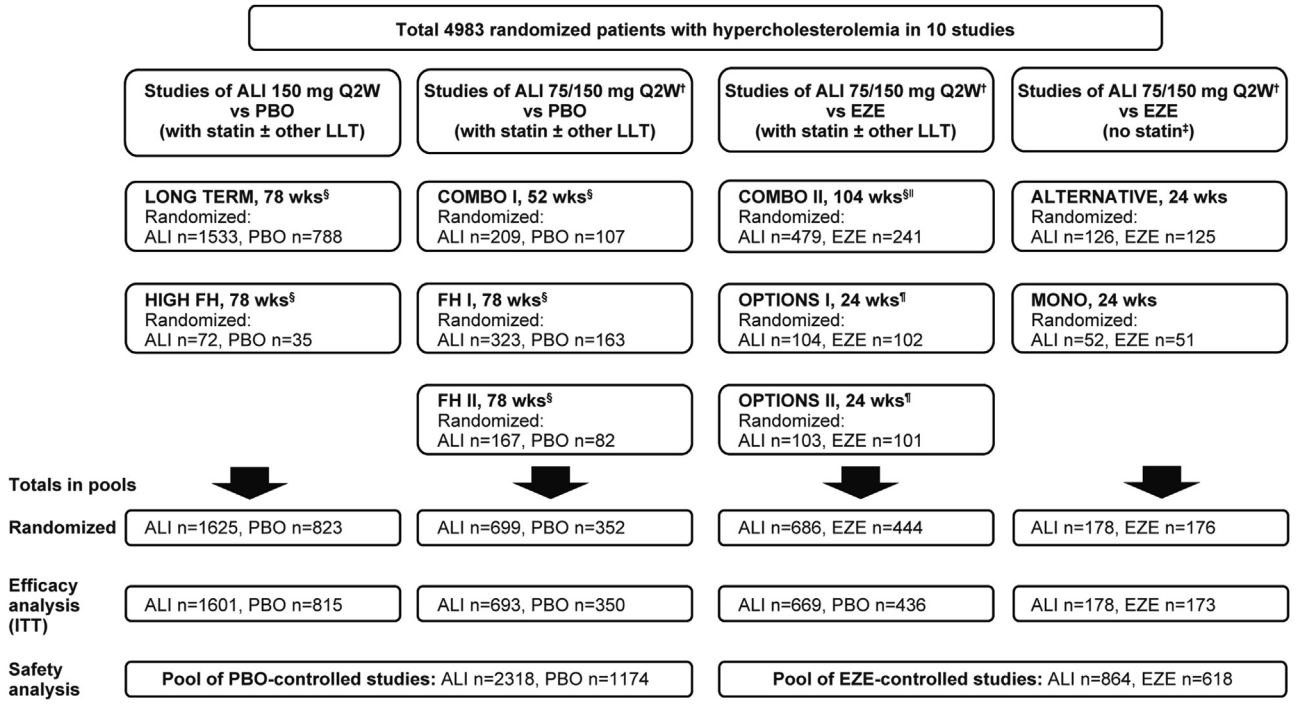

Figure 1. Overview of studies included in this analysis. All patients randomized to either ALI, PBO, or EZE were included. Patients randomized to the statin control arms in OPTIONS I, OPTIONS II, and ALTERNATIVE were not included in this analysis. The ITT population included all randomized patients with a baseline and at least one postbaseline LDL-C measurement, regardless of treatment adherence. The safety population includes all randomized patients who received at least one dose or part of a dose of study treatment. Supplementary Table 1 lists the number of patients in the efficacy and safety analysis for the individual studies. Study references and clinicaltrials.gov identifiers: LONG TERM, NCT01507831[8]; HIGH FH, NCT01617655[5]; FH I NCT01623115[4]; FH II, NCT01709500[4]; COMBO I, NCT01644175[6]; COMBO II, NCT01644188[2]; OPTIONS I, NCT01730040[1]; OPTIONS II, NCT01730053[3]; ALTERNATIVE, NCT01709513[7]; MONO, NCT01644474.[9] †75/150-mg Q2W indicates that the starting dose of 75-mg Q2W could be increased to 150-mg Q2W at week 12, if LDL-C was above prespecified levels at week 8. ‡Concomitant nonstatin LLT apart from ezetimibe allowed in ALTERNATIVE; no concomitant LLT allowed in MONO. §Concomitant statin at maximally tolerated doses (atorvastatin 40 to 80 mg, rosuvastatin 20 to 40 mg, or simvastatin 80 mg; lower doses were allowed with an investigator-approved reason). ‖No concomitant nonstatin LLT allowed in COMBO II. ¶Concomitant statin and doses were atorvastatin 20 or 40 mg in OPTIONS I and rosuvastatin 10 or 20 mg in OPTIONS II. ALI = alirocumab; EZE = ezetimibe; ITT = intention-to-treat; LLT = lipid-lowering therapy; PBO = placebo; Q2W = every 2 weeks.

Prespecified end points included percentage change in Lp(a) and LDL-C from baseline at week 12 (before potential dose adjustment) and week 24 (and weeks 52 to 104 for longer trials), analyzed using an intention-to-treat (ITT) approach that included all data regardless of adherence to treatment and also using only on-treatment data. Analytical methods and statistical analysis methods are described in the Supplementary Material.

