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Effectiveness and safety of bictegravir/emtricitabine/tenofovir alafenamide in HIV late presenters

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ABSTRACT

Objectives: The efficacy of BIC/FTC/TAF in HIV late presenters initiating antiretroviral therapy (ART) has not been sufficiently evaluated.
Methods: The aim of this study was to assess the effectiveness and tolerability of BIC/FTC/TAF compared to other first-line antiretroviral regimens in treatment-naïve adult individuals from the CoRIS Cohort starting ART with CD4 counts <200 cells/mm^3 and/or AIDS-defining conditions between January 1st 2019 and November 30th 2020. Logistic regression models were used to estimate odds ratios (ORs) of association between initial regimen and achievement of viral suppression (VS) (primary objective), defined as HIV RNA <50 cop/mL, and immunological recovery (IR) (secondary objective), defined as CD4 count >200 cells/mm^3, at weeks 24 and 48 after initiation of ART.
Results: We evaluated 314 individuals (84.7% men, median age 40 years). Of them, 158 initiated with BIC/FTC/TAF. At inclusion, 117 had an AIDS-defining condition. In multivariable analyses, individuals with AIDS-defining conditions initiating ART with BIC/FTC/TAF achieved higher rates of VS at 24 weeks than other regimens (aOR: 0.2; 95% CI: 0.06–0.64) and, at 48 weeks, than DTG/ABC/3TC (aOR: 0.06; 95% CI: 0.01–0.76) and DTG + TDF/3TC (aOR: 0.2; 95% CI: 0.47–0.9). No other differences in VS or IR were observed. At 24 and 48 weeks after ART initiation, treatment discontinuations were lower with BIC/FTC/TAF than with other regimens (3.2% and 7.6% vs. 24.4% and 37.8%, respectively; $P < 0.005$).
Conclusion: Our results suggest that BIC/FTC/TAF could be a preferred regimen as initial therapy in HIV late presenters because of its high effectiveness and good tolerability.

1. Introduction

Bictegravir (BIC) is an integrase inhibitor with high antiviral potency and a high genetic barrier to resistance. Its pharmacokinetic profile allows its administration once a day without the need of a booster [1]. As initial therapy, BIC in combination with emtricitabine and tenofovir alafenamide (BIC/FTC/TAF) has demonstrated high efficacy and a favourable safety and tolerability profile [2,3], being non-inferior to dolutegravir (DTG)-containing regimens at 48, 96, and 144 weeks of follow-up [4,5]. Therefore, BIC/FTC/TAF is considered a preferred regimen as initial antiretroviral therapy (ART) in current HIV clinical guidelines [6,7].

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Late presentation of HIV infection, defined by the presence of a CD4+ cell count <200 cells/mm^3 or AIDS-defining conditions, remains a major problem among people living with HIV [8,9]. Many ART regimens have demonstrated to decrease their efficacies when they are used in this context [10–12]. This loss of performance is especially noticeable in late presenters with AIDS-defining conditions because drug interactions between antiretroviral drugs and drugs necessary for the treatment of AIDS-defining conditions are common and may result in greater or lesser exposure to drugs, which may increase the frequency and/or severity of toxicities and affect the therapeutic response [13]. These considerations underscore the importance of evaluating the effectiveness of each ART regimen in late presenters [14].

The performance of BIC/FTC/TAF as initial ART in late presenters has been insufficiently evaluated. The number of late presenters included in the pivotal BIC/FTC/TAF studies was small (GS-US-380–1489: 36 patients and GS-1490: 44 patients). As is common in initial phase 3 trials for new HIV drugs, patients with serious infections or AIDS-related diseases were excluded from these clinical trials [2,3]. In addition, data from real-world observational studies analysing this scenario are limited. Therefore, it is important to add more evidence regarding the efficacy and safety of BIC/FTC/TAF as an initial therapy in late presenters. To this end, we developed the following study.

2. Methods

2.1. Study design

We developed a study, nested in the Cohort of the Spanish AIDS Research Network (CoRIS) [15], to evaluate the effectiveness and tolerability of BIC/FTC/TAF in comparison with other regimens as initial ART in late presenters.

2.2. Study population

We selected all HIV late presenters (defined by CD4 count <200 cells/mm^3 or a previous or ongoing AIDS-defining condition) enrolled in the CORIS who started ART between January 1st 2019 and November 30th 2020. Of them, we excluded for all the analyses those who started ART in the context of a clinical trial or with no follow-up after initiation of ART.

