Patient-reported outcomes in the single-tablet regimen (STaR) trial of rilpivirine/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate in antiretroviral treatment-naive adults infected with HIV-1 through 48 weeks of treatment

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Patient-reported outcomes in the single-tablet regimen (STaR) trial of rilpivirine/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate in antiretroviral treatment-naive adults infected with HIV-1 through 48 weeks of treatment

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ABSTRACT

This 96-week, randomized, open-label study was designed to assess the efficacy and safety of two single-tablet regimens in treatment naïve HIV-1-infected adults: rilpivirine (RPV) + emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) and efavirenz (EFV) + FTC/TDF. Assessments included patient-reported Medication Adherence Self-Report Inventory, SF-12v2 Quality of Life assessment, HIV Treatment Satisfaction Questionnaire, and HIV Symptom Index Questionnaire through Week 48. Additional evaluations included study drug discontinuations due to treatment-emergent adverse events (TEAEs). A total of 786 participants (n=394 RPV/FTC/TDF, n=392 EFV/FTC/TDF) were included. Fewer RPV/FTC/TDF-treated than EFV/FTC/TDF-treated participants discontinued study drug due to TEAEs (2.5% vs. 8.7%), with 41% (14/34) TEAE-related discontinuations in the EFV/FTC/TDF group occurring within the first four weeks of treatment. Treatment adherence and satisfaction remained high through Week 48 and quality of life improved from baseline in both groups. There were no significant between-group differences in virologic success (HIV-1 RNA <50 copies/mL) regardless of adherence (<95% or ≥95%). Significant between-group differences favouring RPV/FTC/TDF were observed for the HIV SIQ symptoms of difficulty falling or staying asleep (p = .022) and diarrhea or loose bowel movements (p = .002). In conclusion, 48-week treatment with RPV/FTC/TDF or EFV/FTC/TDF was associated with high adherence, high treatment satisfaction, and improved quality of life. TEAE-related discontinuations and patient-reported symptoms indicate that RPV/FTC/TDF may be somewhat better tolerated than EFV/FTC/TDF.

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Introduction

Long-term adherence to antiretroviral treatment (ART) for HIV infections can be challenging to achieve, despite the progress made in simplifying regimens by decreasing dose frequency and reducing toxicity (Aldir, Horta, & Serrado, 2014; Boyd, 2009; Nachega, Mugavero, Zeier, Vitoria, & Gallant, 2011).

Patient-reported assessment of adherence is relatively easy to conduct, yet sensitive enough to detect significant associations between nonadherence and greater rates of hospitalization and emergency room visits (Brigido et al., 2001; Garcia de Olalla et al., 2002; Juday, Gupta, Grimm, Wagner, & Kim, 2011), as well as between nonadherence and worsening of virologic outcomes (Ammassari et al., 2001; Barfod et al., 2005; Cahn et al., 2004, 2013; Gardner et al., 2008, 2010; Glass et al., 2008).

Furthermore, clinicians’ assessment of adherence is poor (Gross, Bilker, Friedman, Coyne, & Strom, 2002; Miller et al., 2002; Murri et al., 2004; Paterson et al., 2000) and rarely agrees with that of the patients (Wagner et al., 2001). For these reasons, the International Association of Physicians in AIDS Care (IAPAC), the United States Department of Health and Human Services (DHHS), and the National Institute for Health and Clinical Excellence (NICE) have each recommended using patient-reported adherence over other methods (“Medicines Adherence”, 2009; Panel on Antiretroviral Guidelines for Adults and Adolescents, 2014; Thompson et al., 2012).

In addition, patient-reported symptoms have benefits over provider-reported adverse events (AEs) (Edelman, Gordon, & Justice, 2011; Justice, Rabeneck, Hays, Wu, & Bozzette, 1999), since they have been associated with low treatment satisfaction and poor adherence (Ammassari
et al., 2001; Duran et al., 2001; Jordan et al., 2005) as well as with increased virologic failure rates (de Boer, Prins, Sprangers, Smit, & Nieuwkerk, 2011), whereas provider-reported AEs demonstrate no such correlations (Flandre et al., 2002).

The single-tablet regimen (STR) consisting of rilpivirine (25 mg), emtricitabine (200 mg), and tenofovir disoproxil fumarate (300 mg) (RPV/FTC/TDF; Complera® in US, Eviplera® in EU) was approved in the USA and the European Union in 2011 for treatment of HIV-1 infections in treatment-naive adults with HIV-1 RNA ≤100,000 copies/mL (“Gilead Sciences, Inc.”, 2014; “Gilead Sciences International Limited”, 2014) based on results from two trials (ECHO and THRIVE; Cohen et al., 2013). However, due to differences in dosing requirements between components, these trials required twice-daily dosing in order to preserve the double-blind design and do not reflect the potential benefits of once-daily single-tablet dosing.

