Benefits of switching to a fixed-dose single-tablet elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide co-formulation from free multi-tablet antiretroviral regimens in people living with HIV: A real-world study

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Research Article

Keywords: Elvitegravir, cobicistat, emtricitabine, drug combination, real-world study, drug tolerance, safety, HIV

Posted Date: October 19th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2170371/v1

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Abstract

Background

Fixed-dose single-tablet drug formulations reduce pill burden and improve medication adherence and treatment efficacy in HIV patients taking antiretroviral therapy (ART). This study aimed to describe a single-center experience using co-formulated elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF) for the treatment of HIV-infected patients in Southwest China.

Methods

This prospective study enrolled consecutive HIV-infected patients admitted to the Chongqing Public Health Medical Center from October 2019 to April 2021. The patients who switched from the freely-available standard regimens (available through the Chinese national antiretroviral treatment program) to the EVG/COBI/FTC/TAF tablet were enrolled. Baseline characteristics, HIV viral suppression (< 50 RNA copies/mL), immune status, laboratory indices, and patient-reported outcomes were recorded and analyzed.

Results

During the study period, 246 patients switched to EVG/COBI/FTC/TAF, and the most common regimen used before switching was tenofovir disoproxil fumarate + lamivudine + efavirenz (76.0%). The mean age of enrolled patients was 43.7 ± 13.8 years, and 84.6% of our study population was male. The mean baseline CD4 + T-lymphocyte count was 227.45 ± 177.01 cells/µl. Adverse drug reactions (ADRs) (n = 130, 52.9%), inconvenience (n = 64, 26.0%), and poor therapeutic effect (n = 52, 21.1%) were the reasons for switching therapy. After 24 weeks of EVG/COBI/FTC/TAF treatment, 100 patients underwent drug efficacy evaluation, and the viral suppression rate was observed to be significantly higher than baseline (99% vs. 90%, p = 0.001). Triglyceride, total cholesterol, and low-density lipoprotein levels were found to be higher than baseline (all p <0.001). The proportion of patients with hyperglycemia and albuminuria was significantly reduced after switching (p < 0.05). Analysis of responses to the HIV treatment satisfaction questionnaire showed that patient satisfaction increased after switching (p < 0.001) ART drug regimen.

Conclusions

Switching from a multi-tablet regimen to the fixed-dose EVG/COBI/FTC/TAF single-tablet ART regimen was effective and well-tolerated in Chinese HIV-infected patients. Patient satisfaction increased significantly after switching.
Currently available antiretroviral drugs are highly effective against HIV infection, and antiretroviral therapy (ART) has led to striking improvements in survival and disease remission in HIV-1-infected individuals [1, 2]. The Chinese national antiretroviral treatment program provides therapeutic ART drugs at no cost to the patient, and the most commonly used therapeutic regimen is the tenofovir disoproxil fumarate plus lamivudine plus efavirenz regimen. However, some patients are not satisfied with the free ART regimens due to the commonly felt side effects, the increased dosing frequency and the high number of pills per dose, resulting in poor patient compliance with the recommended therapeutic protocol [3, 4]. Switching to an alternative regimen that has less side effects and reduces the pill burden and dosing frequency might thus improve adherence and treatment outcomes [5, 6].

More single-tablet ART regimens are becoming available internationally, which is likely helpful in reducing the drug compliance burden on patients, and may ensure patient adherence and improved efficacy of ART [7]. The elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF) tablet is a four-in-one single-tablet regimen that contains elvitegravir (150 mg), cobicistat (150 mg), emtricitabine (200 mg), and tenofovir alafenamide fumarate (10 mg). EVG/COBI/FTC/TAF has been available for use in China since October 2018 and has been covered by the National Healthcare Security Program from the end of 2019, and is emerging as the new regimen of choice for people living with HIV (PLWH) in China.

Nevertheless, data regarding the effectiveness and safety of this regimen in a real-world setting is presently sparse in China. This study aimed to describe our single-center experience with respect to the use of EVG/COBI/FTC/TAF tablets for the treatment of HIV in Chongqing, China.

