Updated Cost-Effectiveness Analysis of Evolocumab in Patients With Clinically Evident Atherosclerotic Cardiovascular Disease

EE5

Gregg C. Fonarow[1], Cameron Cook[2], Eduard Sidelnikov[3], Guillermo Villa[3]

[1]Division of Cardiology, David Geffen School of Medicine, University of California, Los Angeles Medical Center, Los Angeles, CA, USA; [2]Amgen Inc., Thousand Oaks, CA, USA; [3]Amgen (Europe) GmbH, Rotkreuz, Switzerland

BACKGROUND

- Despite advances in care, patients with clinically evident ASCVD remain at substantial risk of recurrent CV events. In many of these patients, LDL-C remains inadequately controlled, leaving patients at increased risk of ASCVD.[1]
- Evolocumab is a fully human PCSK9i monoclonal antibody that lowers LDL-C from baseline by approximately 60% and reduces the risk of CV events in patients with clinically evident ASCVD.[2-4]
- The 2026 ACC/AHA/Multisociety Guideline on the Management of Dyslipidemia recommends PCSK9i monoclonal antibodies as nonstatin treatment options for LDL-C lowering and an LDL-C goal of < 55 mg/dL in patients with established clinical ASCVD who are at very high risk.[5]
- A previous cost-effectiveness analysis of evolocumab in patients with clinically evident ASCVD demonstrated that evolocumab meets accepted cost-effectiveness thresholds.[6]
- Changes in clinical guidance around LDL-C goals and evolocumab pricing warrant an updated economic evaluation in a clinically evident ASCVD patient population.
  - Evolocumab is now available in the US at a lower annualised direct-to-patient price of $3,107.[7]

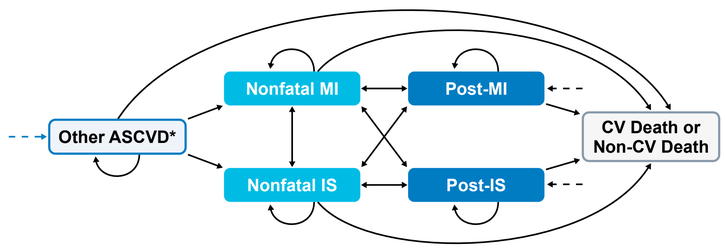
OBJECTIVE

- To evaluate the cost-effectiveness of evolocumab plus standard therapy (statins with or without ezetimibe) vs standard therapy alone in adults with clinically evident ASCVD and LDL-C ≥ 70 mg/dL at the direct-to-patient price of $3,107 per year.

METHODS

- A previously published Markov cohort state-transition model (**Figure 1**) was used to simulate patients with clinically evident ASCVD over a lifetime horizon.[8]
  - Health states included other ASCVD (defined as clinically evident ASCVD other than MI or IS), MI, IS, post-MI, post-IS, CV death, and non-CV death; RV was modelled as a procedure.
- Baseline characteristics and event rates from a representative real-world cohort in the US with LDL-C ≥ 70 mg/dL were applied (**Table 1**).
- The base case assumed a US payer perspective and used evolocumab CVOT-based risk reduction estimates. Scenario analyses varied the analysis perspective and CV-risk reduction estimates (**Figure 2**).
- Cost-effectiveness was assessed using a WTP threshold of $120,000 per QALY gained, which was selected based on the 2025 AHA/ACC Statement on Cost/Value Methodology in Clinical Practice Guidelines.[9]
- A deterministic univariate sensitivity analysis was performed by modifying model parameters across plausible values.

FIGURE 1. MARKOV COHORT STATE-TRANSITION MODEL DIAGRAM[8]



*Defined as clinically evident ASCVD other than MI or IS.
ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; IS, ischaemic stroke; MI, myocardial infarction.

FIGURE 2. ANALYSES

US Payer Perspective*

BASE CASE
- Evolocumab CVOT-based CV risk–reduction estimates

SCENARIO 1
- CTT Collaboration 2010 meta-analysis–based CV risk–reduction estimates

Societal Perspective†

SCENARIO 2
- Evolocumab CVOT-based CV risk–reduction estimates

SCENARIO 3
- CTT Collaboration 2010 meta-analysis–based CV risk–reduction estimates

Outcomes
- MACE: MI, IS, or CV death
- RV procedures
- Costs
- Life-years
- QALYs
- ICERs

*The base case and scenario 1 include direct medical costs associated with the modelled ASCVD health states and CV events (Table 1).
†Scenarios 2 and 3 include the same direct medical costs as the base case and scenario 1, plus indirect costs associated with nonfatal MI and IS
CTT, Cholesterol Treatment Trialists'; CV, cardiovascular; CVOT, cardiovascular outcomes trial; ICER, incremental cost-effectiveness ratio; IS, ischaemic stroke; MACE, major adverse cardiovascular event; MI, myocardial infarction; QALY, quality-adjusted life-year; RV, revascularisation.

