Virologica Sinica 40 (2025) 835–841

Contents lists available at ScienceDirect

Virologica Sinica

journal homepage: www.keaipublishing.com/en/journals/virologica-sinica
www.virosin.org

Research Article

Efficacy and safety of switching from lopinavir/ritonavir-based regimens to bictegravir/emtricitabine/tenofovir alafenamide in people living with HIV: A multicenter retrospective study

Jiantao Fu [a,1], Yifan Guo [a,1], Guoxiang Zheng [b], Zongxing Yang [b], Jinchuan Shi [b], Dingyan Yan [b], Jianhua Yu [b,*], Lijun Sun [c,*], Hongxin Zhao [a,*]

[a] Clinical Center for HIV/AIDS, Beijing Ditan Hospital, Capital Medical University, Beijing, 100015, China
[b] Department of Infectious Diseases, Affiliated Hangzhou Xixi Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, 310023, China
[c] Center for Infectious Diseases, Beijing Youan Hospital, Capital Medical University, Beijing, 100015, China

ARTICLE INFO

Keywords:
Human immunodeficiency virus (HIV)
Virological suppression
LPV/r
BIC/FTC/TAF
Metabolic outcomes

ABSTRACT

In China, approximately 13% of people living with human immunodeficiency virus (HIV) (PLWH) are receiving lopinavir/ritonavir (LPV/r)-based regimens. These PLWH typically have a history of either treatment failure or intolerance to first-line efavirenz-based regimens. Given the considerable pill burden and adverse effects associated with LPV/r, treatment optimization is important for this population. This multicenter retrospective study aimed to evaluate the efficacy and safety of switching from LPV/r-based regimens to the single-tablet regimen of bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF). Virological suppression rates (HIV-RNA < 40 copies/mL) were primarily compared between the 48-week periods before and after switching to BIC/FTC/TAF. CD4 counts and metabolic data were also assessed. A total of 461 PLWH were recruited between January 2021 and December 2023, with 92.2% being male, a median age of 38 years, and a median antiretroviral therapy duration of 8 years. Prior to initiating LPV/r, 23.0% (106/461) had documented virological failure. During LPV/r treatment, 18.9% (20/106) of these individuals experienced viral rebound. Among all participants, the overall virological suppression rates significantly increased from 94.6% (pre-switch) to 98.6% (post-switch) ($P < 0.001$). Notably, among participants with prior virological failure, suppression rates improved significantly from 81.1% to 97.2% ($P < 0.001$), whereas no significant difference was observed in those without such history (from 98.6% to 99.2%, $P = 0.764$). The median triglyceride level decreased from 2.4 mmol/L to 1.8 mmol/L ($P < 0.001$), while no difference in CD4 counts was observed. These findings demonstrate that BIC/FTC/TAF is an effective and metabolically favorable treatment option for PLWH switching from LPV/r based regimens, regardless of whether they have a prior history of virological failure.

INTRODUCTION

Lopinavir/ritonavir (LPV/r) is a boosted protease inhibitor (PI) characterized by a high barrier to the development of human immunodeficiency virus (HIV) drug resistance. It is typically combined with two nucleoside reverse-transcriptase inhibitors (NRTIs) to form a triple-drug, multi-tablet regimen (Croxtall and Perry, 2010). In China, LPV/r-based regimens are recommended as alternative therapies for people living with HIV (PLWH) who have experienced treatment failure or cannot tolerate first-line efavirenz (EFV)-based regimens. According to data from the National Center for AIDS/STD Control and Prevention, approximately 13% of PLWH in China are currently receiving LPV/r-based regimens (Zhao et al., 2020). However, these regimens are associated with a higher pill burden, more complex dosing schedules,

* Corresponding authors.
E-mail addresses: yujhmc@126.com (J. Yu), sunlijunkity@163.com (L. Sun), 13911022130@163.com (H. Zhao).
[1] Jiantao Fu and Yifan Guo contributed equally to this work.

https://doi.org/10.1016/j.virs.2025.10.003
Received 15 January 2025; Accepted 14 October 2025
Available online 20 October 2025

and a higher incidence of side effects, including dyslipidemia and gastrointestinal disturbances (Hulgan et al., 2011; Boyd et al., 2013, 2017), which may negatively impact adherence and long-term outcomes.

In resource-limited settings, NRTI mutations-often followed by the development of non-nucleoside reverse-transcriptase inhibitor (NNRTI) resistance-are frequently observed (van Zyl et al., 2011; Hosseinipour et al., 2013; Paton et al., 2017). According to international guidelines and previous studies (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2025; Paton et al., 2017; Paton et al., 2022; D2EFT Study Group, 2024), dolutegravir (DTG)-based regimens are non-inferior to boosted PI plus NRTIs and are recommended as second-line therapy for PLWH who experience failure of first-line NNRTI-based therapy. Bictegravir (BIC) has a high resistance barrier and have similar activity to that of DTG (Deeks, 2018). BIC, co-formulated with tenofovir alafenamide (TAF) and emtricitabine (FTC) into a single-tablet regimen (BIC/FTC/TAF), represents a significant advancement in treatment options, providing a high genetic barrier to the development of HIV-1 resistance, along with high efficacy, safety and tolerability (Deeks, 2018; Aboud et al., 2019; Ambrosioni et al., 2022; Sax et al., 2023; Wang et al., 2024; Yuan et al., 2024). However, clinical trial data and real-world studies regarding the use of BIC/FTC/TAF in PLWH who experienced failure of first-line NNRTI-based regimens remain limited (Chang et al., 2021). This evidence gap is particularly relevant for China, where approximately 13% of PLWH remain on LPV/r-based regimens. For this specific population, switching to BIC/FTC/TAF could be significant for those PLWH to improve long-term outcomes, given its simplified dosing and fewer side effects. Therefore, we conducted this study to investigate the clinical outcomes of switching to BIC/FTC/TAF among such LPV/r-treated PLWH in China. The findings of this study may provide insights for optimizing antiretroviral therapy (ART) strategies and improve long-term outcomes for this group of PLWH.