2.3. Outcomes

The primary outcome was the proportion of individuals achieving viral suppression (VS), defined as HIV RNA viral load <50 copies/mL at 24 and 48 weeks (±12 weeks) after ART initiation. Secondary outcomes included the proportion of individuals achieving immunological recovery (IR), defined as CD4 count >200 cells/mm^3 at 24 and 48 weeks (±12 weeks) after ART initiation, the time to VS during the first 48 weeks after ART initiation, and the proportion of individuals who discontinued their initial regimen, including reasons for discontinuation, during the first 24 and 48 weeks of ART. Outcomes were analysed both in the entire study population and in subgroups categorized by the presence or absence of AIDS-defining conditions.

Discontinuation reasons were categorized into the following: treatment failure, adverse events (AE), availability of simplified treatment, drug interaction, patient's preference, cost reduction, toxicity prevention, other, and unknown.

For the analyses of VS and IR at 24 and 48 weeks after ART initiation, we included only cases with available data within the assessment window. When multiple measurements were available within that window, we used the most recent one. We conducted two types of analyses: intention-to-treat (ITT) and on-treatment (OT). In the ITT analysis, outcomes were assessed based on the initial regimen, disregarding subsequent changes; thus, participants were assumed to have remained on their initial regimen once started. In the OT analysis, individuals who changed their initial regimen before 24 or 48 weeks were excluded from the analysis.

2.4. Statistical analysis

Our primary analysis was to compare outcomes between participants initiating ART with BIC/FTC/TAF and those on alternative regimens. As a secondary analysis, to elucidate potential differences between alternative regimens, we compared outcomes between participants initiating ART with regimens prescribed to more than 5% of participants and those on BIC/FTC/TAF. We used logistic regression models to estimate odds ratios (ORs) of association between the initial regimen and the achievement of VS and IR at weeks 24 and 48 after ART initiation.

For the analyses of time to VS within the initial 48 weeks after ART initiation, an individual's follow-up commenced at ART initiation and concluded at the occurrence of VS, death, the last study contact, or after 48 weeks, whichever happened first. We applied the multiple decrement method to compute the cumulative incidence of VS and used proportional hazards models on the sub-distribution hazard to estimate sub-distribution hazard ratios (sHR) for VS, considering deaths before VS as competing events.

Multivariable models were adjusted for potential confounding factors, including sex (male, female), age at ART initiation (<30, 30–49, ≥50 years), transmission category (men who have sex with men [MSM], heterosexual, other/unknown), educational level (no or compulsory education, secondary or university education, unknown), country of origin (Spain, foreign-born), CD4 cell count (<50, ≥50 cells/mm^3, unknown) viral load (<100,000, >100,000 copies/mL, unknown) within 6 months before ART initiation, and the presence of AIDS at baseline (no, yes).

To account for clustering of individuals within centres, we applied robust methods to estimate standard errors and calculate 95% CIs and *P* values. Wald tests were used to derive *P* values.

2.5. Ethical approval and informed consent

The CoRIS was approved by the Clinical Research Ethics Committee of the Gregorio Marañón General University Hospital. All patients agree to participate in CoRIS by signing an informed consent form. This study was approved by the Comité de Ética de la Investigación Provincial de Córdoba.

2.6. Role of the funding source

This work was funded by an Investigator Sponsored Research (ISR) grant from Gilead Sciences (IN-ES-380–6277) awarded to AR. Gilead Science were not in position to veto study design, data collection, data analysis, data interpretation, or writing of the manuscript.

3. Results

Between January 1st 2019 and November 30th 2020, 357 late presenters initiated ART within the CORIS. Among them, 314 individuals were eligible for our study, while 43 were excluded (41 who initiated ART within a clinical trial and 2 who lacked follow-up after ART initiation). Of the participants, 117 (37.7%) had AIDS-defining conditions. A total of 158 participants initiated ART with BIC/FTC/TAF and 156 with other regimens (Table S1). Baseline characteristics were similar between participants who initiated ART with BIC/FTC/TAF and those who initiated with other regimens (Table 1).

Table 1
Sociodemographic and clinical characteristics at antiretroviral therapy (ART) initiation according to initial ART regimen.

