Evolocumab consistently lowers low-density lipoprotein cholesterol among diverse patient populations

Erik Stroes
Jennifer G. Robinson
Frederick J. Raal
Robert Dufour
David Sullivan
Helina Kassahun
Yuhui Ma
Scott M. Wasserman
Michael J. Koren

Video Abstract

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Abstract

Statins are the first-line treatment for hypercholesterolemia in patients at high risk for cardiovascular mortality. But some patients require additional LDL cholesterol lowering to reach risk-stratified LDL-cholesterol levels or to further reduce cardiovascular risk. Clinical trials have demonstrated that the PCSK9 inhibitor evolocumab effectively lowers LDL cholesterol and is well tolerated. A new analysis of data from a subset of these trials extends these findings by evaluating LDL cholesterol lowering in patients receiving different evolocumab dosage regimens. Researchers performed a pooled analysis of data from four randomized 12-week phase 3 clinical trials comparing evolocumab to placebo or ezetimibe. Two subcutaneous evolocumab dosage regimens were examined: 140 mg every two weeks, and 420 mg monthly. Patients received evolocumab either as monotherapy or with background lipidlowering therapies, consisting of a statin alone or with ezetimibe. The primary outcome was the difference in percent change from baseline in LDL cholesterol, calculated using mean week 10 and week 12 values. This outcome was compared among prespecified patient subgroups defined by demographic and disease characteristics. The results showed no substantial differences in LDL cholesterol lowering across dosage regimens or subgroups. Compared to placebo, the two-week regimen led to a mean 66% reduction from baseline LDL-cholesterol, while the monthly regimen led to a mean 65% reduction. Compared to ezetimibe, the two-week regimen led to a mean 39% reduction and the monthly regimen led to a 40% reduction. The researchers also looked at treatment differences among patient subgroups defined by age, gender, race, ethnicity, region, glucose tolerance status, and cardiovascular risk. They found that regardless of dosing regimen, evolocumab was linked to statistically significant mean reductions in LDL-cholesterol from baseline across all subgroups when compared with treatment with placebo or ezetimibe. Certain low-magnitude variations in LDL-cholesterol lowering were found among subgroups, which led to significant quantitative interaction P values. But when tested by qualitative interaction, these values were not significant. Importantly, adverse event rates were similar across groups treated with each evolocumab dosing regimen or control. Overall, these efficacy and safety data support that evolocumab has a favorable benefit-risk profile at two different dosage regimens across diverse patient populations.