

Efficacy and Safety of PCSK9 Inhibitors in Patients With Atherosclerotic Cardiovascular Disease at a Tertiary Hospital in the Northeast of Thailand

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Abstract

Background: Elevated low-density lipoprotein cholesterol (LDL-C) remains inadequately controlled in Thai patients with atherosclerotic cardiovascular disease (ASCVD) despite intensive statin-ezetimibe therapy. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors offer substantial LDL-C reduction, but real-world data from Thailand remain limited.

Objective: To evaluate the longitudinal effectiveness and safety of alirocumab and evolocumab in Thai patients with ASCVD.

Methods: This retrospective cohort study included 137 ASCVD patients initiating PCSK9 inhibitor therapy at Queen Sirikit Heart Center of the Northeast, Thailand (January 2021 to May 2024), with 12-month follow-up. Patients were grouped by treatment group (continued or switched), and LDL-C at baseline and months 3, 6, 9, and 12 was compared using a linear mixed-effects model. Target attainment (< 70 and < 55 mg/dL) was analyzed using generalized estimating equations.

Results: Mean (SD) age was 63.2 (9.9) years (66.4% male), and a total of 79.6% had chronic coronary syndrome. Mean baseline LDL-C was 155.4 mg/dL, decreasing to 56.3 mg/dL at month 3 and remaining stable through month 12 (55.2 mg/dL). LDL-C targets of < 70 and < 55 mg/dL were achieved in 65%-78% and 54%-69% of patients, respectively. Cardiovascular events occurred in 2 patients (1.4%), with no myocardial infarction or stroke. Adverse events occurred in 6.5% of patients, with no serious drug-related discontinuations. Switching between agents did not compromise lipid-lowering efficacy.

Conclusions: PCSK9 inhibitors were associated with sustained LDL-C reduction and infrequent adverse events among Thai ASCVD patients in real-world practice, supporting their effectiveness and the importance of treatment continuity and access.

Keywords: PCSK9 inhibitors, Alirocumab, Evolocumab, LDL-C, Atherosclerotic cardiovascular disease, Real-world study

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Introduction

Atherosclerotic cardiovascular disease (ASCVD) remains a leading cause of morbidity and mortality worldwide and in Thailand, with patients carrying substantial residual risk of recurrent events despite advances in preventive therapy.¹⁻⁴ Elevated low-density lipoprotein cholesterol (LDL-C) is causally linked to atherosclerotic progression,⁵⁻⁷ and current guidelines support the “lower-the-better” principle. The 2019 European Society of Cardiology/European Atherosclerosis Society guidelines recommend an LDL-C target

of < 55 mg/dL for very high-risk patients, whereas the 2018 American College of Cardiology/American Heart Association and Thai Acute Coronary Syndrome guidelines set a target of < 70 mg/dL for patients with established ASCVD.⁸⁻¹⁰ However, Thai data show only 26.5% of patients achieve recommended LDL-C targets,¹¹ consistent with international findings identifying statin intolerance and insufficient efficacy of high-intensity statin-ezetimibe therapy as major barriers to goal attainment.^{12, 13}

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, including evolocumab and alirocumab, reduce LDL-C by approximately 50%-60% through inhibition of LDL-C receptor degradation, and have demonstrated cardiovascular benefit in the FOURIER and ODYSSEY OUTCOMES trials, respectively.^{14, 15} However, outcomes observed in randomized controlled trials may not fully represent routine clinical practice in Thailand. Access to PCSK9 inhibitors may be influenced by medication cost, reimbursement and institutional eligibility criteria, drug availability, and long-term injectable therapy. In addition, long-term therapy may be affected by patients' perceptions, adherence and treatment sustainability. These factors may influence the magnitude and sustainability of LDL-C reduction and are not adequately captured in controlled trials. Although real-world studies from other countries have supported the effectiveness and tolerability of PCSK9 inhibitors,^{16, 17} longitudinal evidence from Thai patients remains limited, particularly regarding treatment patterns, nonstandard dosing intervals, switching between agents, and sustained LDL-C goal attainment.

Therefore, this study aimed to evaluate the longitudinal effectiveness and documented safety outcomes of alirocumab and evolocumab in Thai patients with ASCVD treated at a tertiary cardiac center. LDL-C levels were assessed at baseline and at 3, 6, 9, and 12 months. The study also examined real-world treatment patterns, including continuation of PCSK9 inhibitor therapy and agent switching, to provide evidence relevant to lipid management within the Thai healthcare setting.

Methods

Study Design and Population

This retrospective descriptive cohort study reviewed medical records of patients with ASCVD who newly received PCSK9 inhibitor therapy at Queen Sirikit Heart Center of the Northeast, Thailand, between 1 January 2021 and 31 May 2024. Evolocumab has been available at this center since February 2020, and alirocumab since May 2022. All patients were followed for 12 months to evaluate long-term effectiveness and safety.

Patients were eligible if they met all of the following criteria, including age ≥ 18 years, newly initiated PCSK9 inhibitor therapy either as monotherapy for dyslipidemia or in combination with other lipid-lowering agents, received at least one dose of PCSK9 inhibitors with documented follow-up during the study period, and at least one posttreatment lipid profile available.