Results

Patient numbers included in the analysis are shown in Figure 1 (further details for individual studies are listed in Supplementary Table 1). Baseline characteristics, including median Lp(a) levels, were generally similar between alirocumab and control groups within each of the 4 study pools (Table 1). There was a higher proportion of men in all groups (~60%), most patients were white (~90%; Table 1). Overall, median baseline Lp(a) levels were higher in patients with HeFH (26.0 mg/dl) versus non-FH (22.9 mg/dl; $p = 0.0004$; Supplementary Table 2). Median baseline Lp(a) levels were lower in studies performed without concomitant statin versus studies performed with statin ($p < 0.0001$; Supplementary Table 3). Furthermore, in an analysis of studies for which baseline PCSK9 levels were available, median baseline levels of free and total PCSK9 were lower in the MONO study (no statin) versus studies performed with statin ($p < 0.0001$; Supplementary Table 3). Correlation analyses suggested that higher baseline PCSK9 levels were associated with higher baseline Lp(a) levels (Supplementary Figure 1). Across the pools, ~30% of patients displayed Lp(a) >50 mg/dl at baseline (Table 1); baseline characteristics for these patients are listed in Supplementary Table 4. Baseline Lp(a) and LDL-C levels for the individual studies are listed in Supplementary Table 5.

Compared with placebo or ezetimibe, alirocumab significantly reduced Lp(a) and LDL-C from baseline at both weeks 12 and 24 in each pool (Table 2). Dose increase from 75 to 150 mg was associated with an additional 7.1% reduction in Lp(a) across studies performed with statins (Supplementary Table 6) although no additional effect was seen in studies performed without statin. Reductions in Lp(a) were maintained up to end of study in the 78-week and 104-week studies (Figure 2). Among patients with baseline Lp(a) ≥50 to <75 mg/dl, 47.1% to 61.7% of alirocumab-treated patients across the study pools achieved Lp(a) <50 mg/dl by week 24 (Supplementary Table 7).