The single-tablet regimen (STaR) trial, a randomized open-label study in treatment-naive adults, was designed to mimic STR-based clinical practice and has demonstrated non-inferior efficacy and better tolerability of RPV/FTC/TDF compared with the STR consisting of efavirenz (600 mg), FTC, and TDF (EFV/FTC/TDF; Cohen et al., 2014). The current analysis presents the patient-reported data on adherence, symptoms, and treatment satisfaction from that trial, together with discontinuations due to treatment-emergent AEs (TEAEs).

Methods

Study design

Details of the trial have been published previously (Cohen et al., 2014). This was a 96-week, international, multicenter, open-label, Phase 3b study (GS-US-264-0110, NCT01309243, EUDRACT 2010-024007-27), designed to assess the safety and efficacy of once-daily STRs, RPV/FTC/TDF (QD with a meal of ≥500 kcal) compared with EFV/FTC/TDF (once daily [QD] on an empty stomach, preferably at bedtime), in HIV-1 positive (HIV-1 RNA ≥2500 copies/mL), treatment-naive adults randomized by HIV-RNA strata (≥100,000 copies/mL vs. >100,000 copies/mL). All analyses were based on the participants who received ≥1 dose of study drug (safety population). The study was conducted in accordance with the Declaration of Helsinki. All treatments were approved by institutional review boards and all participants provided a written informed consent.

Patient-reported treatment adherence

Participants were asked to complete an abbreviated version of the Medication Adherence Self-Report Inventory (M-MASRI; Walsh, Mandalia, & Gazzard, 2002), which was administered at each study visit (Weeks 4, 8, 12, 16, 24, 32, 40, and 48). Missing questionnaires were excluded from the analysis and between-group comparisons were performed using the Wilcoxon rank sum test. In addition, participants rated their treatment adherence over the previous 30 days using a linear visual analog scale (VAS), ranging from 0% (taken zero doses of prescribed regimen) to 100% (taken every dose of prescribed regimen). Mean VAS responses were summarized using descriptive statistics only. Investigator-reported adherence was also assessed via pill count and summarized categorically (<95% and ≥95%).

Patient-reported outcomes (PROs)

The HIV Treatment Satisfaction Questionnaire (HIVTSQ; Woodcock & Bradley, 2001, 2006) consists of 10 questions assessing the impact of HIV treatment on participants’ lifestyle and well-being. For each question, participants responded with a score from 0 (least favorable) to 6 (most favorable). Overall treatment satisfaction is the sum of these scores (maximum 60). Patients were assessed at Weeks 24 and 48. Missing values were handled using standard, pre-defined criteria: if more than one response was missing on an individual questionnaire, then the total treatment satisfaction score was considered “missing”; otherwise, the missing value was imputed from the average score for the rest of that questionnaire and the total treatment satisfaction score was calculated. Missing questionnaires were excluded from the analysis. For each treatment group, descriptive statistics were used to summarize the mean score for each question and mean total treatment satisfaction. In addition, total treatment satisfaction scores were analyzed using an analysis of variance (ANOVA) model, with treatment as a covariate.

The HIV Symptom Index Questionnaire (HIV SIQ; Justice et al., 2001) is a 20-item questionnaire designed to assess the presence and perceived distress due to symptoms during the previous four weeks. Scores for each question range from 0 (no symptom) to 4 (symptom bothers a lot). The HIV SIQ was administered at baseline and at each study visit. As part of the pre-specified analysis, responses for each question were characterized as “no symptom” (score 0) or “with symptom” (score grades of 1, 2, 3, or 4) and summarized using descriptive statistics. Analyses by symptom severity were not performed. Missing questionnaires were excluded from the analysis. For each visit, within-group comparisons versus baseline were performed using the McNemar test. Between-group differences were evaluated using the Cochran-Mantel–Haenszel row mean score test with modified ridit scores,
and the $p$-values refer to the entire distribution of changes in symptom status: absent to present, absent to absent, present to present, present to absent.