	BIC/FTC/TAF N = 158	Other regimens N = 156	*P* value
Sex [N (%)]			0.790
Male	133 (84.2)	133 (85.3)	
Female	25 (15.8)	23 (14.7)	
Age, years [N (%)]			
Median (IQR)	40 (33–51)	40 (33–52)	0.622
<30	28 (17.7)	24 (15.4)	0.836
30–49	85 (53.8)	88 (56.4)	
≥50	45 (28.5)	44 (28.2)	
Transmission category [N (%)]			0.224
Men who have sex with men	86 (54.4)	82 (52.6)	
Heterosexual	59 (37.3)	53 (34.0)	
Injection drug users	1 (0.6)	3 (1.9)	
Other/Unknown	12 (7.6)	18 (11.5)	
Country of origin [N (%)]			0.282
Spain	78 (49.4)	76 (48.7)	
Other in Western Europe	14 (8.9)	11 (7.0)	
Eastern Europe	5 (3.2)	0	
sub-Saharan Africa	5 (3.2)	8 (5.1)	
Northern Africa	1 (0.6)	3 (1.9)	
Latin America	54 (34.2)	56 (35.9)	
Other	1 (0.6)	2 (1.3)	
Educational level [N (%)]			0.069
No/compulsory education	22 (13.9)	20 (12.8)	
Upper secondary/university	98 (62.0)	80 (51.3)	
Unknown	38 (24.0)	56 (35.9)	
CD4 count, cells/mm3 [N (%)]			
Median (IQR)	103 (51–154)	97 (42–171)	0.978
<50	37 (23.4)	40 (25.6)	0.024
≥50	115 (72.8)	98 (62.8)	
Unknown	6 (3.8)	18 (11.5)	
Viral load, copies/mL [N (%)]			
Median (IQR)	249,621 (86,500–851,138)	273,000 (65,000–690,000)	0.510
<100,000	40 (25.3)	44 (28.2)	0.305
≥100,000	109 (69.0)	97 (62.2)	
Unknown	9 (5.7)	15 (9.6)	
AIDS diagnosis [N (%)]			0.066
No	107 (67.7)	90 (57.7)	
Yes	51 (32.3)	66 (42.3)	

3.1. Viral suppression

Viral suppression at 24 and 48 weeks after ART initiation was assessed in 147 (93.0%) and 137 (86.7%) of participants who initiated ART with BIC/FTC/TAF and in 140 (89.7%) and 127 (81.4%) of participants who initiated ART with other regimens, respectively. The reasons for exclusion from these analyses are detailed in Table S2. The proportion of participants achieving VS with BIC/FTC/TAF or alternative regimens was comparable at both 24 and 48 weeks after ART initiation (Fig. 1). Crude (ORc) and adjusted (ORa) odds ratios for achieving VS were also similar between BIC/FTC/TAF (used as reference) and other regimens, both at week 24 (ORc [95% CI]: 0.65 [0.3–1.43]; ORa: 0.61 [0.27–1.36]) and week 48 (ORc: 0.69 [0.31–1.54]; ORa: 0.61 [0.27–1.42]) after ART initiation. Nearly identical results were observed in the OT analyses (not shown) and in the subgroup of participants without AIDS-defining conditions (VS at week 24: 69% vs. 71.1%; VS at week 48: 82.8% vs. 82.9%).

Conversely, participants with AIDS-defining conditions achieved higher rates of VS with BIC/FTC/TAF compared to other regimens at both 24 and 48 weeks after ART initiation (Fig. 1). This difference remained statistically significant after adjusting for relevant confounders at week 24 (ORa [95%CI]: BIC/FTC/TAF (reference) vs. 0.2 [0.06–0.64]; $P = 0.007$ for other regimens) but not at week 48 ($P = 0.058$). We also evaluated the relationship between the initial ART and the achievement of VS, comparing BIC/FTC/TAF to each alternative regimen. At week 24, we observed lower ORa for the association between VS and DTG/ABC/3TC (ORa [95%CI]: BIC/FTC/TAF (reference) vs. 0.17 [0.04–0.68; $P = 0.012$) or DRV/COBI/FTC/TAF (ORa [95%CI]: BIC/FTC/TAF (reference) vs. 0.8 [0.01–0.52]; *P* value = 0.008). Similarly, at week 48, comparable results were found for DTG/ABC/3TC (ORa [95% CI]: BIC/FTC/TAF (reference) vs. 0.06 [0.01–0.76]; $P = 0.03$) and DTG + FTC/TDF (ORa [95% CI]: BIC/FTC/TAF (reference) vs. 0.2 [0.47–0.9]; $P = 0.035$).