TABLE 1. PARTICIPANT CHARACTERISTICS AND KEY MODEL INPUTS

	Value	Source
Clinical and demographic characteristics		
Age, mean, years	66	Fonarow 2017[8]
Female, %	39	
LDL-C, mean, mg/dL	104	
Ezetimibe use, %	7.0	
Statin use, %	100.0	
Event rates		
Cost discounting, %	3.0	2025 AHA/ACC Statement on Cost/Value Methodology in Clinical Guidelines[9]
Outcomes discounting, %	3.0	
Time horizon	Lifetime	
Composite MACE rate per 100 patients-years	6.4	Fonarow 2017[8]
RV rate per 100 patient-years	3.3	
Intervention effect, hazard ratio: trial based*		
Nonfatal MI	0.73	FOURIER[2]
Nonfatal IS	0.79	
Coronary RV	0.78	
CV-related death†	0.77	FOURIER-OLE[3]
Intervention effect, rate ratio per 39 mg/dL LDL-C reduction: trial based, CTT Collaboration		
Nonfatal MI	0.80, 0.73	FOURIER,[2] CTT Collaboration[10]
Nonfatal IS	0.85, 0.79	
Coronary RV	0.84, 0.75	
CV-related death†	0.84, 0.86	FOURIER-OLE,[3] CTT Collaboration[10]
Costs		
Treatment cost (annual), USD		
Ezetimibe	15.58	Merative Micromedex RED BOOK[11]
Statin	7.57	
Evolocumab‡	3,107.00	AmgenNow[12,13]
Direct cost (annual),§ USD		
Other ASCVD**	10,374.96	Fonarow 2017[8]
Nonfatal MI, post-MI	63,565.40, 10,374.96	
Nonfatal IS, post-IS	56,392.87, 10,759.40	
CV-related death	93,408.82	
Coronary RV	72,474.61	
Indirect cost,§,†† USD		
Nonfatal MI	70,707.41	Fonarow 2017[8]
Nonfatal IS	45,723.79	
Utilities		
Other ASCVD**	0.824	Fonarow 2017[8]
Nonfatal MI, post-MI	0.672, 0.824	
Nonfatal IS, post-IS	0.327, 0.524	
Injection-site reaction	−0.0003	
Discontinuation over 3 years, %	15	FOURIER[2]

*Hazard ratios from FOURIER and FOURIER-OLE were converted to rate ratios per 38.67 mg/dL (1 mmol/L) LDL-C reduction using: rate ratio per 38.67 mg/dL = hazard ratio^(1/[absolute LDL-C reduction/38.67]).
†The CV death estimate was derived from FOURIER-OLE rather than FOURIER, as FOURIER was not powered to detect a treatment effect on mortality.
‡The direct-to-patient price of evolocumab was made available in October 2025.
§Costs were inflated to 2025 USD.
**Assumed to be equivalent to the post-MI health state.
††Used in the societal perspective scenarios.
ACC, American College of Cardiology; AHA, American Heart Association; CTT, Cholesterol Treatment Trialists'; CV, cardiovascular; IS, ischaemic stroke; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular event; MI, myocardial infarction; OLE, open-label extension; RV, revascularisation; USD, US dollars.

RESULTS

- In the base-case analysis, evolocumab added to standard therapy was associated with improved outcomes in MACE (1.51 vs 1.81), RV (0.70 vs 0.79), life-years (11.52 vs 10.70), and QALYs (7.83 vs 7.20) vs standard therapy alone in patients with clinically evident ASCVD; however, incremental costs were increased by $20,055, resulting in an ICER of $31,837 per QALY gained **(Table 2)**.
- Evolocumab added to standard therapy improved health outcomes and was cost-effective across all scenario analyses. Notably, evolocumab was dominant (more effective and cost-saving) in the societal-perspective scenario using CTT Collaboration–based estimates.