The 12-item Medical Outcomes Study Short-Form (SF-12v2) quality of life questionnaire (Ware, Kosinski, & Keller, 1996) encompasses eight health domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Mean score changes for each domain and the composites of physical health (most heavily influenced by domains of physical functioning, role physical, bodily pain, general health, and vitality) and mental health (most heavily influenced by domains of general health, vitality, social functioning, role emotional, and mental health) are presented. Each of the 12 items requires responses with raw scores of 1–3 or 1–5. For each domain and composite, these raw scores are added up and converted to values ranging from 0 to 100, using the following formula: [(actual raw score − lowest possible raw score)/possible raw score range] × 100. The SF-12v2 was administered at baseline and at Weeks 24 and 48. Questionnaires with any missing responses were considered “missing” and excluded from the analysis. For the physical and mental health composite scores, within-group mean changes from baseline were evaluated using the Wilcoxon signed rank test and between-group differences were evaluated using the Wilcoxon rank sum test.

Supportive investigator-reported outcomes

Investigator-reported outcomes used to assess treatment tolerability included the proportion of participants experiencing at least one TEAE leading to permanent treatment discontinuation and duration of exposure prior to discontinuation by system organ class and preferred term (MedDRA Version 15). Duration of exposure was based on those participants who permanently discontinued treatment due to TEAEs prior to Week 48.

In addition, virologic success and failure rates by adherence (via pill count) were assessed using the Snap-shot algorithm (Guidance for Industry, 2013). Rates were compared using the Cochran–Mantel–Haenszel test stratified by baseline HIV-1 RNA ($\leq$100,000 copies/mL, >100,000 copies/mL).

Results

Baseline characteristics and patient disposition

Out of 991 individuals screened for this trial, 799 were found eligible and randomized, 786 of whom (RPV/FTC/TDF, 394; EFV/FTC/TDF, 392) received at least one dose of study medication. A majority of participants were men (92.9%) and white (67.2%), with a mean age of 37 years. Demographic and clinical characteristics at baseline were similar between treatment groups (Table 1).

Fewer participants who received RPV/FTC/TDF permanently discontinued study drug for any reason compared to those who received EFV/FTC/TDF (Table 1). The overall rate of TEAEs that led to permanent discontinuation of study drug was significantly lower in the RPV/FTC/TDF group compared to the EFV/FTC/TDF group (2.5% vs. 8.7%, $p < .001$), with a similar pattern of individual TEAEs (Table 2). Of the study drug discontinuations due to TEAE in the EFV/FTC/TDF group, 41% occurred in the first four weeks (Figure 1). More RPV/FTC/TDF-treated than EFV/FTC/TDF-treated participants discontinued study drug due to lack of efficacy and more participants in the EFV/FTC/TDF group than in the RPV/FTC/TDF group withdrew consent (Table 1).

Treatment adherence, quality of life, and treatment satisfaction

In both groups, participants reported a high overall adherence to treatment assessed via M-MASRI at each visit (97–99%), and similar proportions (RPV/FTC/TDF, 49%; EFV/FTC/TDF, 48%) reported having never missed a dose over the course of 48 weeks. This is consistent with measurements of adherence based on the investigator count of returned study medications through Week 48 (RPV/FTC/TDF, 97%; EFV/FTC/TDF, 97%).

Table 1. Baseline characteristics and patient disposition (safety population).

<table>
<thead>
<tr>
<th></th>
<th>RPV/FTC/TDF (N = 394)</th>
<th>EFV/FTC/TDF (N = 392)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>37 ± 10</td>
<td>37 ± 11</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>366 (92.9)</td>
<td>364 (92.9)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>266 (67.7)</td>
<td>262 (66.8)</td>
</tr>
<tr>
<td>Hispanic or Latino, n (%)</td>
<td>59 (15.0)</td>
<td>75 (19.1)</td>
</tr>
<tr>
<td>BMI (kg/m²), mean ± SD</td>
<td>25.3 ± 4.4</td>
<td>25.9 ± 4.9</td>
</tr>
<tr>
<td>CD4 cell count (/µL), mean ± SD</td>
<td>395.7 ± 179.6</td>
<td>385.2 ± 186.8</td>
</tr>
<tr>
<td>HIV-1 RNA (log₁₀ copies/ml), mean ± SD</td>
<td>4.8 ± 0.7</td>
<td>4.8 ± 0.6</td>
</tr>
<tr>
<td>Permanently discontinued study drug, n (%)</td>
<td>54 (13.7)</td>
<td>72 (18.4)</td>
</tr>
</tbody>
</table>

Primary Reason, n (%)

<table>
<thead>
<tr>
<th>Reason</th>
<th>RPV/FTC/TDF</th>
<th>EFV/FTC/TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAE</td>
<td>10 (2.5)</td>
<td>34 (8.7)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0.0)</td>
<td>1 (0.3)*</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>2 (0.5)</td>
<td>0</td>
</tr>
<tr>
<td>Lack of efficacy</td>
<td>12 (3.0)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Investigator’s discretion</td>
<td>3 (0.8)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Withdraw consent</td>
<td>5 (1.3)</td>
<td>13 (3.3)</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>15 (3.8)</td>
<td>13 (3.3)</td>
</tr>
<tr>
<td>Participant noncompliance</td>
<td>6 (1.5)</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Protocol violation</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
</tr>
</tbody>
</table>

Note: BMI indicates body mass index; EFV/FTC/TDF, efavirenz/emtricitabine/tenofovir disoproxil fumarate; RPV/FTC/TDF, rilpivirine/emtricitabine/tenofovir disoproxil fumarate, TEAE, treatment-emergent adverse event.