**Methods**

**Study design and participants**

This is a single-center prospective cohort study, which enrolled treatment experienced HIV-infected patients who switched from free ART regimens to EVG/COBI/FTC/TAF tablet from October 2019 to April 2021 at Chongqing Public Health Medical Center, China. A total of 302 HIV-infected patients were screened. 32 patients did not meet the inclusion criteria, 10 patients changed their treatment plan during the follow-up, and 14 patients had too many missing follow-up data. Finally, 246 patients completed the study (Figure 1). This study was approved by the Medical Ethics Review Committee of the Chongqing Public Health Medical Treatment Center (Study approval number: 2021-030-02-KY). Written informed consent was obtained from each participant.

The inclusion criteria for participants were as follows: 1) 18 years of age or older, 2) switched to the EVG/COBI/FTC/TAF tablet for any reason from a previously initiated free ART regimen which had been taken for at least 24 weeks. 3) willing to provide written informed consent. Patients who met the following criteria were excluded: 1) those who did not receive the EVG/COBI/FTC/TAF regimen consecutively for 24 weeks after regimen switch, and 2) those who did not complete the 24-week follow-up at our center.
Data Collection

Baseline was considered to be the time point of switching to the EVG/COBI/FTC/TAF tablet. Demographic characteristics, clinical features, and laboratory data of the participants were collected from electronic medical records at baseline and follow-up visits, including sex, age, ART use, CD4 + T-cell count, CD4+/CD8 + ratio, HIV RNA levels, liver and renal function test results, blood glucose levels, blood lipid levels, and urinalysis results.

Viral suppression was defined as an HIV viral load of < 50 RNA copies/mL after antiviral therapy for 6 months [8]. Dyslipidemia was evaluated using multiple indicators. Hypercholesterolemia was defined as a total cholesterol (TC) level of $\geq$ 6.24 mmol/l. Hypertriglyceridemia was defined as a triglyceride level of $\geq$ 1.675 mmol/l. High low-density lipoprotein (LDL) was defined as an LDL level of $\geq$ 3.36 mmol/l. Low high-density lipoprotein (HDL) was defined as an HDL level of $\leq$ 1.04 mmol/l [9]. Abnormal liver function was defined as an alanine aminotransferase (ALT) concentration of $>$ 50 U/l, an aspartate aminotransferase (AST) level $>$ 40 U/l, or a total bilirubin (TBil) level of $>$ 20.5 µmol/l. Mild and moderate renal insufficiency were defined as an estimated glomerular filtration rate (eGFR) of 50–90 mL/min/1.73 m$^2$ and 20–50 mL/min/1.73 m$^2$, respectively [10].

Patient-reported outcomes were also collected by requesting participants to answer HIV treatment satisfaction questionnaires (HIV-TSQ) [11] at baseline, at 4 weeks, and at 24 weeks after regimen switch.

Statistical analysis

Continuous variables were expressed as means ± standard deviation (SD) or medians [interquartile range (IQR)] if non-normally distributed, according to Kolmogorov-Smirnov testing. Categorical variables were expressed as numbers and percentages (%) and analyzed using the Chi-squared or the Fisher exact test. Wilcoxon signed-rank tests were used to compare CD4 + T-cell counts and CD4+/CD8 + ratios. Continuous data with a normal distribution were analyzed using analysis of variance (ANOVA). The Bonferroni method was used for the post-hoc multiple comparisons of safety profiles, and Fisher's least significant difference (LSD) method was used for comparison of the satisfaction of patients. Two-sided $p$-values of $< 0.05$ were considered statistically significant. All statistical analyses were conducted using Statistical Package for Social Sciences (SPSS) software (IBM SPSS Statistics for Windows, Version 19, IBM Corp., Armonk, NY, USA).