Patients were excluded if medical records were incomplete, missing, or unretrievable, or a documented contraindication to PCSK9 inhibitor therapy was present.

Operational Definitions

ASCVD was defined as a history of acute coronary syndrome, myocardial infarction, stable coronary artery disease, stable/unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack, peripheral artery disease, or atherosclerotic aortic disease.⁹

Statin intolerance was operationally defined as the inability to tolerate at least 2 different statins due to muscle-related adverse effects that improved or resolved upon discontinuation or dose reduction.¹⁵

High-intensity statin was defined as atorvastatin 40-80 mg or rosuvastatin 20-40 mg daily; moderate-intensity statin referred to atorvastatin 10-20 mg, rosuvastatin 5-10 mg, simvastatin 20-40 mg, or pitavastatin 2-4 mg daily.⁹

Recurrent major adverse cardiac events were defined as cardiovascular death, recurrent myocardial infarction, rehospitalization for cardiovascular causes, repeat coronary revascularization, or ischemic stroke occurring during follow-up.⁹

Study Outcomes

The primary outcome was the percentage change in LDL-C from baseline at months 3, 6, 9, and 12. Secondary outcomes included the proportion of patients achieving LDL-C targets of < 70 mg/dL and < 55 mg/dL at each time point and the composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization, respectively.

Safety outcomes were assessed by reviewing medical records at each follow-up period and included treatment-emergent adverse events, serious adverse events, and predefined events of interest (injection-site reactions, myalgia/muscle-related events, hepatotoxicity, and new-onset diabetes mellitus).

Statistical Analysis

Continuous variables are presented as mean (SD) or median (IQR), as appropriate based on distribution (Shapiro-Wilk test); categorical variables are summarized as frequencies and percentages. Baseline characteristics among the treatment groups (continued alirocumab, continued evolocumab, alirocumab then switch, and evolocumab then switch) were compared using one-way analysis of variance or the Kruskal-Wallis test for continuous variables, and the chi-square or Fisher exact test for categorical variables.

Longitudinal changes in LDL-C and other lipid parameters were analyzed using a linear mixed-effects model, with group, time, and group-by-time interaction as fixed effects and a subject-specific random intercept to account for within-subject correlation. Missing data were handled under a missing-at-random assumption.

The proportions of patients achieving LDL-C targets (< 70 and < 55 mg/dL) at each time point, a prespecified secondary outcome, were summarized by group with 95% CIs. For continued alirocumab, continued evolocumab, alirocumab then switch, generalized estimating equations (GEE) models estimated adjusted odds ratios (ORs), 95% CIs, and *P* values, including group-by-time interaction terms; the evolocumab then switch was reported descriptively due to its small sample size and complete separation.

Exploratory analysis of switching subgroups based on divergent longitudinal LDL-C trajectories observed during data exploration, an exploratory comparison of the magnitude and trajectory of LDL-C reduction between the alirocumab then switch and evolocumab then switch was performed using estimated marginal means with Bonferroni adjustment. This comparison was not among the prespecified primary or secondary outcomes and was undertaken to characterize observed real-world switching patterns; findings should therefore be interpreted as hypothesis-generating rather than confirmatory.

All tests were 2-sided, with *P* < .05 considered statistically significant. Analyses were performed using SPSS, version 29.0 (IBM Corp).

Results

Patient and Lesion Characteristics

The baseline characteristics of the 137 patients were determined (Table 1). The study population comprised 31 patients who continued alirocumab, 79 continued evolocumab, 21 alirocumab then switch, and 6 evolocumab then switch. Overall, the mean (SD) age was 63.2 (9.9) years and 66.4% were male. Most had chronic coronary syndrome (79.6%), and prior coronary revascularization was frequent, with 63.5% had undergone percutaneous coronary intervention (PCI) and 29.2% coronary artery bypass grafting. Cardiometabolic comorbidities were common (type 2 diabetes 34.3%, dyslipidemia 67.2%, and hypertension 51.1%), indicating a very high cardiovascular risk profile.

Most patients received high-intensity statins (77.4%) and ezetimibe (89.8%), as well as guideline-directed cardiovascular therapies, including aspirin (81%), P2Y12 inhibitors (61.3%), and β -blockers (74.5%). Median LDL-C remained elevated at 144 mg/dL despite intensive lipid-lowering therapy.

The only statistically significant difference among the treatment groups was the proportion of patients with a history of PCI, which was highest in the alirocumab then switch group (85.7%), followed by the evolocumab then switch group (83.3%), the continued alirocumab group (77.4%), and the continued evolocumab group (50.6%) ($P = .003$). No significant between-group differences were observed in age, sex, cardiovascular risk factors, background lipid-lowering therapy, baseline LDL-C levels, or other laboratory parameters (Supplementary S1).

The reasons for initiation and the dosage interval of PCSK9 inhibitors at initiation were determined (Table 2). Most patients started PCSK9 inhibitor therapy because of very high-risk ASCVD, particularly disease involving multiple vascular bed involvement (73.7%) and recurrent ASCVD events (24.8%). Statin intolerance due to myositis (16.1%) or hepatitis (5.8%) and familial hypercholesterolemia (11.7%) were additional key indications. Familial hypercholesterolemia was significantly more prevalent in the continued alirocumab and evolocumab then switch subgroups ($P = .005$). At initiation, 82.5% of patients received subcutaneous injections every 2 weeks, with significant variation among groups ($P = .01$) (nonrecommended dosing intervals are detailed in Supplementary S2).