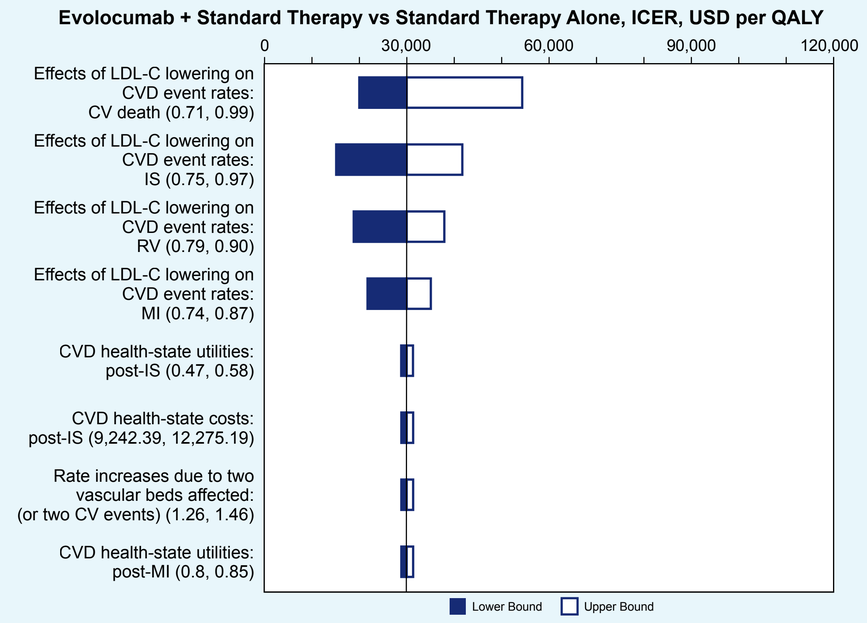
TABLE 2. COST-EFFECTIVENESS RESULTS FOR BASE-CASE AND SCENARIO ANALYSES

Analysis	Event Rates		Cost, USD		Life-Years		QALYs		Estimated VBP,* USD/Year	ICER, USD/QALY
	MACE	RV	Total	Δ	Total	Δ	Total	Δ		
Base case: US payer perspective, evolocumab CV-outcomes efficacy data†										
Standard therapy alone	1.81	0.79	233,284		10.70		7.20			
Evolocumab + standard therapy	1.51	0.70	253,339	20,055	11.52	0.82	7.83	0.63	8,715	31,837
Scenario 1: US payer perspective, CTT Collaboration 2010 meta-analysis rate ratio per 38.67 mg/dL LDL-C reduction†										
Standard therapy alone	1.81	0.79	233,284		10.70		7.20			
Evolocumab + standard therapy	1.38	0.59	242,646	9,361	11.45	0.75	7.83	0.63	9,803	14,924
Scenario 2: Societal perspective, evolocumab CV-outcomes efficacy data‡										
Standard therapy alone	1.81	0.79	284,012		10.70		7.20			
Evolocumab + standard therapy	1.51	0.70	294,306	10,294	11.52	0.82	7.83	0.63	9,701	16,341
Scenario 3: Societal perspective, CTT Collaboration 2010 meta-analysis rate ratio per 38.67 mg/dL LDL-C reduction‡										
Standard therapy alone	1.81	0.79	284,012		10.70		7.20			
Evolocumab + standard therapy	1.38	0.59	278,115	−5,897	11.45	0.75	7.83	0.63	11,353	Cost-saving§

The values are rounded; therefore, the reported differences may not match the exact subtractions.
*Estimated using the cost-effectiveness WTP threshold recommended by the 2025 AHA/ACC Statement on Cost/Value Methodology in Clinical Practice Guidelines ($120,000 per QALY). Values represent the model-estimated theoretical maximum net price at which the ICER would remain under this threshold. Estimates do not represent actual drug prices in the marketplace.
†The base case and scenario 1 include direct medical costs associated with the modelled ASCVD health states and CV events (Table 1).
‡Scenarios 2 and 3 include the same direct medical costs as the base case and scenario 1, plus indirect costs associated with nonfatal MI and IS.
§The ICER value was negative (−$9,401 per QALY gained), indicating greater effectiveness and lower total costs with evolocumab + standard therapy vs standard therapy alone (ie, indicative of cost saving).
ACC, American College of Cardiology; AHA, American Heart Association; CTT, Cholesterol Treatment Trialists'; CV, cardiovascular; ICER, incremental cost-effectiveness ratio; IS, ischaemic stroke; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular events; MI, myocardial infarction;
QALY, quality-adjusted life-year; RV, revascularisation; USD, US dollars; VBP, value-based price; WTP, willingness-to-pay.