Results

Characteristics of the patients

The data from 246 HIV-infected patients were collected. All participants completed the 24-week post-switching follow-up. Among them, 232 had at least one efficacy evaluation; 246 had at least one safety evaluation. As shown in Table 1, the mean age was 43.7 ± 13.8 years, and 208/246 (84.6%) patients were
male. The main mode of infection (HIV risk factors) was sexual transmission (n = 245, 99.6%), including heterosexual transmission (n = 134, 54.5%) and homosexual transmission (n = 111, 45.1%). Mean CD4 + T-lymphocyte count was 227.45 ± 177.01 cells/µl. The main ART regimen of the 246 HIV infected patients before switching to the single-dose regimen were tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) + efavirenz (EFV) (n = 187, 76.2%), zidovudine (AZT)/3TC + EFV (n = 23, 5.7%), and TDF + 3TC + lopinavir/ritonavir (LPV/r) (n = 13, 5.3%). ADRs (n = 130, 52.9%), inconvenience (n = 64, 26.0%), and poor therapeutic effect (n = 52, 21.1%) were the main reasons for switching antiviral therapy.

Table 1
Clinical characteristics of participants.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients (n = 246)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.7 ± 13.8</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>208 (84.6%)</td>
</tr>
<tr>
<td>Mode of infection (HIV risk factors)</td>
<td></td>
</tr>
<tr>
<td>Heterosexual</td>
<td>134 (54.5%)</td>
</tr>
<tr>
<td>Homosexual</td>
<td>111 (45.1%)</td>
</tr>
<tr>
<td>Intravenous drug use</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Baseline CD4 + T-cell count (cells/µl)</td>
<td>227.5 ± 177.0</td>
</tr>
<tr>
<td>ART regimen used before switching</td>
<td></td>
</tr>
<tr>
<td>AZT/3TC + LPV/r</td>
<td>6 (2.4%)</td>
</tr>
<tr>
<td>AZT/3TC + NVP</td>
<td>12 (4.9%)</td>
</tr>
<tr>
<td>AZT/3TC + EFV</td>
<td>23 (9.3%)</td>
</tr>
<tr>
<td>TDF + 3TC + LPV/r</td>
<td>13 (5.3%)</td>
</tr>
<tr>
<td>TDF + 3TC + NVP</td>
<td>5 (2.0%)</td>
</tr>
<tr>
<td>TDF + 3TC + EFV</td>
<td>187 (76.0%)</td>
</tr>
<tr>
<td>Reasons for switching treatment regimens</td>
<td></td>
</tr>
<tr>
<td>Adverse drug reaction</td>
<td>130 (52.9%)</td>
</tr>
<tr>
<td>Inconvenience</td>
<td>64 (26.0%)</td>
</tr>
<tr>
<td>Poor therapeutic effect</td>
<td>52 (21.1%)</td>
</tr>
</tbody>
</table>

Data are shown as number (%) or mean ± standard deviation.

3TC: lamivudine; AZT: zidovudine; EFV: efavirenz; LPV/r: lopinavir/ritonavir; NVP: nevirapine; TDF: tenofovir disoproxil fumarate.
Art Effect And Immune Function Recovery

After 24 weeks of treatment with EVG/COBI/FTC/TAF, the mean CD4 + T-cell count ($p = 0.064$) and CD4/CD8 ratio ($p = 0.49$) were numerically increased compared with baseline, but with no statistically significant differences. After 24 weeks of treatment with EVG/COBI/FTC/TAF, the viral suppression rate was 99% (99/100), compared to 90% (90/100) at baseline ($p = 0.001$), based on data analysis from patients who completed HIV viral load testing (Table 2).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline</th>
<th>24 weeks</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 + T-cell count*</td>
<td>327 (241, 483)</td>
<td>420 (231.5, 564.5)</td>
<td>0.064</td>
</tr>
<tr>
<td>CD4+/CD8 + ratio**</td>
<td>0.62 (0.40, 0.79)</td>
<td>0.65 (0.37, 0.87)</td>
<td>0.49</td>
</tr>
<tr>
<td>Viral suppression rate***, n (%)</td>
<td>90 (90%)</td>
<td>99 (99%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data are shown as median (interquartile range).

