Another statin option in HIV

In *The Lancet HIV*, Judith Aberg and colleagues present results of the INTREPID study.1 This study was a multicentre, double-blind, double-dummy, randomised clinical trial comparing the safety and lipid lowering effects of pitavastatin (4 mg daily) and pravastatin (40 mg daily) in 252 people with HIV and dyslipidaemia. Study participants were on suppressive antiretroviral therapy (ART), more than 80% were white men, and those with glucose intolerance, established diabetes, or coronary artery disease were not eligible to participate.

At 12 weeks, LDL cholesterol decreased more with pitavastatin than with pravastatin and these effects were sustained at 52 weeks. The proportion of adverse events were similar between the two treatment groups and no effect on fasting glucose, insulin, or glycosylated haemoglobin was recorded. This finding is important given the increased risk of diabetes with statins, particularly with high-dose statin therapy2 and with rosuvastatin.3 HIV clinicians will welcome the results of the INTREPID trial because they establish pitavastatin as an additional appropriate option to treat dyslipidemia also in HIV.

Because pitavastatin is considered to be a weaker LDL-lowering drug than atorvastatin and rosuvastatin,4 we are reassured by the efficacy of pitavastatin in INTREPID (median LDL cholesterol decrease of 31.1%). However, pitavastatin fared better in a randomised, placebo-controlled trial5 that the authors previously did in people without HIV (median LDL cholesterol concentration decrease of 38.1%). Statins are believed to be less effective at lowering LDL cholesterol concentrations in HIV than in the general population because of drug interactions or concurrent use of antiretroviral drugs that promote dyslipidaemia. This notion was confirmed in a large retrospective analysis6 of 550 people with HIV and 5170 seronegative patients starting statin therapy but the difference was relatively small (~25.6% adjusted LDL cholesterol change in people with HIV versus ~28.3% in seronegative people).

Importantly, we do not yet know whether statin treatment translates into meaningful clinical benefits in people with HIV. Statin therapy reduces atherosclerotic plaque in people with HIV7 but conclusive data that statins reduce the cardiovascular event rate in this population are not yet available.8,9 This finding is perhaps surprising given the substantial attention to the notion of accelerated atherosclerosis, or even accelerated aging, in people with HIV in the past few years.

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Lancet HIV 2017
Published Online
April 13, 2017
http://dx.doi.org/10.1016/S2352-3018(17)30072-3
Hopes are therefore high that the ongoing REPRIEVE trial (NCT02344290), sponsored by the manufacturer of pitavastatin and the US National Heart Lung and Blood Institute, will answer this question.14 REPRIEVE investigators intend to randomise 6500 people with HIV aged 40–75 years without known cardiovascular disease to pitavastatin 4 mg per day versus placebo and assess the cardiovascular event rate during 6 years of follow-up. Meanwhile, that lipid-lowering treatment with statins is as relevant to people with HIV at increased cardiovascular risk as it is in the general population remains a reasonable but unproved assumption.

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HK received grants and travel funds paid to her institution from Gilead Sciences, financial support paid to the institution for advisory boards by MSD, Gilead Sciences. PET’s institution received grants and advisory board fees from Gilead, lecture fees from Schwabe Pharma, and grants from Viiv.