3.2. Time to viral suppression

The median time to achieve VS from ART initiation was 17 weeks (IQR: 9–41) for participants who initiated ART with BIC/FTC/TAF and 25 weeks (13–48+) for those initiating with any other regimen: 20 (10–47) in DTG+FTC/TDF, 22 (8–48+) in DTG/ABC/3TC, and 45 (25–48+) in DRV/COBI/FTC/TAF (Fig. 2).

In our multivariable analyses, initiating ART with a regimen other than BIC/FTC/TAF was associated with a lower likelihood of achieving VS within the first 48 weeks after ART initiation (adjusted sHR: 0.69; 95% CI: 0.52–0.92; $P = 0.011$). However, in a comparative analysis of individual regimens, DRV/COBI/FTC/TAF was the only regimen that showed a significantly lower likelihood of VS compared to BIC/FTC/TAF (adjusted sHR: 0.36; 95% CI: 0.21–0.59; $P < 0.001$). Similar results were observed among participants initiating ART with AIDS-defining conditions (adjusted

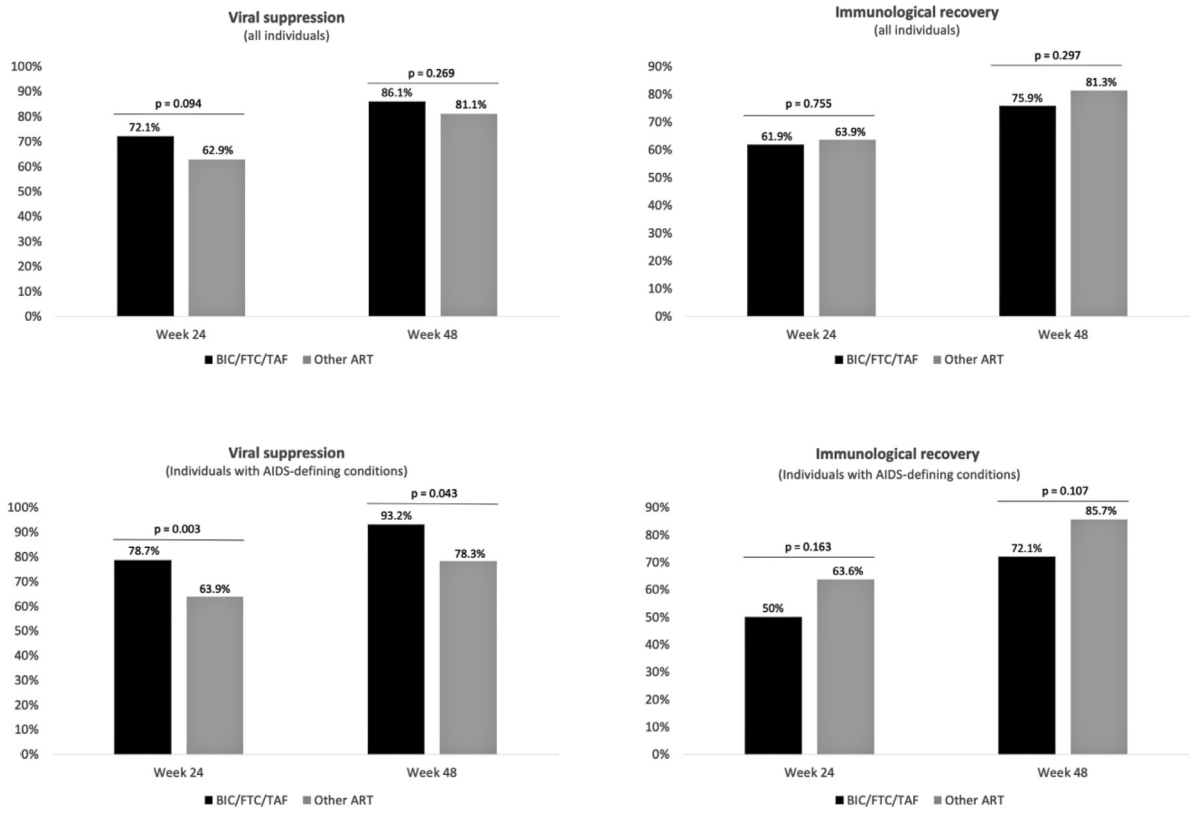

Figure 1. Viral suppression and immunological recovery at 24 and 48 weeks after ART initiation.

