Infection and Drug Resistance

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ORIGINAL RESEARCH

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

Hui-Min Chang[1–3]
Pei-Yun Chou[4,5]
Chen-Hsi Chou[2]
Hung-Chin Tsai[4–6]

[1]Department of Pharmacy, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; [2]Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [3]Department of Pharmacy and Master Program, Collage of Pharmacy and Health Care, Tajen University, Pingtung, Taiwan; [4]Section of Infectious Diseases, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; [5]National Yang Ming Chiao Tung University, Taipei, Taiwan; [6]Institute of Biomedical Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan

Purpose: This study evaluated the real-world tolerability and treatment effectiveness of BIC/FTC/TAF in treatment-experienced patients living with HIV-1 in Taiwan, especially in those with viremia at switch.

Patients and Methods: This was a retrospective cohort study of adult patients in Taiwan with HIV-1 who received BIC/FTC/TAF from between November 2019 and November 2020. The primary endpoint was the rate of viral suppression (plasma HIV RNA load <50 copies/mL) while on BIC/FTC/TAF. The secondary endpoints included durability of treatment, incidence of and reasons for discontinuation of BIC/FTC/TAF, and changes in weight and lipid profiles.

Results: A total of 175 patients were switched to BIC/FTC/TAF. Among them, 74 patients (42%) were using INSTI based regimen, 34 patients (19%) NNRTI based regimen and 65 patients (37%) with PI based regimen before switching. Before starting BIC/FTC/TAF, 84.6% of the patients were virologically suppressed, of whom 97.3% maintained suppression while on BIC/FTC/TAF. Overall, 15.4% of the patients (n=27) had a detectable viral load before BIC/FTC/TAF, of whom 81.5% achieved and maintained virologic suppression on BIC/FTC/TAF during follow-up. Only two patients discontinued BIC/FTC/TAF due to adverse events, with rash being the predominant cause. By month 12, the median changes in weight was +4 kg (IQR, −1.8 to 8.2). There were no significant differences from baseline to the end of follow-up in triglycerides (p = 0.07), total cholesterol (p = 0.92), LDL-C (p = 0.12), and HDL-C (p = 0.053).

Conclusion: The results of this real-world cohort study suggest that switching to BIC/FTC/TAF may be an option to achieve and maintain virological suppression, even in patients with residual viremia at baseline. Our results also demonstrated a low discontinuation rate, a moderate gain in weight, and no significant increases in lipid levels with BIC/FTC/TAF. However, studies with larger sample sizes are warranted to evaluate the clinical implications of our findings.

Keywords: Biktarvy, bictegravir, switching, virological failure, viremia

Correspondence: Hung-Chin Tsai
Section of Infectious Diseases, Department of Medicine, Kaohsiung Veterans General Hospital, #386 Ta-Chung 1st Road, Kaohsiung, 813, Taiwan
Tel +886-7-3422121 ext. 2029
Fax +886-7-346-8292
Email hctsai1011@yahoo.com.tw

Chen-Hsi Chou
Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan
Email chenhsi@mail.ncku.edu.tw

Introduction

A single tablet regimen (STR) has been associated with better drug compliance,[1] improved quality of life[2] and being less likely to develop resistance[3,4] compared to multiple tablet regimens. Integrase strand transfer inhibitors (INSTIs) can reduce viral load rapidly with a low rate of drug–drug interactions and good tolerability,