Table 1. Baseline Characteristics of Patients Receiving PCSK9 Inhibitors

Characteristic	No. (%)					P Value
	Overall (N = 137)	Continued Alirocumab (n = 31)	Continued Evolocumab (n = 79)	Alirocumab Then Switch (n = 21)	Evolocumab Then Switch (n = 6)	
Age, mean (SD), y	63.2 (9.9)	59.0 (12.2)	64.9 (9.3)	63.0 (8.2)	59.5 (3.1)	.06
Male, No. (%)	91 (66.4)	19 (61.3)	56 (70.9)	12 (57.1)	4 (66.7)	.60
Body weight, median (IQR), kg	66.3 (58.6-74.8)	66.7 (58.3-76.0)	67.0 (60.0-74.5)	61.0 (53.9-68.6)	66.5 (49.0-71.7)	.20
BMI, median (IQR), kg/m ²	25.0 (22.5-27.6)	25.5 (22.7-27.6)	24.9 (22.5-27.8)	24.6 (22.4-26.6)	24.0 (20.2-26.4)	.50
Systolic BP, mean (SD), mmHg	132.8 (18.6)	128.9 (15.6)	135.3 (20.0)	131.0 (16.6)	126.0 (18.0)	.29

Table 1. Baseline Characteristics of Patients Receiving PCSK9 Inhibitors (Continued)

Characteristic	No. (%)					P Value
	Overall (N = 137)	Continued Alirocumab (n = 31)	Continued Evolocumab (n = 79)	Alirocumab Then Switch (n = 21)	Evolocumab Then Switch (n = 6)	
Diastolic BP, mean (SD), mmHg	77.0 (10.2)	76.7 (11.2)	77.7 (9.7)	76.4 (9.5)	72.2 (14.8)	.60
Medical history and cardiovascular risk factors						
Acute coronary syndrome	19 (13.9)	6 (19.4)	9 (11.5)	3 (14.3)	1 (16.7)	.62
Chronic coronary syndrome	109 (79.6)	23 (74.2)	64 (81.0)	17 (81.0)	5 (83.3)	.87
Post-PCI	87 (63.5)	24 (77.4)	40 (50.6)	18 (85.7)	5 (83.3)	.003
Post-CABG	40 (29.2)	5 (16.1)	29 (36.7)	6 (28.6)	0	.07
Type 2 diabetes mellitus	47 (34.3)	12 (38.7)	26 (32.9)	5 (23.8)	4 (66.7)	.23
Dyslipidemia	92 (67.2)	23 (74.2)	48 (60.8)	18 (85.7)	3 (50.0)	.10
Hypertension	70 (51.1)	16 (51.6)	41 (51.9)	11 (52.4)	2 (33.3)	.85
Stroke	3 (2.2)	1 (3.2)	1 (1.3)	1 (4.8)	0	.43
Chronic kidney disease	16 (11.7)	2 (6.5)	10 (12.7)	3 (14.3)	1 (16.7)	.64
Current smoke	3 (2.2)	0	2 (2.5)	0	1 (16.7)	.22
Prior medications						
Lipid-modifying medications						
High intensity statin	106 (77.4)	25 (80.6)	59 (74.7)	17 (81)	5 (83.3)	.85
Moderate intensity statin	17 (12.4)	3 (9.7)	12 (15.2)	1 (4.8)	1 (16.7)	.52
Low intensity statin	3 (2.2)	0	3 (3.8)	0	0	.77
Ezetimibe	123 (89.8)	27 (87.1)	72 (91.1)	18 (85.7)	6 (100.0)	.74
Cardiovascular medications						
Aspirin	111 (81.0)	24 (77.4)	64 (81.0)	18 (85.7)	5 (83.3)	.93
P2Y12 inhibitor	84 (61.3)	21 (67.7)	44 (55.7)	14 (66.7)	5 (83.3)	.38
β-blocker	102 (74.5)	21 (67.7)	57 (72.2)	19 (90.5)	5 (83.3)	.26
ACE inhibitor or ARB or ARNI	73 (53.3)	16 (51.6)	44 (55.7)	11 (52.4)	2 (33.3)	.76
Antidiabetes drug	56 (40.9)	15 (48.4)	31 (39.2)	7 (33.3)	3 (50.0)	.68

Table 1. Baseline Characteristics of Patients Receiving PCSK9 Inhibitors (Continued)

	No. (%)					
Characteristic	Overall (N = 137)	Continued Alirocumab (n = 31)	Continued Evolocumab (n = 79)	Alirocumab Then Switch (n = 21)	Evolocumab Then Switch (n = 6)	P Value
Laboratory parameters						
LDL-C, median (IQR), mg/dL	144.0 (106.5-189.5)	168.0 (133.0-216.0)	136.0 (106.0-180.0)	141.0 (97.5-182.5)	184.5 (98.8-203.5)	.16
HDL-C, median (IQR), mg/dL	48.0 (40.5-55.0)	48.0 (37.8-51.8)	48.0 (41.5-55.5)	50.5 (43.8-57.8)	39.0 (29.8-56.3)	.42
Triglycerides, median (IQR), mg/dL	132.0 (101.0-203.5)	152.0 (113.8-222.3)	126.0 (98.0-178.5)	133.5 (83.5-217.0)	178.5 (130.0-276.3)	.26
Total cholesterol, median (IQR), mg/dL	209.0 (160.5-253.0)	226.5 (184.8-285.0)	188.0 (159.5-241.5)	208.0 (157.0-239.8)	255.0 (147.0-291.5)	.17

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCI, percutaneous coronary intervention; PCSK9, proprotein convertase subtilisin/kexin type 9.