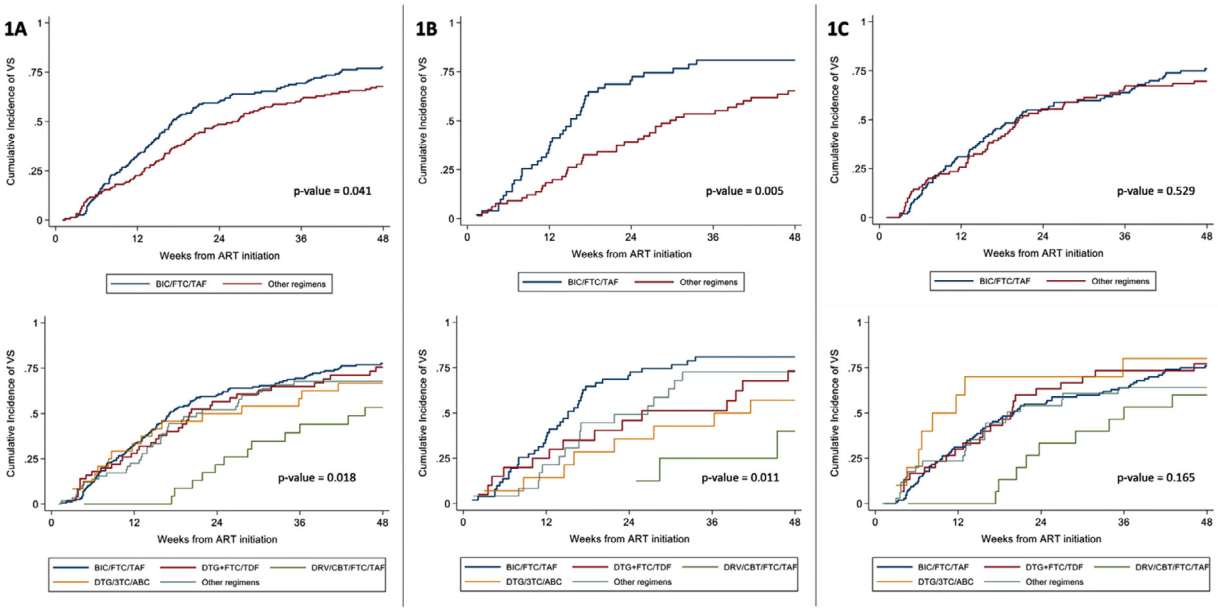

Figure 2. Time to VS during the first 48 weeks after ART initiation according to initial regimen for (1A) all individuals, (1B) individuals with AIDS-defining conditions and (1C) individuals without AIDS-defining conditions.

sHR: 0.49; 95% CI: 0.29–0.85; $P = 0.011$). In a comparative analysis of individual regimens performed within the subgroup of participants with AIDS-defining conditions, BIC/FTC/TAF demonstrated a significantly higher likelihood of achieving VS compared to DRV/COBI/FTC/TAF (adjusted sHR: 0.18; 95% CI: 0.07–0.45; $P < 0.001$) and DTG/ABC/3TC (adjusted sHR: 0.34; 95% CI: 0.13–0.88; $P = 0.026$).

3.3. Immunological recovery

We evaluated the achievement of IR at 24 and 48 weeks after ART initiation in 147 (93.0%) and 133 (84.2%) participants who initiated ART with BIC/FTC/TAF and in 135 (86.5%) and 123 (78.8%) who initiated ART with alternative regimens, respectively. The reasons for exclusion from these analyses are detailed in Table S2.

Table 2
Treatment discontinuations during the first 24 and 48 weeks after initiation of antiretroviral therapy (ART) and reason for discontinuation, according to initial regimen.

