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Real-life experience with bictegravir/emtricitabine/tenofovir alafenamide in a large reference clinical centre

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Background: The use of bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) is mainly based on robust, pivotal clinical trials.

Objectives: To provide data on clinical use of BIC/FTC/TAF in real life.

Patients and methods: This was an observational, retrospective and single-centre study. We included all adult, treatment-naive (TN) and treatment-experienced (TE) people living with HIV (PLWH) starting BIC/FTC/TAF from 8 June 2018. We evaluated effectiveness [on treatment (OT), modified intention-to-treat (mITT) and intention-to-treat (ITT)], tolerability and safety in those patients who reached 6 months of follow-up (M6).

Results: We included 1584 PLWH [213 TN (13%) and 1371 TE (87%)]. The median (IQR) follow-up was 16 (7–21) months, with 81% and 53% of PLWH reaching M6 and M12, respectively. By OT, mITT and ITT, HIV-RNA <50 copies/mL was 77%, 70% and 62% at M6 and 92%, 77% and 63% at M12 for TN PLWH and 94%, 89% and 83% at M6 and 93%, 85% and 78% at M12 for TE PLWH, respectively. In PLWH carrying an M184V/I substitution, OT RNA <50 copies/mL was 89.5% at M6. The median CD4 cell count increased from 329 to 511/μL in TN PLWH and from 630 to 683/μL in TE PLWH at M6. Of the total, 1148 (88%) PLWH continued on BIC/FTC/TAF at M6. The most frequent known reason for discontinuation was toxicity [42 (69%) cases]; only 7 cases were considered virological failures (0.6% of the total OT cohort at M6), with no emerging resistance substitutions.

Conclusions: In real life, BIC/FTC/TAF showed high rates of virological suppression and also in PLWH carrying lamivudine/emtricitabine resistance substitutions. The tolerability and safety of BIC/FTC/TAF were good, with high persistence observed for patients on this regimen at M6.

Introduction

The use of bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) is mainly based on robust, pivotal randomized clinical trials (RCT) of both treatment-naive (TN)[1–3] and treatment-experienced (TE)[4–6] people living with HIV (PLWH). To date, real-life data concerning BIC/FTC/TAF remain limited.

The international Conference on Antiretroviral Drug Optimization (CADO) suggests that target product profile characteristics of an ideal antiretroviral (ARV) regimen should comprise safety, efficacy, tolerability, durability, stability and convenience; it should also be suitable for special populations and economical for treatment.[7] In both the updated IAS–USA[8] and European AIDS Clinical Society (EACS) guidelines,[9] two single-tablet, three-drug regimens (BIC/FTC/TAF and dolutegravir/lamivudine/abacavir) and one two-drug regimen (dolutegravir/lamivudine) containing integrase strand transfer inhibitors (InSTI) are approved combinations for initial treatments of PLWH. Moreover, for naive individuals, rapid ART initiation [and immediate ART initiation in some situations, such as primary HIV infection (PHI)] has been increasingly proposed in these guidelines, especially given study results that suggest better outcomes when clinicians initiate ART promptly. BIC/FTC/TAF meets the recommended characteristics for an ART regimen administered in rapid initiation, including a high genetic barrier to resistance, activity against HBV and rapid suppression of viraemia.

For TE PLWH, clinicians should tailor treatment in accordance with acute and long-term toxicities, previous exposure to ARV drugs and proven/suspected resistance. The use of the combination BIC/FTC/TAF has grown over time as a simplification

strategy in virologically suppressed PLWH with susceptible strains; however, clinicians have also used such drug regimens in cases with proven or suspected resistance to lamivudine/emtricitabine or other NRTI.[10] In this specific setting, many clinicians may consider that the two remaining active components (bictegravir and tenofovir alafenamide) plus the potential reduction of replication fitness conferred by the lamivudine resistance serve as an appropriate therapeutic option.[11]