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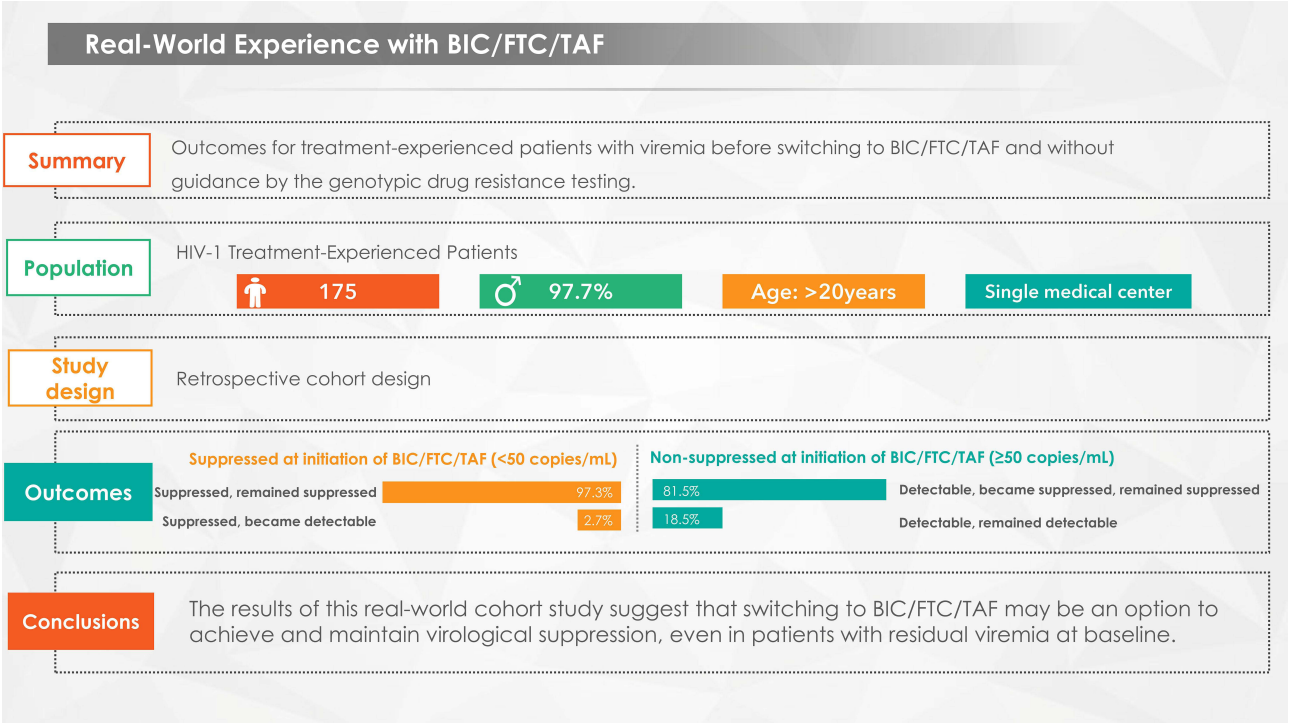
Graphical Abstract



making them a suitable treatment option for both treatment-naïve and treatment-experienced patients with HIV-1 infection.[5,6] In the last decade, three INSTIs have been approved by the Food and Drug Administration (FDA): raltegravir (RAL), elvitegravir (EVG), and dolutegravir (DTG). RAL is not co-formulated with Nucleoside analog reverse-transcriptase inhibitors (NRTIs), whereas EVG requires pharmacological boosting with cobicistat.[5,7] DTG was the first approved second-generation INSTI, and it differs from RAL and EVG in a higher genetic barrier and improved resistance profile.[8] A novel integrase inhibitor, bictegravir (BIC) is now available for the treatment of HIV-1 infection, and it is co-formulated with FTC and TAF as an STR.[9] BIC offers several advantages over other first-line INSTI-based regimens as EVG, including a low potential for drug–drug interactions due to the lack of a pharmacological booster, a high genetic barrier to resistance, and administration without regard to meals.[10] This higher resistance barrier is evident in the results of prospective clinical trials.[11,12] Based on these results, the International AIDS Society (IAS) recommends BIC or DTG based regimen as the initial therapy for HIV-1 infected individuals and also as a switching regimen in viral suppressed patients.[13] During the lifelong treatment of people living with human immunodeficiency virus (PLWH), they commonly switch ART regimens. Some studies have shown that a substantial number of patients (up to 55.5%) may modify their regimen overtime, where 25%–44% of them modify their initial treatment within the first years of treatment. The reasons for switching regimens include drug-related adverse events (AEs), virological failure (VF), drug toxicity, and simplification of a current regimen.[14–17] In this context that two-drug regimens (2-DR) were approved in the USA and Europe for the treatment of virologically suppressed or treatment naïve patients.[18] Biktarvy has been recommended as the first-line antiretroviral (ARV) therapy for HIV-1-infected patients in Taiwan since October 2019. However, very few studies have investigated the efficacy and safety of BIC/FTC/TAF in Asian populations or in viremic patients who switch to BIC/FTC/TAF.[19] Therefore, the purpose of this study was to assess the 12-month post-marketing tolerability and treatment effectiveness of HIV treatment experienced patients

switching to BIC/FTC/TAF regardless of pre-switching viral suppression in Taiwan.