Table 2. Reason and Dosage Interval for PCSK9 Inhibitors at Initiation

Variable	No. (%)					P Value
	Overall (N = 137)	Continued Alirocumab (n = 31)	Continued Evolocumab (n = 79)	Alirocumab Then Switch (n = 21)	Evolocumab Then Switch (n = 6)	
Reasons for initiation of PCSK9 inhibitors*						
ASCVD with multiple vascular bed involvement	101 (73.7)	22 (71)	56 (70.9)	19 (90.5)	4 (66.7)	.30
ASCVD with multiple attack	34 (24.8)	7 (22.6)	21 (26.6)	4 (19)	2 (33.3)	.84
Statin intolerance (myositis)	22 (16.1)	4 (12.9)	16 (20.3)	1 (4.8)	1 (16.7)	.34
Statin intolerance (hepatitis)	8 (5.8)	0	4 (5.1)	3 (14.3)	1 (16.7)	.07
Familial hypercholesterolemia	16 (11.7)	8 (25.8)	4 (5.1)	2 (9.5)	2 (33.3)	.005
Dosage interval for PCSK9 inhibitors at initiation						
Subcutaneous every 2 wk	113 (82.5)	31 (100)	56 (70.9)	20 (95.2)	6 (100)	.01

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; PCSK9, proprotein convertase subtilisin/kexin type 9.

* Reason for initiation was determined using a hospital appropriateness assessment form approved by the Pharmacy and Therapeutics Committee in March 2020 and based on criteria derived from the FOURIER trial.

The estimated marginal means of LDL-C over 12 months derived from a linear mixed-effects model. In the overall cohort, LDL-C declined from 155.4 mg/dL at baseline to 56.3 mg/dL at month 3 and remained substantially lower than baseline throughout the follow-up, with values of 73.3, 75.3, and 55.2 mg/dL at months 6, 9, and 12, respectively.

A similar pattern of rapid LDL-C reduction followed by sustained control was observed across all treatment groups. Continued evolocumab was associated with consistently lower LDL-C levels compared with continued alirocumab throughout follow-up. The alirocumab then switch achieved comparable or even lower LDL-C levels than continued evolocumab from month 6 onward, whereas the evolocumab then switch ($n = 6$) showed more variable estimates, with higher values at months 6 and 9 that likely reflect the small sample size rather than a true treatment effect, as evidenced by the wide 95% CIs (60.5-165.8 mg/dL at month 9) (Table 3).

The time effect was statistically significant ($P < .001$), whereas the group effect ($P = .12$) and group $\times$ time interaction ($P = .61$) were not significant, indicating that the pattern of LDL-C reduction over time did not meaningfully differ across the treatment groups. These findings indicate that PCSK9 inhibitor therapy, whether continued or switched, achieved robust and durable LDL-C lowering in this very high-risk population.

The longitudinal patterns of LDL-C according to treatment group are illustrated (Figure 1). All treatment groups demonstrated a marked initial reduction in LDL-C at month 3. The fluctuations were observed in the continued alirocumab group and, particularly, in the small evolocumab then switch group. The latter group had an estimated marginal mean LDL-C level of 113.2 mg/dL at month 9 before declining to 52 mg/dL at month 12. However, this apparent fluctuation should be interpreted cautiously because the group included only 6 patients and therefore had relatively large standard errors.