Table 1
Baseline characteristics of all randomized patients in the 10 studies

Treatment groups	Placebo-controlled studies				Ezetimibe-controlled studies			
	Concomitant statin				Concomitant statin		No concomitant statin	
	Alirocumab 150 mg (n=1625)	Placebo (n=823)	Alirocumab 75/150 mg* (*n*=699)	Placebo (n=352)	Alirocumab 75/150 mg* (*n*=686)	Ezetimibe (n=444)	Alirocumab 75/150 mg* (*n*=178)	Ezetimibe (n=176)
Age (years), mean ± SD	60.0 ± 10.8	60.2 ± 10.6	55.6 ± 12.9	55.5 ± 12.5	61.6 ± 9.7	62.3 ± 9.7	63.1 ± 8.1	61.9 ± 9.1
Male	1018 (62.6%)	496 (60.3%)	397 (56.8%)	216 (61.4%)	483 (70.4%)	294 (66.2%)	98 (55.1%)	94 (53.4%)
White	1505 (92.6%)	760 (92.3%)	634 (90.7%)	312 (88.6%)	582 (84.8%)	385 (86.7%)	163 (91.6%)	163 (92.6%)
Black	54 (3.3%)	25 (3.0%)	36 (5.2%)	22 (6.3%)	39 (5.7%)	26 (5.9%)	11 (6.2%)	11 (6.3%)
Asian	15 (0.9%)	9 (1.1%)	10 (1.4%)	2 (0.6%)	39 (5.7%)	25 (5.6%)	2 (1.1%)	2 (1.1%)
American Indian or Alaska Native	28 (1.7%)	18 (2.2%)	4 (0.6%)	1 (0.3%)	6 (0.9%)	1 (0.2%)	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	1 (0.3%)	0	0	1 (0.6%)	0
Other	23 (1.4%)	11 (1.3%)	15 (2.1%)	14 (4.0%)	20 (2.9%)	7 (1.6%)	1 (0.6%)	0
Body mass index, (kg/m^2), mean ± SD	30.1 ± 5.7	30.5 ± 5.4	30.0 ± 5.5	30.1 ± 6.0	30.3 ± 5.9	30.7 ± 5.6	29.7 ± 6.4	28.4 ± 5.5
Heterozygous familial hypercholesterolemia	348 (21.4%)	174 (21.1%)	490 (70.1%)	245 (69.6%)	26 (3.8%)	18 (4.1%)	14 (7.9%)	25 (14.2%)
Cardiovascular risk level								
Very high	1451 (89.3%)	751 (91.3%)	438 (62.7%)	224 (63.6%)	601 (87.6%)	371 (83.6%)	73 (41.0%)	62 (35.2%)
High	174 (10.7%)	72 (8.7%)	261 (37.3%)	128 (36.4%)	85 (12.4%)	73 (16.4%)	29 (16.3%)	47 (26.7%)
Moderate	0	0	0	0	0	0	71 (39.9%)	65 (36.9%)
Concomitant medication								
Maximally tolerated statin	1625 (100.0%)	823 (100.0%)	699 (100.0%)	352 (100.0%)	479 (69.8%)	241 (54.3%)	0	0
High-intensity statin†	744 (45.8%)	367 (44.6%)	527 (75.4%)	266 (75.6%)	421 (61.4%)	260 (58.6%)	0	0