Virological suppression in both TN and TE patients in RCT with BIC/FTC/TAF has been excellent. In a recent meta-analysis, suppression rates and tolerance for TN and TE patients were very high, whilst discontinuation rates were very low.[12] It is worth mentioning, though, that patients in RCT are carefully selected and expected to show high levels of therapy adherence. Additionally, for some individuals, clinical use of the regimen differs on many occasions from that recommended by manufacturers and regulatory agencies. Use of BIC/FTC/TAF has extensively gone beyond approved indications; indeed, many patients with suspected or documented resistance to lamivudine/emtricitabine (and possibly other drugs) receive this combination as well. Data in this clinical scenario remain further limited. This aspect is particularly relevant in contexts wherein the use of PrEP is expanding; the prevalence of lamivudine/emtricitabine has been reported to be higher.[13] Real-life studies provide, then, complementary information to that obtained from RCT[14] and are relevant to the understanding of the genuine use and performance of a given treatment combination. Real-life data for BIC/FTC/TAF are lacking.

Our institution is a large teaching university hospital that hosts all clinical and surgical specialties. The HIV Unit actively monitors close to 6000 PLWH, most of whom are on ART. The aim of our study was to provide an updated description of the clinical use of BIC/FTC/TAF—which remains one of the most frequently prescribed ART regimens—in a real-life clinical setting.

Patients and methods

The HIV Unit of the Hospital Clinic of Barcelona currently attends to 6000 PLWH, of whom more than 95% receive ART. The active cohort increases by approximately 200 naive PLWH each year.

This was an observational, retrospective and single-centre study. We included all adult TN and TE patients receiving BIC/FTC/TAF since 8 June 2018. We describe the demographics, HIV-related characteristics and available comorbidities of the population. For TE PLWH, previous ARV regimens were recorded and the last regimen before BIC/FTC/TAF initiation was reported, including the reason for the BIC/FTC/TAF prescription. The primary objective was to assess the proportion of PLWH with HIV-1 RNA <50 copies/mL at 6 and 12 months of follow-up (M6 and M12, respectively). Additional secondary endpoints included changes in CD4+ cell count, safety and resistance.

Effectiveness, defined as HIV-RNA <50 copies/mL, was evaluated on the basis of on treatment (OT; discontinuation/missing = excluded), modified intention-to-treat (mITT; discontinuation = failure, missing = excluded) and intention-to-treat (ITT; discontinuation/missing = failure); patients without a reported viral load (VL) value in the corresponding window (without discontinuation and not lost to follow-up) were not included. We assessed tolerability and safety (drug-related adverse events) for PLWH reaching, at least, the M6 mark. All participants who received at least one dose of study drug were included in primary efficacy and safety analyses. Virological failure was defined as HIV RNA VL >50 copies/mL in two consecutive determinations or a single determination >1000 copies/mL, OT.

We assessed ARV resistance tests performed before BIC/FTC/TAF initiation in both TN and TE PLWH. Furthermore, we evaluated the presence of resistance substitutions in all genotype tests performed before the first dose of BIC/FTC/TAF, according to the Stanford HIV Drug Resistance Database, Version 9.0. For TN PLWH this was mostly the baseline genotype; for TE PLWH with more than one test performed, a historical cumulative genotype was evaluated. We also report the proportion of cases with HIV-RNA <50 copies/mL OT in PLWH carrying specific substitutions conferring decreased susceptibility to lamivudine/emtricitabine, tenofovir disoproxil fumarate/tenofovir alafenamide and/or InSTI.

Resistance testing was performed using Sanger population sequencing until May 2015 and using ultra-deep sequencing (UDS) using a 1% frequency threshold for variant detection since May 2015. For ultra-deep sequencing, we reported only substitutions detected in 20% of sequences or higher.

