Etravirine demonstrates a favourable safety and tolerability profile: pooled 96-week results from the Phase III DUET trials

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Abstract

Background

The next-generation NNRTI etravirine (ETR; TMC125) demonstrated superior efficacy versus placebo, and a tolerability profile generally similar to efavirenz (EFV) in two Phase III trials in treatment-experienced, HIV-1-infected patients (DUET-1 and DUET-2). This report shows the safety results from a pre-specified pooled analysis of the DUET-1 and DUET-2 trials.

Methods

Patients with documented NNRTI resistance and ≥3 primary protease inhibitor (PI) mutations were randomised to ETR 200 mg or placebo bid, both with a background regimen (BR) of darunavir with low-dose ritonavir (DRV/r), investigation selected NNRTI ± enfuvirtide (ENF). Incidence and severity of adverse events (AEs) were recorded. To account for the differences in treatment duration, incidences were adjusted for total patient years of exposure.

Results

Few treatment-related and no serious AEs were reported in ETR or placebo. Treatment duration was similar in the two groups. The incidence of AEs and grades 3–4 liver abnormalities was generally comparable between treatment groups. When adjusted for total patient years of exposure, the incidence of any grade 3–4 AE, grade 3–4 NNRTIs, and grade 3–4 liver abnormalities was similar between the treatment groups.

Conclusions

Apart from rash, ETR demonstrates a tolerability profile generally similar to placebo over 96 weeks in the DUET trials.

Mean change from baseline in lipids: pooled 96-week analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ETR 200 mg (n=599)</th>
<th>Placebo (n=604)</th>
<th>Mean change from baseline</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL-cholesterol</td>
<td>70.1</td>
<td>68.7</td>
<td>1.4</td>
<td>0.653</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>95.3</td>
<td>93.7</td>
<td>1.6</td>
<td>0.056</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>113</td>
<td>105</td>
<td>8</td>
<td>0.118</td>
</tr>
</tbody>
</table>

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Conclusions

• Consistent with previous results at 24 and 48 weeks, the incidence of AEs was similar in both treatment groups, with the exception of rash, which occurred more commonly in the ETR group.

• No safety signals were associated with longer treatment with ETR and there were no unexpected safety concerns between Weeks 48 and 96.

• The incidence of nervous system, psychiatric and hepatic AEs was low and comparable between the ETR and placebo groups.

• The incidence of laboratory abnormalities, including lipid abnormalities, was low and similar in the two groups.

• The incidence of AEs adjusted for patient exposure was similar and often lower in the ETR group than the placebo group.

• Apart from rash, ETR demonstrates a tolerability profile generally similar to placebo in treatment-experienced, HIV-1-infected patients over 96 weeks.