Methods

Study Design and Setting

This study had a retrospective cohort design; it was conducted at Kaohsiung Veterans General Hospital (VGHKS) which is one of the largest medical centers in Kaohsiung and is responsible for health care of approximately 25% of HIV infected individuals in the city and about up to 5% of the HIV infected patients in Taiwan.

The inclusion criteria was male or female patients aged 20 years or above with confirmed HIV-1 infection who was switched their prior ART regimen to BIC/FTC/TAF between 1 November 2019 and 30 November 2020. These individuals were then followed until February 2021. Patients who had no plasma viral load (VL), lipid profile and weight measurements taken during the study period before and after switching to BIC/FTC/TAF were excluded, as were those who died or were lost to follow-up within 4 weeks of switching and those who were hospitalized during the follow-up period were also excluded. Censoring events in this study included the development of virological failure (plasma HIV RNA load >50 copies/mL), switch to another ART, loss to follow-up, or end of observation (February 28, 2021), which ever occurred first.

Procedures

In Taiwan, PLWH are provided with free-of-charge medical services at designated hospitals, which include cART and laboratory monitoring of viral hepatitis, lipids, liver and renal function, sugars and HbA1c, CD4 count and plasma VL. The current national HIV treatment guidelines suggest using either one of the TDF/FTC/EFV (Atripla®), ABC/3TC/DTG (Triumeq®), TAF/FTC/RPV (Odefsey) and BIC/TAF/FTC (Biktarvy®) in ART naïve and viral suppressed patients.

All stable PLWH are followed at outpatient clinics of designated hospitals around Taiwan every 3 months, and blood tests are performed every 3 to 6 months. However, genotypic drug resistance testing is not mandatory due to financial constraints.

Data Collection and Laboratory Investigations

A case report form was used to collect information on baseline demographics and serial laboratory data, included age, sex, weight, body mass index (BMI), CD4 count, HIV-1 VL, prior ART and duration of ART before switching to BIC/FTC/TAF, fasting glucose and HbA1c, and fasting lipids, which included triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). The primary reason for switching to BIC/FTC/TAF and the primary reason for discontinuation of BIC/FTC/TAF, were abstracted from the medical records if available. Also, descriptions of adverse events (AEs) and adherence measured by proportion of day cover were summarized based on electronic medical records. Of note, all AEs were documented when there was not a clear alternative etiology noted by the clinician including prior dermatological history or if the clinician specifically documented that the AE was attributed to BIC/FTC/TAF. The inclusive criteria for virologically failing patients were defined as plasma HIV RNA more than 50 copies/mL before or after switching.

Body weight and body mass index (BMI) calculations (weight in kilograms divided by height in meters, squared [kg/m2]) were performed at each clinic visit. Baseline body mass index (BMI) was classified as being underweight (<18.5 kg/m2), normal (18.5–23.9 kg/m2), overweight (24–26.9 kg/m2), and obese (≥27 kg/m2).[20]

Ethics Statement

This study was approved by the Ethics Committee and the institutional Review Board of the Kaohsiung Veterans General Hospital (VGHKS19-CT4-02). The study subjects were signed the written informed consent and all the participants had their records used in this study. This study complied with the Declaration of Helsinki.

Statistical Analysis

Baseline data are presented as number (%) or median (interquartile range [IQR]). Categorical data were compared using chi-squared or Fisher's exact tests. Continuous data were analyzed using *t*-test or Wilcoxon rank sum test, according to the distribution. Paired t-tests were also used to compare the changes of lipid and weight prior to switch and after switching. Time to virological failure (VF) analyses were performed using the Kaplan–Meier curves. In creating the survival curves, time to VF was estimated from the date of BIC/FTC/TAF initiation to the date of VF; in absence of VF, we used the date of last clinic visit as the follow-up time. To assess the influence of various demographic and clinical parameters on the

occurrence of VF, univariable and multivariable Cox proportional hazards regression models were applied. Multivariable models were adjusted for age and VL at baseline, CD4 count at baseline, HIV transmission category, intravenous drug abuser (IVDU), ever single-tablet regimen used, and length of time on ART before the switch. In the multivariate analysis, variables with $P < 0.1$ by univariate analysis were included. All statistical tests were two tailed and a p-value of less than 0.05 was considered statistically significant.

