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Lipid Lowering Effects of Rosuvastatin in HIV-Infected Patients With A Boosted Protease Inhibitor as Part of their Highly Active Antiretroviral Therapy

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Introduction

- Highly active antiretroviral therapy (HAART) has transformed the human immunodeficiency virus (HIV) from a terminal disease to a manageable chronic disorder.
- Hyperlipidemia has become a common issue in the management of HIV due to factors, including the aging of our population, comorbid conditions, and the use of certain antiretrovirals, such as protease inhibitors (PI).[1,2,3]
- PI are substrates and inhibitors of the cytochrome P450 (CYP450) system, particularly the CYP3A4 isoenzyme.[4,5]
- Although most statins rely on CYP3A4 for elimination, rosuvastatin is primarily excreted unchanged in the urine.[5]
- A recent study in HIV-negative subjects evaluated the bioequivalence of rosuvastatin and lopinavir/ritonavir when administered alone and in combination, and showed an increase in plasma concentrations of the statin when administered in conjunction with the PI.[6]
- Paradoxically, patients experienced a blunted lipid-lowering response when rosuvastatin was coadministered with lopinavir/ritonavir in spite of the enhanced serum levels, questioning the utility of this agent in patients on HAART.
- We conducted a retrospective analysis to evaluate the response to rosuvastatin in HIV-infected patients on PI-based regimens.

Objectives

Primary Outcomes:
- Difference in low density lipoprotein (LDL) serum concentrations after addition of 3 months of rosuvastatin therapy.
- Difference in the total cholesterol / high density lipoprotein ratio (TC:HDL) after addition of 3 months of rosuvastatin therapy.

Secondary Outcomes:
- Difference in TC, HDL, triglyceride (TG) levels after addition of 3 months of rosuvastatin therapy.

Methods

- Retrospective chart review of 83 HIV-infected patients treated at Saint Michael's Medical Center in Newark, NJ from March 2004 to October 2008.
- Key inclusion criteria:
  Patients ≥ 18 years of age, treatment with either a PI, concomitant treatment with rosuvastatin for at least 3 months, and a lipid profile drawn before and after rosuvastatin was initiated
- Key exclusion criteria
  Presence of other antilipemics coadministered with rosuvastatin and patients were also exicuded if treated with two PIs (except ritonavir) or a PI in combination with a non-nucleoside reverse transcriptase inhibitor
- The Student's T-test was utilized to measure changes from baseline in total cholesterol, LDL, HDL, and triglyceride levels.

Results

Table 1. Baseline Characteristics

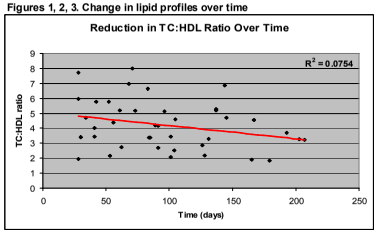
	Total (N=26)
Male sex, n (%)	15 (58)
Race, n (%)	
White	1 (4)
Black	18 (69)
Hispanic	7 (27)
Mean age, y	50
Mean CD4 cell count (cell/mm^3)	440
Mean Viral Load, n (%)	
< 50 copies/mL	7 (27)
< 400 copies/mL	11 (42)
≥ 400 copies/mL	8 (31)
Boosted Protease Inhibitor, n (%)	
Lopinavir/r (Kaletra®)	12 (46)
Fosamprenavir/r (Lexiva®)	4 (15)
Atazanavir/r (Reyataz®)	4 (15)
Saquinavir/r (Invirase®)	3 (12)
Tipranavir/r (Aptivus®)	2 (8)
Darunavir/r (Prezista®)	1 (4)
Background Antiretrovirals, n (%)	
Emtricitabine/Tenofovir (Truvada®)	8 (31)
Lamivudine/Zidovudine (Combivir®)	2 (8)
Abacavir/Lamivudine (Epzicom®)	3 (12)
Tenofovir (Viread®)*	4 (15)
Rosuvastatin dose, n (%)	
5 mg	4 (15)
10 mg	21 (81)
40 mg	1 (4)

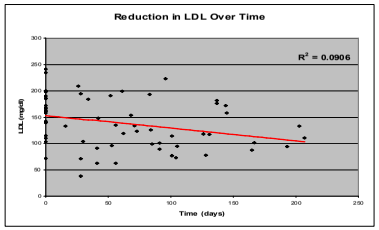
N/n, number of patients; y, years; mm^3, cubic millimeter; mL, milliliter; r, ritonavir (Norvir®)
* Tenofovir administered alone or in combination with either didanosine EC or abacavir

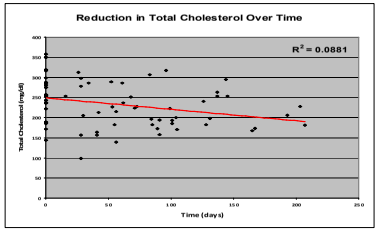
Table 2. Results Table

Laboratory Parameter	Baseline	3 months Post-Rosuvastatin	% Change	P value
TC (mg/dl)	258	213	-17.5%	**0.0003**
TG (mg/dl)	271	239	-11.5%	0.233
LDL (mg/dl)	167	118	-29.3%	**0.0002**
HDL (mg/dl)	52	54	2.5%	0.63
TC:HDL	5.37	4.27	-20.5%	0.07

Figures 1, 2, 3. Change in lipid profiles over time







Discussion

- Rosuvastatin significantly reduced LDL and TC (29.3% and 17.5%, respectively).
- Rosuvastatin appeared well tolerated, although one patient discontinued therapy due to myalgias and an increased creatine kinase.
- Virological response was not affected by the addition of the antilipemic agent.

Conclusions

- Rosuvastatin may have a role in the treatment of dyslipidemia in HIV-infected patients on PI-based HAART.
- A large randomized, controlled study is needed to provide to confirm these findings and the overall safety in this population.

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