Statistical analyses

Qualitative variables are described by frequency and column percentage, and quantitative variables are described by median and IQR. A logistic regression model including the main demographic (age, sex, transmission route) and immuno-virological (baseline VL and CD4 T cell count, presence of M184V/I or other substitutions) variables was used to determine prognostic factors of reaching virological suppression (ITT) at M6 and M12. All tests were two-tailed and a statistical significance of 0.05 was used. Statistical analyses were performed using Stata 17 software (StataCorp LLC, College Station, TX, USA).

Results

Baseline characteristics of the cohort

Between 8 June 2018 and 30 June 2021, 1605 PLWH received at least one dose of BIC/FTC/TAF. Of them, 21 (1.3%) received at least one additional ARV drug (18 of them darunavir with or without other drugs) and were excluded from the analysis. In the end, we included 1584 PLWH. The median (IQR) follow-up time on BIC/FTC/TAF was 16 (7.1–21.2) months for the entire cohort, 16.4 (7.6–21.3) months for the TE cohort and 11.2 (5–18) months for the TN cohort of PLWH.

Of the 1584 patients included overall in the baseline cohort, 87% were male and the median (IQR) age was 43 (34–52) years. Additionally, 32% of patients were aged 50 years or older and 72% were MSM. Of the total, 213 were TN PLWH; 1371 were TE PLWH and 7% of PLWH underwent initiation of follow-up monitoring during the PHI (documented as acute or recent HIV infection of less than 6 months after infection). In TN PLWH, PHI accounted for 10% of cases. Overall, 12% had positive HCV serology and 3% active chronic HBV, 3% had estimated glomerular filtration rates by Cockcroft-Gault (eGFRCG) at 30–60 mL/min (none had <30) and 10% of those who underwent a DEXA scan presented with osteoporosis (T-score −2.5 or higher). Baseline characteristics of the entire cohort are shown in Table 1.

In TE PLWH, the reasons for BIC/FTC/TAF prescription were known in 1046 (92%) cases who reached M6. The main reasons included simplification from other ARV regimens in 337 (32%) cases, avoidance of relevant drug–drug interactions (DDI) that manifested with the previous ARV regimen in 332 (32%) cases and toxicity caused by the previous regimen in 152 (15%) cases. All

Table 1. Baseline characteristics of 1584 PLWH who received at least one dose of BIC/FTC/TAF

	Overall	TN	TE
Demographic characteristics			
N (%)	1584 (100)	213 (100)	1371 (100)
male, *n* (%)	1379 (87)	194 (91)	1185 (86)
age (years), median (IQR)	43 (34–52)	35 (29–42)	44 (36–53)
age ≥50 years, *n* (%)	506 (32)	21 (10)	485 (35)
HIV acquisition route *n* (%)			
MSM	1140 (72)	143 (67)	997 (73)
heterosexual	257 (16)	39 (18)	218 (16)
injecting drug users	71 (4)	2 (1)	69 (5)
other/unknown	116 (8)	29 (14)	87 (6)
HIV-related characteristics			
time since HIV diagnosis (years), median (IQR) [*n*]	8 (3–15) [1550]	0 (0–3) [207]	10 (5–17) [1343]
primary (acute/recent) HIV infection[a], *n* (%)	110 (7)	21 (10)	89 (6)
HIV-RNA VL (copies/mL), median (IQR) [*n*]	<50 (<50–176) [1509]	68 500 (19 600–261 000) [207]	<50 (<50–<50) [1302]
HIV-1 RNA <50 copies/mL, *n* (%)	1068 (71)	0 (0)	1068 (82)
HIV-1 RNA >100 000 copies/mL, *n* (%)	138 (9)	92 (44)	46 (4)
CD4 count (cells/μL), median (IQR) [*n*]	584 (385–805) [1295]	357 (194–496) [205]	628.5 (441–846) [1090]
CD4 count <200 cells/μL, *n* (%)	111 (9)	55 (27)	56 (5)
CD4 count >500 cells/μL, *n* (%)	788 (61)	50 (24)	738 (68)
Coinfections and comorbidities			
HCV serology[b], *n* (%)	194 (12)	6 (3)	188 (14)
active chronic HBV[c], *n* (%)	48 (3)	2 (1)	46 (3)
eGFRCG (mL/min), median (IQR) [*n*]	90 (81–90) [1522]	90 (90–90) [209]	90 (79–90) [1313]
eGFRCG >90 mL/min, *n* (%)	897 (59)	187 (89)	710 (54)
eGFRCG >60–90 mL/min (IQR), *n* (%)	583 (38)	21 (10)	562 (43)
eGFRCG 30–60 mL/min (IQR), *n* (%)	42 (3)	1 (0)	41 (3)
DEXA scan available, *n*	150	69	81
osteopenia *n* (%)	85 (57)	31 (45)	54 (67)
osteoporosis *n* (%)	15 (10)	2 (3)	13 (16)