Results

Study Population

We included a total of 175 patients with a median follow-up of 52.7 weeks (IQR 41.9–63.3). The baseline characteristics of the study participants are summarized in Table 1. Briefly, their medium age (IQR) was 39 (32–49) years old with man consisted of 97.7%. The HIV transmission risk factor included MSM (65.2%) and intravenous drug abuser (9.2%). At baseline, 147 of the patients had virological suppression (VS; <50 copies/mL), with a median CD4 count (range) of 536 (376–722) cells/mm3.

The most common ARTs used prior to BIC/FTC/TAF were an INSTI (42.3%) plus two nucleoside analog reverse-transcriptase inhibitors (2NRTIs), followed by a protease inhibitor (PI; 37.1%) plus 2NRTIs, and a non-nucleoside/nucleotide reverse transcriptase inhibitor (NNRTI; 19.4%) plus 2NRTIs. Prior to switching to BIC/FTC/TAF, 91 patients (52%) were taking an STR, and 27 patients had detectable viral load (≥50 copies/mL).

The most common reasons for switching to BIC/FTC/TAF were treatment simplification (37.1%), toxicity/intolerance to ART (24%), and reimbursement requirements (16%).

Virologic Response

The virologic suppression rate was 94.9% (166/175) in our cohort. Of the 148 patients who were suppressed at the switch, 144 (97.3%) maintained viral suppression while on BIC/FTC/TAF. Of the four (2.7%) patients who became detectable, two had a VF (57.5 and 52.4 copies/mL, respectively) at the end of follow-up, and two were lost to follow-up. Kaplan–Meier plots showed that patients with higher baseline VL had a 16.27 times higher risk of VF (log rank P<0.0001; Figure 1). In addition, Table 2 provides results from univariable and multivariable Cox proportional hazards models for the occurrence of VF (defined as HIV

Table 1 Characteristics of the Study Population at Baseline

	Treatment-Experienced N=175
Age (year), median (IQR)	39 (32–49)
HIV-1 risk factors, No. (%)	
Unprotected heterosexual	15 (8.6)
Bisexual	29 (16.6)
MSM	106 (60.6)
MSM/IVDU	8 (4.6)
IVDU	8 (4.6)
Unknown	9 (5.1)
Sex M, No. (%)	171(97.7)
Baseline CD4 count, cells/μL, median (IQR)	536 (376–722)
Baseline HIV-1 RNA, log copies/mL	
<20	135 (77.6)
20–50	12 (6.9)
50–1000	13 (7.5)
>1000	14 (8.0)
Weight (kg), median (IQR)	67 (59.6–74)
Body mass index, kg/m^2 (%)	
Underweight (<18.5)	9 (5.1)
Normal (18.5≤BMI<24)	102 (58.3)
Overweight (24≤BMI<27)	42 (24)
Obesity (≥27)	22 (12.6)
Co-infection, No. (%)	
HAV	113 (64.6)
HBV	66 (37.7)
HCV	19 (10.9)
Median years since HIV diagnosis at baseline (IQR)	7.8 (5.2–11.6)
Prior cART duration (years), median (IQR)	6.3 (3.9–8.6)
ART regimen prior to switch, No. (%)	
STR (single-tablet regimen)	
INSTI/ NRTI	67 (38.3)
NNRTI/ NRTI	24 (13.7)
MTR (multiple-tablet regimen)	
INSTI/ NRTI	7 (4)
NNRTI/ NRTI	10 (5.7)
PI/NRTI	65 (37.1)
Other	2 (1.1)
Duration of BIC/FTC/TAF (years), median (IQR)	52.7 (41.9–63.3)

Note: One patient had no baseline viral load data.
Abbreviations: ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; IVDU, intravenous drug user; MSM, men who have sex with men; NRTIs, nucleoside reverse transcriptase inhibitors; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