	BIC/FTC/TAF N = 158	No BIC/FTC/TAF					*P* value[a]
		DTG+FTC/TDF N = 50	DTG/ABC/3TC N = 24	DRV/CBT/FTC/TAF N = 24	Other regimens N = 58	Total N = 156	
During the first 24 weeks							
Treatment changes [N (%)]	5 (3.2)	20 (40.0)	2 (8.3)	3 (12.5)	13 (22.4)	38 (24.4)	<0.001
Reason for treatment change [N (%)]							
Treatment failure	0	0	0	0	2 (3.4)	2 (1.3)	0.153
Adverse event	3 (1.9)	8 (16.0)	1 (4.2)	2 (8.3)	3 (5.2)	14 (9.0)	0.006
Simplified treatment available	0	6 (12.0)	0	1 (4.2)	1 (1.7)	8 (5.1)	0.004
Drug interaction	0	0	1 (4.2)	0	0	1 (0.6)	0.313
Patient's wish/decision	2 (1.3)	0	0	0	1 (1.7)	1 (0.6)	0.569
Cost reduction	0	1 (2.0)	0	0	0	1 (0.6)	0.313
Toxicity prevention	0	4 (8.0)	0	0	5 (8.6)	9 (5.8)	0.002
Other	0	1 (2.0)	0	0	1 (1.7)	2 (1.3)	0.153
During the first 48 weeks							
Treatment changes [N (%)]	12 (7.6)	30 (60.0)	4 (16.7)	5 (20.8)	20 (34.5)	59 (37.8)	<0.001
Reason for treatment change [N (%)]							
Treatment failure	2 (1.3)	1 (2.0)	1 (4.2)	0	2 (3.4)	4 (2.6)	0.401
Adverse event	4 (2.5)	8 (16.0)	1 (4.2)	2 (8.3)	3 (5.2)	14 (9.0)	0.014
Simplified treatment available	1 (0.6)	13 (26.0)	1 (4.2)	1 (4.2)	5 (8.6)	20 (12.8)	<0.001
Drug interaction	0	0	1 (4.2)	1 (4.2)	0	2 (1.3)	0.153
Patient's wish/decision	4 (2.5)	0	0	0	1 (1.7)	1 (0.6)	0.181
Cost reduction	0	1 (2.0)	0	0	0	1 (0.6)	0.313
Toxicity prevention	0	5 (10.0)	0	0	6 (10.3)	11 (7.1)	0.001
Other	1 (0.6)	2 (4.0)	0	0	2 (3.4)	4 (2.6)	0.172
Unknown	0	0	0	1 (4.2)	1 (1.7)	2 (1.3)	0.153

[a] *P* value for the difference in percentages between BIC/FTC/TAF and no BIC/FTC/TAF.

The proportion of late presenters achieving IR at both time points was comparable between the study groups (Fig. 1). Both ORc and ORa for achieving IR were similar between BIC/FTC/TAF (used as reference) and alternative regimens, both at week 24 (ORc [95% CI]: 1.08 [0.66–1.78]; ORa: 1.22 [0.67–2.22]) and week 48 (ORc: 1.38 [0.72–2.65]; ORa: 1.72 [0.79–3.73]) after ART initiation. Rates of IR were also similar among participants with or without AIDS-defining conditions (Fig. 1), even after adjusting for significant confounders. Comparable results were obtained in the OT analyses (not shown).

3.4. Treatment discontinuations

The rate of treatment discontinuations within the initial 24 weeks after ART initiation was significantly lower among individuals commencing ART with BIC/FTC/TAF (3.2%) compared to those starting on alternative regimens (24.4%) ($P < 0.001$). This difference was primarily driven by lower percentages of discontinuations attributed to adverse events (1.9% vs. 9.0%, $P = 0.006$), treatment simplification (0% vs. 5.1%, $P = 0.004$), and toxicity prevention (0% vs. 5.8%, $P = 0.002$) (Table 2). A comprehensive breakdown of the types of AE leading to first-line regimen discontinuation and substitution regimens is provided in Table 3. The results for discontinuations within the initial 48 weeks after initiation of ART were consistent with those observed during the first 24 weeks (Table 2 and 3). Similar findings were observed among participants who initiated ART with and without AIDS-defining conditions (details not shown).

4. Discussion

In the CORIS real-world European cohort, late presenters who initiated ART with BIC/FTC/TAF demonstrated substantial achievement to VS and IR at both 24 and 48 weeks of follow-up. Compared to alternative regimens, initiating ART with BIC/FTC/TAF in late presenters was associated with a shorter time to VS and lower rates of ART discontinuation, primarily attributed to its enhanced safety and tolerability profile.