Table 1
Characteristics of 461 PLWH who switched from LPV/r-based regimens to BIC/FTC/TAF.

Characteristics	
Age, years	38 (34, 45)
Male	425 (92.2%)
Nadir CD4 count, cells/μL	250 (98, 408)
Baseline HIV RNA, copies/mL (Log10)	4.5 (3.8, 5.1)
ART duration, years	8 (6, 10)
Initial ART regimens	
NVP based	33 (7.2%)
EFV based	321 (69.6%)
LPV/r based	105 (22.8%)
RAL based	2 (0.4%)
Regimens before switching to BIC/FTC/TAF	
LPV/r+3 TC + TDF	348 (75.5%)
LPV/r+3 TC + AZT	84 (18.2%)
LPV/r+3 TC	17 (3.7%)
LPV/r+3 TC + ABC	7 (1.5%)
LPV/r + DTG	3 (0.7%)
LPV/r + RAL	1 (0.2%)
LPV/r + DTG + TDF	1 (0.2%)
Virological failure before LPV/r use	106 (23.0%)
Reasons for BIC/FTC/TAF switch	
Simplify regimens	248 (53.8%)
Dyslipidemia	27 (5.9%)
Diarrhea	12 (2.6%)
Other adverse events	30 (6.5%)
Virological failure	19 (4.1%)
Unrecorded	125 (27.1%)

Notes: Data are presented as median (IQR) or n (%) unless specified otherwise. Abbreviations: 3TC, lamivudine; ABC, abacavir; AZT, zidovudine; BIC, bictegravir; DTG, dolutegravir; FTC, emtricitabine; LPV/r, ritonavir-boosted lopinavir; NVP, nevirapine; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

RESULT

Study population and characteristics

From January 2021 to December 2023, a total of 461 participants who switched from LPV/r-based regimens to BIC/FTC/TAF were screened (Fig. 1). Baseline characteristics are summarized in Table 1. Generally, 92.2% (425/461) were males, with a median age of 38 years (IQR: 34–45) and median ART duration 8 years (IQR: 6–10). At baseline, the median nadir CD4 count was 250 cells/μL (IQR: 98–408), and the median baseline HIV RNA level was 4.53 log10 copies/mL (IQR: 3.82–5.06). Regarding regimens, 69.6% PLWH initiated ART with EFV-based regimens and the majority of PLWH (75.5%) were on LPV/r + 3TC (lamividine) + TDF (tenofovir disoproxil) before switching to BIC/FTC/

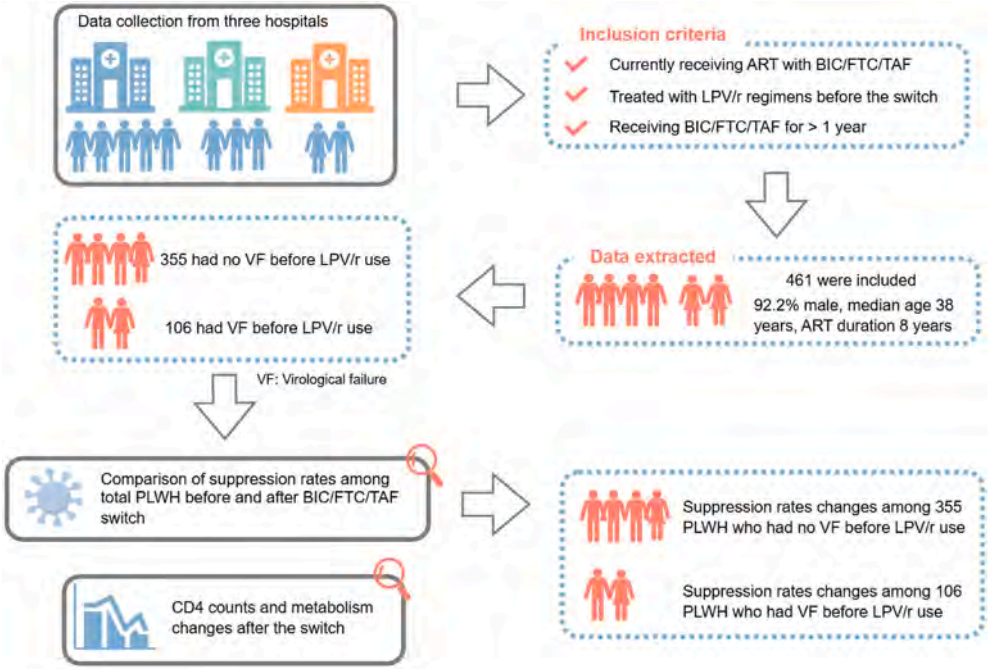

Fig. 1. Flowchart of PLWH included and excluded for this study.

TAF, followed by LPV/r + 3TC + AZT (zidovudine) (18.2%). A total of 106 (23.0%) PLWH experienced virological failure before LPV/r-based regimens used. Among these, 20 PLWH still had virological non-suppression despite treatment with LPV/r-based regimens.

The most common reason for switching to BIC/FTC/TAF was regimen simplification (248/461, 53.8%), shown in Table 1. And 19 (4.12%) PLWH switched to BIC/FTC/TAF due to virological failure.