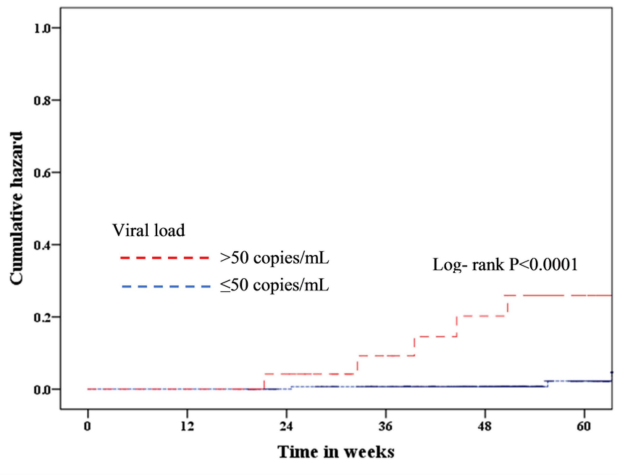


Figure 1 Kaplan–Meier estimates of time to virological failure relative to the baseline HIV-1 viral load.

RNA level of ≥50 copies/mL). Univariate Cox regression was performed to determine the factors associated with time to VF. HR indicates the relative risks associated with VF in the study group compared with the reference group. The time to VF was significantly different in patients who were IVDUs (HR 15.44; 95% CI 3.8–62.1; P < 0.0001), had a baseline CD4 cell count of ≥500 cells/mm3 (versus <200 cells/mm3; HR; 13.68; 95% CI 2.5–75; P=0.005), baseline VL of ≤ 50 copies/mL (versus >50 copies/mL; HR 9.39; 95% CI 2.5–35.33; P =0.001) and prior cART duration of >12 months (versus ≤12 months; HR 0.21; 95% CI 0.04–1.03; P = 0.055). After controlling for the aforementioned factors by multivariate Cox regression analysis, the factors significantly associated with time to VF was IVDU (HR 15.23; 95% CI 3.79–61.25; P = 0.0001). Of the 27 patients who were viremic before switching to BIC/FTC/TAF, 22 (81.5%) achieved and maintained suppression (Table 3). The majority of the viremic patients (51.9%) were on a PI-based regimen, 25.9% used an INSTI-based regimen, and 22.2% used a NNRTI-based regimen before switching to BIC/FTC/TAF. Of the remaining five patients (18.5%) with a detectable viral load, three were lost to follow-up before 12 weeks of treatment; the viral load of one of these patients was not assessed, and the other two had a viral load <200 copies/mL (85.9 and 100 copies/mL, at week 6 and week 8, respectively). One patient on prior EVG/COB/FTC/TAF (HIV-1 RNA viral load: 437,000 copies/mL) and one patient on LPV/r/3TC/AZT (HIV-1 RNA viral load: 102,000 copies/mL) with poor compliance were switched to BIC/FTC/TAF, and the viral load was reduced in both while not achieving viral suppression (5290 and 5100 copies/mL).

Immunological Response

The median CD4+ T cell count showed a slight but not significantly increase from 536cells/lL (IQR 376–722) before starting BIC/FTC/TAF to 557 cells/ul (IQR 381–735) at W48 (p = 0.31) after switching.

Discontinuation and Adverse Drug Reactions

Of the 175 patients, 28 (16%) reported AEs in a total of 30 events. The estimated rate of any AEs leading to discontinuation was 1.1%. A total of 3 patients reporting rash, two discontinued BIC/FTC/TAF and one patient reported resolution of the rash after concurrent use of an antihistamine agent. The most frequent AEs were neuropsychiatric toxicity (5.7%) and gastrointestinal toxicity (2.9%). Other AEs, each representing less than 1%, included palpitation, tremor, and tinnitus. No symptoms were life-threatening or led to the hospitalization and most symptoms were tolerated then subsided.

Change in Weight and Lipids

At 6 and 12 months, the median weight change from baseline was +2 kg (IQR, −1 to 6 kg, P = 0.007) and +4 kg (IQR −0.67 to 6.57 kg, P < 0.0001), respectively, in the treatment-experienced patients. The subgroup of 45 patients who switched from EVG/COB/FTC/TAF to BIC/FTC/TAF gained a median of 2 kg (IQR, 0.8 to 5 kg) at 12 months compared to those who remained on their baseline regimen. Individuals who were underweight gained a median of 8 kg (IQR, 1.8 to 8.85 kg), those who were normal weight gained 3.4 kg (IQR, 0 to 6 kg), those who were overweight gained 0.4 kg (IQR, −2 to 4.5 kg), and those who were obese gained 0 kg (IQR, −4.3 to 3.5 kg) (Figure 2).