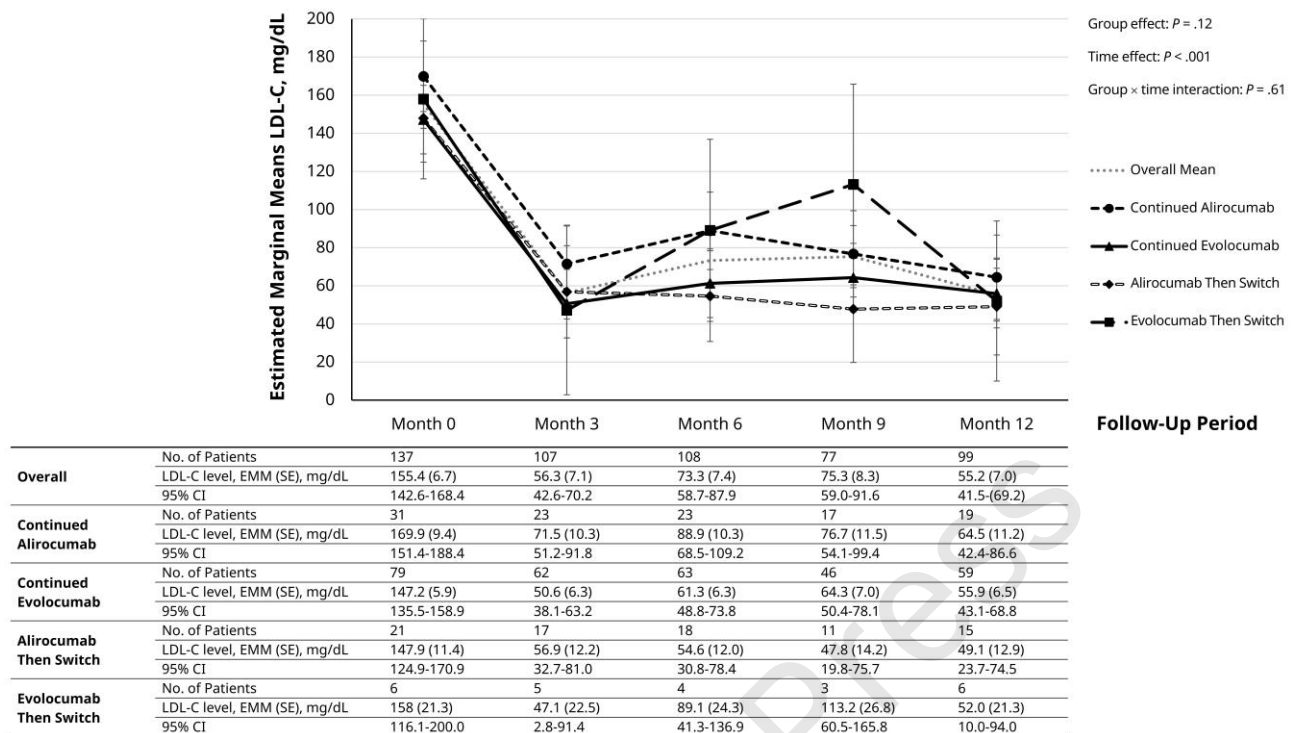
Other lipid parameters showed variable patterns of change over follow-up (Supplementary S3). Triglycerides decreased significantly over time ($P = .03$) and total cholesterol showed a borderline reduction ($P = .05$), but neither differed by treatment group nor showed a significant group-by-time interaction (all $P > .05$). High-density lipoprotein cholesterol (HDL-C) remained stable throughout follow-up (all $P > .05$). Unlike the group-dependent LDL-C reduction described above, changes in these parameters were generally consistent across treatment groups. Consistent with these absolute LDL-C values, the percent reduction in LDL-C from baseline ranged from approximately 42.6% to 71.2% across treatment groups and follow-up time points, with reductions generally sustained through month 12 (Supplementary S4). These findings indicated that PCSK9 inhibitor therapy, whether continued or switched, achieved robust and durable LDL-C lowering in this very high-risk population.

Table 3. Estimated Marginal Means of LDL-C by Treatment Group and Follow-Up Period From Linear Mixed-Effects Model

Follow-Up Period	Estimated Marginal Means (95% CI) of LDL-C, mg/dL				
	Overall (N = 137)	Continued Alirocumab (n = 31)	Continued Evolocumab (n = 79)	Alirocumab Then Switch (n = 21)	Evolocumab Then Switch (n = 6)
Month 0	155.4 (142.6-168.4)	169.9 (151.4-188.4)	147.2 (135.5-158.9)	147.9 (124.9-170.9)	158.0 (116.1-200.0)
Month 3	56.3 (42.6-70.2)	71.5 (51.2-91.8)	50.6 (38.1-63.2)	56.9 (32.7-81.0)	47.1 (2.8-91.4)
Month 6	73.3 (58.7-87.9)	88.9 (68.5-109.2)	61.3 (48.8-73.8)	54.6 (30.8-78.4)	89.1 (41.3-136.9)
Month 9	75.3 (59-91.6)	76.7 (54.1-99.4)	64.3 (50.4-78.1)	47.8 (19.8-75.7)	113.2 (60.5-165.8)
Month 12	55.2 (41.5-69.2)	64.5 (42.4-86.6)	55.9 (43.1-68.8)	49.1 (23.7-74.5)	52.0 (10.0-94.0)

Abbreviation: LDL-C, low-density lipoprotein cholesterol.

Figure 1. Estimated Marginal Means LDL-C by Treatment Group at Each Follow-Up Period



Abbreviations: EMM, estimated marginal mean from the linear mixed-effects model; LDL-C, low-density lipoprotein cholesterol; SE, standard error.

Attainment of the LDL-C target of < 70 mg/dL ranged from 65% to 78% across the follow-up periods, while attainment of the more stringent target of < 55 mg/dL ranged from 54% to 69% (Table 4). For both thresholds, the lowest attainment rate was observed at month 6, with recovery to near-baseline levels by months 9 and 12. Target attainment (< 70 mg/dL for LDL-C) varied by treatment group, ranging from 50% to 81% among patients who continued evolocumab or alirocumab and 74% to 84% among those who switched from alirocumab. The evolocumab then switch ($n = 6$) showed the greatest variability (0%-83.3% for < 70 mg/dL; 0%-66.7% for < 55 mg/dL) and was excluded from multivariable modeling owing to its small sample size.