Virologic response

Fig. 2A summarized virologic suppression rates before and after switching to BIC/FTC/TAF. Overall, a significant improvement in virologic outcomes was observed following the switch. The proportion of PLWH achieving virologic suppression increased significantly from 94.6% pre-switch to 98.6% post-switch ($P < 0.001$). The prevalence of low-level viremia decreased from 1.3% to 0.7%, while virologic failure declined from 4.1% to 0.7% ($P < 0.001$). After adjusting for baseline viral load, gender, and age in the ordinal logistic regression model, these improvements remained statistically significant (adjusted $P = 0.013$). We then evaluated the effectiveness of BIC/FTC/TAF in PLWH (106/461) with a history of virologic failure prior to LPV/r use. In this subgroup, virologic suppression rates improved significantly after switching to BIC/FTC/TAF (81.1%–97.2%, $P < 0.001$, adjusted $P = 0.001$; Fig. 2B). Among those PLWH who were virologically suppressed before the switch (86/106), BIC/FTC/TAF also maintained good viral suppression (85/86, 98.8%; Fig. 2C). Additionally, when comparing suppression rates in PLWH without such a history, no difference was found (98.6% vs. 99.2%, $P = 0.789$; Fig. 2D).

Furthermore, comparative analysis of PLWH with (n = 106) versus without (n = 355) virologic failure revealed significant baseline difference in disease progression (Table 2). PLWH with historical virological failure (PLWH with HVF) showed poorer immunologic status (median nadir CD4 count 192 vs. 265 cells/μL, $P = 0.003$) and higher baseline viremia level (median 4.8 vs. 4.4 log10 copies/mL, $P = 0.047$). While both groups showed comparable pre-switch regimen compositions ($P = 0.308$), the HVF cohort more frequently initiated on the first-line EFV-based regimens (76.4% vs. 67.6%; $P < 0.001$). The NVP-based regimens served as a first-line ART option prior to the adoption of EFV-based regimens in China, which may partly explain the longer ART duration observed in PLWH with HVF (median 10 vs. 8 years,

Table 2
Characteristics of PLWH with or without a history of virologic failure prior to LPV/r use.

Characteristics	PLWH with HVF	PLWH without HVF	*P* value
n	106	355	
Gender			0.347
Male	100 (94.3%)	325 (91.5%)	
Female	6 (5.7%)	30 (8.5%)	
Age	41 (37, 47)	38 (33, 45)	0.002
ART duration, years	10 (7, 12)	8 (6, 9)	<0.001
Initial regimens			<0.001
NVP based	22 (20.8%)	11 (3.1%)	
EFV based	81 (76.4%)	240 (67.6%)	
LPV/r based	2 (1.9%)	103 (29%)	
RAL based	1 (0.9%)	1 (0.3%)	
Nadir CD4 count, cells/μL	192 (69, 342)	265 (117, 427)	0.003
Baseline HIV RNA, copies/mL (Log10)	4.8 (4.0, 5.2)	4.4 (3.8, 5.0)	0.047
Pre-switch regimens			0.308
LPV/r+3 TC + TDF	81 (76.4%)	267 (75.2%)	
LPV/r+3 TC + AZT	21 (19.8%)	63 (17.7%)	
LPV/r+3 TC	1 (0.9%)	16 (4.5%)	
LPV/r+3 TC + ABC	1 (0.9%)	6 (1.7%)	
LPV/r + DTG	1 (0.9%)	2 (0.6%)	
LPV/r + RAL	1 (0.9%)	0 (0%)	
LPV/r + DTG + TDF	0 (0%)	1 (0.3%)	
Pre-switch suppression rate			<0.001
VS	86 (81.1%)	350 (98.6%)	
LLV	3 (2.8%)	3 (0.8%)	
VF	17 (16%)	2 (0.6%)	
Post-switch suppression rate			0.179
VS	103 (97.2%)	352 (99.2%)	
LLV	1 (0.9%)	2 (0.6%)	
VF	2 (1.9%)	1 (0.3%)	

Notes: Data are presented as median (IQR) or n (%) unless specified otherwise.

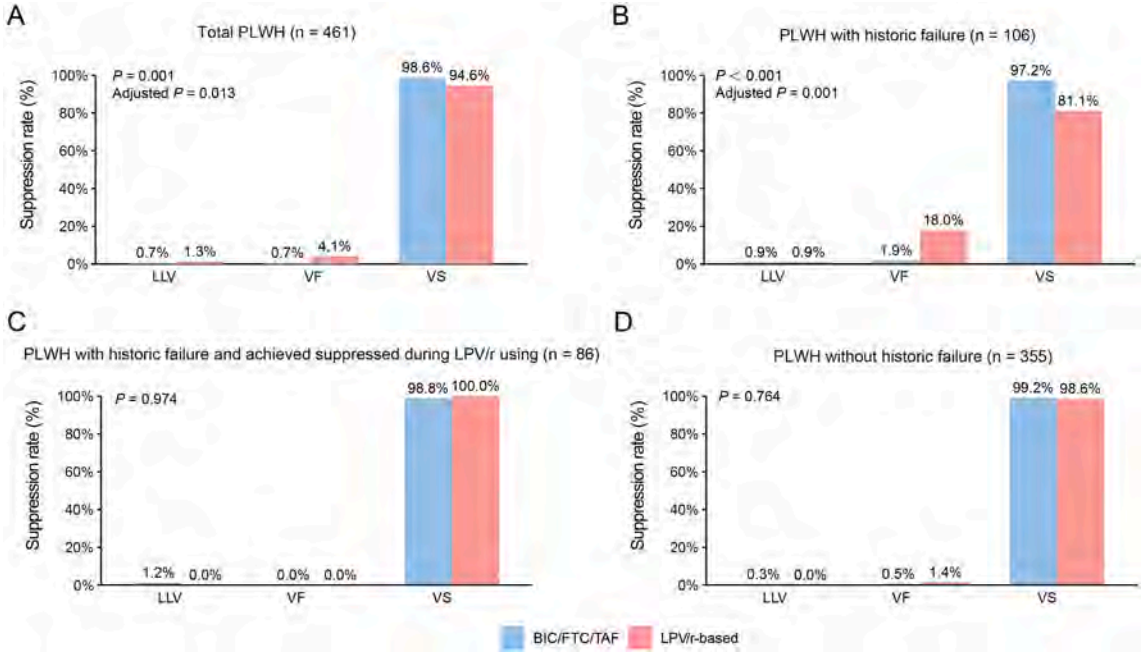

Fig. 2. Suppression rates in PLWH before and after BIC/FTC/TAF switch. **A** Comparison of suppression rates in the total population (n = 461); **B** Suppression rates in PLWH with virological failure before LPV/r use (n = 106); **C** Suppression rates in PLWH with virological failure prior to LPV/r use who achieved virological suppressed before switching to BIC/FTC/TAF (n = 86); **D** Suppression rates in PLWH without historical virological failure (n = 355). McNemar-Bowker test was used to compare suppression rate, while the ordinal logistic regression was used to assess the suppression rate change after adjusting for baseline viral load, gender, and age; VS: virological suppression; VF: virological failure; LLV: low-level viremia.