Figure 3 shows the lipid parameter changes between baseline and the last clinical visit across. No significant changes were observed in any of the fasting lipid parameters evaluated (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides) during follow-up.

Discussion

This retrospective cohort study of Taiwanese PLWH treated with BIC/FTC/TAF demonstrated a good viral suppression

Table 2 Factors Associated with Time to Virological Failure by Multivariate Cox Regression

Outcome	VF ≥ 50 Copies/mL			
No. of Patients	N =175			
	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
VL at baseline		0.001		
>50 copies/mL	9.39 (2.5–35.33)			
≤50 copies/mL	1.00 (Reference)			
Age at baseline		0.74		
>50 yr	2.57 (0.23–28.45)			
30–50 yr	1.99 (0.24–16.5)			
<30 y	1.00 (Reference)			
IVDU		<0.0001		<0.0001
Yes	15.44 (3.8–62.1)		15.23 (3.79–61.25)	
No	1.00 (Reference)		1.00 (Reference)	
CD4 count at baseline, cells/mm3		0.005		
<200	13.68 (2.5–75)			
200–499	2.4 (0.4–14.4)			
≥500	1.00 (Reference)			
Prior cART duration		0.055		
≤ 12 months	0.21 (0.04–1.03)			
>12 months	1.00 (Reference)			
Ever STR before switch		0.21		
Yes	0.47 (0.1–1.6)			
No	1.00 (Reference)			

rate of 94.9% in treatment-experienced patients after more than 1 year of follow-up. Among 27 viremic patients before switching to BIC/FTC/TAF, 81.5% (22/27) achieved and maintained suppression. The most frequent AEs were neuropsychiatric toxicity (5.7%) and gastrointestinal toxicity (2.9%). Only two patients (1.1%) discontinue BIC/FTC/TAF due to AEs.

In our cohort study, we found that high VL before the switch was significantly associated with VF. This is consistent with other studies reporting that high baseline VL was associated with delay of viral suppression and increased chance of virological failure.[21,22] We also identified the factors significantly associated with shorter time to VF was intravenous drug abuser, which is consistent with a previous study reporting that active drug use or heavy alcohol use was associated with poor ART adherence, regardless of whether it was ongoing or recently reinitiated.[23]

BIC/FTC/TAF has demonstrated noninferiority to dolutegravir based regimen for individuals who are ART-naive and those virologically suppressed on another regimen.[12,24–26] However, little was known about patients with VF switching to BIC/FTC/TAF. In the present study, effective viral suppression was demonstrated in the patients who were viremic (n=27) on switching to BIC/FTC/TAF from another regimen. At the end of follow-up, 81.5% of these patients achieved virologic suppression. At the end of follow-up, only five patients had a detectable viral load (3 were lost follow-up and 2 had frequently missing visits). In previous studies, PI-based ART regimens have been significantly associated with developing a quantifiable viral load, possibly due to prescribing PI-based regimens for patients who previously experienced virologic failure or adherence problems.[16,17] Similar to previous studies, 51.9% of the viremic patients were on a PI-based regimen before switching in our study. In the DAWNING study,[27] patients with VF on first-line NNRTI + 2 NRTIs switched to DTG or LPV/RPV + 2 NRTIs, and the results showed that DTG

Table 3 Results of the 27 Study Participants Who Were Viremic Before Switching to BIC/FTC/TAF

