New Findings Highlight the Potential Utility of Pitavastatin for People Living with HIV in Support of the REPRIEVE Trial

Pitavastatin may have favorable effects to lower cholesterol and dampen inflammation thereby improving cardiovascular disease risk for people living with HIV. Ongoing studies are needed to determine if pitavastatin also prevents cardiovascular disease events such as heart attacks and strokes.

Boston, MA (PRWEB) April 24, 2017 -- Pitavastatin, a relatively new statin, has relevance to the cardiovascular health of individuals with HIV because it is not known to have significant interactions with antiretroviral therapy (ART). Among people living with HIV, statins may have favorable effects to both lower cholesterol levels and dampen inflammation in the bloodstream.

While lowering cholesterol and dampening inflammation are beneficial effects of statins, the ultimate goal of statin therapy is to prevent a major cardiovascular disease (CVD) event such as a heart attack or stroke. Indeed, the NIH-funded REPRIEVE trial (www.reprievetrial.org), currently underway, is testing whether and how pitavastatin prevents a major cardiovascular event among individuals with HIV who are considered at low-to-moderate CVD risk using conventional methods, including the American College of Cardiology’s ASCVD risk estimator and LDL cholesterol levels. In REPRIEVE, 6,500 such individuals are being randomized to pitavastatin 4 mg daily or placebo and are being followed for an average of four to five years.

This past month, three interrelated papers were published which advance our understanding of the unique effects of pitavastatin in HIV and reinforce the choice of pitavastatin as a promising CVD prevention strategy being studied among individuals with HIV. All three papers stem from the INTREPID trial, a randomized trial conducted among 252 individuals with HIV and abnormal cholesterol, comparing the effects of 12 months of pitavastatin (4 mg/day) vs. pravastatin (40 mg/day), another statin that tends not to interact with ART.

In INTREPID, statin effects on measures of cholesterol and inflammatory/immune markers in the blood were primarily assessed. By contrast, the REPRIEVE trial will determine whether pitavastatin prevents actual cardiovascular events among individuals with HIV who are not already prescribed a statin. A substudy of REPRIEVE will also assess pitavastatin’s effects on immune activation and coronary plaque to determine the degree to which pitavastatin protects the cardiovascular system via lowering cholesterol, dampening of inflammation, and/or directly effecting coronary plaque.

Pitavastatin versus Pravastatin in Adults with HIV-1 Infection and Dyslipidemia: 12 week and 52 Week Results of a Phase 4 Multicenter Randomized, Double-blind Superiority Trial. In this paper published in Lancet HIV, Aberg and colleagues assessed the effects of pitavastatin vs. pravastatin on lipid levels and glucose, as well as the safety/tolerability of both agents. Pitavastatin was more efficacious in lowering LDL cholesterol (-29.7% vs. -20.5%, P=0.0007) and non-HDL cholesterol (-26.1% vs. -19.0%, P=0.0120) compared to pravastatin over 52 weeks. Neither pitavastatin nor pravastatin increased blood glucose, an important consideration as individuals with HIV are often at increased risk of developing diabetes. Both drugs were well tolerated, with relatively few serious adverse events. Myalgia was reported in only 2% of those on either statin in INTREPID. https://www.ncbi.nlm.nih.gov/pubmed/28416195

Effects of Pitavastatin and Pravastatin on Markers of Immune Activation and Arterial Inflammation in HIV. In this paper published by Toribio et al. in AIDS, the authors compared effects of pitavastatin vs. pravastatin on
critical immune activation indices and measures of arterial inflammation. Over 52 weeks, pitavastatin resulted in more significant lowering of sCD14, a key marker of immune activation (-10.0% vs. +0.6%, p=0.02), oxidized LDL (oxLDL), a marker of coronary plaque formation (-26.9% vs. -17.5%, P=0.02), and Lp-PLA2, a marker of arterial inflammation (-26.6% vs. -15.5%, P=0.005). Indeed, the effects were largest in those with the highest levels of immune activation and inflammation, to begin with. This paper suggests an important mechanism by which pitavastatin may help to prevent CVD in HIV that is being further tested in REPRIEVE. 

Greater Remnant Lipoprotein Cholesterol Reduction with Pitavastatin Compared with Pravastatin in HIV-infected Patients. In this paper published in AIDS, Joshi and colleagues examined the effects of pitavastatin and pravastatin on key proteins related to coronary plaque formation, including triglyceride rich remnant lipoprotein RLP-C and the risk ratios of specific proteins, apolipoprotein B/apolipoprotein A1. The pattern of abnormal cholesterol among individuals with HIV is often characterized by increased triglyceride and RLP levels, which may contribute to excess CVD in the HIV population. Pitavastatin lowered RLP by -11.6mg/dL vs. -8.5mg/dL (P=0.01) compared to pravastatin and also lowered the key risk ratio of apolipoprotein B/apolipoprotein A1 by -0.21 vs. -0.13, (P<0.001 pitavastatin vs. pravastatin). https://www.ncbi.nlm.nih.gov/pubmed/28121706

These recently published findings demonstrate that pitavastatin is a safe and effective choice to lower cholesterol among people living with HIV. These findings also offer insight into the mechanisms by which pitavastatin may work to prevent cardiovascular disease. However, more research is needed to determine if pitavastatin is able to prevent cardiovascular disease events such as heart attack and stroke in the setting of HIV. The REPRIEVE trial, being conducted at more than 100 sites in the US and internationally and currently enrolling participants, will ultimately provide the answer to this important question.
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