A Potential New Treatment for Atherosclerosis in People With HIV

Scientists are looking at whether blocking the receptor PCSK9 could reduce heart disease in people living with HIV.

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It's not just beta blockers, ACE inhibitors and statins that might help protect people living with HIV from developing heart problems. According to a clinical trial published in the Journal of the American College of Cardiology, scientists are also studying a monoclonal antibody that aims to manage abnormal blood lipid levels by blocking a receptor that plays a key role in cholesterol regulation.

Franck Boccara, MD, of Hôpitaux de l'Est Parisien and Sorbonne University, and colleagues enrolled 464 people living with HIV who had elevated cholesterol levels or mixed lipidemia. The participants were randomized two to one to receive either the experimental monoclonal antibody evolocumab or a placebo once monthly.

Evolocumab (brand name Repatha) blocks PCSK9, a protein that plays a role in low-density lipoprotein (LDL)—"bad cholesterol"—metabolism, enhancing the liver's ability to remove LDL from the blood. Evolocumab is currently approved for adults with established cardiovascular disease to reduce the risk for heart attack and stroke and the need for coronary revascularization procedures and for people with inherited conditions that lead to high cholesterol. It has not been well studied in people living with HIV.

The participants were primarily older (mean age 56), male (83%) and white (80%), and had been living with HIV for a mean of 17 years. Almost all, 97%, had an undetectable viral load (fewer than 50 copies). More than one in three (36%) had atherosclerotic cardiovascular disease. Roughly 27% also had been diagnosed with type 2 diabetes, and 28% currently smoked, both of which can increase heart disease risk.

All participants were also taking a maximally tolerated dose of statins, the standard of care for managing elevated cholesterol. For 21% of participants, that meant they weren't taking any statins, due to either a potential interaction between statins and their other medications or for other reasons. In the end, 79% were actually on a high-intensity statin regimen, with slightly more people on statins in the evolocumab group.

The researchers followed the participants for 24 weeks, checking their LDL and other lipid levels at the outset and again at six months.

At the end of the trial, evolocumab reduced LDL levels by 57%. What's more, 73% of people in the evolocumab arm saw their LDL cholesterol drop below 70 mg/dl, compared with just 8% of those in the placebo group. Evolocumab also significantly reduced levels of other lipids linked to atherosclerosis. The study didn't follow participants long enough to look at whether the drug reduced actual heart attacks or other heart-related events.

While 446 people made it to the end of the trial, there were twice as many discontinuations in the evolocumab group compared with the placebo group (eight versus four people). Five of those in the evolocumab arm discontinued because of adverse events, compared with two in the placebo group.

These findings led Vijay Nambi, MD, PhD, of Baylor College of Medicine, and colleagues, writing in an accompanying commentary, to call the results "an important first step" toward new options for people living with HIV. At least two other trials—another one also testing evolocumab—are underway to evaluate ways to target LDL receptors to reduce the risk for heart disease in people living with HIV.

Still, they added that the cost of such drugs "will remain a challenge."

"The investigators should be congratulated for conducting this first randomized controlled trial to establish the short-term efficacy and safety of a PCSK9 inhibitor in individuals with HIV infection," wrote Nambi and colleagues. "We look forward to seeing the results of the additional 24 weeks of follow-up from this study as well as other trials that are evaluating the effect of lipid modification on atherosclerosis and [cardiovascular disease] events in HIV disease."

Click here to read the study abstract

Click here to read the accompanying commentary.

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