*: The number of cases with assessed CD4 + T-cell counts were 73 at baseline and 137 at week 24.

**: The number of cases with assessed CD4+/CD8 + ratios were 73 at baseline and 104 at week 24.

***: The number of cases with assessed viral suppression rates were 100 both at baseline and at week 24.

ART: antiretroviral therapy;
EVG/COBI/FTC/TAF: elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide.

Safety Evaluation After Switching Art Regimen

The indicators of liver function, renal function, blood glucose level, lipid profile, β2 micro-globulin content, and routine urinalysis were determined, and safety profile was evaluated at five time points, including at weeks 12 and 24 before switching, at baseline, and at week 12 and 24 after switching. After switching, no significant differences in liver function and renal function were found; however, blood glucose ($p = 0.005$) and urinary protein ($p < 0.001$) showed a decreasing trend, and blood lipids showed an increasing trend, including triglyceride levels ($p < 0.001$), TC ($p < 0.001$), and LDL levels ($p < 0.001$) (Table 3 and Supplementary Table S1).
Table 3
Changes in liver and renal function, blood glucose levels, and blood lipid levels before and after switching ART regimen.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline *</th>
<th>12 weeks *</th>
<th>24 weeks *</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood lipid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides (&gt; 1.695 mmol/l)</td>
<td>91 (45.3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>122 (66.7%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>106 (62.7%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total cholesterol (&gt; 6.24 mmol/l)</td>
<td>36 (17.9%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>57 (31.1%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>40 (23.7%)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>0.002</td>
</tr>
<tr>
<td>High-density lipoprotein (&lt; 1.04 mmol/l)</td>
<td>85 (42.3%)</td>
<td>58 (31.7%)</td>
<td>71 (42%)</td>
<td>0.055</td>
</tr>
<tr>
<td>Low-density lipoprotein (&gt; 3.36 mmol/l)</td>
<td>29 (14.4%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>59 (32.2%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>43 (25.4%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ALT (&gt; 40 U/l)</td>
<td>42 (19.3%)</td>
<td>24 (12.3%)</td>
<td>24 (13.6%)</td>
<td>0.075</td>
</tr>
<tr>
<td>AST (&gt; 35 U/l)</td>
<td>30 (13.8%)</td>
<td>27 (13.8%)</td>
<td>20 (11.4%)</td>
<td>0.197</td>
</tr>
<tr>
<td>LDH (&gt; 245 U/l)</td>
<td>9 (4.2%)</td>
<td>8 (4.1%)</td>
<td>12 (6.9%)</td>
<td>0.512</td>
</tr>
<tr>
<td>BUN (&gt; 8.3 mmol/l)</td>
<td>8 (3.7%)</td>
<td>5 (2.6%)</td>
<td>7 (4%)</td>
<td>0.654</td>
</tr>
<tr>
<td>CREA (&gt; 106 µmol/l)</td>
<td>11 (5%)</td>
<td>11 (5.6%)</td>
<td>10 (5.7%)</td>
<td>0.984</td>
</tr>
<tr>
<td>UA (&gt; 430 µmol/L)</td>
<td>48 (22%)</td>
<td>58 (29.7%)</td>
<td>54 (30.9%)</td>
<td>0.301</td>
</tr>
<tr>
<td>β2 microglobulin (&gt; 1.84 mg/l)</td>
<td>22 (10.4%)</td>
<td>11 (5.7%)</td>
<td>13 (7.5%)</td>
<td>0.516</td>
</tr>
<tr>
<td>Serum cystatin C (&gt; 1.3 mg/l)</td>
<td>26 (12.3%)</td>
<td>22 (11.4%)</td>
<td>20 (11.5%)</td>
<td>0.852</td>
</tr>
<tr>
<td>eGFR (&lt; 60 mL/min)</td>
<td>6 (2.8%)</td>
<td>3 (1.5%)</td>
<td>7 (4%)</td>
<td>0.611</td>
</tr>
<tr>
<td>Blood glucose (&gt; 6.11 mmol/l)</td>
<td>74 (35.4%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>47 (24.7%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>33 (19.4%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.005</td>
</tr>
<tr>
<td>Urine specific gravity (&lt; 1.010, &gt; 1.030)</td>
<td>6 (2.9%)</td>
<td>7 (3.7%)</td>
<td>6 (3.9%)</td>
<td>0.758</td>
</tr>
<tr>
<td>Urine protein (positive)</td>
<td>39 (18.8%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20 (10.6%)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>12 (7.2%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Urine occult blood (positive)</td>
<td>39 (18.8%)</td>
<td>27 (14.3%)</td>
<td>27 (16.3%)</td>
<td>0.225**</td>
</tr>
<tr>
<td>Urine glucose (positive)</td>
<td>6 (2.9%)</td>
<td>3 (1.6%)</td>
<td>3 (1.8%)</td>
<td>0.503**</td>
</tr>
</tbody>
</table>

