EFFECT OF FALDAPREVIR ON ATAZANAVIR PHARMACOKINETICS IN PATIENTS WITH HIV/HCV CO-INFECTION

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BACKGROUND

Faldaprevir (FDV) is a potent inhibitor of HCV NS3/4A, with activity against HCV genotypes 1, 4, 5, and 6, which are common in the HIV/HCV co-infected population. FDV is a substrate of CYP3A4, a moderate inhibitor of CYP3A4 at 240 mg dose, and a weak inhibitor of CYP3A4 at 120 mg. Closest characterized statement (CMAA) is a mild inhibitor of CYP3A4. In healthy subjects, no clinically relevant effect on the pharmacokinetics (PK) of tenofovir, darunavir, and saquinavir was observed.

METHODS

Individuals on an ATV/r regimen with baseline bilirubin levels >2.5 x ULN were excluded from the study. This was a PK substudy of the STARTVerso4 trial, which was approved by the relevant ethics committees and regulatory authorities and conducted in accordance with the Declaration of Helsinki. Individual participants provided written informed consent in writing.

RESULTS

- The effect of ATV/r on FDV PK was evaluated by comparison with historical data from 6,090 subjects receiving ATV/r-based ART.
- The safety profile of FDV in this HIV/HCV co-infected population was similar to that observed in STARTVerso4, a Phase III trial in an HCV/HIV co-infected population.

TABLE 1. Comparison of mean steady-state PK parameters of ritonavir before and after administration of faldaprevir

<table>
<thead>
<tr>
<th>PK parameter</th>
<th>Ritonavir (N=11)</th>
<th>Ritonavir (N=12)</th>
<th>Adjusted GMR (N=11)</th>
<th>Adjusted GMR (N=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMR (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cmax,ss</td>
<td>2,000</td>
<td>109.37</td>
<td>Not determined</td>
<td>Not determined</td>
</tr>
<tr>
<td>AUC0–24h,ss</td>
<td>2,000</td>
<td>225.13</td>
<td>Not determined</td>
<td>Not determined</td>
</tr>
<tr>
<td>T1/2,ss</td>
<td>2,000</td>
<td>67.25</td>
<td>Not determined</td>
<td>Not determined</td>
</tr>
</tbody>
</table>

CONCLUSION

- No clinically relevant changes in the steady state PK of FDV were observed with ATV/r.
- The safety profile of FDV in HIV/HCV co-infected patients was consistent with that observed in STARTVerso4, a Phase III trial in an HCV/HIV co-infected population.

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