First-Time Heart Attacks and Strokes will be Prevented by Evolocumab

Researchers assessed whether adding the PCSK9 inhibitor evolocumab to standard therapy reduces first major adverse cardiovascular events (MACE) compared with placebo in adults with atherosclerosis or high-risk diabetes but without previous myocardial infarction or stroke.

Study

This international, double-blind, randomized, placebo-controlled trial included adults at high cardiovascular risk without prior myocardial infarction or stroke. Eligible participants had atherosclerosis or high-risk diabetes, were on stable lipid-lowering therapy, and had LDL cholesterol of at least 90 mg/dl or equivalent non-HDL or apolipoprotein B thresholds. Participants were assigned in a 1:1 ratio to receive either subcutaneous evolocumab 140 mg every two weeks or a matching placebo, stratified by region and baseline LDL cholesterol.

Investigators and participants remained blinded to assignment. Two primary endpoints were prespecified:

1. Three-point MACE: coronary heart disease death, myocardial infarction, or ischemic stroke.
2. Four-point MACE, the same, plus ischemia-driven arterial revascularization.

A blinded TIMI Clinical Events Committee adjudicated all outcomes. Lipid substudies measured biochemical effects, and Cox proportional hazards models estimated hazard ratios (HRs) with 95% confidence intervals (CIs). The study included 12,257 participants, excluding 44 due to site irregularities. Follow-up spanned a median of 4.5 years. The trial was funded by Amgen (ClinicalTrials.gov NCT03872401).

Findings

Among 12,257 randomized participants (median age 66 years, 43% women), 6,129 received evolocumab and 6,128 received placebo. About two-thirds had qualifying atherosclerosis without prior events, and 59% had diabetes. The median baseline LDL cholesterol level was 122 mg/dL, and most participants received statins, with 68% at high intensity. Evolocumab reduced LDL cholesterol by 55% versus placebo at 48 weeks, yielding a median on-treatment LDL of 45 mg/dl.

Evolocumab significantly reduced the risk of first cardiovascular events. Three-point MACE occurred in 336 evolocumab patients and 443 placebo patients, with a 5-year Kaplan-Meier estimate of 6.2% versus 8.0% (HR 0.75; 95% CI 0.65–0.86; P<0.001). The four-point MACE

endpoint occurred in 747 versus 907 patients (13.4% vs 16.2%; HR 0.81; 95% CI 0.73–0.89; P<0.001). Key secondary outcomes, including myocardial infarction alone (HR 0.64; 95% CI 0.52–0.79), also favored evolocumab. Mortality endpoints were exploratory but numerically lower in the evolocumab group.

Efficacy was consistent across age, sex, race, geography, baseline LDL cholesterol quartiles, and background use of statins or ezetimibe. Fine-Gray competing-risk analyses confirmed the robustness of the primary findings. Although most participants were White (93%), the treatment benefit appeared uniform. Safety profiles were comparable between groups, with no excess in serious adverse events or treatment discontinuations. The magnitude of benefit mirrored the Cholesterol Treatment Trialists' Collaboration (CTTC) projections relating LDL reduction to event risk.

Conclusion

Adding evolocumab to optimized background therapy significantly lowered the risk of first MACE in adults with atherosclerosis or high-risk diabetes who had not yet suffered a myocardial infarction or stroke. Benefits were consistent across key clinical subgroups and achieved without new safety signals.

These findings reinforce the concept of earlier, intensive LDL cholesterol lowering to prevent initial cardiovascular crises, reduce procedural interventions, and maintain functional independence for patients while easing the burden on healthcare systems.

Source:

https://www.news-medical.net/news/20251111/Evolocumab-shows-clear-benefit-in-preventing-first-time-heart-attacks-and-strokes.aspx