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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, patients infected with HIV have persistent low-grade inflammation[1]. This inflammation has been shown to be associated with increased risk of cardiovascular diseases risk, other non-AIDS morbidities, and mortality[2,3].
- Statins possess pleiotropic anti-inflammatory activities in addition to lipid lowering effects[4].
- 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[4,5].
- 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.

Materials and Methods

- A randomized, double-blind, crossover study
- 24 HIV-infected dyslipidaemic patients, receiving atazanavir/ritonavir-based antiretroviral agents
- Pitavastatin 2 mg/day or placebo for 12 weeks, followed by 2 weeks of washout period, and then 12 weeks of another treatment arm
- Safety and plasma lipid profiles have been reported previously (ClinicalTrials.gov NCT02442700)[6]
- Plasma collected at 12 weeks of treatment
- Cytokines measured by multiplex ELISA (Bio-Plex ®)
- Hs-CRP measured by immunoturbidimetric assay
- Compared by Wilcoxon signed ranks test

Results

- Twenty-four HIV-infected individuals were included in this study. Baseline characteristics of subjects are shown in Table 1.
- Most patients (83.3%) had 100% drug compliance.
- None of the patients reported any adverse event.

Table 1. Baseline characteristics of subjects who received placebo first compared to those who received pitavastatin first

Characteristics	Placebo (n=12)	Pitavastatin (n=12)	Total (n=24)
Age, years (median, IQR)	45.0 (42.0-52.3)	47.5 (40.3-57.8)	45.5 (41.0-54.0)
Male sex, %	50.0	66.7	58.3
CD4+ T cell count, cells/mm^3 (median, IQR)	740.0 (568.8-862.3)	627.5 (540.3-738.3)	661.5 (559.0-827.0)
Undetectable HIV viral load, %	91.7	100.0	95.8
Duration of ATV/r use, months (median, IQR)	36 (24-36)	42 (30-54)	36 (24-48)
Comorbidities, %			
- None	66.7	33.3	50.0
- Dyslipidaemia	16.7	33.3	25.0
- Chronic hepatitis B or C	16.7	16.7	16.7
- Others	0	16.7	8.3
Cardiovascular risk factors, %			
- <2	91.7	58.3	75.0
- ≥ 2	8.3	41.7	25.0
Baseline lipid profiles, mg/dL (median, IQR)			
- Total cholesterol	249.0 (216.8-263.8)	226.5 (211.3-269.5)	242.5 (215.0-264.0)
- LDL-cholesterol	144.0 (131.0-164.5)	139.5 (117.5-167.5)	144.0 (127.0-160.0)
- HDL-cholesterol	42.0 (35.8-46.8)	36.5 (32.3-51.3)	41.0 (34.0-46.0)
- Triglyceride	184.5 (150.8-358.5)	203.0 (135.3-464.5)	190.0 (145.0-355.0)

* No significant difference between groups for all characteristics

**Current smoking, systolic blood pressure ≥ 140 mmHg or on antihypertensive drugs, HDL <40 mg/dL, first degree relative <55 years in male and <65 years in female, and age >45 years in male or >55 years in female

Results (cont.)

- As compared to placebo, treatment with pitavastatin resulted in significantly lower plasma total cholesterol (TC) and LDL cholesterol (LDL) levels.
- However, pitavastatin did not have a significant effect on plasma levels of IL-1β, IL-6, IL-8, IL-10, TNF-α, MCP-1, IP-10, and high-sensitivity CRP (hs-CRP) (p=NS) at 12th week.

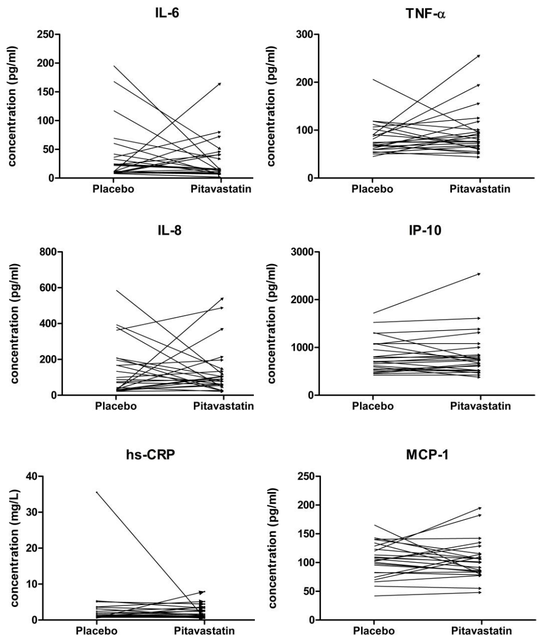

Figure 1. Levels of representative plasma cytokines and hs-CRP after 12 weeks of placebo or pitavastatin

Results (cont.)

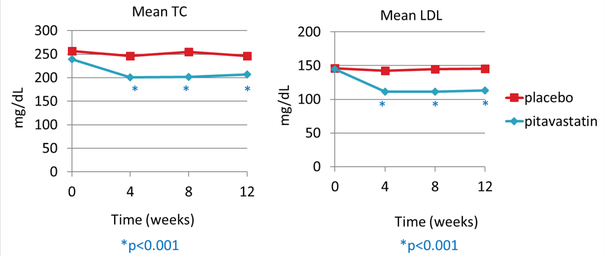

Figure 2. Serum levels of TC and LDL after receiving placebo or pitavastatin, compared by multilevel mixed effect linear regression

Conclusions

- This preliminary study shows that treatment of virologically-suppressed HIV-infected patients with 2 mg/day of pitavastatin for 12 weeks does not have an effect on plasma IL-1β, IL-6, IL-8, IL-10, TNF-α, MCP-1, IP-10 and hs-CRP
- Further study of cellular markers of activation, other biomarkers, as well as the effect of different doses and durations of pitavastatin is warrant.

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Disclosure: None