Ezetimibe (EZB) lowers cholesterol by blocking cholesterol absorption in the intestine. Data on stable PI-based HAART for at least 6 weeks prior to study entry were analyzed. Addition of EZB to low dose statin effectively lowers LDL and TC and appears to be safe and well-tolerated. We enrolled 20 subjects; 12 (60%) men, 18 (90%) African American, 2 (10%) Latino; mean (SD) age was 49.1 (8.5) years. ART included RTV-boosted PIs in 17 (85%) patients, 3 (15%) were on nelfinavir; 19 were on pravastatin, 1 on atorvastatin. Cholesterol changes are described in the table. Patients were receiving LPV/RTV, LPV and RTV trough concentrations did not change after addition of EZB. One patient experienced elevated CPK possibly related to study medication; no other laboratory abnormalities or adverse effects were seen.

**Table 1. Demographics (N=20)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (n=20)</th>
<th>Wk 6 (n=20)</th>
<th>p-value</th>
<th>Wk 12 (n=20)</th>
<th>Wk 18 (n=16)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mg/dL)</td>
<td>228.8 (42.4)</td>
<td>203.4 (37.7)</td>
<td>0.003</td>
<td>206.9 (35.8)</td>
<td>0.008</td>
<td>208.1 (37.3)</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>139.3 (25.4)</td>
<td>124.0 (33.6)</td>
<td>0.039</td>
<td>122.4 (28.8)</td>
<td>0.010</td>
<td>122.0 (28.6)</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>163.3 (112.6)</td>
<td>154.0 (70.9)</td>
<td>NS</td>
<td>162.4 (102.3)</td>
<td>NS</td>
<td>156.8 (64.6)</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>60.2 (23.9)</td>
<td>58.6 (16.6)</td>
<td>NS</td>
<td>58.3 (18.8)</td>
<td>NS</td>
<td>55.9 (17.6)</td>
</tr>
</tbody>
</table>

**Conclusions:** Addition of EZB to low dose statin effectively lowers LDL and TC and appears to be safe and well-tolerated.

**ABSTRACT**

**Objectives:** Ezetimibe (EZB) lowers cholesterol by blocking cholesterol absorption in the intestine. Data regarding its use are limited in HIV-infected patients. Our main objective was to assess LDL reduction 18 weeks after addition of EZB 10mg/day to statin-treated patients on protease inhibitor (PI)-based antiretroviral therapy (ART).

**Methods:** HIV-infected adults on stable PI-based ART were enrolled in this prospective pilot study if their LDL was not at goal (per National Cholesterol Education Program III guidelines) despite therapy with a statin (pravastatin 20 mg or atorvastatin 10 mg). In a subgroup of patients on lopinavir/ritonavir (LPV/RTV), trough LPV and RTV concentrations were obtained before and after addition of EZB. Data were analyzed using repeated measures ANOVA on ranks with Bonferroni adjustment.

**Results:** We enrolled 20 subjects; 12 (60%) men, 18 (90%) African American, 2 (10%) Latino; mean (SD) age was 49.1 (8.5) years. ART included RTV-boosted PIs in 17 (85%) patients, 3 (15%) were on nelfinavir; 19 were on pravastatin, 1 on atorvastatin. Cholesterol changes are described in the table. Patients were receiving LPV/RTV, LPV and RTV trough concentrations did not change after addition of EZB. One patient experienced elevated CPK possibly related to study medication; no other laboratory abnormalities or adverse effects were seen.

**BACKGROUND**

- Lipid abnormalities are common in HIV-infected patients.
- Controlling this cardiovascular risk factor is essential in decreasing the risk of myocardial infarction (MI) and other atherosclerotic complications; however, HMG-CoA reductase inhibitor (statin) therapy often fails to meet target lipid goals in this patient population.
- Ezetimibe (EZB) inhibits absorption of cholesterol in the intestine, resulting in a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood.
- Two clinical studies in HIV-infected individuals evaluating EZB monotherapy reported a 10-12% reduction in LDL cholesterol after 6 weeks of treatment.
- A 24-wk study in 23 HIV-infected patients evaluated addition EZB to pravastatin 20mg/day and showed an additional 7% decrease in LDL.

Our main objective was to assess lipid changes in HIV-infected patients after addition of EZB to stable statin and PI-based HAART.

**METHODS**

**Study Design**

- Prospective pilot study

**Inclusion criteria**

- HIV-infected adults (> 18 years) on stable PI-based HAART for at least 6 weeks prior to study entry
- Hypercholesterolemia treated with atorvastatin (ATR) 10mg/day or pravastatin (PRA) 20mg/day, and LDL-cholesterol not at goal based on National Cholesterol Education Program III (NCEP)
- Laboratory values within normal limits

**Exclusion criteria**

- Pregnant or breastfeeding women
- Active alcohol or substance abuse
- Presence of decompensated heart failure, MI within 1 year, severe vascular disease, poorly controlled diabetes mellitus

**Primary Objective**

- To assess LDL reduction at 18 weeks

**Secondary Objectives**

- To assess TC, LDL, TG, HDL reductions at 6, 12, and 18 weeks of EZB therapy
- To assess safety of the addition of EZB to statin therapy in HIV-infected patients on PIs
- To evaluate lopinavir/ritonavir trough concentrations before and after addition of EZB (baseline and week 6) in a subgroup of patients on LPV/RTV

**Statistical Analysis**

- Data were analyzed using repeated measures ANOVA on ranks with Bonferroni adjustment

**RESULTS**

**Table 2. Cholesterol Changes**

<table>
<thead>
<tr>
<th>Week</th>
<th>TC (mg/dL)</th>
<th>LDL (mg/dL)</th>
<th>TG (mg/dL)</th>
<th>HDL (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>228.8 (42.4)</td>
<td>139.3 (25.4)</td>
<td>124.0 (33.6)</td>
<td>58.6 (16.6)</td>
</tr>
<tr>
<td>Wk 6</td>
<td>203.4 (37.7)</td>
<td>124.0 (33.6)</td>
<td>122.4 (28.8)</td>
<td>58.3 (18.8)</td>
</tr>
<tr>
<td>Wk 12</td>
<td>206.9 (35.8)</td>
<td>122.4 (28.8)</td>
<td>118.5 (27.8)</td>
<td>55.9 (17.6)</td>
</tr>
<tr>
<td>Wk 18</td>
<td>208.1 (37.3)</td>
<td>120.2 (26.8)</td>
<td>116.8 (46.4)</td>
<td>56.9 (17.6)</td>
</tr>
</tbody>
</table>

**Graph 1. Cholesterol Changes**

**Limitations and conclusion**

- Study limitations: Our cohort of minimal patients had many baseline risk factors for cardiovascular disease
- Our strict inclusion criteria of low-dose statins may have led to a blunted cholesterol-lowering response to combination therapy with statins and EZB

**Conclusions:** Adding ezetimibe to statins resulted in a significant reduction of TC and LDL in all studies at all visits (p<0.05), without significant changes in TG or HDL

At 7 of 20 patients (35%) achieved their NCEP III LDL goal at study completion

**Pharmacokinetic substudy**

- 13 of 20 patients were on LPV/RTV at study entry and completed the PK substudy. No changes in the trough concentrations of LPV or RTV were observed after addition of EZB.

**Acknowledgements**

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**References**

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