*Cause of death was septic shock.
Table 2. Most frequently reported treatment-emergent adverse events leading to permanent study drug discontinuation (≥1 participants in either group; Safety population).

<table>
<thead>
<tr>
<th>System Organ Class, n (%) preferred term</th>
<th>RPV/FTC/TDF (N = 394)</th>
<th>EFV/FTC/TDF (N = 392)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE leading to permanent study drug discontinuation</td>
<td>10 (2.5)*</td>
<td>34 (8.7)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>1 (0.3)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>0</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>3 (0.8)</td>
<td>7 (1.8)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>1 (0.3)</td>
<td>18 (4.6)</td>
</tr>
<tr>
<td>Abnormal dreams</td>
<td>0</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Depression</td>
<td>0</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>1 (0.3)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Nightmare</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>0</td>
<td>7 (1.8)</td>
</tr>
<tr>
<td>TOX skin eruption</td>
<td>0</td>
<td>2 (0.5)</td>
</tr>
</tbody>
</table>

Note: EFV/FTC/TDF indicates efavirenz/emtricitabine/tenofovir disoproxil fumarate; RPV/FTC/TDF, rilpivirine/emtricitabine/tenofovir disoproxil fumarate; TEAE, treatment-emergent adverse event.

*Permanent study drug discontinuation could be due to >1 TEAE.

**Neither was considered by the investigator to be toxic epidermal necrolysis or Stevens-Johnson syndrome.

*p < .001 vs. EFV/FTC/TDF.

Symptoms (HIV SIQ)

For each HIV SIQ item, there were no significant baseline score differences between groups. In addition, no individual symptom was reported significantly more often at Week 48 than at baseline. At Week 48, two HIV SIQ symptoms had a significant between-group difference in symptom status change from baseline (see the Methods section for details of data analysis), both in favor of RPV/FTC/TDF: difficulty falling or staying asleep (with symptom: RPV/FTC/TDF, 45.4%; EFV/FTC/TDF, 45.4%; p = .022; Figure 3(a)) and diarrhea or loose bowel movements (with symptom: RPV/FTC/TDF, 26.0%; EFV/FTC/TDF, 39.4%; p = .002; Figure 3(b)). For difficulty falling asleep, there was also a significant advantage of RPV/FTC/TDF over EFV/FTC/TDF at Weeks 4 and 8, and for diarrhea at Weeks 8, 12, 16, 24, 32, and 40 (Figure 3). There were also transient significant between-group differences, all in favor of RPV/FTC/TDF, for the symptoms of feeling dizzy or light-headed (Weeks 4, 8, 12, 16, and 24), feeling nervous or anxious (Weeks 4 and 8), fatigue or loss of energy (Weeks 4 and 8), problems with having sex (Week 24), hair loss or changes in the way hair looks (Week 32), and nausea or vomiting (Week 8). Data for all HIV SIQ symptoms are presented in the Supplemental Figure.

Discussion

Overall, the treatment-naive participants in this study showed high levels of patient-reported adherence and treatment satisfaction in both treatment groups, which was reflected with an improvement in quality of life in both groups. In addition, RPV/FTC/TDF may be somewhat better tolerated than EFV/FTC/TDF, as indicated by a significantly lower rate of patients who discontinued treatment due to TEAEs and lower rates of some patient-reported symptoms in the RPV/FTC/TDF group.

In this era of simplified, once-daily STR dosing, reducing the incidence of symptoms associated with an HIV treatment remains an important strategy for improving treatment adherence. Poor adherence has been associated with increased overall symptom burden including trouble sleeping, fatigue, and anxiety (Al-Dakkak et al., 2013; Ammassari et al., 2001; Gay et al., 2011), as well as worse virologic outcomes (Behrens et al., 2014; King, Brun, & Kempf, 2005). In the Snapshot analysis performed in this study, a higher proportion of participants in the <95% adherence stratum in the EFV/FTC/TDF group discontinued treatment due to AEs, suggesting a tolerability-related decline in adherence. In these treatment-naive participants, reductions from baseline in the occurrence of most of the HIV SIQ...
items were similar between treatments, perhaps reflecting improved well-being due to higher CD4 counts, lower viral replication, or less worry about HIV.