[a]Documented HIV infection of <6 months after infection at the time of follow-up initiation.
[b]Positive HCV antibodies.
[c]Positive HBVsAg.

reasons for BIC/FTC/TAF prescription are shown in Table 2. Previous ARV regimens were also known in 1046 (92%) TE PLWH. The TE PLWH population had a median (IQR) of 2 (1–4) previous ARV regimens. The last regimen included an InSTI in 721 (69%) cases, an NNRTI in 207 (20%) cases and a PI in 93 (8%) cases. Details of the last previous ARV regimen are shown in Table 3.

Follow-up of cohort at M6 and M12

The flow chart and distribution of the cohort are shown in Figure 1. Of the1584 PLWH included at baseline, 1299 reached M6. Of the 1299 who reached M6 (BIC/FTC/TAF initiation before 1 January 2021), 1148 continued receiving BIC/FTC/TAF. Only 151 (13%) discontinued such treatment before reaching M6 (90 are missing cases and 61 are documented discontinuations). Of the documented 61 cases, causes for discontinuation included: toxicity in 42 (69%) cases, with neuropsychiatric and gastrointestinal side effects occurring in two-thirds of cases; virological failures in 7 (11.5%) cases; simplification in 4 (7%) cases; avoidance of DDI in 3 (5%) cases; and other causes (7.5%) in the remaining cases.

Suppression rates at M6 and M12

In accordance with the three predefined analyses, the proportion of PLWH with VL <50 copies/mL are shown in Figure 2(a and b). Suppression rates were lower than 80% for TN PLWH, although higher at M12 (92% OT). TE PLWH had a suppression rate of 94% at M6 and 93% at M12 (OT). For PLWH who were undetectable at baseline, 96% remained undetectable at M6 (OT), whilst 3% had a VL of 50–200 copies/mL.

Resistance substitutions

At least one genotypic resistance test (before BIC/FTC/TAF initiation) was performed in 715 of 1148 patients reaching M6 OT. Overall, 80% of PLWH underwent one genotype test (98% for TN PLWH, baseline genotype before ART initiation), 14% underwent two genotype tests and 4% underwent three genotype tests. Three TE PLWH underwent seven genotype tests. Of the total 715 PLWH with at least one genotype test performed, at least one resistance substitution to any family (according to the Stanford HIV Drug Resistance Database, Version 9.0) was found in 371 (52%).

Table 2. Reasons for BIC/FTC/TAF prescription in 1046 TE PLWH

Causes of prescription	*N* (%)
Simplification	337 (32)
Avoidance of DDI	332 (32)
Side effects from previous ART regimen	152 (15)
ART discontinued by patient	64 (6)
Patient's preference	30 (3)
Virological failure of previous ART regimen	18 (2)
Other causes	52 (10)

Table 3. Last previous ARV regimen in 1046 TE PLWH before initiation of BIC/FTC/TAF

Previous ART regimens	*N* (%)
InSTI based	721 (69)
elvitegravir based	552 (77)
dolutegravir based	92 (13)[a]
raltegravir based	86 (10)
NNRTI based	207 (20)
efavirenz based	87 (42)
rilpivirine based	84 (41)
other NNRTI based	46 (17)
PI based	93 (8)
darunavir based	71 (76)
other PI based	22 (24)
Other ARV combinations (two, three or four drugs)	25 (3)

[a]Including four cases of dual therapy (dolutegravir/lamivudine) and 88 cases of different triple combinations.

