HIV/AIDS - Research and Palliative Care

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Effectiveness and Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide in People with HIV: A Real-World Data from the Spanish BICSTaR Cohort

Alexy Inciarte[1–3], Celia Miralles[4], Ana Silva-Klug[5], Boris Revollo[6], Miguel García Deltoro[7], Joaquín Portilla[8,9], Antonio Antela[10], Manuel Ángel Castaño Carracedo[11], Cristina De Álvaro[12], Johanna Ramroth[13], Ana González-Cordón[1–3], Josep Mallolas[1–3]

[1]HIV Unit, Clínic Hospital, Barcelona, Spain; [2]Barcelona University, Barcelona, Spain; [3]August Pi I Sunyer Biomedical Investigations Institute (IDIBAPS), Barcelona, Spain; [4]Internal Medicine Department, Álvaro Cunqueiro Hospital, Vigo, Spain; [5]HIV Unit, Bellvitge University Hospital, L'Hospitalet de Llobregat, Spain; [6]Infectious Diseases Department, Germans Trias I Pujol University Hospital, Badalona, Spain; [7]Infectious Diseases Department, Consorcio General University Hospital, Valencia, Spain; [8]Internal Medicine Department, Dr Balmis General University Hospital, Alicante, Spain; [9]Biosanitary Investigation Institute (ISABIAL), Alicante, Spain; [10]Infectious Diseases Unit, Clinic University Hospital (CHUS), Santiago de Compostela, Spain; [11]Infectious Diseases Department, Regional University Hospital, Málaga, Spain; [12]Medical Department, Gilead Sciences SLU, Madrid, Spain; [13]Real-World Evidence, Gilead Sciences Ltd, Uxbridge, UK

Correspondence: Alexy Inciarte, HIV Unit, Hospital Clínic de Barcelona, Villarroel 170, Barcelona, 08036, Spain, Tel +34697159341, Email alexyss_@hotmail.com

Background: Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a single-tablet regimen recommended as first-line HIV treatment in international guidelines. This analysis aimed to assess the effectiveness and safety of B/F/TAF in real-world Spanish clinical practice.

Methods: This was an analysis of the Spanish subset from the BICSTaR study in treatment-naïve (TN) and treatment-experienced (TE) people with HIV who started treatment between November 2019 and July 2021 (European study registration: EUPAS22185). The primary endpoint was virologic suppression (HIV-1 RNA <50 copies/mL); additional endpoints included CD4 cell count changes, treatment persistence, adverse events, weight changes, and the 36-Item Short Form Survey mental and physical component summary (MCS/PCS) scores at 12 months.

Results: In total, 249 people with HIV initiated B/F/TAF treatment (62 TN, 187 TE). At 12 months, virologic suppression was achieved by 86% of TN and 98% of TE participants, with 91% of those TE participants with baseline HIV-1 RNA ≥50 copies/μL achieving suppression. Median CD4 count increased by 296 cells/μL in TN (p<0.001) and 12 cells/μL in TE (p=0.302) participants. Persistence at 12 months was high in all participants, with 95% still on treatment. Overall, none of TN and less than 3% of TE participants discontinued B/F/TAF due to drug-related adverse events, all of which were mild or moderate. Median weight increase was 2.9 kg in TN (p<0.001) and 1.0 kg in TE (p<0.001) participants. Median MCS scores improved in the TN group (8.4-point increase, p<0.001) but not in the TE group (0.4-point increase, p=0.767), while PCS scores remained stable both among TN and TE.

Conclusion: These real-world findings strongly support B/F/TAF use in TN and TE people with HIV in Spain, demonstrating high 12-month persistence and effectiveness, and mental health benefits in TN participants, with minimal adverse events.