#	Age	HIV-1 Risk Factor	Drug Abuse	ART Regimen Prior to Switch	Prior cART Duration (Years)	Continuous Follow-Up	Baseline CD4 Count, Cells/μL	Baseline HIV-1 RNA, log Copies/mL	Last CD4 Count, Cells/μL	Last HIV-1 Viral Load, log Copies/mL	Ever Viral Suppression Before Switch
1	31	MSM		NRTI/PIs	4.5	Y	554	648	552	<20	Y
2	35	MSM		NRTI/PIs	7.2	Y	240	95	335	25.2	Y
3	29	MSM	Y	NRTI/PIs	5.5	N	611	276	611	276	Y
4	39	MSM		NRTI/PIs	6.5	Y	33	274,000	109	22.1	Y
5	51	MSM		NRTI/PIs	3.7	Y	534	186	609	<20	Y
6	34	Unknown		NRTI/PIs	6.8	Y	412	502	288	<20	Y
7	37	Bisexual	Y	NRTI/NNRTI	5.9	Y	25	79,100	305	<20	Y
8	49	IVDU	Y	NRTI/NNRTI	3.5	Y	778	165	823	<20	Y
9	28	MSM	Y	NRTI/NNRTI	3.2	N	101	12,400	105	<20	N
10	32	MSM		NRTI/PIs	11.3	N	2	63,100	3	85.9	N
11	31	Bisexual		NRTI/INSTI	1	Y	97	355	610	27	Y
12	43	MSM	Y	NRTI/PIs	7.7	Y	126	19,100	150	<20	Y
13	26	MSM		NRTI/INSTI	3.7	Y	239	55.7	275	<20	Y
14	32	MSM		NRTI/INSTI	4.1	Y	230	346	221	<20	N
15	36	MSM	Y	NRTI/PIs	7.4	N	7	271,000	338	100	N
16	50	MSM	Y	NRTI/INSTI	14.5	Y	32	437,000	208	5290	Y
17	38	MSM	Y	NRTI/INSTI	2.3	Y	378	454	499	21.6	Y
18	31	MSM		NRTI/NNRTI	4	Y	369	97,500	558	<20	Y
19	46	MSM		NRTI/PIs	7.1	Y	791	209	997	<20	Y
20	36	MSM	Y	NRTI/INSTI	0.7	Y	555	105	741	40.8	Y
21	28	MSM		NRTI/NNRTI	3	Y	70	126,000	253	<20	Y
22	25	MSM		NRTI/INSTI	Unknown	Y	28	1,210,000	260	<20	N
23	52	MSM	Y	NRTI/PIs	12.6	Y	29	102,000	82	5100	N
24	51	Heterosexual		NRTI/NNRTI	7.8	Y	445	460	701	<20	Y
25	48	MSM		NRTI/PIs	14.2	N	95	7360	93	<20	Y
26	42	MSM		NRTI/PIs	13.8	Y	159	30,000	182	<20	Y
27	36	MSM		NRTI/PIs	9.7	Y	232	79,500	274	<20	Y

Abbreviations: ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; IVDU, intravenous drug user; MSM, men who have sex with men; NRTIs, nucleoside reverse transcriptase inhibitors; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Y, yes; N, No.

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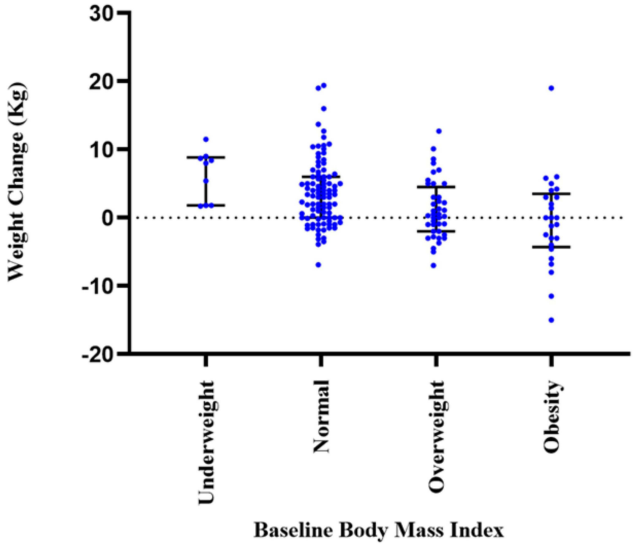

Figure 2 Baseline body mass index and individuals weight change After BIC/FTC/TAF treatment.

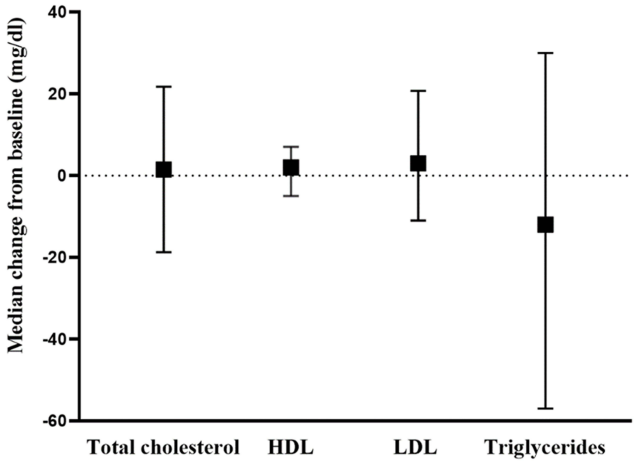

Figure 3 Individuals changes from baseline in lipid profile.
Abbreviations: LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol.