In the multivariable-adjusted GEE model, the odds of target attainment did not differ significantly between patients who continued evolocumab and those who continued alirocumab, or between the alirocumab then switch and the continued alirocumab reference group, for either the < 70 mg/dL threshold (adjusted OR [95% CI], 1.38 [0.67-2.85]; $P = .38$ and 1.68 [0.61-4.63]; $P = .32$) or the < 55 mg/dL threshold (adjusted OR [95% CI], 0.93 [0.47-1.85]; $P = .83$ and 1.20 [0.43-3.3]; $P = .70$). Neither the group effect nor the group $\times$ time interaction reached statistical significance for either threshold (all $P \geq .53$).

Clinical Events

During the 12-month follow-up period, clinical events were infrequent, occurring in 2 of 137 patients (1.4%), consisting of one death (0.7%) and one coronary revascularization (0.7%) (Table 5). No cases of myocardial infarction, stroke, or hospitalization for unstable angina

were observed. Given the small number of events, no meaningful between-group comparison of the composite cardiovascular outcome could be performed.

Safety

Adverse drug reactions associated with PCSK9 inhibitor therapy were determined. A total of 9 adverse events (6.5%) were reported among 137 patients, the most common being myalgia or muscle-related events (3 patients [2.2%]), followed by local injection-site reactions (2 patients [1.5%]). Other reported events, each occurring in a single patient (0.7%), included dizziness/vertigo/tinnitus, lower limb numbness, generalized allergic reaction, and gastrointestinal irritation (Table 6). No serious or life-threatening adverse events were reported during the follow-up period.

Table 4. Proportion of Patients Achieving LDL-C Targets Over Time (GEE-Adjusted Analysis)

Parameter	No. (%)				GEE Model <i>P</i> Value (Group/Time/Interaction) ^a	Adjusted OR (95% CI) ^b	<i>P</i> Value ^b
	Month 3	Month 6	Month 9	Month 12			
Panel A: Patients Achieving LDL-C < 70 mg/dL							
Overall (N = 137)	83 (78.0)	68 (65.0)	53 (69.0)	74 (76.0)	NA	NA	NA
Treatment group	NA	NA	NA	NA	.57/.13/.53	NA	NA
Continued alirocumab (n = 31)	16 (74.0)	10 (50.0)	12 (74.0)	13 (73.0)	NA	1 [Reference]	NA
Continued evolocumab (n = 79)	50 (81.0)	45 (72.0)	31 (65.0)	44 (74.0)	NA	1.38 (0.67-2.85)	.38
Alirocumab then switch (n = 21)	13 (75.0)	13 (74.0)	9 (84.0)	12 (83.0)	NA	1.68 (0.61-4.63)	.32
Evolocumab then switch (n = 6)	4 (80.0)	0	1 (33.3)	5 (83.3)	NA ^c	NA ^c	NA ^c
Panel B: Patients Achieving LDL-C < 55 mg/dL							
Overall (N = 137)	74 (69.0)	57 (54.0)	45 (58.0)	60 (61.0)	NA	NA	NA
Treatment group	NA	NA	NA	NA	.75/.07/.62	NA	NA
Continued alirocumab (n = 31)	16 (73.0)	9 (44.0)	10 (62.0)	12 (67.0)	NA	1 [Reference]	NA
Continued evolocumab (n = 79)	42 (67.0)	37 (58.0)	26 (54.0)	35 (58.0)	NA	0.93 (0.47-1.85)	.83
Alirocumab then switch (n = 21)	12 (69.0)	11 (63.0)	8 (75.0)	9 (62.0)	NA	1.20 (0.43-3.35)	.70
Evolocumab then switch (n = 6)	4 (80.0)	0	1 (33.3)	4 (66.7)	NA ^c	NA ^c	NA ^c

Abbreviations: GEE, generalized estimating equations; LDL-C, low-density lipoprotein cholesterol; NA, not applicable.

^a *P* values were derived from a GEE model with a logit link and exchangeable correlation structure, specifying treatment group, time, and group × time interaction as fixed effects. The time effect was tested separately for each LDL-C threshold (< 70 and < 55 mg/dL). Neither the group effect nor the group × time interaction reached statistical significance for either threshold, indicating that the temporal pattern of target attainment did not differ meaningfully across treatment groups.

^b Adjusted for baseline LDL-C level, age, sex, and post PCI. Continued alirocumab served as the reference group.

^c The evolocumab then switch (n = 6) was excluded from the multivariable logistic regression model owing to the small sample size and resultant model instability. Findings for this subgroup are presented descriptively only (see percentages above) and should not be interpreted as evidence of reduced treatment effectiveness following the switch.

Table 5. Clinical Events During the 12-Month Follow-Up Period

Clinical Event	No. (%)				
	Overall (N = 137)	Continued Alirocumab (n = 31)	Continued Evolocumab (n = 79)	Alirocumab Then Switch (n = 21)	Evolocumab Then switch (n = 6)
All-cause death	1 (0.7)	1 (3.2)	0	0	0
Revascularization	1 (0.7)	0	1 (1.3)	0	0
Total	2 (1.4)	1 (3.2)	1 (1.3)	0	0