Data are shown as numbers (%).

The difference between different letters was significant between the two groups (p < 0.05).

*: The number of cases at different time points is not identical for different items, and it is therefore not possible to give a uniform number of cases at each time point.

**: Fisher’s exact probability method.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; CREA: creatinine; eGFR: estimated glomerular filtration rate; LDH: lactate dehydrogenase; UA: uric acid.
Adverse Drug Reactions And Satisfaction Survey

The incidence of ADRs was assessed by patient self-reporting before switching to EVG/COBI/FTC/TAF and 4 and 24 weeks after switching. The main ADRs before switching were neurological disorders, including dizziness (43.3%) and excessive dreams (21.2%). ADRs were significantly reduced after switching to EVG/COBI/FTC/TAF (Table 4). The HIV-TSQ scores at baseline and 4 and 24 weeks after switching to EVG/COBI/FTC/TAF were 40.7 ± 9.7, 66.6 ± 11.7, and 94.4 ± 12.9, respectively. Patient satisfaction increased significantly (p < 0.001) after switching to the fixed-dose single-tablet ART regimen.

**Table 4**
Self-reported ADRs before and after treatment with EVG/COBI/FTC/TAF.

<table>
<thead>
<tr>
<th>ADRs</th>
<th>Baseline (n = 245)</th>
<th>4 weeks (n = 245)</th>
<th>24 weeks (n = 245)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>8 (3.3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 (0.8%)&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0 (0%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.005*</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (2.9%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 (0.4%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0 (0%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.007*</td>
</tr>
<tr>
<td>Anorexia</td>
<td>2 (0.8%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.332*</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12 (4.9%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0 (0%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0 (0%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Rash</td>
<td>1 (0.4%)</td>
<td>1 (0.4%)</td>
<td>0 (0%)</td>
<td>&gt; 0.999*</td>
</tr>
<tr>
<td>Dizziness</td>
<td>106 (43.3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 (0.4%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0 (0%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Excessive dreams</td>
<td>52 (21.2%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 (0.4%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2 (0.8%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1 (0.4%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>&gt; 0.999*</td>
</tr>
<tr>
<td>Fatigue</td>
<td>8 (3.3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0 (0%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0 (0%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Other</td>
<td>18 (7.3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 (0.4%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15 (6.1%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Data are shown as numbers (%).

The difference between different letters was significant between the two groups (p < 0.05)

* Fisher’s exact probability method

Other = cough, runny nose, joint pain, and chest tightness.

ADRs: adverse drug reactions;

EVG/COBI/FTC/TAF: elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide.

**Discussion**
The present study was conducted to describe our single-center experience of HIV-infected patients when switching from the ARVs to the fixed-dose single-tablet EVG/COBI/FTC/TAF regimen. The main reasons for switching therapy were ADRs, inconvenience, and poor therapeutic effect. After switching, the reported ADRs decreased, blood lipids levels increased, blood glucose levels decreased, and proteinuria decreased. The viral inhibition rate increased from 90% before switching to 99% after switching and patient satisfaction increased when using the single-dose combined tablet.

