Potential cardiovascular risk reduction with evolocumab in the real world: a simulation in patients with a history of myocardial infarction from the HEYMANS register

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Background/Introduction: FOURIER included 22,351 patients with a history of myocardial infarction (MI) and a median low-density lipoprotein cholesterol (LDL-C) of 2.4 mmol/L. Reducing LDL-C with evolocumab reduced the risk of major cardiovascular (CV) events by 1.3%, in absolute terms, over 2.2 years. Whether similar benefits might be observed in real-world evidence from evolocumab use is unknown.

Purpose: Simulate CV risk and assess the potential CV risk reduction among a large European cohort of evolocumab users with a history of MI.

Methods: We used interim data from HEYMANS, a register of patients initiating evolocumab in routine clinical practice across 12 European countries, from August 2015 with follow-up through July 2020. Demographic and clinical characteristics, lipid-lowering therapy (LLT), and lipid values were collected from routine medical records (6 months prior to evolocumab initiation through 30 months post initiation). Patients with a history of MI were considered and two sub-cohorts were created: recent MI (MI $\leq$1 year before evolocumab initiation) and remote MI (MI $>$1 year before evolocumab initiation). For each patient, we 1) simulated their CV risk using three different sources, correcting for age and LDL-C: i) the REACH equation, ii) FOURIER, iii) an observational study including FOURIER-like patients; 2) calculated their absolute LDL-C reduction on evolocumab; 3) simulated their relative risk reduction (RRR) by randomly sampling from the inverse probability distribution of the rate ratio per 1 mmol/L from the key secondary endpoint in the FOURIER landmark analysis; 4) calculated their absolute risk reduction (ARR) and number needed to treat (NNT) over 2 years (recent MI) or 10 years (remote MI).

Results: Our analysis included 90 recent MI and 489 remote MI patients initiating evolocumab in clinical practice per local reimbursement criteria, with up to 24 months follow-up. Median (inter-quartile range) age was 59 (53–67) and 61 (53–68) years in recent MI and remote MI patients, respectively. LDL-C before evolocumab was 3.8 (3.2–4.6) and 3.6 (3.0–4.5) mmol/L. Absolute LDL-C reduction on evolocumab was 2.2 (1.4–2.8) and 2.2 (1.6–2.8) mmol/L, meaning relative LDL-C reduction of 60% (44%-73%) and 62% (47%-72%), respectively. Predicted ARR with evolocumab was substantial, whether over 2 years (recent MI) or over 10 years (remote MI). See Table 1.

Conclusions: This cohort of evolocumab users in clinical practice had a higher baseline LDL-C and CV risk than patients enrolled in FOURIER. LDL-C reduction and RRR were very similar in recent MI and remote MI patients. However, patients with a recent MI had a higher short-term CV risk and therefore showed a larger ARR on evolocumab.

Table 1. CV risk simulation in recent MI and remote MI patients[a]

	REACH equation[1]	FOURIER[2]	Observational study[3]
	Recent MI (n=90)		
Annualized CV risk at baseline	5% (3%-7%)	5% (4%-6%)	9% (7%-12%)
2-year CV risk at baseline	10% (6%-14%)	10% (7%-12%)	18% (13%-23%)
2-year CV risk on evolocumab	6% (4%-9%)	6% (5%-8%)	11% (9%-15%)
RRR from a 2.2 (1.4-2.8) mmol/L reduction	34% (23%-49%)		
2-year ARR	3% (2%-5%)	3% (2%-5%)	6% (3%-9%)
2-year NNT	33	31	18
	Remote MI (n=489)		
Annualized CV risk at baseline	3% (2%-6%)	4% (3%-5%)	5% (4%-6%)
10-year CV risk at baseline	30% (20%-44%)	31% (25%-40%)	38% (30%-47%)
10-year CV risk on evolocumab	20% (14%-30%)	22% (17%-27%)	27% (21%-33%)
RRR from a 2.2 (1.6-2.8) mmol/L reduction	35% (25%-44%)		
10-year ARR	9% (5%-13%)	9% (6%-13%)	11% (7%-15%)
10-year NNT	11	11	9

[a]Figures represent medians (inter-quartile ranges)

[1]Am J Med. 2012 Jul;125(7):695-703.e1.; [2]N Engl J Med. 2017 May 4;376(18):1713-1722.; [3]Eur Heart J Qual Care Clin Outcomes. 2019 Jul 1;5(3):225-232.