Our findings further support the robust efficacy and favourable safety profile observed among the late presenters who participated in BIC/FTC/TAF phase 3 clinical trials. In the GS-US-380–1489 and 1490 clinical trials, 99% of late presenters initiating ART with BIC/FTC/TAF achieved VS after 48 weeks of follow-up [2,3]. As anticipated from clinical trials settings, this percentage was slightly higher than the 86.1% observed in our study.

In the real world, only two cohort studies have evaluated the performance of BIC/FTC/TAF as initial therapy in late presenters. The first study examined the effectiveness and persistence of recommended 3-drug regimens in treatment-naïve individuals with CD4 cell counts <200/mm^3 enrolled in the US OPERA cohort at two different time points: July 31st 2019 [16] and December 31st 2021 [17]. The second study compared the virological effectiveness and discontinuation patters of BIC/FTC/TAF vs. DTG/ABC/3TC in late presenters initiating ART in Taiwan [18]. In contrast, our study conducted in Europe, has been the first to analyse the performance of BIC/FTC/TAF in late presenters initiating ART with AIDS-defining conditions.

In both of those cohorts, initiating ART with BIC/FTC/TAF was linked to lower rates of ART discontinuation when compared to alternative regimens. This finding aligns within our study results. Like the Taiwanese cohort, we observed that differences in the rate of initial ART discontinuation between BIC/FTC/TAF and alternative regimens was primarily attributed to a reduced proportion of AE associated with BIC/FTC/TAF leading to ART discontinuation.

However, it's worth nothing that in the OPERA cohort, this association was not identified [16]. Nevertheless, caution should be exercised when interpreting this lack of association, as 56% of the

Table 3
Treatment discontinuations due to adverse events (AEs) during the first 24 weeks after initiation of antiretroviral therapy (ART) and substitution regimen, according to initial regimen.

	BIC/FTC/TAF N = 158	No BIC/FTC/TAF					*P* value[a]
		DTG+FTC/TDF N = 50	DTG/ABC/3TC N = 24	DRV/CBT/FTC/TAF N = 24	Other regimens N = 58	Total N = 156	
Any adverse event [N (%)]	3 (1.9)	8 (16.0)	1 (4.2)	2 (8.3)	3 (5.2)	14 (9.0)	0.006
Renal	0	4 (8.0)	0	0	2 (3.4)	6 (3.8)	0.013
Skin	0	1 (2.0)	0	1 (4.2)	0	2 (1.3)	0.153
Gastrointestinal	1 (0.6)	0	0	1 (4.2)	0	1 (0.6)	0.993
Neuropsychiatric	0	2 (4.0)	0	0	0	2 (1.3)	0.153
Liver	1 (0.6)	0	0	0	0	0	0.320
Other	1 (0.6)	1 (2.0)	1 (4.2)	0	1 (1.7)	3 (1.9)	0.308
Substitution regimen [N (%)]	DTG/ABC/3TC	DTG/ABC/3TC	DRV/COBI/FTC/TAF	DTG/ABC/3TC	DTG/3TC	DTG/ABC/3TC	
	1 (33.3)	3 (37.5)	1 (100.0)	1 (50.0)	1 (33.3)	4 (28.6)	
	DRV/COBI/FTC/TAF	DRV/COBI/FTC/TDF		BIC/FTC/TAF	EFV+3TC/ABC	BIC/FTC/TAF	
	1 (33.3)	2 (25.0)		1 (50.0)	1 (33.3)	2 (14.3)	
	DTG/RPV	BIC/FTC/TAF			No ART	DRV/COBI/FTC/TDF	
	1 (33.3)	1 (12.5)			1 (33.3)	2 (14.3)	
		DRV+RTV+FTC/TDF				DTG/3TC	
		1 (12.5)				2 (14.3)	
		DTG/3TC				DRV/COBI/FTC/TAF	
		1 (12.5)				1 (7.1)	
						DRV+RTV+FTC/TDF	
						1 (7.1)	
						EFV+3TC/ABC	
						1 (7.1)	
						No ART	
						1 (7.1)	

[a] *P* value for the difference in percentages between BIC/FTC/TAF and no BIC/FTC/TAF.

participants had unknown reasons for ART discontinuation. Regardless of the specific cause, the available evidence suggests the high durability of BIC/FTC/TAF as an initial therapy option for late presenters [17].