$P < 0.001$). Of note, despite these baseline differences and lower suppression rate before BIC/FTC/TAF switching (81.1% vs. 98.6%, $P < 0.001$), both two group achieved comparable virologic suppression rates following switching to BIC/FTC/TAF (97.2% vs 99.2%; $P = 0.179$). Those findings suggested that BIC/FTC/TAF could be generally effective for PLWH with LPV/r-based regimens.

CD4 recovery and metabolism outcomes

The changes in CD4 counts, creatinine (CRE), glucose (GLU), triglyceride (TG) and total cholesterol (TC) (pre-switch vs. post-switch) were presented in Table 3. Overall, there was no difference in CD4 counts before and after the switch (median 603 vs. 599 cells/μL, $P = 0.632$). Regarding metabolic changes, a significant increase in CRE levels was observed [from a median of 72.4 (58.7, 82.7) pre-switch to 86.5 (77, 98.6), adjusted $P < 0.001$], while TG declined from 2.4 (1.8, 3.4) pre-switch to 1.8 (1.1, 2.6) post-switch (adjusted $P < 0.001$). Although the median level of TG after the switch remained slightly above the normal threshold (1.7 mmol/L), the reduction of TG could reduce cardiovascular disease risk (Park et al., 2024). There was no significant change observed in TC and GLU after adjusting for the baseline age, gender, TC and GLU. Then we compared those indicators in PLWH with LPV/r+3 TC + TDF, as this regimen was the main type before BIC/FTC/TAF switch. Interestingly, though both switching from TDF to TAF and the use of LPV/r would increase the level of lipids (Carr et al., 1998; Surial et al., 2021), the level of lipids decreased after switching from LPV/r+3 TC + TDF. This finding suggested switching from LPV/r to BIC could balance even eliminate the effect of switching from TDF to TAF on lipid.

DISCUSSION

Our multicenter retrospective study demonstrated that switching from LPV/r-based regimens to BIC/FTC/TAF significantly improved virological suppression rates (94.6%–98.6%, $P < 0.001$) and reduced TG levels in Chinese PLWH. The improvement of suppression rates was particularly notable among PLWH with a history of virologic failure, where suppression rates increased from 81.1% to 97.2% ($P < 0.001$).

The suppression rates of PLWH with historical virologic failure before the switch were consistent with previous studies: 83% in SECOND-LINE trail (Boyd et al., 2013), 86% in Europe Africa Research Network for Evaluation of Second-line Therapy (EARNEST) trail (Hakim et al., 2018) and 87% in NADIA trail (Paton et al., 2022). Within this subgroup, NNRTI resistance mutations were commonly observed, frequently accompanied by NRTI resistance mutations (Paton et al., 2017; Tsai et al., 2023). DTG plus two NRTIs has been considered an second-line regimen when NNRTI plus NRTI regimen failed and has demonstrated maintained a good viral suppression, regardless of whether the full activity of at least one NRTI was confirmed (Aboud et al., 2019; Paton et al., 2022). However, data on BIC/FTC/TAF in this setting remains limited.

Herein, our study provides some evidence about the efficacy of BIC/FTC/TAF in this setting. The significant improvement in virologic supression after switching to BIC/FTC/TAF in PLWH with historical virologic failure suggests that BIC/FTC/TAF may have high efficacy in settings where confirmation of NRTI activity is unavailable. The sustained high suppression rate (85/86, 98.8%) in those PLWH who were already suppressed during LPV/r use further confirms this. Besides, a robust suppression rate of 90.0% (18/20, data not shown) with BIC/FTC/TAF was also observed in PLWH who had virological non-suppression with LPV/r-based regimens. Given the high barrier to resistance of LPV/r, virological non-suppression in those PLWH may be primarily attributed to poor adherence, unwanted side effects and drug–drug interactions (Stebbing et al., 2007; Lathouwers et al., 2011; Zheng et al., 2014). Therefore, we believe the virological superiority likely stems from two benefits provided by BIC/FTC/TAF. First, BIC's high genetic barrier to resistance might provide clinical benefits even in those PLWH who had archived NRTI resistance mutations, as a high suppression rate was observed in PLWH who were already suppressed before the switch. Second, regimen simplification reduces pill burden from typically 4–6 pills/day to a single tablet, which might potentially improve adherence and enhance the virological outcome.

Switching from LPV/r was associated with improvements in fasting lipids (Eron et al., 2010; Arribas et al., 2014; Gatell et al., 2017), which might be attributed to the reduced interference with the normal function of hepatic lipid-metabolizing enzymes (Loos et al., 2022). In our study, PLWH experienced changes in all components of LPV/r-based regimens: NRTIs were switched to FTC and TAF, while LPV/r was switched to BIC. Since both switching from TDF to TAF and the use of LPV/r would increase the level of lipids (Carr et al., 1998, 1999; Surial et al., 2021; Martínez-Sanz et al., 2023; Damas et al., 2024), lipids changes might depend on whether PLWH were taking regimens containing TDF. Interestingly, when we compared the changes among PLWH with LPV/r+3 TC + TDF, no difference in TC was observed, while the TG was reduced. This finding suggested the lipid effects of switching from TDF to TAF were balanced or even eliminated by switching from LPV/r to BIC. Overall, the reduction of TG after switching to BIC/FTC/TAF was consistent with results reported by Eric S. Daar et al. (2018), which might help reduce the risk of cardiovascular mortality (Nordestgaard and Varbo, 2014; Park

Table 3
Changes in CD4 counts and metabolism data after the BIC/FTC/TAF switch.

