Repatha® (evolocumab) clinical trials:

CLINICAL EVIDENCE FOR INITIATING REPATHA® DURING HOSPITALIZATION FOR ACS[1,2]

Learn more about clinical studies that examine targeting LDL-C in the acute setting for ACS patients[1,2]

INDICATIONS

Repatha® is indicated:

- In adults with established cardiovascular disease to reduce the risk of myocardial infarction, stroke, and coronary revascularization.
- As an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH) to reduce LDL-C.

IMPORTANT SAFETY INFORMATION

Contraindication: Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to evolocumab or any of the excipients in Repatha®. Serious hypersensitivity reactions including angioedema have occurred in patients treated with Repatha®.

ACS = acute coronary syndrome; LDL-C = low-density lipoprotein cholesterol.

Please see additional Important Safety Information throughout.

Repatha® (evolocumab) injection 140 mg/mL

FOURIER TRIAL

Further Cardiovascular **Ou**tcomes **R**esearch With PCSK9 **I**nhibition in Subjects With **E**levated **R**isk

The objective of FOURIER was to evaluate the effectiveness of Repatha® (evolocumab) to reduce CV events in patients with established CVD who remained at risk despite high- or moderate-intensity statin therapy.[3] 81% of patients had previously experienced ≥1 MI.[4] The FOURIER trial included MI patients with a median time of approximately 3.4 years since their most recent previous MI.[3]
The impact of initiating Repatha® in the acute phase of ACS on LDL-C lowering was not studied.[3]

EVACS TRIAL

Evolocumab in **A**cute **C**oronary **S**yndrome

In EVACS, an investigator-sponsored study conducted in the US, Repatha® was administered in-hospital early postinfarction. The study assessed the mean percent change in LDL-C from baseline, comparing placebo and Repatha® groups at day 30.[1]

EVOPACS TRIAL

Evolocumab for Early Reduction of LDL-Cholesterol Levels in **P**atients With **A**cute **C**oronary **S**yndromes

In EVOPACS, an investigator-sponsored study conducted in Switzerland, Repatha® was administered in-hospital in the acute phase of ACS. The percent change in LDL-C from baseline to week 8 was assessed.[2]

Adding Repatha® to statin therapy during hospitalization after ACS may help patients achieve the guideline-recommended LDL-C level[1,2]

IMPORTANT SAFETY INFORMATION (continued)

Hypersensitivity Reactions: Hypersensitivity reactions, including angioedema, have been reported in patients treated with Repatha®. If signs or symptoms of serious hypersensitivity reactions occur, discontinue treatment with Repatha®, treat according to the standard of care, and monitor until signs and symptoms resolve.

CV = cardiovascular; CVD = cardiovascular disease; MI = myocardial infarction.

FOURIER TRIAL

Further Cardiovascular **Ou**tcomes **R**esearch With PCSK9 **I**nhibition in Subjects With **E**levated **R**isk

IN FOURIER, REPATHA® ADDED TO A STATIN WAS STUDIED IN ESTABLISHED CVD PATIENTS WHO REMAINED AT RISK OF ANOTHER CV EVENT[4]

27,564 patients with established CVD and LDL-C ≥70 mg/dL and/or non–HDL-C ≥100 mg/dL despite high- or moderate-intensity statin therapy[4]

Patients were aged ≥40 to ≤85 years with prior MI, stroke, or symptomatic PAD[3,*]

81% of patients already experienced ≥1 MI[3]

Median baseline LDL-C for enrolled patients was 92 mg/dL[3]

of patients were receiving high- or moderate-intensity statin therapy[3]

of patients in the Repatha® arm were on high-intensity statins[3]

Study Design: FOURIER was a double-blind, randomized, placebo-controlled, event-driven trial in 27,564 adult patients with established cardiovascular disease and with LDL-C ≥70 mg/dL and/or non–HDL-C ≥100 mg/dL despite high- or moderate-intensity statin therapy. Patients received either subcutaneous injections of Repatha® (140 mg every 2 weeks or 420 mg once monthly) or placebo. On stable background lipid-lowering therapy, median LDL-C at baseline was 92 mg/dL.[4]