Two other significant findings from these two studies, which our study also confirmed, are the comparable likelihood of achieving VS after 48 weeks of ART initiation in late presenters commencing ART with BIC/FTC/TAF or DTG-based regimens, and the higher likelihood of achieving VS after 48 weeks of ART initiation in late presenters starting ART with BIC/FTC/TAF compared to those initiating with DRV/COBI/FTC/TAF. Pending the results of the LAPTOP trial [19], the available evidence suggests that late presenters should initiate ART with integrase inhibitors-based ART rather than DRV/COBI/FTC/TAF.

Another observation from the OPERA cohort was a lower likelihood of achieving a CD4 count >200 cells/mm^3 with DRV and DTG-based regimens compared to BIC/FTC/TAF [17]. These results, which were not initially found in their earlier analyses [16], have not been confirmed in our study, possibly due to the lower number of individuals included in our study.

Our study is the first to assess the effectiveness and the tolerability of BIC/FTC/TAF as initial ART in late presenters with AIDS-defining conditions. In this critical scenario, where achieving VS as early as possible is paramount to prevent subsequent complications, our findings indicated that BIC/FTC/TAF, when compared other regimens, was associated with higher rates of VS at 24 weeks after ART initiation, an increased likelihood of achieving VS within the first 48 weeks after ART initiation, and greater ART persistence during the initial 48 weeks after ART initiation.

Interestingly, late presenters with AIDS-defining conditions achieved a higher percentage of VS with BIC/FTC/TAF as initial therapy compared to those without such conditions. The exact reason for this discrepancy remains uncertain. Drawing from a study by Sax P. et al, which demonstrated an association between higher VS rates and greater adherence at 24 weeks after ART initiation [20], it is plausible that late presenters with AIDS-defining conditions exhibited higher adherence rates compared to their counterparts without AIDS-defining conditions. Unfortunately, we cannot confirm this hypothesis because our study did not provide adherence data.

Nevertheless, regardless of the underlying cause, the proportion of VS achieved with BIC/FTC/TAF as initial ART in late presenters was notably distinct from that seen with other regimens, including recommended DTG-based regimens. The significant disparity supports our conclusion that the likelihood of achieving VS with BIC/FTC/TAF is superior to that of DTC/3TC/ABC and DTG + FTC/TDF at 48 weeks after ART initiation in late presenters with AIDS-defining conditions. Based on our comprehensive findings, we advocate for considering BIC/FTC/TAF as the preferred initial ART regimen for individuals with AIDS-defining conditions.

This study boasts several strengths. The CORIS, a large prospective cohort, is highly representative of the HIV population diagnosed with HIV since 2014 in Spain. Consequently, the participants included in this study offer a robust reflection of contemporary late presenters initiating ART. This provides us with a precise understanding of real-world prescription practices and the associated health outcomes within our clinical context. Additionally, our study benefits from the exceptional data quality maintained within the CORIS database. The incidence of unavailable data and estimated data entry errors remained minimal, ensuring the accuracy and reliability of our statistical analyses.

This study is not without its limitations. Despite the generous time window for the 24 and 48-week results (±12 weeks), ca. 5% of the participants lacked HIV viral load or CD4 cell count data during these periods. This was primarily due to a reduction in blood draws, a consequence of the COVID-19 pandemic. While we did

not identify significant differences in baseline characteristics between included and excluded individuals (except for a higher percentage of MSM among the included individuals), we cannot rule out the possibility that those without available data might exhibit different rates of VS or IR, although this seems less unlikely. Another limitation pertains to the relatively narrow eligibility and follow-up timeframe since BIC/FTC/TAF's approval in Spain in June 2018. Nevertheless, the number of participants initiating ART with BIC/FTC/TAF in our study was sufficient to evaluate the study outcomes. Additional analyses with larger participant cohorts and extended follow-up periods may potentially reveal differences between BIC/FTC/TAF and other preferred regimens, such as DTG/3TC, if they indeed exist.

In summary, BIC/FTC/TAF stands out as an excellent choice for initiating therapy in HIV late presenters, particularly among those with AIDS-defining conditions. This is attributed to its remarkable effectiveness in swift HIV replication and its minimal incidence of ART discontinuations.

Declarations

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2023.107016.

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