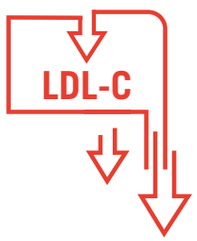
When initiated in hospital at acute phase of ACS,

EVOPACS concluded Repatha® substantially reduced LDL-C at 8 weeks and the safety and tolerability of Repatha® were consistent with previous trials[1]

Repatha® (evolocumab) injection 140 mg/mL

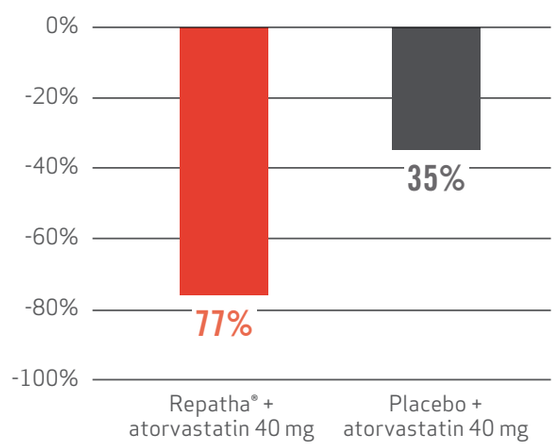


When administered in the acute phase of ACS, high-intensity statins result in LDL-C reduction[2-4]

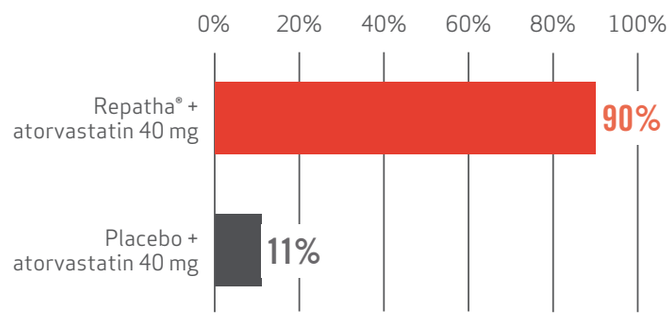
Nearly two-thirds of ACS patients fail to achieve guideline-recommended LDL-C goals despite high-intensity statin treatment[5]

95% of patients on Repatha® added to statin achieved the ACC/AHA Guidelines-recommended threshold of below 70 mg/dL vs just 37% of patients on placebo + statin.[1,6]

% reduced from baseline LDL-C at week 8[1]



% of patients who reached LDL-C <55 mg/dL at week 8[7]



The results are consistent with safety and tolerability data from previous studies.[1]

Study Design: EVOPACS is 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. 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 low- or moderate-intensity statin, or ≥125 mg/dL in statin-naïve patients or patients not on stable statin therapy.[1]

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.[1]

Indications

- **Prevention of Cardiovascular Events**: In adults with established cardiovascular disease, Repatha® is indicated to reduce the risk of myocardial infarction, stroke, and coronary revascularization.
- **Primary Hyperlipidemia (including Heterozygous Familial Hypercholesterolemia):** Repatha® is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C).

Important Safety Information

- **Contraindication:** Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to Repatha®. Serious hypersensitivity reactions including angioedema have occurred in patients treated with Repatha®.

Please see additional Important Safety Information on back page.

Repatha® (evolocumab) injection 140 mg/mL

Although reduction of CV events was not explored as an endpoint in EVOPACS, more than 200 studies with more than 2 million patients have established that elevated LDL-C causes CV events such as a heart attack.[8] FOURIER showed that adding Repatha® to stable statin therapy reduced the risk of CV events and delivered a 27% relative risk reduction in heart attack.[9]

FOR PATIENTS WITH ESTABLISHED CV DISEASE,

ADD REPATHA® TO LOWER THE RISK OF AN MI BY DRAMATICALLY LOWERING LDL-C

ACC/AHA=American College of Cardiology/American Heart Association; ACS=acute coronary syndrome; CV=cardiovascular; ESC=European Society of Cardiologists; LDL-C=low-density lipoprotein cholesterol; MI=myocardial infarction; NSTEMI=non-ST-elevation myocardial infarction; STEMI=ST-elevation myocardial infarction; UA=unstable angina.

Important Safety Information

- **Allergic Reactions:** Hypersensitivity reactions (e.g. angioedema, rash, urticaria) have been reported in patients treated with Repatha®, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic 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 (including HeFH):** The most common adverse reactions (>5% of patients treated with Repatha® and occurring 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.

  Allergic reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated patients, respectively. The most common allergic 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 occurring 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 assigned to Repatha® compared with 7.7% in those assigned to placebo.
- **Immunogenicity:** Repatha® is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity with Repatha®.

References: 1. Koskinas KC, Windecker S, Pedrazinni G, et al. Evolocumab for early reduction of LDL-cholesterol levels in patients with acute coronary syndromes (EVOPACS). *J Am Coll Cardiol.* 2019. doi:10.1016/j.jacc.2019.08.010 **2.** Ray KK, Cannon CP, McCabe CH, et al. Early and late benefits of high-dose atorvastatin in patients with acute coronary syndromes. *J Am Coll Cardiol.* 2005;46:1405-1410. **3.** Schwartz GG, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes. The MIRACL Study: a randomized controlled trial. *JAMA.* 2001;285:1711-1718. **4.** Patti G, Pasceri V, Colonna G, et al. Atorvastatin pretreatment improves outcomes in patients with acute coronary syndromes undergoing early percutaneous coronary intervention. *J Am Coll Cardiol.* 2007;49:1272-1278. **5.** Gencer B, Koskinas KC, Räber L, et al. Eligibility for PCSK9 inhibitors according to American College of Cardiology (ACC) and European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) Guidelines after acute coronary syndromes. *J Am Heart Assoc.* 2017; doi: 10.1161/JAHA.117.006537 **6.** Grundy SM, Stone NJ, Bailey AL, et al. 2018. 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.* 2018: doi:https://doi.org/10.1016/j.jacc.2018.11.003 **7.** Koskinas KC. EVOlocumab for early reduction of LDL-cholesterol levels in Patients with Acute Coronary Syndromes (EVOPACS): a randomized, double-blind, placebo-controlled multicenter study. Presented at: ESC World Congress of Cardiology; August 31-September 4, 2019; Paris, France. **8.** Ference BA, Ginsberg HN, Graham I, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J.* 2017;38:2459-2472. **9.** Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med.* 2017;376:1713-1722.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

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USA-145-82062 03-20