Characteristics	Baseline	Pre-switch	Post-switch	*P*	Adjusted *P*
Overall [a]					
CD4 count, cells/μL	250 (98, 408)	603 (453, 790)	599 (468, 790)	0.632	0.384
CRE, μmol/L	70 (60.7, 77.7)	72.4 (58.7, 82.7)	86.5 (77.0, 98.6)	< 0.001	< 0.001
TG, mmol/L	1.39 (0.9, 2.2)	2.4 (1.8, 3.4)	1.8 (1.1, 2.6)	< 0.001	< 0.001
TC, mmol/L	4.03 (3.5, 4.7)	5.1 (4.2, 5.6)	5.0 (4.2, 5.5)	0.297	0.345
GLU, mmol/L	5.36 (4.9, 6.0)	5.6 (5.0, 6.3)	5.6 (5.1, 6.2)	0.910	0.784
LPV/r+3 TC + TDF [b]					
CD4 count, cells/μL	267 (121, 414)	603 (440, 795)	608 (480, 811)	0.119	0.149
CRE, μmol/L	69.1 (61.0, 76.6)	73.1 (61.4, 83.2)	87.3 (77.5, 98.0)	< 0.001	< 0.001
TG, mmol/L	1.4 (0.9, 2.2)	2.3 (1.8, 3.3)	1.8 (1.1, 2.5)	< 0.001	< 0.001
TC, mmol/L	4 (3.5, 4.6)	5.1 (4.1, 5.6)	4.9 (4.2, 5.5)	0.593	0.710
GLU, mmol/L	5.4 (4.9, 6.0)	5.6 (5.0, 6.2)	5.5 (5.1, 6.2)	0.182	0.967

Notes: Data were presented as median (IQR). Paired *t*-test was used to compare the differences in various indicators before and after the switch. A multivariable linear regression model adjusted for age, gender, baseline viral load and index was used to estimate the average Δindicator (post-switch minus pre-switch values).
The reference ranges for metabolic parameters: CRE (creatinine, 57–97 μmol/L), TG (triglyceride, 0.57–1.71 mmol/L), TC (total cholesterol, 2.9–5.68 mmol/L), GLU (3.9–6.1 mmol/L).

[a] Data was available for 461 participants in CD4 counts and 287 in metabolism data. Pre-switch and post-switch CD4 count represented the current CD4 levels before switching to BIC/FTC/TAF and 48 weeks after the switch.

[b] Data was available for 315 participants in CD4 counts and for 215 in metabolism data.

et al., 2024). Additionally, BIC inhibits the tubular secretion of CRE caused by, which subsequently contributed to the increase in serum CRE observed in our study. This increased level of CRE has been well-documented as clinically insignificant (Deeks, 2018).

There were some limitations in our study. As a single-arm retrospective observational study, the results may not be generalized to all population. The study design may exclude those who discontinued BIC/FTC/TAF before 48 weeks, which might introduce survivorship bias. Although another study from our large cohort demonstrated a 92.5% persistence rate of BIC/FTC/TAF at 48 weeks (unpublished), there was still limited survivorship bias in this study. Besides, the favorable virological outcomes after the switch should be interpreted with caution, due to the lack of historic resistance data. Potential side effects of BIC/FTC/TAF (e.g., weight gain trends or nephrotoxicity markers beyond creatinine elevation) were not collected, which may lead to underestimation of risks associated with prolonged use. Furthermore, the observation duration in this study was short, and long-term follow-up studies are needed to elucidate the impact on virologic response, bone mineral density, and mental health.

However, our findings may also extend current knowledge. To our knowledge, this is the first real-world efficacy assay of virologic efficacy and metabolic changes associated with switching from LPV/r-based regimens to BIC/FTC/TAF in Chinese clinical practice. This makes our findings particularly relevant for regimen optimization in China, where LPV/r remains widely used. Besides, the multicenter design involving three hospitals and a larger sample size could provide more comprehensive data reflecting diverse clinical setting.

CONCLUSIONS

This multicenter retrospective study demonstrated that switching to BIC/FTC/TAF could be effective across all PLWH with LPV/r-based regimens in China. The regimen switch significantly improved virological suppression rates among PLWH with prior virological failure, while also effectively maintaining high suppression rates in PLWH without such a history. Additionally, the switch led to favorable metabolic outcomes in reducing triglyceride levels.

MATERIALS AND METHODS

Research design

This study was a multicenter retrospective observational study aimed at evaluating the clinical outcomes of PLWH who switched from LPV/r-based regimens to the BIC/FTC/TAF in China. As described in Fig. 1, a total of 461 participants were screened from January 2021 to December 2023. The inclusion criteria included: (1) PLWH currently receiving ART with BIC/FTC/TAF; (2) prior to switching to BIC/FTC/TAF, they had been treated with an LPV/r-based regimen; (3) the duration of BIC/FTC/TAF treatment >1 year.

The primary objective of this study was to evaluate the viral suppression outcomes in PLWH before and after the switch to BIC/FTC/TAF. Secondary objectives involved evaluating the changes in CD4 counts, fasting glucose (GLU), fasting lipids, which included triglyceride (TG), total cholesterol (TC), and creatinine (CRE).