Although captured in different ways than the TEAEs, the patient-reported data in this analysis are generally consistent in their pattern with TEAE data from the primary STaR report (Cohen et al., 2014) and from the randomized, double-blind, double-dummy ECHO and THRIVE trials, in which the incidence of TEAEs leading to permanent study drug discontinuation and the incidence of dizziness were lower with RPV+FTC/TDF compared with EFV+FTC/TDF (Nelson et al., 2013). According to approved labeling (“Edurant® (rilpivirine) tablets,” 2014; “Sustiva® (efavirenz) capsules and tablets”, 2013), a systematic review (Kenedi & Goforth, 2011), and ECHO and THRIVE data (Mills et al., 2013), nervous system and psychiatric disorders generally develop during the first days of treatment, so the higher rate of study drug discontinuation observed during the first four weeks of EFV/FTC/TDF treatment was not unexpected. These observations are also consistent with the higher rates of several HIV SIQ items in the early stages of the trial (Supplemental Figure).

Neither RPV (“Edurant® (rilpivirine) tablets”, 2014) nor EFV (“Sustiva® (efavirenz) capsules and tablets”, 2013) is associated with diarrhea, but in this predominantly male population, RPV/FTC/TDF-treated participants reported this symptom significantly less often than those treated with EFV/FTC/TDF. Likewise, in the ECHO and THRIVE trials, diarrhea was less

**Figure 1.** Permanent study drug discontinuations due to treatment-emergent adverse events by duration of exposure (Safety population). EFV/FTC/TDF indicates efavirenz/emtricitabine/tenofovir disoproxil fumarate; RPV/FTC/TDF, rilpivirine/emtricitabine/tenofovir disoproxil fumarate.

**Figure 2.** Mean change from baseline in patient-reported quality of life at Week 48 (SF-12v2; Safety population). **p < .001 vs. baseline via the Wilcoxon signed rank test; †p < .05 RPV/FTC/TDF vs. EFV/FTC/TDF via the Wilcoxon rank sum test. EFV/FTC/TDF indicates efavirenz/emtricitabine/tenofovir disoproxil fumarate; RPV/FTC/TDF, rilpivirine/emtricitabine/tenofovir disoproxil fumarate; SF-12v2, Medical Outcomes Study Short-Form.
frequently reported as a TEAE in men treated with RPV + FTC/TDF than those treated with EFV + FTC/TDF (Hodder et al., 2012). Gastrointestinal symptoms in general (Nelson et al., 2010), and taste disturbances/nausea (Al-Dakkak et al., 2013; Ammassari et al., 2001) and diarrhea (Gupta, Ordonez, & Koenig, 2012; Hill & Balkin, 2009) in particular have been shown to be significant factors in patient adherence to treatment; however, in this study, no difference in adherence was observed between treatments.

There are several limitations of this trial. As with any long-term questionnaire-based study, the quality (completeness) of questionnaire data may decrease over time, but there is little reason to think that factors affecting the quality of questionnaires would differ between groups. In addition, this was an open-label study, which is associated with inherent limitations; for example, participants may have preferred to be randomized to a newer treatment and their PRO data may have been biased by that preference. Also, the PRO instruments used in this study demonstrated ceiling effects (i.e., a majority of participants responded with the highest possible score, making it difficult to differentiate between the groups). Finally, the predominantly white, male study population in this study is not reflective of the global, US, or EU HIV-positive population (per UNAIDS; “Report on the Global AIDS”, 2008). Therefore, the outcomes observed in this study may not be generalizable to other HIV-infected populations.

In conclusion, these patient-reported results of a multicenter, randomized, open-label trial indicate that patients who received the STRs of either RPV/FTC/TDF or EFV/FTC/TDF for 48 weeks were highly adherent to medication and overall very satisfied with their treatment, which was reflected in an improved quality of life. Differences in TEAE-related discontinuations and the occurrence of some patient-reported symptoms (sleep difficulties, diarrhea) suggest that RPV/FTC/TDF may be somewhat better tolerated than EFV/FTC/TDF, especially during the first four weeks of treatment.

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No potential conflict of interest was reported by the authors.

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Supplementary material
Supplementary Figure 1 and Table 1 are available via the “Supplementary” tab on the article’s online page (http://dx.doi.org/10.1080/09540121.2015.1096890).
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