Lipid-lowering therapies other than statin	450 (27.7%)	225 (27.3%)	375 (53.6%)	205 (58.2%)	51 (7.4%)	41 (9.2%)	43 (24.2%)	48 (27.3%)
Aspirin	1019 (62.7%)	529 (64.3%)	349 (49.9%)	171 (48.6%)	481 (70.1%)	307 (69.1%)	80 (44.9%)	82 (46.6%)
Lipids, mean ± SD (mg/dL)								
Low-density lipoprotein cholesterol (Friedewald formula)	125.9 ± 45.9	125.3 ± 44.5	129.0 ± 47.3	130.3 ± 45.4	109.4 ± 35.6	105.0 ± 36.2	176.5 ± 66.8	177.4 ± 66.0
High-density lipoprotein cholesterol	49.8 ± 12.3	49.8 ± 12.4	50.5 ± 15.4	49.7 ± 14.4	48.0 ± 13.2	48.3 ± 13.1	50.5 ± 15.7	53.3 ± 16.3
Non-high-density lipoprotein cholesterol	155.8 ± 49.4	155.4 ± 48.6	155.5 ± 50.0	155.8 ± 48.4	139.3 ± 39.7	135.4 ± 41.8	211.7 ± 75.1	210.8 ± 77.4
Fasting triglycerides, median (Q1:Q3)	132.0 (93.8 : 182.3)	134.5 (94.7 : 188.5)	114.0 (85.0 : 161.0)	111.0 (86.0 : 156.0)	129.0 (96.0 : 185.0)	134.0 (97.0 : 187.0)	147.5 (105.0 : 218.0)	130.0 (89.5 : 201.5)
Apolipoprotein B	103.5 ± 28.9	103.3 ± 28.8	106.1 ± 29.3	105.6 ± 27.8	94.3 ± 23.0	92.3 ± 23.5	131.0 ± 38.7	128.6 ± 36.6
Apolipoprotein A-1	146.2 ± 25.1	146.7 ± 27.1	143.7 ± 27.3	142.5 ± 27.1	142.0 ± 23.8	142.7 ± 24.7	150.4 ± 26.3	153.9 ± 27.7
Lipopotein(a), median (Q1:Q3)	22.2 (7.7 : 66.1)	21.5 (6.7 : 66.8)	29.0 (10.0 : 81.0)	26.0 (8.0 : 75.0)	26.0 (8.0 : 74.0)	24.0 (10.0 : 61.0)	17.0 (6.0 : 44.5)	15.0 (7.0 : 39.0)
Distribution of Lipoprotein(a) baseline levels								
<30	896 (56.3%)	459 (56.6%)	340 (50.4%)	183 (53.4%)	353 (52.5%)	234 (54.0%)	112 (65.1%)	110 (65.9%)
≥30 to <50	190 (11.9%)	85 (10.5%)	91 (13.5%)	39 (11.4%)	69 (10.3%)	63 (14.5%)	22 (12.8%)	26 (15.6%)
≥50 to <75	172 (10.8%)	99 (12.2%)	62 (9.2%)	35 (10.2%)	83 (12.3%)	46 (10.6%)	17 (9.9%)	11 (6.6%)
≥75 to <100	123 (7.7%)	66 (8.1%)	65 (9.6%)	24 (7.0%)	64 (9.5%)	33 (7.6%)	10 (5.8%)	10 (6.0%)
≥100	211 (13.3%)	102 (12.6%)	117 (17.3%)	62 (18.1%)	104 (15.5%)	57 (13.2%)	11 (6.4%)	10 (6.0%)

