Atazanavir

Its role in HIV treatment

Telemed News update

CME, October 2009
How much do you know about atazanavir?

Across:

3 Which nucleotide reverse transcriptase inhibitor does lower atazanavir plasma levels by 20-40%?
4 Which complications may you expect in view of the fact that atazanavir prolong the PR interval on ECG’s?
5 How many times per day a patient should take atazanavir?

Down:

1 To which HIV drug-class does belong atazanavir
2 Atazanavir is not active against which virus type
Overview

- Azatanavir (ATV) is a protease inhibitor (PI) approved for the treatment of HIV-1 infection
- ATV is the first PI approved for once-daily dosing
- ATV is both a substrate and inducer of cytochrome P450 (CYP3A4) and an inhibitor and inducer of P-glycoprotein
- Drug-drug interactions are frequent with other drugs metabolized by CYP3A4
- Bioavailability is enhanced by food
Dosage

- ATV 400 mg (two 200-mg capsules) once daily, taken with food

OR

- ATV 300 mg (one 300-mg capsule or two 150-mg capsules) with ritonavir 100 mg once daily (all as a single dose with food) if combined with any of the following:
  - tenofovir
  - efavirenz
Side effects

- Atazanavir causes unconjugated bilirubinemia in over 40% of patients but results in less than 2% discontinuations.

- PR interval prolongation may occur in some patients and ATV should be used with caution in patients with preexisting conduction system disease or when administered with other drugs that may prolong the PR interval.
Drug-drug interactions

ATV should not be used with proton pump inhibitors, such as omeprazole; a 76% reduction in ATV area under the concentration-time curve (AUC) and a 78% reduction in ATV trough plasma concentration (Cmin) were observed when boosted ATV was coadministered with omeprazole 40 mg.

Proton pump inhibitors reduce the effects of ATV.
## Drugs that are contraindicated with ATV

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drugs within class that are contraindicated with REYATAZ</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimycobacterials</td>
<td>Rifampin</td>
<td>Rifampin substantially decreases plasma concentrations of atazanavir, which may result in loss of therapeutic effect and development of resistance.</td>
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<tr>
<td>Antineoplastics</td>
<td>Irinotecan</td>
<td>Atazanavir inhibits UGT1A1 and may interfere with the metabolism of irinotecan, resulting in increased irinotecan toxicities.</td>
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<tr>
<td>Benzodiazepines</td>
<td>Midazolam, triazolam</td>
<td></td>
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<tr>
<td>Ergot Derivatives</td>
<td>Dihyderoergotamine, ergotamine, ergonovine, methylergonovine</td>
<td>Potential for serious and/or life-threatening events such as acute ergot toxicity characterized by peripheral vasospasm and ischemia of the extremities and other tissues.</td>
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<tr>
<td>GI Motility Agent</td>
<td>Cisapride</td>
<td>Potential for serious and/or life-threatening reactions such as cardiac arrhythmias.</td>
</tr>
<tr>
<td>Herbal Products</td>
<td>St. John’s wort (<em>Hypericum perforatum</em>)</td>
<td>Patients taking REYATAZ should not use products containing St. John’s wort because coadministration may be expected to reduce plasma concentrations of atazanavir. This may result in loss of therapeutic effect and development of resistance.</td>
</tr>
<tr>
<td>HMG-CoA Reductase Inhibitors</td>
<td>Lovastatin, simvastatin</td>
<td>Potential for serious reactions such as myopathy including rhabdomyolysis.</td>
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<tr>
<td>Neuroleptic</td>
<td>Pimozide</td>
<td>Potential for serious and/or life-threatening reactions such as cardiac arrhythmias.</td>
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<tr>
<td>Protease Inhibitors</td>
<td>Indinavir</td>
<td>Both REYATAZ and indinavir are associated with indirect (unconjugated) hyperbilirubinemia.</td>
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</tbody>
</table>
Efficacy

- Ritonavir-boosted ATV (ATV/r) has similar antiviral activity as lopinavir boosted in both antiretroviral-naive and -experienced patients.
- ATV impact on lipids is less than other PIs and it is suitable for those patients in whom hyperlipidemia is undesirable.
- Ritonavir enhances the bioavailability of ATV but may result in some elevation of lipids.
- Tenofovir lowers ATV plasma levels by 20-40% and ritonavir boosting of ATV is recommended with tenofovir.

Atazanavir, with or without ritonavir should not be coadministered with proton pump inhibitors, U.S. Food and Drug Administration, Consumer Updates, 30/04/2009