Introduction

• TDF (in combination with FTC) is a NRTI backbone in most recommended regimens in US/EU treatment guidelines
• TDF has limitations and can be improved
  - Dose adjustment when CrCl < 50 mL/min; Nephrotoxicity; Loss of bone mineral density
  - Likely relationship between TFV exposure and renal or bone toxicity
• TAF is a novel prodrug of TFV with distinct metabolic design to maximize antiviral potency and clinical safety
  - TAF provides comparable efficacy to TDF at one-tenth the dose, resulting in lower TFV concentrations and fewer off-target effects
• Exposure of TAF is increased in the presence of cobicistat
  - Dose adjustment when CrCl < 50 mL/min; Nephrotoxicity; Loss of bone mineral density

Methods (cont’d)

• Study treatments administered in the morning under fed conditions
• Safety assessed throughout study
• Plasma TFV, FTC, EVO and COBI concentrations were determined (as applicable per treatment) via LC/MS/MS
• PK parameters estimated via noncompartmental methods (WinNonLin v.6.3)
• A parametric (normal theory) ANOVA was used for generation of geometric mean ratio (GMR) for TAF (AUC_{0→∞}, C_{max}) and FTC (AUC_{0→∞}, C_{max})
  - Treatment 1: F/TAF (25 mg TAF dose)
  - Treatment 2: F/TAF (10 mg TAF dose), EVO + COBI

Results

Table 1. Demographics

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled/completed</td>
<td>116/116</td>
</tr>
<tr>
<td>Sex (male/female), n</td>
<td>76/40</td>
</tr>
<tr>
<td>Mean age, years (range)</td>
<td>55.4 (24-81)</td>
</tr>
<tr>
<td>Mean weight, kg (range)</td>
<td>75.7 (48.9, 108)</td>
</tr>
</tbody>
</table>

Safety

Table 1. Demographics

<table>
<thead>
<tr>
<th>Study 1 (F/TAF 25 mg)</th>
<th>Study 2 (E/C/F/TAF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled/completed</td>
<td>116/116</td>
</tr>
<tr>
<td>Sex (male/female), n</td>
<td>76/40</td>
</tr>
<tr>
<td>Mean age, years (range)</td>
<td>55.4 (24-81)</td>
</tr>
<tr>
<td>Mean weight, kg (range)</td>
<td>75.7 (48.9, 108)</td>
</tr>
</tbody>
</table>

Safety

Study 1 (F/TAF 25 mg)

- No deaths occurred
- One serious AE occurred in the F/TAF 25 mg arm (cornal herniorrhaphy); unrelated to study drug
- No other AEs were Grade 3 or 4 in severity
- One AE reported in >1 subject was:
  - Gastrointestinal (nausea, constipation, vomiting, diarrhea), headache, dizziness, tension headache, toothache

Study 2 (E/C/F/TAF)

- No deaths occurred
- One serious AE occurred in the E/C/F/TAF 18 mg arm (peritoneal hemorrhage); unrelated to study drug
- No other AEs were Grade 3 or 4 in severity
- One AE reported in >1 subject was:
  - Gastrointestinal (nausea, constipation, vomiting, diarrhea), headache, dizziness, tension headache, toothache

Figure 1. Study Design; Two Randomized, Open Label, Single Dose, Two-Way, Cross-Over Studies in Healthy Volunteers

Methods

- To establish bioequivalence for F/TAF to E/C/F/TAF as a bridge to the safety and efficacy of E/C/F/TAF
- To evaluate the safety and tolerability of single oral doses of EVG, FTC, and TAF as administered as FDC tablets (E/C/F/TAF and F/TAF)

Figure 2. TAF Pharmacokinetics Study 1: Mean (± SD) Plasma TAF Concentration-time Profiles

Figure 3. TAF Pharmacokinetics Study 2: Mean (± SD) Plasma TAF Concentration-time Profiles

Conclusions

- F/TAF (200/10 mg + EVO + COBI) is bioequivalent to E/C/F/TAF
- F/TAF (200/25 mg) is bioequivalent to E/C/F/TAF
- Through bioequivalence, the safety and efficacy of F/TAF FDC is bridged to that established in clinical studies of E/C/F/TAF

Acknowledgments

We extend our thanks to study participants and their families as well as the study teams.

Disclosures

© 2015 Gilead Sciences, Inc. All rights reserved.