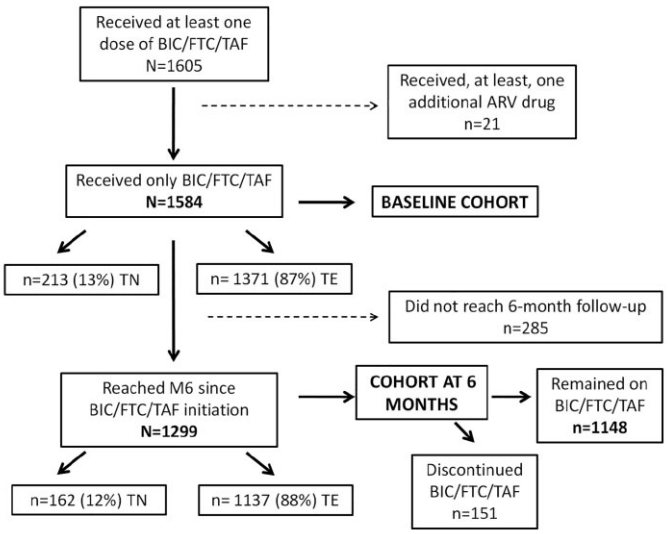

Figure 1. Flow chart of the cohort of PLWH who received at least one dose of BIC/FTC/TAF.

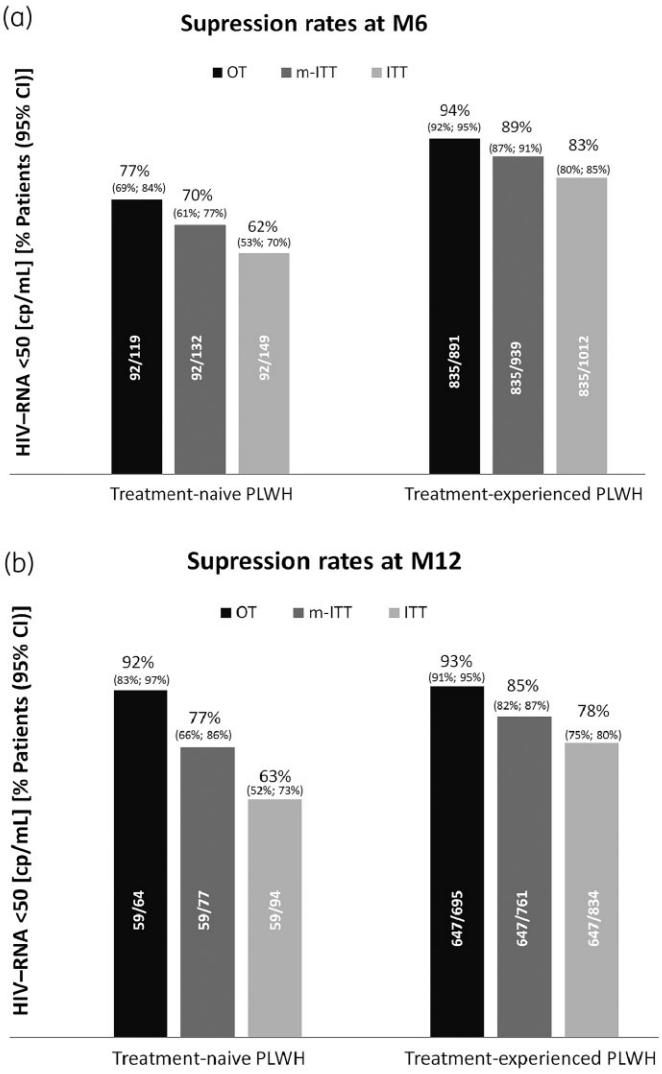

Figure 2. Effectiveness of BIC/FTC/TAF at 6 months (a) and 12 months (b) since initiation in TN and TE PLWH.

