Alirocumab Lowers Cholesterol in Individuals on Insulin

Alirocumab improves cholesterol levels in individuals with insulin-treated diabetes who are receiving maximal statin therapy.

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December 17, 2017 — Individuals with insulin-treated diabetes who were at risk for cardiovascular disease and receiving maximum tolerated statin therapy had lower cholesterol levels when receiving alirocumab than those receiving placebo, a recent study demonstrated.

Lawrence A. Leiter, MD, with the University of Toronto in Toronto, Ontario, and associates reported their findings in the December 2017 edition of *Diabetes, Obesity and Metabolism*.

Previous studies have shown that alirocumab, a monoclonal antibody targeting proprotein convertase subtilisin/kexin type 9 (PCSK9), reduced cholesterol levels in individuals already on maximum tolerated statin therapy. Study authors noted concern regarding "the safety of the concomitant administration of 2 injectable agents (alirocumab, a monoclonal antibody, and insulin, a biological agent)." The ODYSSEY DM-INSULIN trial compared the efficacy and safety of alirocumab with placebo in a randomized double-blind study of individuals with insulin-treated diabetes, hypercholesterolemia, and risk factors for cardiovascular disease.

A total of 441 individuals with type 2 diabetes (T2D) and 76 individuals with type 1 diabetes (T1D) were randomized 2:1 to receive a subcutaneous injection of 75 mg of alirocumab or placebo, respectively, every 2 weeks for 24 weeks. The alirocumab dose was increased to 150 mg at 12 weeks if the 8-week low-density lipoprotein (LDL) cholesterol level was not below a goal of 1.8 mmol/L (70 mg/dL).

The primary efficacy end point was percent change in LDL cholesterol level from baseline at 24 weeks. Participants were monitored for adverse events through 32 weeks.

Participants with T2D given alirocumab had a -49.0% change in LDL cholesterol level compared with those given placebo (95% CI -54.4% to -43.6%; $P < .001$). Similarly, participants with T1D given alirocumab had a -47.8% change in LDL cholesterol level compared with those given placebo (95% CI -60.7% to -35.0%; $P < .001$).

Significant reductions in secondary end points, including non–high-density lipoprotein cholesterol level, apolipoprotein B level, total cholesterol level, and lipoprotein (a) level were also noted, but measures of glycemic control including hemoglobin A1c level, fasting plasma glucose level, daily insulin dose, and antihyperglycemic medication use were unchanged from baseline.

Adverse events, including headache, cognitive disorder, allergic dermatitis, myalgia, and injection site reactions, were reported by 64.5% of participants in the alirocumab group and

64.1% of participants in the placebo group. One death from myocardial infarction occurred in the placebo group.

“The present study showed. . . that alirocumab produced significant LDL cholesterol reductions in individuals with both T2D and T1D receiving insulin treatment who were at high cardiovascular risk,” according to study authors, who also noted that there was “no apparent effect on overall safety or measures of glycemic control.”

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Leiter LA, Cariou B, Müller-Wieland D, et al. Efficacy and safety of alirocumab in insulin-treated individuals with type 1 or type 2 diabetes and high cardiovascular risk: the ODYSSEY DM-INSULIN randomized trial. *Diabetes Obes Metab*. 2017;19(12):1781-1792. doi:10.1111/dom.13114