Table 6. Adverse Drug Reactions Associated With PCSK9 Inhibitor Therapy

Adverse Event	No. (%)				
	Overall (N = 137)	Continued Alirocumab (n = 31)	Continued Evolocumab (n = 79)	Alirocumab Then Switch (n = 21)	Evolocumab Then Switch (n = 6)
Local injection-site reaction	2 (1.5)	0	0	2 (9.5)	0
Myalgia/muscle-related event	3 (2.2)	1 (3.2)	2 (2.5)	0	0
Dizziness, vertigo, tinnitus	1 (0.7)	0	1 (1.3)	0	0
Lower limb numbness	1 (0.7)	0	1 (1.3)	0	0
General allergic reaction	1 (0.7)	0	1 (1.3)	0	0
Gastrointestinal irritation	1 (0.7)	0	1 (1.3)	0	0
Total	9 (6.5)	1 (3.2)	6 (7.7)	2 (9.5)	0

Discussion

This real-world study demonstrated that treatment with PCSK9 inhibitors (alirocumab and evolocumab) in Thai patients with ASCVD at a tertiary cardiac center achieved rapid and sustained LDL-C reduction throughout 12-month follow-up. LDL-C decreased from 155.4 mg/dL at baseline to 56.3 mg/dL at month 3, remaining significantly reduced through 12 months. These findings align with the FOURIER trial, which reported a 59% LDL-C reduction with evolocumab¹⁴ and the ODYSSEY LONG TERM trial, which demonstrated a 61% reduction with alirocumab.¹⁸ Overall, these findings suggested that the real-world LDL-C-lowering efficacy observed in Thai patients is comparable to that reported in controlled trial settings, despite treatment heterogeneity in the routine practice.

Regarding LDL-C target attainment, 65%-78% of patients achieved LDL-C < 70 mg/dL, while 54%-69% achieved the stricter target of < 55 mg/dL across follow-up. These rates were slightly lower than those reported in the network meta-analysis by Toth et al.¹⁹ This difference may reflect real-world treatment adjustments, including dose interval extension or temporary discontinuation after reaching target LDL-C, as well as reimbursement restrictions and financial or access barriers that may have limited continuation of therapy (Supplementary S5). Such individualized management in routine clinical practice, in contrast to the fixed dosing schedules used in randomized trials, may have contributed to greater variability in sustained LDL-C control.

In the switching subgroup analyses, no clear difference in LDL-C trajectory was observed. The evolocumab then switch was very small (n = 6) and showed marked fluctuations; therefore, any apparent differences between switch patterns should be interpreted cautiously.

Possible explanations include unmeasured post-switch adherence, device familiarity, or differences in drug access. Because this was a retrospective analysis, the reasons for these patterns could not be determined.

Clinical outcomes were favorable, with cardiovascular events occurring in only 2 of 137 patients (1.4%), including one death and one repeat revascularization, and no cases of myocardial infarction, stroke, or hospitalized unstable angina. Although these findings are reassuring, the small number of events precludes meaningful between-group comparisons. Larger long-term real-world studies are needed to further evaluate clinical outcomes,²⁰ particularly in Thai populations.

Safety outcomes were generally comparable across groups, with an overall adverse event rate of 6.5%, primarily myalgia (2.2%) and injection-site reactions (1.5%), and no serious adverse events reported. No cases of new-onset diabetes mellitus or glucose intolerance were documented during the 12-month follow-up; however, the retrospective design, incomplete glycemic surveillance, relatively small sample size, low event rates, and the potential for underreporting warrant cautious interpretation. These findings are broadly consistent with the ODYSSEY APPRISE study,²¹ but larger prospective studies are needed to better define the long-term safety and tolerability of PCSK9 inhibitors.

Limitations

Several limitations of this study warrant consideration. First, the retrospective design precludes control of confounding factors, including diet, physical activity, and medication adherence, which may influence LDL-C levels. Second, the relatively small sample size, particularly within subgroups such as the switching cohorts and the evolocumab then switch (n = 6), limits the statistical power for between-group comparisons. Third, incomplete laboratory data at certain time points introduces potential information bias. Fourth, the 12-month follow-up period, while sufficient to demonstrate short-term lipid-lowering efficacy, is inadequate to evaluate long-term cardiovascular outcomes. Finally, clinically driven dose adjustments and treatment switching in real-world practice may introduce variability in observed LDL-C values, complicating direct comparison with data from controlled clinical trials.

Conclusions

In this real-world study conducted at a tertiary cardiac center in northeastern Thailand, treatment with PCSK9 inhibitors (alirocumab and evolocumab) was associated with sustained LDL-C reduction, and a proportion of Thai patients with ASCVD achieving guideline-recommended targets over 12 months of follow-up. Cardiovascular events and adverse effects were infrequent during follow-up, and no serious drug-related harm leading to treatment discontinuation was documented. Switching between agents did not appear to compromise lipid-lowering efficacy. These findings should be interpreted cautiously, but they suggest that PCSK9 inhibitors may be a useful treatment option in routine clinical practice. Larger prospective studies are needed to confirm long-term effectiveness and safety.

Additional Information

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Ethics Approval: This study was approved by the Khon Kaen University Human Research Ethics Committee (HE671404 on 11 January 2024). All data were accessed retrospectively from preexisting routine clinical records. Data prior to January 2024 were generated through standard physician-directed care and accessed retrospectively under initial ethics approval. Follow-up data through July 2025 were covered under ethics approval and committee review (No. 660201.2.3/3236 on 9 July 2025).

