Pharmacokinetic interaction between etravirine and lopinavir/ritonavir in HIV-negative volunteers

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Abstract

Objectives
Etravirine (ETR; TMC125) is a next-generation NNRTI with demonstrated activity in treatment-experienced, HIV-1-infected patients. A previous interaction trial in HIV-negative volunteers demonstrated 17% increase of ETR exposure when co-administered with the soft gel formulation of lopinavir/ritonavir (LPV/r) with low-dose ritonavir (RTV). This study re-evaluated the pharmacokinetics of ETR and LPV when LPV/r was administered as the Meltrex formulation in HIV-negative healthy volunteers.

Methods
In an open-label, randomized, two-way, two-period crossover trial, ETR 200mg bid was given for 8 days. After 14 days washout, LPV/r 400/100mg bid was administered for 16 days. ETR 200mg bid was co-administered on days 9–16. Study drug formulations were assessed over 12 hours for the ETR, LPV, and RTV alone and after co-administration. Pharmacokinetic (PK) parameters were obtained by non-compartmental analysis and analyzed by linear mixed-effects model. Safety and tolerability were assessed.

Sixteen volunteers participated (11 male/five female). PK results are given below:

Results

PK and safety parameters and statistical analyses

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<tbody>
<tr>
<td>ETR</td>
<td>LPV</td>
<td>RTV</td>
<td></td>
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<tr>
<td></td>
<td>Alone</td>
<td>With ETR</td>
<td></td>
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<tr>
<td></td>
<td>[mean ± SD]</td>
<td>[mean ± SD]</td>
<td>[mean ± SD]</td>
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<tr>
<td>AUC</td>
<td>125 ± 72</td>
<td>107 ± 53</td>
<td>84 ± 21</td>
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<tr>
<td>C_{max}</td>
<td>5.3 ± 1.9</td>
<td>4.2 ± 1.5</td>
<td>3.8 ± 1.6</td>
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<tr>
<td>C_{min}</td>
<td>3.5 ± 0.8</td>
<td>2.7 ± 0.6</td>
<td>2.4 ± 0.6</td>
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<tr>
<td>C_{eff}</td>
<td>2.7 ± 0.6</td>
<td>2.1 ± 0.5</td>
<td>1.9 ± 0.4</td>
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<tr>
<td>SD</td>
<td>72 ± 33</td>
<td>53 ± 26</td>
<td>21 ± 9</td>
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<tr>
<td>LSM</td>
<td>125 ± 64</td>
<td>107 ± 47</td>
<td>84 ± 17</td>
</tr>
<tr>
<td>CI</td>
<td>1.76–1.98</td>
<td>1.63–1.96</td>
<td>1.49–1.65</td>
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Conclusions

ETR had no clinically relevant effect on the pharmacokinetics of LPV and RTV. When co-administered with the Meltrex® formulation of LPV/r, ETR PK parameters decreased by 30–45%. The effect of the Meltrex® formulation of LPV/r on ETR is comparable to that seen with DRV/r. ETR can be co-administered with LPV/r without dose adjustments.

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References


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