SD = standard deviation.
* 75/150 mg indicates that the starting dose of 75-mg Q2W could be increased to 150-mg Q2W at week 12, if LDL-C had not decreased to predetermined levels at week 8.
† Atorvastatin 40 to 80 mg daily or rosuvastatin 20 to 40 mg daily.

Table 2
Percentage changes in plasma concentrations of Lp(a) and LDL-C from baseline to weeks 12 and 24 (intent-to-treat population analysis)

Treatment groups	Week 12			Week 24		
	Alirocumab	Control	Difference alirocumab vs. control	Alirocumab	Control	Difference alirocumab vs. control
Alirocumab 150 mg (n=1601) vs. placebo (n=815) with statin						
Lipoprotein(a)	−28.0 ± 0.7	−3.0 ± 0.9	−25.0 ± 1.2*	−29.1 ± 0.7	−4.0 ± 1.0	−25.1 ± 1.2*
Low-density lipoprotein cholesterol	−62.6 ± 0.7	1.1 ± 1.0	−63.8 ± 1.2*	−60.4 ± 0.7	0.5 ± 1.0	−60.9 ± 1.2*
Alirocumab 75/150 mg† (n=693) vs. placebo (n=350) with statin						
Lipoprotein(a)	−21.7 ± 0.9	−3.2 ± 1.3	−18.5 ± 1.6*	−25.0 ± 1.0	−7.7 ± 1.4	−17.4 ± 1.7*
Low-density lipoprotein cholesterol	−44.5 ± 1.0	4.1 ± 1.3	−48.6 ± 1.6*	−48.6 ± 1.0	4.2 ± 1.5	−52.7 ± 1.8*
Alirocumab 75/150 mg† (n=669) vs. ezetimibe (n=436) with statin						
Lipoprotein(a)	−22.0 ± 1.0	1.5 ± 1.3	−23.5 ± 1.7*	−27.1 ± 1.2	−5.3 ± 1.5	−21.8 ± 1.9*
Low-density lipoprotein cholesterol	−49.2 ± 1.2	−22.3 ± 1.5	−26.8 ± 1.9*	−48.9 ± 1.4	−19.3 ± 1.7	−29.6 ± 2.2*
Alirocumab 75/150 mg† (n=178) vs. ezetimibe (n=173) without statin						
Lipoprotein(a)	−20.1 ± 1.9	−7.3 ± 2.0	−12.9 ± 2.8*	−23.3 ± 2.0	−8.9 ± 2.1	−14.4 ± 2.9*
Low-density lipoprotein cholesterol	−47.4 ± 1.5	−16.7 ± 1.6	−30.7 ± 2.2*	−45.6 ± 1.8	−14.8 ± 1.8	−30.9 ± 2.6*