- Deterministic sensitivity analysis results were robust, with ICERs remaining substantially below the WTP threshold across all parameters, including the effect of LDL-C lowering on CV disease event rates (CV death, IS, RV, and MI), which had the greatest influence on model uncertainty (**Figure 3**).

FIGURE 3. TORNADO DIAGRAM SHOWING A DETERMINISTIC SENSITIVITY ANALYSIS OF ICERs



CV, cardiovascular; CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; IS, ischaemic stroke; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; QALY, quality-adjusted life-year; RV, revascularisation; USD, US dollars.

CONCLUSIONS

- **Evolocumab is cost-effective** in patients with clinically evident ASCVD at the current direct-to-patient price as indicated by ICERs substantially below the AHA/ACC-recommended WTP threshold of $120,000 per QALY gained.
- **Evolocumab with standard therapy lowered rates of MACE and RV and increased life-years and QALYs** in patients with clinically evident ASCVD compared to standard therapy alone as indicated across base-case and scenario analyses.
- **Evolocumab was cost-saving, showing lower costs and better outcomes,** in the scenario evaluated from the societal perspective using CTT Collaboration-based risk-reduction estimates. In this scenario, evolocumab was projected to reduce overall societal costs while improving patients' health.

LIMITATIONS

- These findings should be interpreted within the context of the data inputs, event rates, and modelling assumptions used; the results are based on the assumption that the clinical benefits of treatment extend beyond the period with direct follow-up.
- This analysis is only applicable to US patients with clinically evident ASCVD and is not generalisable to primary prevention patients, other populations at lower CV event risk, or patients outside the US.

Acknowledgements

This study was funded by Amgen Inc. Writing and editorial support were provided by Stacie Meaux, PhD, of Red Nucleus and funded by Amgen Inc.

Abbreviations

ACC, American College of Cardiology; **AHA**, American Heart Association; **ASCVD**, atherosclerotic cardiovascular disease; **CTT**, Cholesterol Treatment Trialists'; **CV**, cardiovascular; **CVOT**, cardiovascular outcomes trial; **ICER**, incremental cost-effectiveness ratio; **IS**, ischaemic stroke; **LDL-C**, low-density lipoprotein cholesterol; **MACE**, major adverse cardiovascular event; **MI**, myocardial infarction; **PCSK9**, proprotein convertase subtilisin kexin 9; **QALY**, quality-adjusted life-year; **RV**, revascularisation; **WTP**, willingness-to-pay.

Disclosures

GCF has served as a consultant for Abbott, Amgen Inc., AstraZeneca, Bayer, Boehringer Ingelheim, Cytokinetics, Eli Lilly, Johnson & Johnson, Medtronic, Merck, Novartis, and Pfizer.
CC is an employee of and owns stock in Amgen Inc. **ES** and **GV** are employees of Amgen (Europe) GmbH and own stock in Amgen Inc.

References

1. Watanabe AH, et al. *J Am Heart Assoc*. 2026;15:e044840. **2.** Sabatine MS, et al. *N Engl J Med*. 2017;376:1713-1722. **3.** O'Donoghue ML, et al. *Circulation*. 2022;146:1109-1119. **4.** Repatha® (evolocumab) prescribing information, Amgen. **5.** Blumenthal RS, et al. J *Am Coll Cardiol*. 2026;87:2624-2757. **6.** Fonarow GC, et al. *JAMA Cardiol*. 2019;4:691-695. **7.** Fonarow GC, et al. [preprint July 27, 2026]. medRxiv. doi: 10.64898/2026.07.23.26358791. **8.** Fonarow GC, et al. *JAMA Cardiol*. 2017;2:1069-1078. **9.** Kazi DS, et al. *Circulation*. 2025;152:e332-e358. **10.** Cholesterol Treatment Trialists' Collaboration. *Lancet*. 2010;376:1670-1681. **11.** Merative. Micromedex RED BOOK. www.micromedexsolutions.com. Accessed October 15, 2026. **12.** Amgen Inc.AmgenNow™ direct-to-patient program. https://www.amgennow.com. Accessed October 15, 2026. **13.** Amgen. Amgen makes Repatha® available through AmgenNow, a direct-to-patient program inthe U.S. https://www.prnewswire.com/news-releases/amgen-makes-repatha-available-through-amgennow-a-direct-to-patient-program-in-the-us-302575486.html. Accessed October 15, 2026.

Please scan the QR code for a copy of the poster

© 2026 All rights reserved

ISPOR Europe 2026; Vienna, Austria; 8–11 November 2026