ART for managing HIV infection requires triple therapy, including two nucleotide reverse transcriptase inhibitors (NRTIs) and another core drug, such as a Non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor. Good adherence with the drug regimen is a crucial prerequisite for successful antiretroviral treatment, and adherence is significantly influenced by the pill burden. Single-tablet regimens contain multiple antiretroviral drugs with different mechanisms of action. Such combined pills reduce the pill burden, improving drug adherence and quality of life. Moreover, as more single-tablet regimens are being covered by the National Medical Insurance of China, patient acceptance of these regimens has gradually increased due to significant price reductions, which has also improved adherence to therapeutic protocols.

Integrase inhibitors such as elvitegravir have revealed their potential for viral inhibition in pre-market clinical trials, with increased short- and long-term drug safety and tolerance. They are, thus, recommended by major public health agencies as first-line therapeutic options [5, 12–20]. However, since participants in clinical trials are selected based on strict inclusion and exclusion criteria, the results obtained from these clinical trials cannot fully represent the general population of potential patients. The present study was based on the clinical data of patients switching from drugs recommended by the National Free Antiretroviral Treatment Program to fixed-dose single-tablet EVG/COBI/FTC/TAF therapy, and results from the present study provides clinicians with useful information with respect to the efficacy and safety of a specific fixed-dose single-tablet ART regimen to treat HIV infection.

TDF + 3TC + EFV and AZT/3TC + EFV are the first-line drugs used in the National Free Antiretroviral Treatment Program, and their efficacy have been established by past clinical studies. However, they also have many adverse effects [21, 22]. Side effects of these regimens include neurological abnormalities, gastrointestinal reactions, skin rash, liver function aberrations, and untoward changes to renal function [21, 22]. These adverse effects may be the main reason causing patients to switch to a single-tablet regimen. In addition, the significant reduction in pill burden is another important reason for switching.

The present study showed that after 6 months of treatment, EVG/COBI/FTC/TAF as a single-tablet regimen showed a 99% (99/100) viral suppression rate in a real-world setting, which is significantly higher viral suppression rate than before switching. Nevertheless, there is a paucity of studies on combined EVG/COBI/FTC/TAF treatment regimens in China. In one previous study, other treatment regimens (such as LPV/r-based and EFV-based regimens) achieved 93.8% and 87.8% viral suppression (HIV RNA level of < 40 RNA copies/mL), respectively, at 6 months in previously untreated Chinese patients [23]. In addition to the specific clinical and therapeutic reasons for the different regimens used, different
study populations and different definitions of viral suppression also might contribute to observed differences in results.

In this study, no significant decline in liver and renal function was found in patients treated with EVG/COBI/FTC/TAF, suggesting the superior tolerance of EVG/COBI/FTC/TAF in a real-world setting. The present study observed no significant uric acid changes after switching from ART drugs used in the National Free Antiretroviral Treatment Program to EVG/COBI/FTC/TAF therapy. In the single-dose regimen, TAF is a tenofovir prodrug that can effectively reduce the circulating plasma concentration of tenofovir, resulting in fewer off-target adverse effects, such as proximal tubulopathy and Fanconi syndrome [24].

In a phase III clinical study of EVG/COBI/FTC/TAF use in ART naïve patients, blood lipid levels were increased significantly, mainly in the first year, and there were no significant continuous increases in lipid levels in the second and third years of treatment [25]. Increased blood lipids were also observed in one retrospective study [26]. The increased blood lipids observed in previous studies are consistent with the results of the present study.