THE ADDITION OF REPATHA® RESULTED IN A SUSTAINED AND CONSISTENT LDL-C REDUCTION[4]

- **63% mean reduction** in LDL-C from baseline at week 12 in the statin + Repatha® group compared to statin alone[4]
- **87% of patients achieved LDL-C** ≤70 mg/dL with Repatha® added to a statin at 48 weeks[3]
- Adding Repatha® to a statin can **lower LDL-C in just 4 weeks**[3]

*Symptomatic peripheral arterial disease (history of claudication with ABI <0.85 or previous revascularization or amputation).[5]

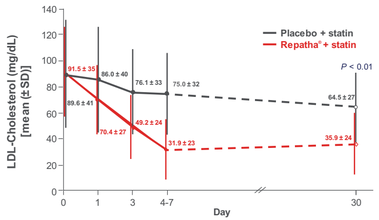
EVACS TRIAL

Evolocumab in **A**cute **C**oronary **S**yndrome

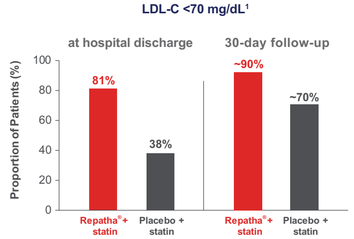
IN EVACS, REPATHA® ADDED TO A STATIN WAS ADMINISTERED IN-HOSPITAL DURING THE EARLY POSTINFARCTION PERIOD, WITHIN 24 HOURS OF HOSPITALIZATION[1]

Repatha® added to statin therapy reduced LDL-C levels throughout hospitalization and at 30-day follow-up more than a statin alone[1]

Mean LDL-C levels in the 2 study groups[1]



LDL-C <70 mg/dL[1]



The number of Repatha® and placebo patients with any adverse event was 10 and 12, respectively, and with a serious adverse event, 2 and 6, respectively[1]

Study Design: The EVACS trial (Evolocumab in Acute Coronary Syndrome) enrolled patients with non–ST-segment–elevation myocardial infarction and troponin I of ≥5 ng/mL and randomly assigned them in a 1:1 ratio to a single dose of evolocumab SQ 420 mg or matching placebo within 24 hours of presentation. There were 57 patients enrolled in the study (30 Repatha® arm; 27 placebo arm). The primary endpoint was the change in LDL-C at 30 days. Other atherogenic lipid outcomes were also measured. All patients received high-intensity statins unless contraindicated and were treated in accordance with current ACS guidelines.[1]

The EVACS trial was not designed to assess a correlation between LDL-C reduction and CV events.[1]

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions in Primary Hyperlipidemia: The most common adverse reactions (>5% of patients treated with Repatha® and more frequently than placebo) were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

From a pool of the 52-week trial and seven 12-week trials: Local injection site reactions occurred in 3.2% and 3.0% of Repatha®-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. Hypersensitivity reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated patients, respectively. The most common hypersensitivity reactions were rash (1.0% versus 0.5% for Repatha® and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

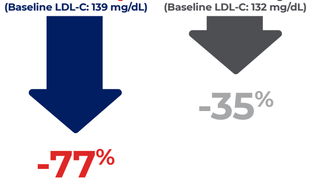
EVOPACS TRIAL

Evolocumab for Early Reduction of LDL-Cholesterol Levels in **P**atients With **A**cute **C**oronary **S**yndromes

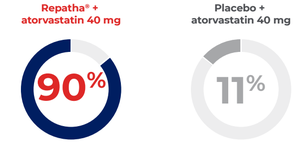
IN THE EVOPACS TRIAL, WHEN INITIATED IN-HOSPITAL AT THE ACUTE PHASE OF ACS, REPATHA® ADDED TO A STATIN REDUCED LDL-C AT 8 WEEKS[2]

