Atazanavir-Cobicistat (Evotaz)

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Antiretroviral Therapy: Studies

Atazanavir-Cobicistat (*Evotaz*)
Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2)

Study 105
Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2)  
Study 105: Study Design

• **Background**: Randomized, partially placebo-controlled, double-blind phase 2 trial to compare the safety and efficacy of cobicistat and ritonavir as pharmacokinetic enhancers administered with atazanavir and fixed-dose tenofovir DF-emtricitabine in treatment-naïve adults with HIV infection

• **Inclusion Criteria** (n = 85)  
  - Age ≥18 years  
  - Antiretroviral treatment-naïve  
  - HIV RNA ≥5000 copies/mL  
  - CD4 count >50 cells/mm³

• **Treatment Arms (all once daily)**  
  - Atazanavir-cobicistat (300/150 mg) + TDF-FTC  
  - Atazanavir 300 mg + Ritonavir 100 mg + TDF-FTC

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2) Study 105: Results

Week 24 and 48: Virologic Response (ITT, Missing=Failure)

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2) Study 105: Results

Adverse Events and Treatment Discontinuations

Conclusion: “Using cobicistat and ritonavir as pharmacoenhancers for atazanavir and administered with emtricitabine/tenofovir DF achieved comparable rates of virologic suppression and CD4 cell count increase with satisfactory safety profiles.”
Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3)

Study 114
Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3)
Study 114: Study Design

**Background**: Randomized, double-blind, double-dummy, active controlled phase 3 trial to compare the safety and efficacy of cobicistat and ritonavir as pharmacokinetic enhancers administered with atazanavir and fixed-dose tenofovir DF-emtricitabine in treatment-naïve adults with HIV infection.

**Inclusion Criteria (n = 692)**
- Age ≥18 years
- Antiretroviral treatment-naïve
- Sensitive to atazanavir, tenofovir, and emtricitabine
- HIV RNA ≥5000 copies/mL

**Treatment Arms (all once daily)**
- Atazanavir-cobicistat (300/150 mg) + TDF-FTC
- Atazanavir 300 mg + Ritonavir 100 mg + TDF-FTC

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3) Study 114: Results

Week 48: Virologic Response (ITT, Missing=Failure)

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3)
Study 114: Results

Adverse Events (AE) and Treatment Discontinuations

Conclusions: “COBI was noninferior to RTV in combination with ATV plus FTC/TDF at week 48. Both regimens achieved high rates of virologic success. Safety and tolerability profiles of the 2 regimens were comparable. Once-daily COBI is a safe and effective pharmacoenhancer of the protease inhibitor ATV.”
Cobicistat-Boosted PIs in Patients with Renal Impairment

Study 118
Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Design

• **Background**: Phase 3, non-comparative, open label, 2 cohort study to compare the safety and efficacy of switching ritonavir to cobicistat in virologically suppressed adults with HIV infection and mild to moderate renal impairment.

• **Inclusion Criteria (n = 73)***
  – Antiretroviral treatment-experienced
  – HIV RNA undetectable x 6 months
  – On regimen of 2 NRTIs + ATV/r or DRV/r
  – Stable renal function with CrCl 50 to 89 mL/min

• **Treatment Arms**
  – Cobicistat 150 mg QD + [Atazanavir 300 mg QD or Darunavir 800 mg QD] + 2 NRTIs

*Note: only ritonavir-to-cobicistat switch cohort presented here

Cobicistat-Boosted PIs in Patients with Renal Impairment Study 118: Results

Week 24 and 48: Virologic Response (Snapshot Analysis)

Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Results

Week 48: Virologic Response, by Different Statistical Analyses

Statistical Analysis

- Cobicistat + [Darunavir or Atazanavir] + 2 NRTIs

<table>
<thead>
<tr>
<th>Statistical Analysis</th>
<th>HIV RNA &lt;50 copies/mL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snapshot</td>
<td>82</td>
</tr>
<tr>
<td>ITT, Missing=Failure</td>
<td>88</td>
</tr>
<tr>
<td>ITT, Missing=Excluded</td>
<td>97</td>
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</tbody>
</table>

Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Results

Week 48: Changes in Creatinine Clearance, by Baseline CrCl

<table>
<thead>
<tr>
<th>Baseline CrCl</th>
<th>Median Change in CrCl from Baseline (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>-3.8</td>
</tr>
<tr>
<td>&lt; 70 mL/min</td>
<td>-1.1</td>
</tr>
<tr>
<td>≥ 70 mL/min</td>
<td>-6.6</td>
</tr>
</tbody>
</table>

# Cobicistat-Boosted PIs in Patients with Renal Impairment

## Study 118: Results

<table>
<thead>
<tr>
<th>Laboratory Value</th>
<th>Cobicistat + [ATV or DRV] + 2 NRTIs (n=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine increase ≥ 0.4mg/dL</td>
<td>4.1%</td>
</tr>
<tr>
<td>Hypophosphatemia (≥ grade 1 increase)</td>
<td>1.4%</td>
</tr>
<tr>
<td>Proteinuria (≥ grade 2 increase)</td>
<td>1.4%</td>
</tr>
<tr>
<td>Normoglycemic glycosuria (≥ grade 1 increase)</td>
<td>0</td>
</tr>
</tbody>
</table>

Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Results

Adverse Events and Treatment Discontinuations

Conclusions: “COBI was noninferior to RTV in combination with ATV plus FTC/TDF at week 48. Both regimens achieved high rates of virologic success. Safety and tolerability profiles of the 2 regimens were comparable. Once-daily COBI is a safe and effective pharmacoenhancer of the protease inhibitor ATV.”

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