Substitutions affecting lamivudine/emtricitabine, tenofovir alafenamide and InSTI activity were specifically addressed.

M184V, M184I or both substitutions were detected in at least one of the previously performed genotype tests (historical genotype) in 47 PLWH (45 of whom were TE). K65R was detected in four PLWH (three of whom were TE). In addition, at least one substitution of a number of other reverse transcriptase substitutions potentially compromising backbone regimen activity, such as thymidine analogue mutations (TAMs) or T69 insertion, were found in 18% of PLWH.

With respect to substitutions conferring resistance to InSTI, 32 of 371 (9%) PLWH with a genotype test amplifying the integrase had at least one substitution conferring reduced activity on InSTI in at least one of the previously performed genotypes (historical genotype). A detailed description of integrase substitutions found is shown in Table S1 (available as Supplementary data at *JAC* Online).

Suppression rates in patients carrying ARV-resistant substitutions

VL levels at M6 were available for 38 of 47 patients with an M184V/I substitution; 34 of 38 had HIV-RNA <50 copies/mL OT. Details of resistance substitutions detected for all ARV families for the four detectable PLWH and 34 undetectable PLWH are shown in Table S2(A and B).

Five out of 32 cases with integrase substitutions identified in historical genotypes had VL >50 copies/mL at M6. Details of resistance substitutions detected for all ARV families for these five PLWH are shown in Table S2(C).

Prognostic factors of virological suppression

In the multivariable and logistic regression analysis, for TN PLWH, the only variable independently related to VL <50 copies/mL at M6 was the baseline CD4 T count [OR=4.81 (95% CI=1.85–12.54) for CD4 T cells >500 compared with <200 cells/μL, P=0.005]; this effect was not seen at M12. For TE PLWH (adjusted by age), baseline CD4 T count at M6 [OR=3.19 (95% CI=1.60–6.36) for CD4 T cells >500 compared with <200 cells/μL, P=0.003] and at M12 [OR=2.37 (95% CI=1.12–5.01) for CD4 T cells >500 compared with <200 cells/μL, P=0.01] and being MSM at M6 [OR=1.72 (95% CI=1.16–2.54), P=0.007] and at M12 [OR=1.93 CI95 (1.27–2.95), P=0.002] were independently associated with higher odds for VL <50 copies/mL. The presence of an M184V/I substitution was not independently associated with lower odds for VL <50 copies/mL [OR=0.55 (95% CI=0.28–1.08), P=0.084].

Discussion

BIC/FTC/TAF is an oral, single-tablet regimen approved for once-a-day treatment of HIV-1 infection in adults with no known substitutions associated with resistance to individual drug components of this combination. As clinical trials of this regimen have shown high efficacy and good tolerance, it is a preferred combination for TN PLWH and in cases of simplification for TE PLWH.[12] Clinical data from real-life use are, however, lacking.

As previously mentioned, PrEP is expanding. Although development of resistance to PrEP components is unusual in cases of infection due to poor adherence to PrEP, resistance does develop rapidly if initiation of PrEP takes place in unrecognized, extremely early HIV infection.[15] Overall reports of transmitted-drug resistance (TDR) in Spain and in Europe describe a low prevalence of lamivudine/emtricitabine resistance. However, given the widening scope of PrEP, this situation might become more frequent in the future[13] and thereby limit the use of two-drug combinations containing lamivudine/emtricitabine.