Data collection

Data were extracted from the medical information systems of three hospitals: Beijing Ditan Hospital, Hangzhou Xixi Hospital and Beijing Youan Hospital. Gender, age, duration of ART, initial regimens, regimens before switching to BIC/FTC/TAF were collected. CD4 counts, HIV viral load, GLU, TG, TC and CRE were obtained from the medical records. CD4 cell counts in blood were determined using flow cytometry-based assays. HIV-1-RNA levels in plasma were quantified using the standard Amplicor-HIV-1 Monitor assay, with a limit of detection of 40 copies/mL. GLU, TG, TC and CRE were analyzed from serum samples using the automatic biochemical analyzer. For laboratory data (e.g. CD4 counts and HIV viral load), measurements were collected at three time points: baseline, 48 weeks prior to the switch to BIC/FTC/TAF, and 48 weeks after the switch. Additionally, the reasons for BIC/FTC/TAF switch and virological failure history prior to the use of LPV/r-based regimens were extracted from medical records.

Definitions

Virological suppression (VS) was defined as HIV-RNA < 40 copies/mL. Low-level viremia (LLV) was considered as HIV-1 RNA between 50 and 200 copies/mL. Virologic failure (VF) was defined as a consistent viral load exceeding 200 copies/mL.

Statistical analysis

Continuous variables did not follow a normal distribution assessed by the Shapiro-Wilk Normality Test, and were described as median measurements and interquartile ranges (IQRs) in this study. Percentages were used to describe categorical data. The comparison was performed with the chi-squared test or Fisher's exact test for categorical variables in Table 2. And the continuous variables comparison was performed with Wilcoxon test in Table 2. The comparison of suppression rate was performed with McNemar-Bowker test in Fig. 2. Then, the ordinal logistic regression was used to assess the suppression rates changes after covariate adjustment. Paired *t*-test to compare the differences in various indicators before and after the switch in Table 3. We evaluated the impact of treatment switching on CD4 counts by calculating per-PLWH ΔCD4 (post-switch minus pre-switch values). A multivariable linear regression model adjusted for age, gender, and baseline viral load was used to estimate the average ΔCD4. The same methodology when assessing the impact of switching on GLU, TG, TC, CRE in Table 3. A two-sided *P*-value <0.05 was considered statistically significant. The statistical analyses in this study were performed using R software, specifically employing the glm function and the MASS package.

DATA AVAILABILITY

The original data in this study can be obtained from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was approved by the Committee of Ethics at Beijing Ditan Hospital (approval number: 2021-022-01), Capital Medical University in Beijing, China. The requirement for informed consent was waived by the Ethics Committee of Beijing Ditan Hospital because of the retrospective nature of the study.

AUTHOR CONTRIBUTIONS

Jiantao Fu: data curation, formal analysis, writing-original draft. Yifan Guo: data curation, writing-original draft. Guoxiang Zheng: data curation. Zongxing Yang: data curation. Jinchuan Shi: data curation. Dingyan Yan: data curation. Jianhua Yu: conceptualization, writing-review & editing. Lijun Sun: conceptualization, writing-review & editing. Hongxin Zhao: conceptualization, methodology, writing-review & editing, supervision.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ACKNOWLEDGEMENT

This work was supported by the Capital's Funds for Health Improvement and Research (CFH2024-2-2175). We warmly thank the R Stats Package (https://github.com/packagestats/) for data processing and the Figdraw for the visualization of the study design. We would like to thank Yipeng Wang (Capital medical university, China) for many inspiring and thought-provoking discussions. We also thank the editor's office for the suggestion that significantly improved the readability of the article.

REFERENCES

Aboud, M., Kaplan, R., Lombaard, J., Zhang, F., Hidalgo, J.A., Mamedova, E., Losso, M. H., Chetchotisakd, P., Brites, C., Sievers, J., Brown, D., Hopking, J., Underwood, M., Nascimento, M.C., Punekar, Y., Gartland, M., Smith, K., 2019. Dolutegravir versus ritonavir-boosted lopinavir both with dual nucleoside reverse transcriptase inhibitor therapy in adults with HIV-1 infection in whom first-line therapy has failed (dawning): an open-label, non-inferiority, phase 3b trial. Lancet Infect. Dis. 19, 253–264.

Ambrosioni, J., Rojas Liévano, J., Berrocal, L., Inciarte, A., de la Mora, L., González-Cordón, A., Martínez-Rebollar, M., Laguno, M., Torres, B., Ugarte, A., Chivite, I., Leal, L., de Lazzari, E., Miró, J.M., Blanco, J.L., Martinez, E., Mallolas, J., 2022. Real-life experience with bictegravir/emtricitabine/tenofovir alafenamide in a large reference clinical centre. J. Antimicrob. Chemother. 77, 1133–1139.

Arribas, J.R., Pialoux, G., Gathe, J., Di Perri, G., Reynes, J., Tebas, P., Nguyen, T., Ebrahimi, R., White, K., Piontkowsky, D., 2014. Simplification to coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus continuation of ritonavir-boosted protease inhibitor with emtricitabine and tenofovir in adults with virologically suppressed hiv (strategy-pi): 48 week results of a randomised, open-label, phase 3b, non-inferiority trial. Lancet Infect. Dis. 14, 581–589.

Boyd, M.A., Kumarasamy, N., Moore, C.L., Nwizu, C., Losso, M.H., Mohapi, L., Martin, A., Kerr, S., Sohn, A.H., Teppler, H., Van de Steen, O., Molina, J.M., Emery, S., Cooper, D.A., 2013. Ritonavir-boosted lopinavir plus nucleoside or nucleotide reverse transcriptase inhibitors versus ritonavir-boosted lopinavir plus raltegravir for treatment of HIV-1 infection in adults with virological failure of a standard first-line art regimen (second-line): a randomised, open-label, non-inferiority study. Lancet 381, 2091–2099.