Fasting glucose concentrations have been observed to be higher among PLWH [27], and this may be attributable to several factors. One study found that abnormally elevated levels of blood glucose were significantly decreased after the switch of the therapy, which may have been related to the long-term use of TDF in 205 of 246 patients before the switch [28]. Even in the absence of protease inhibitor treatment, HIV may directly influence the function of pancreatic beta cells and insulin secretion, which may induce insulin resistance [29, 30]. Polsky et al., have observed that HIV infection and antiretroviral treatment increased the risk of hyperglycemia, regardless of the treatment used [31]. The present study found that blood glucose concentrations were decreased at 24 weeks after switching to EVG/COBI/FTC/TAF, suggesting the enhanced benefit of this treatment regimen for PLWH.

Our study observed that the main ADRs before switching were nervous system-related ADRs including dizziness (43.3%) and excessive dreams (21.2%), possibly associated with EFV use. The incidence of neurological adverse effects was significantly reduced after switching to EVG/COBI/FTC/TAF. One 48-week phase III clinical trial observed that patients treated with the EVG/COBI/FTC/TDF regimen experience less dizziness compared to those receiving EFV/FTC/TDF [32]. As FTC and 3TC may be considered to be therapeutically interchangeable [33], switching to EVG/COBI/FTC/TAF might contribute to the reduced incidence of ADRs. The HIV-TSQ showed that patient satisfaction increased significantly after the switch to EVG/COBI/FTC/TAF because of the reduced ADRs and pill burden.

This study had limitations. This was a single center study, and the sample size was relatively small. In addition, patients were followed-up for 24 weeks only, which is a relatively short period, considering that these patients will have to take lifelong ART. Due to the COVID-19 epidemic, participants had only one efficacy follow-up at 24 weeks. The requisition of immune function laboratory indices in the study was low, and the self-control analysis could not be performed, which may have led to a degree of measurement bias.
Conclusion

In conclusion, switching from a multi-tablet ART regimen to a fixed-dose single-tablet EVG/COBI/FTC/TAF ART regimen was effective and well-tolerated in Chinese HIV-infected patients. Patient satisfaction significantly increased after switching therapy to a fixed-dose single-tablet ART regimen.

Abbreviations

3TC, lamivudine
ALT, alanine aminotransferase
ART, antiretroviral therapy
AST, aspartate aminotransferase
EFV, efavirenz
eGFR, estimated glomerular filtration rate
EVG/COBI/FTC/TAF, elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
HDL, high-density lipoprotein
HIV-TSQ, HIV treatment satisfaction questionnaires
IQR, interquartile range
LDL, low-density lipoprotein
LSD, least significant difference
NNRTI, non-nucleoside reverse transcriptase inhibitor
NRTI, nucleotide reverse transcriptase inhibitors
PLWH, people living with HIV
SD, standard deviation
TC, total cholesterol
TBil, total bilirubin
TDF, tenofovir disoproxil fumarate
Declarations

**Ethics approval and consent to participate:** This study was approved by the Medical Ethics Review Committee of the Chongqing Public Health Medical Treatment Center (Study approval number: 2021-030-02-KY). Written informed consent was obtained from each participant.

**Consent for publication:** Not applicable.

**Availability of data and materials:** All data generated or analyzed during this study are included in this article and its supplementary information files. Other datasets are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that we have no conflicts of interest.

**Funding:** This study was supported by the Chongqing Talent Cultivation Program (cstc2021ycjh-bgzxm0275), the National Science and Technology Major Project of China of the 13th Five-Year Plan (2018ZX10302104) and the Chongqing Science and Technology Commission (cxtc2019jscx-msxmX0120).

**Authors’ contributions:** JN, QC and XD had full access to all of the data used in the study, and take full responsibility for the integrity of the data and the accuracy of the data analysis. JN and YL were involved in the study conceptualization and design. All authors (JN, QC, XD, QZ, HM, YL) were involved in the acquisition, analysis, and interpretation of data. JN and QZ supervised the analysis. JN and XD were involved in the draft of the manuscript. All authors read, critically revised, and approved the manuscript.

**Acknowledgements:** None.

**References**


**Figures**

![Diagram](image-url)
Flowchart of patient inclusion and exclusion.

Abbreviations: DDI Drug-Drug Interaction

**Supplementary Files**

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- [SupplementaryTableS1.docx](#)