+2NRTIs was potent and that 80–85% of the patients achieved viral suppression at Week 48 even for patients with M184V/I ± other NRTI mutations. In the NADIA study, 464 African patients with VF to TDF, 3TC/FTC and NNRTIs were enrolled, and the virological response was assessed after switching to DTG/Darunavir/r or TDF/3TC and ZDV/3TC. Overall, 80% of the patients achieved viral suppression after switching to DTG and 2 NRTIs.[28] Bictegravir and DTG are both second generation INSTIs with a high genetic barrier to resistance. There is potential for the successful use of BIC/FTC/TAF as a treatment option in the setting of VF, similar to the use of DTG as evidenced by the DAWNING and NADIA study. These results strongly suggest that the resistance barrier of BIC/FTC/TAF is high, as has been shown in vitro.[26,29]

In this study, we found that, in general, BIC/FTC/TAF was tolerated very well by most patients. The most frequently reported AEs were neuropsychological (sleeping disturbance, insomnia, and dreamful sleep) and gastrointestinal in our population. No symptoms were life-threatening or led to hospitalization, and most symptoms disappeared quickly after discontinuation of BIC/FTC/TAF. The rate of BIC/FTC/TAF discontinuation because of any AE was 1.1%, with rash being the predominant cause in our study (n=2). However, in investigational trials, the most frequent adverse reactions reported in at least 5% of participants in the BIC/FTC/TAF group were diarrhea, nausea, headache, nasopharyngitis, fatigue and upper respiratory tract infection. Our study observed similar AEs leading to discontinuation compared to the BIC/FTC/TAF Phase 3 trials with approximately 0% to 2%.[11,30] Palmetto et al[19] reported their post-marketing experience of AEs associated with BIC/FTC/TAF between February 2018 and March 2019. A total of 201 patients initiated treatment during the observation period, and 10 AEs (7 rash, 1 insomnia and loss of appetite, 1 thrombocytopenia, and 1 feeling unwell) led to discontinuation. The AEs leading to discontinuation in their observational cohort appeared to be driven mostly by rash, with 4.5% reporting rash compared with <2% reported in the package insert.

We demonstrated an increase in body weight over time after BIC/FTC/TAF therapy in treatment-experienced patients, consistent with prior studies.[31,32] Of note, a slight weight gain was noted when the participants switched from EVG/COB/FTC/TAF, however the mechanism of weight changes associated with INSTIs remains unclear. In a randomized trial, treatment-naïve PLWH receiving bictegravir-containing regimens were found to gain significant weight (+3.4 kg) at week 48.[12] In the present study, we found a greater weight gain among those who were underweight. The overweight and obese individuals did not show weight gain in our study; therefore, all patients may be counseled with regards to healthy eating and exercise habits, and clinicians should not be overly concerned with weight gain or loss. We did not find an increase in lipid profile AEs, which may imply that such events either did not occur or occurred with low intensity.

There are several limitations to this study. First, it was a single-center study with no comparator group, and the results may not be generalized to all population. Second, the duration of observation in this study was short, and further long-term follow-up studies are warranted to elucidate the impact of virologic response. Third, most of the patients did not have baseline data on drug resistance before and after switching. Fourth, this was a retrospective observational cohort study, so it was not possible to characterize AEs in detail, and we also lacked information on the onset timing of BIC/FTC/TAF related AEs. Finally, other potential contributors to weight gain such as psychiatric comorbidities, lifestyle, concomitant medications, prior ART regimen, diet, exercise, and smoking were not evaluated.

Conclusions

The results of this real-world cohort study suggest that switching to BIC/FTC/TAF may be an option for achieving and maintaining virological suppression, even in patients with residual viremia at baseline. Our results also demonstrated a low discontinuation rate, a mild gain in weight, and no significant increases in lipid levels with BIC/FTC/TAF. However, studies with larger sample sizes are warranted to evaluate the clinical implications of our findings.

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Disclosure

The authors report no conflicts of interest in this work.

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