Boyd, M.A., Amin, J., Mallon, P.W., Kumarasamy, N., Lombaard, J., Wood, R., Chetchotisakd, P., Phanuphak, P., Mohapi, L., Azwa, I., Belloso, W.H., Molina, J.M., Hoy, J., Moore, C.L., Emery, S., Cooper, D.A., 2017. Body composition and metabolic outcomes after 96 weeks of treatment with ritonavir-boosted lopinavir plus either nucleoside or nucleotide reverse transcriptase inhibitors or raltegravir in patients with hiv with virological failure of a standard first-line antiretroviral therapy regimen: a substudy of the randomised, open-label, non-inferiority second-line study. Lancet HIV 4, e13–e20.

Carr, A., Samaras, K., Chisholm, D.J., Cooper, D.A., 1998. Pathogenesis of hiv-1-protease inhibitor-associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance. Lancet 351, 1881–1883.

Carr, A., Samaras, K., Thorisdottir, A., Kaufmann, G.R., Chisholm, D.J., Cooper, D.A., 1999. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. Lancet 353, 2093–2099.

Chang, H.M., Chou, P.Y., Chou, C.H., Tsai, H.C., 2021. Outcomes after switching to BIC/FTC/TAF in patients with virological failure to protease inhibitors or non-nucleoside reverse transcriptase inhibitors: a real-world cohort study. Infect. Drug Resist. 14, 4877–4886.

Croxtall, J.D., Perry, C.M., 2010. Lopinavir/ritonavir: a review of its use in the management of HIV-1 infection. Drugs 70, 1885–1915.

D2EFT Study Group, 2024. Dolutegravir plus boosted darunavir versus recommended standard-of-care antiretroviral regimens in people with HIV-1 for whom recommended first-line non-nucleoside reverse transcriptase inhibitor therapy has failed (D(2)EFT): an open-label, randomised, phase 3b/4 trial. Lancet HIV 11, e436–e448.

Daar, E.S., DeJesus, E., Ruane, P., Crofoot, G., Oguchi, G., Creticos, C., Rockstroh, J.K., Molina, J.M., Koenig, E., Liu, Y.P., Custodio, J., Andreatta, K., Graham, H., Cheng, A., Martin, H., Quirk, E., 2018. Efficacy and safety of switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from boosted protease inhibitor-based regimens in virologically suppressed adults with HIV-1: 48 week results of a randomised, open-label, multicentre, phase 3, non-inferiority trial. Lancet HIV 5, e347–e356.

Damas, J., Munting, A., Fellay, J., Haerry, D., Marzolini, C., Tarr, P.E., Steffen, A., Braun, D.L., Stoeckle, M., Bernasconi, E., Nawej Tshikung, O., Fux, C.A., Darling, K. E.A., Béguelin, C., Wandeler, G., Cavassini, M., Surial, B., 2024. Weight, anthropometric and metabolic changes after discontinuing antiretroviral therapy containing tenofovir alafenamide in people with HIV. Clin. Infect. Dis. 79, 990–998.

Deeks, E.D., 2018. Bictegravir/emtricitabine/tenofovir alafenamide: a review in hiv-1 infection. Drugs 78, 1817–1828.

Eron, J.J., Young, B., Cooper, D.A., Youle, M., Dejesus, E., Andrade-Villanueva, J., Workman, C., Zajdenverg, R., Fätkenheuer, G., Berger, D.S., Kumar, P.N., Rodgers, A.J., Shaughnessy, M.A., Walker, M.L., Barnard, R.J., Miller, M.D., Dinubile, M.J., Nguyen, B.Y., Leavitt, R., Xu, X., Sklar, P., 2010. Switch to a raltegravir-based regimen versus continuation of a lopinavir-ritonavir-based regimen in stable HIV-infected patients with suppressed viraemia (switchmrk 1 and 2): two multicentre, double-blin, randomised controlled trials. Lancet 375, 396–407.

Gatell, J.M., Assoumou, L., Moyle, G., Waters, L., Johnson, M., Domingo, P., Fox, J., Martinez, E., Stellbrink, H.J., Guaraldi, G., Masia, M., Gompels, M., De Wit, S., Florence, E., Esser, S., Raffi, F., Pozniak, A.L., 2017. Switching from a ritonavir-boosted protease inhibitor to a dolutegravir-based regimen for maintenance of HIV viral suppression in patients with high cardiovascular risk. Aids 31, 2503–2514.

Hakim, J.G., Thompson, J., Kityo, C., Hoppe, A., Kambugu, A., van Oosterhout, J.J., Lugemwa, A., Siika, A., Mwebaze, R., Mweemba, A., Abongomera, G., Thomason, M.J., Easterbrook, P., Mugyenyi, P., Walker, A.S., Paton, N.I., 2018. Lopinavir plus nucleoside reverse-transcriptase inhibitors, lopinavir plus raltegravir, or lopinavir monotherapy for second-line treatment of HIV (EARNEST): 144-week follow-up results from a randomised controlled trial. Lancet Infect. Dis. 18, 47–57.

Hosseinipour, M.C., Gupta, R.K., Van Zyl, G., Eron, J.J., Nachega, J.B., 2013. Emergence of hiv drug resistance during first- and second-line antiretroviral therapy in resource-limited settings. J. Infect. Dis. 207 (Suppl. 2), S49–S56.

Hulgan, T., Haubrich, R., Riddler, S.A., Tebas, P., Ritchie, M.D., McComsey, G.A., Haas, D.W., Canter, J.A., 2011. European mitochondrial DNA haplogroups and metabolic changes during antiretroviral therapy in AIDS clinical trials group study A5142. AIDS 25, 37–47.

Lathouwers, E., De Meyer, S., Dierynck, I., Van de Casteele, T., Lavreys, L., de Béthune, M.P., Picchio, G., 2011. Virological characterization of patients failing darunavir/ritonavir or lopinavir/ritonavir treatment in the artemis study: 96-week analysis. Antivir. Ther. 16, 99–108.

Loos, N.H.C., Beijnen, J.H., Schinkel, A.H., 2022. The mechanism-based inactivation of CYP3A4 by ritonavir: what mechanism? Int. J. Mol. Sci. 23, 9866.