Our cohort of PLWH receiving BIC/FTC/TAF reflects the current epidemiology of HIV infection in a reference centre in a western/central European city: mainly MSM, a low prevalence of injecting drug users and older age (30% of patients were older than 50). Less than 15% of the patients included in this cohort were TN. This percentage represents a small proportion of the total PLWH receiving BIC/FTC/TAF; however, as in most large reference centres, most naive patients are prioritized for clinical trials. In addition, the number of new PLWH monitored in our institution declined throughout the past year due to the COVID-19 pandemic, including the number of HIV infections, testing/diagnosis or both.[16]

Suppression rates were not as high (to be expected) as those observed in RCT including TN PLWH treated with BIC/FTC/TAF.[1–3] Overall, PLWH with higher CD4 T cell counts and MSM (among TE PLWH) showed higher odds of virological suppression. Patients in RCT undergo a careful selection process, with priority conferred to individuals perceived as adherent. In real life, though, compliance to clinical follow-up and therapy are always less consistent; missing cases are frequently higher and, thus, ITT suppression rates lower. Additionally, a plausible explanation for lower suppression rates is that 10% of TN PLWH in our cohort were documented as having PHI, which often has a very high VL.[17] PLWH with PHI frequently require longer periods to reach virological suppression. Indeed, the OT suppression rate for TN PLWH increased to 92% at M12. It is worth noting that this 10% of the cohort accounts only for the proportion of documented PHI; the real proportion of TN PLWH with PHI might be higher, especially given the frequent testing (every 3 months) recommended locally to be done in the MSM population.[18] Moreover, part of the follow-up time includes months seriously affected by the COVID-19 pandemic in Spain; this might have partially influenced the lower suppression rates initially seen for TN PLWH.[16] Finally, with respect to TE patients, OT suppression rates were very good. Considering only those who had undetectable VL at the moment of BIC/FTC/TAF initiation, 96% remained undetectable and 3% had a VL ranging between 50 and 200 copies/mL.

Conversely, treatment discontinuation in real life is frequently higher than in RCT. The reasons are, however, less well-documented. In our cohort, most causes were unknown. Known toxicity was rather low, though, and consistent with good adherence shown for BIC/FTC/TAF in RCT.

The prevalence of TDR to the InSTI family in Spain is low,[19] although some studies have reported higher prevalence rates of InSTI polymorphic substitutions possibly capable of reducing the activity of first-generation InSTI (raltegravir, elvitegravir/cobicistat).[20,21] In our study, we identified five TN individuals carrying 97A and three TN individuals carrying 157Q detected in the baseline genotype. These substitutions are unlikely to affect newer InSTI, such as dolutegravir, bictegravir or cabotegravir.[20,21] We also identified two cases with an 148K substitution, which may indeed represent some of the real rare cases of TDR to InSTI. Of the total 32 cases of PLWH with detected InSTI substitutions (Table S1) in the historical genotypes, only 5 (15.6%) of these individuals had HIV-RNA >50 copies/mL, of whom 2 also had substitutions compromising tenofovir alafenamide or emtricitabine activity (Table S2C).

As previously explained, TDR to lamivudine/emtricitabine (M184V/I transmission) remains quite low in our setting to date,[22] at least until the use of PrEP has grown expansively. In contrast, M184V/I is amongst the most frequent substitutions found in TE PLWH with previous ART failures. Its value in the old genotype test with years of suppression thereafter is perhaps poor, though, as it may represent a defective virus. Its presence, nonetheless, provides hyper-susceptibility to tenofovir disoproxil fumarate/tenofovir alafenamide, increasing the activity of BIC/FTC/TAF as enhanced dual therapy. The suppression rate at M6 in our cohort was high—close to 90% OT—albeit slightly lower than in previous reports.[11] This is remarkable, though. As shown

in Table S2(B), many of these PLWH also had several accompanying substitutions, such as TAMs or K65R, which could limit tenofovir alafenamide activity as well. Only one patient with an isolated M184 substitution had detectable HIV-RNA at M6 (patient 3; Table S2A). Although the total number of PLWH carrying M184V/I in our cohort was not very high, the presence of these substitutions was not independently associated with lower odds of virological suppression.