Data are adjusted mean percentage change ± standard error.
* p <0.0001 versus control.
† Dose was increased from 75 to 150 mg at week 12 in 43.9% and 17.7% of patients in the ezetimibe-controlled pools without and with concomitant statin, respectively, and in 34.2% of patients in the placebo-controlled pool.

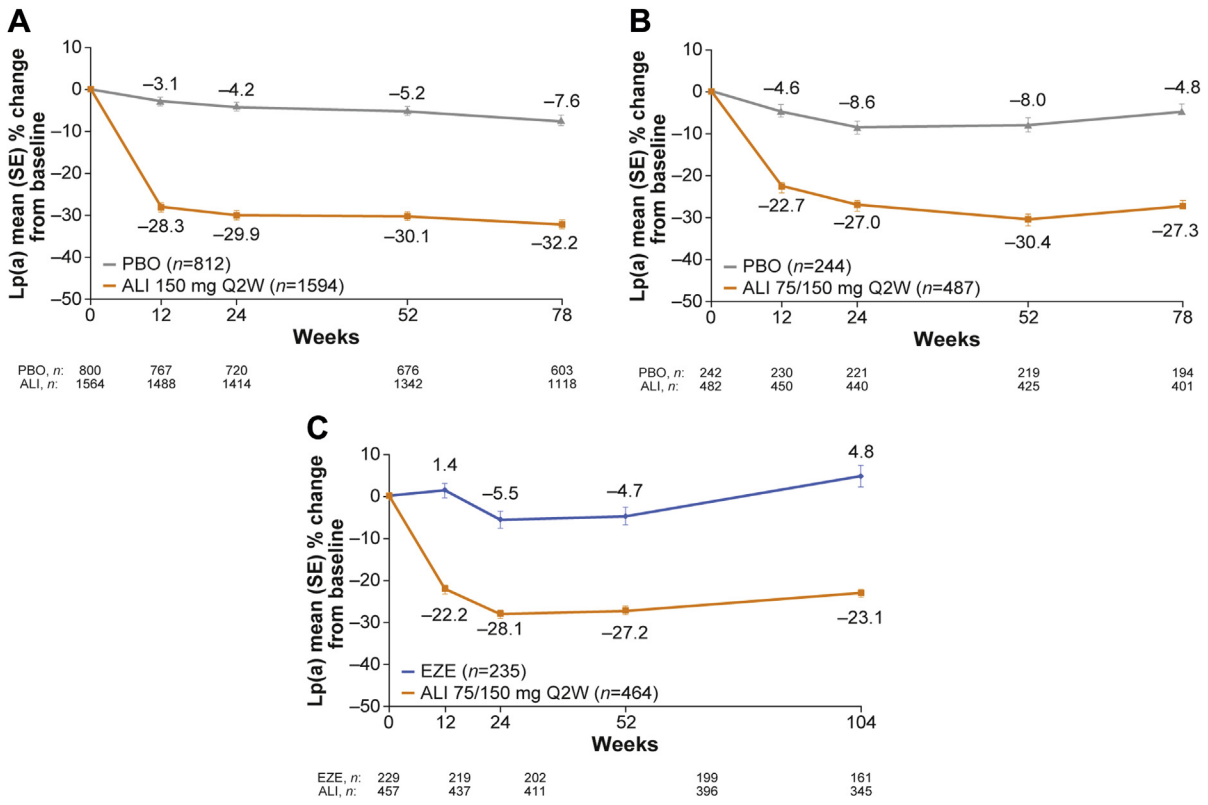

Figure 2. Adjusted mean percentage change in plasma Lp(a) concentration from baseline in *(A)* LONG TERM and HIGH FH; *(B)* FH I and FH II; and *(C)* COMBO II (on-treatment analysis). Values on charts above data points indicate percentage reduction from baseline. Values below the x-axes indicate the number of patients with data available at each time point. Missing data were accounted for by means of multiple imputation. ALI = alirocumab; EZE = ezetimibe; Lp(a) = lipoprotein(a); PBO = placebo; Q2W = every 2 weeks; SE = standard error.

In patients with HeFH from the FH I and FH II studies, Lp(a) was reduced from baseline by 26.9% at week 24 with alirocumab 75/150-mg Q2W versus 8.5% with placebo (mean difference −18.4%; p <0.0001; ITT analysis). Likewise, in patients with HeFH from LONG TERM and HIGH FH, Lp(a) decreased by 26.0% at week 24 in the alirocumab 150-mg Q2W group and by 2.8% in the placebo group (mean difference −23.3%; p <0.0001; ITT analysis).

Percentage Lp(a) reductions with alirocumab were consistent regardless of baseline Lp(a) or LDL-C levels