Martínez-Sanz, J., Serrano-Villar, S., Muriel, A., García Fraile, L.J., Orviz, E., Mena de Cea, Á., Campins, A.A., Moreno, S., 2023. Metabolic-related outcomes after switching from tenofovir disoproxil fumarate to tenofovir alafenamide in adults with human immunodeficiency virus (HIV): a multicenter prospective cohort study. Clin. Infect. Dis. 76, e652–e660.

Nordestgaard, B.G., Varbo, A., 2014. Triglycerides and cardiovascular disease. Lancet 384, 626–635.

Panel on Antiretroviral Guidelines for Adults and Adolescents, 2025. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new.

Park, H.B., Arsanjani, R., Hong, S.J., Yi, J.J., Yi, S.W., 2024. Impact of hypertriglyceridaemia on cardiovascular mortality according to low-density lipoprotein cholesterol in a 15.6-million population. Eur. J. Prev. Cardiol. 31, 280–290.

Paton, N.I., Kityo, C., Thompson, J., Nankya, I., Bagenda, L., Hoppe, A., Hakim, J., Kambugu, A., van Oosterhout, J.J., Kiconco, M., Bertagnolio, S., Easterbrook, P.J., Mugyenyi, P., Walker, A.S., 2017. Nucleoside reverse-transcriptase inhibitor cross-resistance and outcomes from second-line antiretroviral therapy in the public health approach: an observational analysis within the randomised, open-label, earnest trial. Lancet HIV 4, e341–e348.

Paton, N.I., Musaazi, J., Kityo, C., Walimbwa, S., Hoppe, A., Balyegisawa, A., Asienzo, J., Kaimal, A., Mirembe, G., Lugemwa, A., Ategeka, G., Borok, M., Mugerwa, H., Siika, A., Odongpiny, E.L.A., Castelnuovo, B., Kiragga, A., Kambugu, A., 2022. Efficacy and safety of dolutegravir or darunavir in combination with lamivudine plus either zidovudine or tenofovir for second-line treatment of hiv infection (NADIA): week 96 results from a prospective, multicentre, open-label, factorial, randomised, non-inferiority trial. Lancet HIV 9, e381–e393.

Sax, P.E., Arribas, J.R., Orkin, C., Lazzarin, A., Pozniak, A., DeJesus, E., Maggiolo, F., Stellbrink, H.J., Yazdanpanah, Y., Acosta, R., Huang, H., Hindman, J.T., Martin, H., Baeten, J.M., Wohl, D., 2023. Bictegravir/emtricitabine/tenofovir alafenamide as initial treatment for HIV-1: five-year follow-up from two randomized trials. eClinicalMedicine 59, 101991.

Stebbing, J., Nathan, B., Jones, R., McKenna, A., Powles, T., Bower, M., Holmes, P., Gazzard, B., Nelson, M., 2007. Virological failure and subsequent resistance profiles in individuals exposed to atazanavir. AIDS 21, 1826–1828.

Surial, B., Mugglin, C., Calmy, A., Cavassini, M., Günthard, H.F., Stöckle, M., Bernasconi, E., Schmid, P., Tarr, P.E., Furrer, H., Ledergerber, B., Wandeler, G., Rauch, A., 2021. Weight and metabolic changes after switching from tenofovir disoproxil fumarate to tenofovir alafenamide in people living with HIV: a cohort study. Ann. Intern. Med. 174, 758–767.

Tsai, M.S., Sun, H.Y., Chen, C.P., Lee, C.H., Lee, C.Y., Liu, C.E., Tang, H.J., Hung, T.C., Li, C.W., Lee, Y.T., Liou, B.H., Yang, C.J., Hung, C.C., 2023. Switching to coformulated bictegravir, emtricitabine, and tenofovir alafenamide maintained viral suppression in adults with historical virological failures and K65N/R mutation. Int. J. Infect. Dis. 126, 39–47.

van Zyl, G.U., van der Merwe, L., Claassen, M., Zeier, M., Preiser, W., 2011. Antiretroviral resistance patterns and factors associated with resistance in adult patients failing NNRTI-based regimens in the Western Cape, South Africa. J. Med. Virol. 83, 1764–1769.

Wang, R., Sun, L., Wang, X., Zhai, Y., Wang, L., Ma, P., Wu, C., Zhou, Y., Chen, R., Wang, R., Zhang, F., Hua, W., Li, A., Xia, W., Gao, Y., Li, R., Lv, S., Shao, Y., Cao, Y., Zhang, T., Wu, H., Cai, C., Dai, L., 2024. Rapid initiation of antiretroviral therapy with coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus efavirenz, lamivudine, and tenofovir disoproxil fumarate in hiv-positive men who

have sex with men in China: week 48 results of the multicenter, randomized clinical trial. Clin. Infect. Dis. 79, 169–176.
Yuan, J., Deng, C., Li, Q., Sun, Y., Huang, W., Zhang, W., Liu, M., 2024. Human immunodeficiency virus/acquired immune deficiency syndrome antiretroviral therapy initiated on the same day in treatment-naïve people with human immunodeficiency virus: a comparative study of efficacy and regimen. Chin Med J (Engl) 137, 2720–2725.
Zhao, Y., Han, M.J., Gan, X.M., Ma, Y., Zhao, D.C., 2020. Characteristics and viral suppression among people living with HIV from the national free antiretroviral therapy programme, 2019. HIV Med. 21, 701–707.
Zheng, Y., Hughes, M.D., Lockman, S., Benson, C.A., Hosseinipour, M.C., Campbell, T.B., Gulick, R.M., Daar, E.S., Sax, P.E., Riddler, S.A., Haubrich, R., Salata, R.A., Currier, J.S., 2014. Antiretroviral therapy and efficacy after virologic failure on first-line boosted protease inhibitor regimens. Clin. Infect. Dis. 59, 888–896.