95% of patients on Repatha® added to a statin achieved the AHA/ACC Guideline–recommended threshold of below 70 mg/dL vs 37% of patients on placebo + statin[2,5]

% reduced from baseline LDL-C at week 8



% of patients who reached LDL-C <55 mg/dL at week 8



Study Design: EVOPACS was a randomized, double-blind, placebo-controlled, multicenter, investigator-sponsored study conducted in Switzerland evaluating the safety and efficacy of Repatha® when administered in the acute phase of ACS (NSTEMI/UA <72 hours, STEMI <24 hours) typically within 72 hours of symptom onset. There were 308 patients enrolled in the study (155 Repatha® arm; 153 placebo arm). Patients presenting with ACS were included if their LDL-C levels were either ≥70 mg/dL despite high-intensity statin therapy, or ≥90 mg/dL despite low- or moderate-intensity statin, or ≥125 mg/dL in statin-naive patients or patients not on stable statin therapy.[2]

Patients were randomized to receive Repatha® 420 mg once monthly subcutaneously plus high-intensity statin therapy or placebo plus high-intensity statin therapy; 78.2% of patients were not on background statin therapy prior to randomization.[2]

THE SAFETY AND TOLERABILITY OF REPATHA® WERE CONSISTENT WITH PREVIOUS TRIALS[2]

The EVOPACS trial was not designed to assess a correlation between LDL-C reduction and CV events[2]

AHA/ACC = American Heart Association/American College of Cardiology; ESC = European Society of Cardiology; NSTEMI = non–ST-segment–elevation myocardial infarction; STEMI = ST-elevation myocardial infarction; SQ = subcutaneous; UA = unstable angina.

IMPORTANT SAFETY INFORMATION

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Hypersensitivity Reactions: Hypersensitivity reactions, including angioedema, have been reported in patients treated with Repatha®. If signs or symptoms of serious hypersensitivity reactions occur, discontinue treatment with Repatha®, treat according to the standard of care, and monitor until signs and symptoms resolve.

Adverse Reactions in Primary Hyperlipidemia: The most common adverse reactions (>5% of patients treated with Repatha® and more frequently than placebo) were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

From a pool of the 52-week trial and seven 12-week trials: Local injection site reactions occurred in 3.2% and 3.0% of Repatha®-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. Hypersensitivity reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated patients, respectively. The most common hypersensitivity reactions were rash (1.0% versus 0.5% for Repatha® and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

Adverse Reactions in the Cardiovascular Outcomes Trial: The most common adverse reactions (>5% of patients treated with Repatha® and more frequently than placebo) were: diabetes mellitus (8.8% Repatha®, 8.2% placebo), nasopharyngitis (7.8% Repatha®, 7.4% placebo), and upper respiratory tract infection (5.1% Repatha®, 4.8% placebo).

Among the 16,676 patients without diabetes mellitus at baseline, the incidence of new-onset diabetes mellitus during the trial was 8.1% in patients treated with Repatha® compared with 7.7% in patients that received placebo.

Immunogenicity: Repatha® is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity with Repatha®.

Please see full Prescribing Information.

References: 1. Leucker TM, Blaha MJ, Jones SR, et al. Effect of evolocumab on atherogenic lipoproteins during the peri- and early postinfarction period: a placebo-controlled, randomized trial. *Circulation*. 2020;142:419-421. **2.** Koskinas KC, Windecker S, Pedrazzini G, et al. Evolocumab for early reduction of LDL cholesterol levels in patients with acute coronary syndromes (EVOPACS). *J Am Coll Cardiol*. 2019;74:2452-2462. **3.** Sabatine MS, Giugliano RP, Keech AC, et al; FOURIER Steering Committee and Investigators. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med*. 2017;376:1713-1722. **4.** Repatha® (evolocumab) prescribing information, Amgen. **5.** 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. *J Am Coll Cardiol*. 2019;73:e285-e350.

AMGEN®

Cardiovascular

Repatha® (evolocumab) injection 140 mg/mL