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Effects of pitavastatin on atherosclerotic-associated inflammatory biomarkers in HIV-infected patients with dyslipidaemia and receiving atazanavir/ritonavir

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Background: Despite undetectable plasma viral load, HIV-infected patients have persistent low-grade inflammation. This was associated with increased risk of cardiovascular diseases, non-AIDS morbidities, and mortality. Statins possess pleiotropic anti-inflammatory activities in addition to lipid lowering effects. Use of different statins has been shown to be associated with reduced biomarkers of inflammation/immune activation and endothelial dysfunction, although there were some discrepant results. Limited data are available regarding anti-inflammatory effect of pitavastatin in HIV-infected patients. We studied the effect of pitavastatin use in virologically-suppressed HIV-infected patients on atherosclerotic-associated inflammatory biomarkers.

Material/methods: This study was a randomized, double-blind, crossover study that evaluated the effect of pitavastatin versus placebo in HIV-infected dyslipidemic patients, who received atazanavir/ritonavir-based antiretroviral agents, on plasma IL-1β, IL-6, IL-12, TNF-α, IFN-γ, hs-CRP, and IP-10. Patients were randomized to receive 12 weeks of pitavastatin 2 mg/day or placebo, followed by 2 weeks of washout period and 12 weeks of another treatment arm. Safety and plasma lipid profiles have been reported previously (ClinicalTrials.gov NCT02442700). This study explored levels of plasma cytokines collected at 12 weeks of treatment, as measured by multiplex ELISA. Comparison between pitavastatin and placebo arms was made by Wilcoxon signed ranks test.

Results: Twenty-three HIV-infected individuals were included in this study. Median (interquartile range; IQR) age of the patients was 45 (41-57) years and 13 (56.5%) patients were male. Median

(IQR) baseline CD4+ lymphocyte counts was 669 (568-839) cells/mm^3. All patients had undetectable HIV viral load. Median (IQR) baseline plasma total cholesterol and LDL cholesterol levels were 246 (215-265) and 147 (130-167) mg/dL, respectively. Most patients (82.6%) had 100% compliance. As compared to placebo, treatment with pitavastatin resulted in significantly lower plasma LDL cholesterol levels (p<0.001), but did not have significant effect on plasma levels of IL-1β, IL-6, IL-12, TNF-α, hs-CRP, and IP-10 (p=NS). Treatment with pitavastatin, as compared to placebo, was associated with a trend toward lowered levels of plasma IFN-γ, with median (IQR) of 53.1 (0-71.7) versus 33.0 (0-72.0) in the placebo arm (p=0.121).

Conclusions: This preliminary study showed that treatment of virologically-suppressed HIV-infected patients with 2 mg/day of pitavastatin for 12 weeks did not have an effect on plasma IL-1β, IL-6, IL-12, TNF-α, hs-CRP, and IP-10, but had a trend toward lowering IFN-γ. Further study of cellular markers of activation as well as the effect of different doses and durations of pitavastatin is warrant.