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Supplementary Material: Download Supplementary S1-S5 from the following link:

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References

1. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics-2021 update: a report from the American Heart Association. *Circulation*. 2021;143(8):e254-e743. doi:10.1161/CIR.0000000000000950
2. World Heart Federation. *World Heart Report 2023: Confronting the World's Number One Killer*. World Heart Federation; 2023. Accessed 17 July 2026. <https://world-heart-federation.org/wp-content/uploads/World-Heart-Report-2023.pdf>

3. Bureau of Strategy and Planning, Office of the Permanent Secretary, Ministry of Public Health. *Public Health Statistics A.D. 2022*. Ministry of Public Health; 2022. Accessed 17 July 2026. <https://spd.moph.go.th/wp-content/uploads/2023/11/Hstatistic65.pdf>
4. Division of Non-Communicable Diseases, Department of Disease Control, Ministry of Public Health. *Annual Report 2023*. Aksorn Graphic and Design; 2023. Accessed 17 July 2026. <https://ddc.moph.go.th/uploads/publish/1544220240312071253.pdf>
5. Taeviriyakul U, Worrasan A, Chanthadansuwan T. Eligibility for PCSK9 inhibitors and associated cost in patient with atherosclerotic cardiovascular disease at Central Chest Institute of Thailand. *Thai J Clin Pharm*. 2023;29(1):65-73.
6. Riam-Amatakun W, Nuntharatanapong N. Development of PCSK9 inhibitor to lower LDL cholesterol. *Thai Bull Pharm Sci*. 2018;13(1):105-123. doi:10.69598/tbps.13.1.105-123
7. Defesche JC, Gidding SS, Harada-Shiba M, Hegele RA, Santos RD, Wierzbicki AS. Familial hypercholesterolaemia. *Nat Rev Dis Primers*. 2017;3:17093. doi:10.1038/nrdp.2017.93
8. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020;41(1):111-188. doi:10.1093/eurheartj/ehz455
9. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139(25):e1082-e1143. doi:10.1161/CIR.0000000000000625
10. The Heart Association of Thailand under the Royal Patronage of H.M. the King. *Thai Acute Coronary Syndromes Guidelines 2020*. Nextstep D-Sign; 2020. Accessed 17 July 2026. <https://thaiheart.org/media/uploads/thai-acs-guidelines-2020/Thai%20ACS%20Guidelines%202020.pdf>
11. Buddhari W, Uerojanaungkul P, Sriratanasathavorn C, et al. Low-density lipoprotein cholesterol target attainment in patients surviving an acute coronary syndrome in Thailand: results from the Dyslipidaemia International Study (DYSIS) II. *Heart Lung Circ*. 2020;29(3):405-413. doi:10.1016/j.hlc.2019.02.193
12. Ray KK, Molemans B, Schoonen WM, et al. EU-wide cross-sectional observational study of lipid-modifying therapy use in secondary and primary care: the DA VINCI study. *Eur J Prev Cardiol*. 2021;28(11):1279-1289. doi:10.1093/eurjpc/zwaa047
13. Sampson UK, Fazio S, Linton MF. Residual cardiovascular risk despite optimal LDL cholesterol reduction with statins: the evidence, etiology, and therapeutic challenges. *Curr Atheroscler Rep*. 2012;14(1):1-10. doi:10.1007/s11883-011-0219-7
14. Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med*. 2017;376(18):1713-1722. doi:10.1056/NEJMoa1615664
15. Schwartz GG, Steg PG, Szarek M, et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N Engl J Med*. 2018;379(22):2097-2107. doi:10.1056/NEJMoa1801174
16. Stoekenbroek RM, Hartgers ML, Rutte R, de Wijer DD, Stroes ESG, Hovingh GK. PCSK9 inhibitors in clinical practice: delivering on the promise? *Atherosclerosis*. 2018;270:205-210. doi:10.1016/j.atherosclerosis.2017.11.027
17. Chng BLK, Heng WMP, Soon YM, et al. Safety, adherence and efficacy of PCSK9 inhibitors: a retrospective real-world study. *Proc Singapore Healthc*. 2022;31. doi:10.1177/20101058221144115
18. Robinson JG, Farnier M, Krempf M, et al. Efficacy and safety of alirocumab in reducing lipids and cardiovascular events. *N Engl J Med*. 2015;372(16):1489-1499. doi:10.1056/NEJMoa1501031

19. Toth PP, Worthy G, Gandra SR, et al. Systematic review and network meta-analysis on the efficacy of evolocumab and other therapies for the management of lipid levels in hyperlipidemia. *J Am Heart Assoc.* 2017;6(10):e005367. doi:10.1161/JAHA.116.005367
20. Blanco-Ruiz M, Amaya-Pascasio L, de Torres Chacón R, et al. Effectiveness and safety of PCSK9 inhibitors in real-world clinical practice. An observational multicentre study. The IRIS-PCSK9I study. *Atheroscler Plus.* 2021;45:32-38. doi:10.1016/j.athplu.2021.08.009
21. Gaudet D, López-Sendón JL, Aversa M, et al. Safety and efficacy of alirocumab in a real-life setting: the ODYSSEY APPRISE study. *Eur J Prev Cardiol.* 2022;28(17):1864-1872. doi:10.1093/eurjpc/zwaa097

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