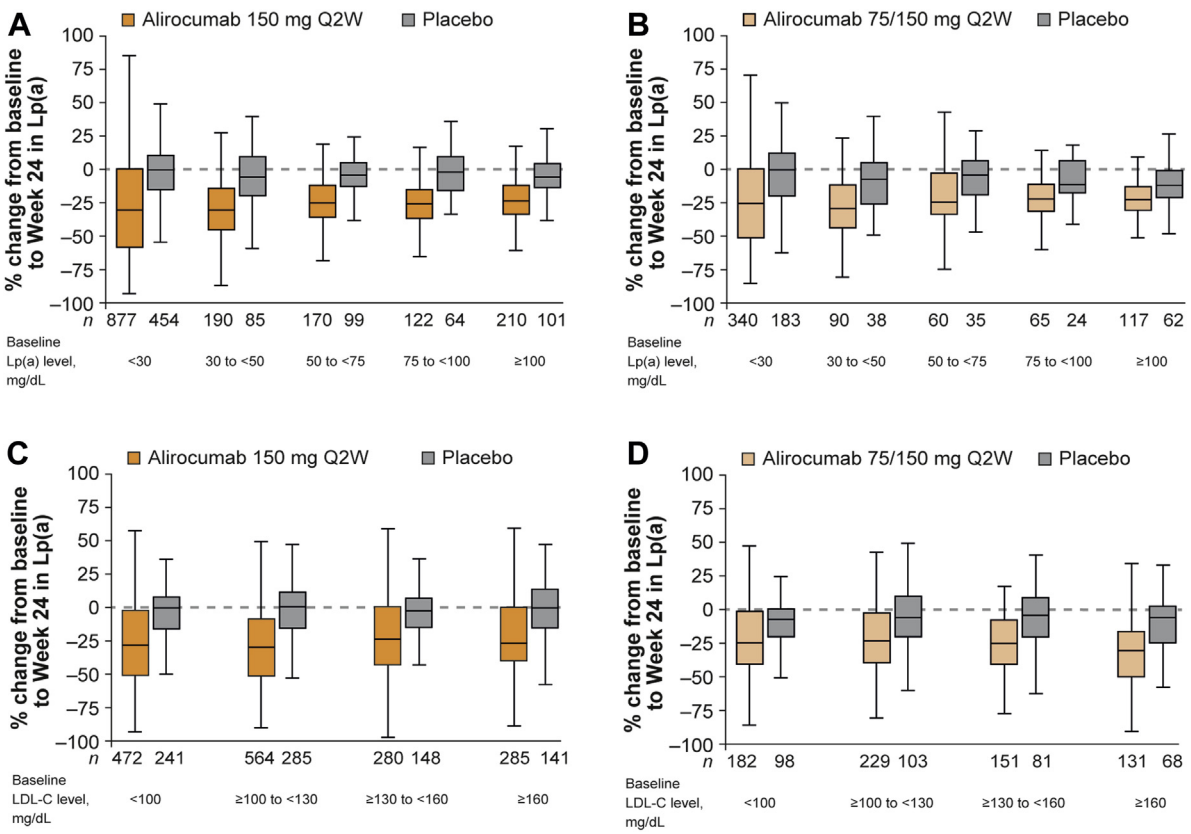

Figure 3. Percentage change in Lp(a) from baseline to week 24 according to baseline Lp(a) levels *(A)* and *(B)* and baseline LDL-C levels (*C* and *D*; placebo-controlled studies only; ITT analysis). Figures are Tukey boxplots: Central lines in boxes indicate median values, upper and lower regions of boxes indicate upper and lower quartiles, respectively, and ends of the upper and lower lines extending from boxes indicate the lowest and highest values still within 1.5 interquartile ranges of the lower and upper quartiles. Interaction p values comparing baseline Lp(a) and LDL-C groups were all >0.05.

(Figure 3). Greater percentage reductions in Lp(a) showed a moderate-to-low correlation with greater percentage reductions in LDL-C (Spearman's correlation coefficient: 0.307; Supplementary Figure 2). A moderate-to-low correlation between percentage reduction in Lp(a) versus LDL-C was also observed in patients with baseline Lp(a) ≥ or <50 mg/dl and in patients with and without HeFH (Supplementary Figures 3 and 4). Similarly, there was a significant trend for greater Lp(a) percentage reductions and lower achieved LDL-C levels (Supplementary Figure 5). Analysis of results by absolute change in Lp(a) levels gave similar results to the analysis by percentage change in Lp(a) (Supplementary Figures 6 and 7).

There was no significant difference in percentage Lp(a) reductions according to race (white vs other racial and ethnic groups); however, there were relatively few patients of other racial and ethnic origin compared with white patients (469 of 4,446; 10.5%; Supplementary Figure 8). There was no difference in percentage Lp(a) reduction either between men and women or by baseline aspirin use (Supplementary Figure 9).

Overall rates of treatment-emergent adverse events in the trials included in this analysis were similar between alirocumab and control patients (Supplementary Table 8). Of treatment-emergent adverse events occurring in ≥5% patients, those occurring in a higher proportion (≥0.5%) of alirocumab-treated patients versus placebo were nasopharyngitis, injection-site reaction, and influenza; in trials versus ezetimibe, these were upper respiratory tract infection, accidental overdose, and headache (Supplementary Table 8).

Discussion

Long-term prospective epidemiological studies reveal a continuous association between increasing Lp(a) levels and risk of coronary heart disease and stroke, independent of LDL-C or non−high-density lipoprotein cholesterol levels.[11] Elevated Lp(a) levels are also associated with increased risk of aortic valve stenosis.[12] European (European Society of Cardiology/European Atherosclerosis Society) and US (National Lipid Association) guidelines state that Lp(a) screening can be considered in high-risk patients such as those with FH.[13,14] In terms of treatment recommendations, statins have little effect on Lp(a), and other currently available treatment options are limited.[14,15] However, to date, there is no evidence from a controlled trial that lowering Lp(a) levels reduce CV events.[14−16]

The ODYSSEY program included a broad population of patients at high risk of atherosclerotic CV disease, who were not at LDL-C goals despite treatment with maximally tolerated statin in most studies. Patients had median Lp(a) levels ranging from 15 to 29 mg/dl, and 33% of them displayed baseline levels of ≥50 mg/dl, a level considered to put them at increased CV risk.[14] Across all study pools,

alirocumab significantly lowered Lp(a) and LDL-C from baseline levels (by 23.3% to 29.1% and 45.6% to 60.4%, respectively, at week 24), with reductions sustained for ≥78 weeks. Safety was comparable across alirocumab and control groups.