The reasons for a clinician to prescribe a regimen with known resistance to its components may vary. First, it can be a clinical choice, considering that, in the case of isolated resistance to lamivudine/emtricitabine, the regimen may retain efficacy. Indeed, two-drug regimens have grown in frequency of administration for both initial therapy and simplification in PLWH.[23–25] In the case of resistance to more than one of the components, the reason may be to provide an alternative therapeutic option to patients unable to tolerate or comply with complex regimens, multiple pills per day and dangerous DDI. A single-tablet regimen with partial activity may be a temporary substitution choice. Finally, clinicians can consider that resistance substitutions detected in old genotypes, followed by years of undetectability, may have low impact.[26]

A very low number of patients received additional ARV drugs to BIC/FTC/TAF (21 of 1605, accounting for 1.3% of the cohort). Several reasons may provide an explanation. First, the BIC/FTC/TAF regimen adapts clinically to various situations including naive and experienced patients—even with known resistance to ARV—as previously discussed. Second, in patients with multiple types of resistance, dolutegravir allows for an increase in dosing (50 mg q12h instead of 50 mg q24h), which is not possible with co-formulated BIC/FTC/TAF. Therefore, it is possible that the majority of the most heavily exposed population of PLWH to ARV are receiving dolutegravir-based regimens. Finally, most cases of regimen switches occurred in those patients with elvitegravir-based ART to avoid DDI (Tables 2 and 3). Such changes (as those from NNRTI regimens) do not risk regimen efficacy, given the high genetic barrier of bictegravir; thus, additional drugs are not required. With the progressively ageing population of PLWH, poly-pharmacy may become more important.[27] Most PLWH receiving ARV regimens with a pharmacokinetic enhancer (PI, elvitegravir) are expected to progressively be changed to non-booster regimens, with BIC/FTC/TAF being an appealing option for such a switch.

Interestingly, the suppression rate in 1371 TE PLWH was 82% at baseline. Of the known reasons for BIC/FTC/TAF prescription, 6% were due to ART abandonment of the previous regimen and 2% due to virological failures. Although both of the following figures may be underestimated, the OT suppression rate in the TE population increased to 94% at M6 and remained at 93% at M12. This may also reflect the choice of three-drug high genetic barrier regimens, such as BIC/FTC/TAF or PI-based regimens, for patients with suboptimal adherence.

Our paper has several strengths. It represents a very large cohort of a typical, current PLWH population, comparable in number to ongoing, multicentre cohorts like that in the BICSTAR study (NCT03580668). The paper does, however, have some major limitations. We do not have data on some relevant comorbidities, such as cardiovascular risk, since such data are not available in our database. However, comorbidities have increasingly been reported in our ageing population of PLWH. For other comorbidities like bone disease, we have data only for a minority of patients. This type of information would have proven interesting in illustrating the profile of patients who were prescribed the three-drug regimen in our cohort. In addition, given the retrospective nature of the paper, there are missing data. Some variables, such as real virological failures, may be underestimated; for other variables like discontinuation reasons, a significant proportion was not known. Finally, many PLWH have started BIC/FTC/TAF recently, so the cohort experienced significant attrition at M6 and M12.

In conclusion, our paper provides an updated profile of BIC/FTC/TAF (one of the most frequently prescribed ART regimens at the moment) use in a real-life context, using a representative cohort of PLWH in a western European city. This observational cohort study supports the high effectiveness, tolerability and safety of BIC/FTC/TAF in clinical practice and demonstrates high persistence over 6 months. In addition, suppression rates remained close to 90% in the PLWH with documented resistance to lamivudine/emtricitabine, even despite accompanying substitutions in several cases.

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Transparency declarations

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Supplementary data

Tables S1 and S2 are available as Supplementary data at *JAC* Online.

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