Tenovir DF Can Be Used Safely in Combination with Didanosine-EC 250mg: Effects on Lymphocytes, CD4, Viral Load, and GFR

Introduction

• A paradoxical CD4 decline despite complete HIV RNA viral suppression was reported in a retrospective cohort analysis of 289 patients receiving didanosine (ddi) 400 mg/day with tenofovir DF (TDF)1
• TDF increases ddi plasma concentrations up to 60% following 400 mg/day of ddi
  – Mechanism of this drug interaction is by inhibition of purine nucleoside phosphorylase degradation of ddi
  – In adults weighing >65kg, ddi dose should be reduced to 250 mg/day when co-administered with TDF (300 mg/day) to attain similar systemic exposure3
• Limited data exist on the safety and efficacy of TDF + ddi when the recommended lower dose (250 mg) of ddi is used

Objectives

• To evaluate the safety and efficacy of a lower dose of ddi (250 mg/day) when given with TDF (300 mg/day) in HAART regimens
• To evaluate the effects of ddi (250 mg/day) administered with TDF (300 mg/day) on CD4 counts

Methods

• Retrospective observational cohort of 72 HIV-infected patients from two clinics
  • All patients receiving HAART with TDF 300 mg and ddi-EC (enteric-coated) from July 2005 to July 2007 were included in the analysis

Results

Table 1. Baseline Demographics (N=72)

<table>
<thead>
<tr>
<th>Patient Group at Baseline</th>
<th>Mean (range) age, years</th>
<th>Male</th>
<th>Female</th>
<th>Race/Ethnicity</th>
<th>Risk Factor</th>
<th>ARV Treatment</th>
<th>ARV-Experienced (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARV-Naive (n=9)</td>
<td>Mean (range) years on HAART</td>
<td>7.5 (1.0-16.0)</td>
<td>7/9</td>
<td>28%</td>
<td>53%</td>
<td>12%</td>
<td>7/9</td>
</tr>
<tr>
<td>ARV-Experienced HIV RNA &lt; 400 c/mL (n=15)</td>
<td>Mean (range) years on HAART</td>
<td>7.5 (1.0-16.0)</td>
<td>15/23</td>
<td>49%</td>
<td>60%</td>
<td>12%</td>
<td>15/23</td>
</tr>
<tr>
<td>HIV RNA ≥ 400 c/mL (n=48)</td>
<td>Mean (range) years on HAART</td>
<td>7.5 (1.0-16.0)</td>
<td>48/2</td>
<td>28%</td>
<td>20%</td>
<td>12%</td>
<td>48/2</td>
</tr>
</tbody>
</table>

Table 2. HIV RNA Response

<table>
<thead>
<tr>
<th>Patient Group at Baseline</th>
<th>Baseline HIV RNA copies/mL</th>
<th>Percent of Patients with HIV RNA &lt; 400 copies/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARV-Naive (n=9)</td>
<td>36,384 (544 to 2,133,523)</td>
<td>67 78 78 78</td>
</tr>
<tr>
<td>ARV-Experienced HIV RNA &lt; 400 c/mL (n=15)</td>
<td>81 (&lt;50 to 1,488)</td>
<td>73 47 87 87</td>
</tr>
<tr>
<td>HIV RNA ≥ 400 c/mL (n=48)</td>
<td>4,213 (6,161 to 16,298)</td>
<td>40 44 56 60</td>
</tr>
</tbody>
</table>

Figure 1. Median HIV RNA Change from Baseline

Figure 2. CD4 Cell Counts in ARV-Naive Patients (N=9)

Figure 3. CD4 Cell Counts in ARV-Experienced Patients with Baseline HIV RNA < 400 c/mL (N=15)

Figure 4. GFR Estimated by MDRD Equation* (N=72)

Conclusions

• In contrast to a previous report1 with TDF and ddi 400 mg, no patient discontinued this regimen because of CD4 cell count decline using the recommended lower dose of ddi 250 mg/day with TDF
• Significant viral load reduction was observed through 3 years
• ddi-associated toxicities were the most common reasons for treatment discontinuation
• Renal function remained relatively stable throughout the 36 month observation period as only 1 patient discontinued due to renal impairment
• Overall, TDF and ddi-EC 250 mg/day was safe and effective in this predominantly highly-experienced population

References