Background

Protease-inhibitor containing antiretroviral therapy for the treatment of HIV-1 infection is associated with elevated triglyceride and LDL-cholesterol levels which may expose patients to an increased risk of coronary artery disease (CAD).

We previously reported 24 week data from a substudy from the Atlantic trial in which we found 1:

- 49 % increase in HDL-cholesterol in NVP - treated patients
- and increases in ApolipoproteinAl (19%), lipoproteinAl (+38%) and HDL particle size (+3%) in these patients

We concluded that the lipid and lipoprotein changes in the nevirapine treated patients result in an anti-atherogenic plasma lipid profile, which has been proven to decrease the incidence of coronary artery disease in other settings.

The objective of the current study was to examine the longer term lipoprotein profiles after 96 weeks of treatment with either a protease inhibitor based, NRTI-based or NNRTI-based regimen from patients included in the Atlantic study.

Methods

The Atlantic Study is an ongoing, randomized, open-label comparative study of three triple antiretroviral regimens for the treatment of HIV-1 infection. Patients were treated with stavudine and didanosine plus the addition of either the non-nucleoside reverse transcriptase inhibitor nevirapine (NVP), the protease inhibitor indinavir (IDV) or the nucleoside reverse transcriptase inhibitor lamivudine (3TC). Standard dosing schedules were used, except for NVP and ddI, which were dose adjusted.

Inclusion criteria Atlantic Study:
- naive, asymptomatic HIV-1 infected patients
- HIV-1 viral load > 500 c/ml
- CD4+ cell count > 200x10^9/L

Inclusion criteria current analysis:
- patients on sustained randomized treatment for at least 96 weeks
- HDL-cholesterol results available at both week 0 and 96
- Week 96 was defined as the closest available timepoint to week 96, but after week 70

Fasting was not mandatory for blood draws.

Concentrations of plasma cholesterol, HDL cholesterol, and triglycerides were measured in a single laboratory using enzymatic assays. LDL-cholesterol concentrations were calculated by the Friedewald formula.

Results

After 96 weeks of treatment we found a 40% increase in HDL-cholesterol and a 6% decrease in the ratio of total over HDL-cholesterol in the patients randomly assigned to the NVP-containing treatment arm. This lipid profile is associated with a decreased incidence of CAD in other settings. HDL-cholesterol did also increase in the 3TC-treated patients but to a lesser extent without any significant changes in the ratio of total over HDL-cholesterol.

In contrast, in the IDV treated patients we found marked increases in total-, LDL-cholesterol and triglycerides together with a 25% increase in the ratio of total over HDL-cholesterol. This lipid profile is associated with an increased incidence of CAD in other settings. These differential changes in lipoprotein profile between regimens may contribute to the choice of initial anti-HIV treatment, particularly if demonstrated to be associated with a different incidence of CAD over the longer term.

The Atlantic study team

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1 M. van der Valk, J. Kastelein, R. Murphy et al. Nevirapine containing potent antiretroviral therapy results in an anti-atherogenic plasma lipid profile: AIDS in press

Table shows absolute and percentage rise with standard errors

Figures show percent change from baseline with standard errors by treatment arm