No difference in effect was observed across subgroups including race and gender. Certain segments of the population are known to have higher levels of Lp(a); for example, African-Americans and, to a lesser extent, patients of Hispanic origin.[14] However, our analysis was limited by the relatively low proportion of participants of other racial and ethnic origin (~10% overall) in the studies. Alirocumab significantly lowered Lp(a) levels in patients with HeFH, with reductions maintained up to 78 weeks. Although contentious, it has been suggested that patients with FH who are already at high risk of developing coronary heart disease may have particularly elevated levels of Lp(a).[17] In this pooled analysis, patients with HeFH had slightly higher median baseline levels of Lp(a) compared with the non-FH patients (26.0 vs 22.9 mg/dl).

In the current analysis, the percentage reductions in Lp(a) were not dependent on baseline levels of Lp(a) or LDL-C. A moderate-to-low correlation between greater percentage reductions in LDL-C and Lp(a) was found, which was stronger than that reported for the phase 2 analysis[10] but which does not account for all the variation observed. The exact mechanism(s) involved in the lowering of Lp(a) by alirocumab is still unclear and requires further investigation. Alirocumab is considered to reduce LDL-C by preventing PCSK9-mediated LDL receptor degradation, thereby increasing the number of LDL receptors available to remove LDL-C from the circulation.[18] Statins also reduce LDL-C by increasing the number of LDL receptors, but most studies have shown little effect of these agents on Lp(a), suggesting that Lp(a) is not cleared through the LDL receptor. It has been proposed that the LDL receptor may become an important route for Lp(a) catabolism following administration of a PCSK9 antibody, owing to a supraphysiological increase in the number of LDL receptors combined with the very low level of LDL-apolipoprotein (apo) B.[19] However, recent data strongly suggest a contribution of non-LDL receptor−mediated mechanisms in Lp(a) clearance. It was previously reported that 2 homozygous FH patients carrying null variants and no functioning LDL receptors showed significant reductions in Lp(a) but no change in LDL-C after treatment with evolocumab.[20] Non−LDL-receptor mechanisms for Lp(a) clearance are supported by recent in vitro studies, suggesting a role for sortilin (a type 1 sorting receptor) in both Lp(a) internalization by hepatocytes and apo(a) secretion.[21,22]

Statin treatment is known to increase PCSK9 levels,[23,24] and in the present analysis, we found a correlation between higher baseline Lp(a) and PCSK9 levels, and furthermore, baseline Lp(a) and PCSK9 levels were lower in studies performed without versus with statin. However, interpretation of this is limited because PCSK9 data were only available for one of the studies performed without statin (MONO), in which patients were at moderate CV risk[9]; other factors may be responsible for the difference in baseline Lp(a) levels between groups.

The consistent reductions in Lp(a) observed across the ODYSSEY studies expand the previous data set from alirocumab phase 2 studies, both in numbers of patients studied and demonstration of maintenance of effect up to 104 weeks,[10] suggesting that PCSK9 inhibition with alirocumab not only effectively lowers LDL-C but also has a substantial, sustained effect on Lp(a). Reductions in Lp(a) reported for evolocumab, another PCSK9 inhibitor, were broadly consistent with those observed with alirocumab.[25]

Long-term clinical benefit of alirocumab treatment on the incidence of major CV events is being assessed in the ODYSSEY OUTCOMES clinical study (ClinicalTrials.gov identifier: NCT01663402), and results may provide further insight into the impact of alirocumab-induced reductions in LDL-C and Lp(a) on CV risk. Furthermore, specific studies are underway or completed in nonwhite populations (NCT02289963; NCT02107898; NCT02584504[26]).

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Disclosures

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Supplementary Data

Supplementary data related with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2016.09.010.

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