Keywords: B/F/TAF, health-related quality of life, HIV-1, prospective non-interventional cohort study, real-world evidence, virologic suppression

Introduction

HIV is a major global public health challenge. According to the latest UNAIDS report, an estimated 39.9 million people were living with HIV, and 1.3 million people acquired HIV, in 2023.[1] The Spanish government reported between 136,436 and 162,307 people with HIV in 2022, which is an HIV prevalence of approximately 0.31% of the total Spanish

Received: 9 May 2025
Accepted: 9 December 2025
Published: 17 December 2025

population. In 2022, 2,956 new HIV diagnoses were reported in Spain, from which 49% involved late diagnosis.[2] Other reports including multiple European countries have reported a similar rates of late diagnosis (52.7%).[3] In 2021, 306 deaths (0.7 per 1000) were due to HIV and AIDS-related complications.[3] Access to effective HIV prevention, diagnosis, treatment, and care has transformed HIV into a manageable chronic health condition, enabling people with HIV to lead long and healthy lives.[4]

Antiretroviral therapy (ART) is recommended for everyone with HIV, and people with HIV should start ART as soon as possible after diagnosis, ideally on the same day.[5] According to the current guidelines,[6] initial ART should include two (or, in specific scenarios, one) nucleoside/nucleotide reverse transcriptase inhibitors combined with a third drug, including integrase strand transfer inhibitors (INSTIs), which represent a significant advancement in ART and improvement in HIV treatment.[7] The selection of a regimen should be personalized based on efficacy, side effects, dosing, drug interactions, resistance test results, comorbidities, HBV coinfection or lack of HBV vaccination response, drug availability, cost, and pregnancy considerations.[6,8]

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a single-tablet regimen supported by long-term efficacy data, with an established safety profile and a high barrier to genetic resistance.[9] Recommended by international guidelines for both treatment-naïve (TN) and treatment-experienced (TE) people with HIV,[5,6] its effectiveness, safety, and tolerability are well supported by real-world evidence, making it a reliable choice in clinical practice.[10]

BICSTaR (BICtegravir Single TAblet Regimen), a multinational, observational, prospective, non-interventional cohort study, evaluated the effectiveness and safety of B/F/TAF in TN and TE adults with HIV during routine clinical practice. Twelve-month results for the pooled BICSTaR cohort, including 1552 people with HIV enrolled across 12 countries, have been published.[11] In the present paper, we present detailed findings from the Spanish cohort of the BICSTaR study at 12 months, offering valuable insights into the real-world application of B/F/TAF in Spain.

Methods

Study Design and Study Population

This prospective study was an analysis of Spanish participants within the broader BICSTaR cohort. It was set in eight geographically diverse major hospitals: Hospital Álvaro Cunqueiro (Vigo), Hospital Clínico Universitario de Santiago (Santiago de Compostela), Hospital niversitari de Bellvitge (L'Hospitalet de Llobregat), Hospital Universitari Germans Trias i Pujol (Badalona), Hospital Clínic de Barcelona (Barcelona), Hospital General Universitario de Alicante (Alicante), Consorcio Hospital General Universitario de Valencia (Valencia), and Hospital Regional Universitario de Málaga (Málaga). The study population comprised TN and TE adults with HIV aged ≥18 years who were starting treatment with B/F/TAF (50 mg/200 mg/25 mg) in routine clinical care. For this analysis, we included individuals who had started B/F/TAF between November 2019 and July 2021, with follow-up until February 2023. We collected enrollment and study variables from routine standard care, utilizing electronic case report forms (Medidata Rave Electronic Data Capture System; Medidata, New York, NY, USA) accessed via a secure web portal by the participating sites.

Study Endpoints and Assessments

The primary endpoint was to evaluate HIV-1 RNA suppression, defined as HIV-1 RNA <50 copies/mL, 12 months after initiating or switching to B/F/TAF.

Secondary objectives included change from baseline in CD4 count (Month 12) and the cumulative incidence of investigator-assessed adverse events (AEs), serious AEs (SAEs), drug-related AEs (DRAEs), and drug-related SAEs (Month 12).

The exploratory endpoints examined reasons for initiating B/F/TAF treatment in TN participants and switching to B/F/TAF in TE participants. Treatment persistence and causes for discontinuing treatment were explored. The proportion of participants discontinuing B/F/TAF within 12 months was used as an indicator of treatment persistence. Weight, body mass index, and lipid parameters at Month 12 were also assessed. Laboratory parameters, such as total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglycerides, were analyzed

according to routine clinical practice using standardized methods. The TC/HDL ratio was also calculated as a marker of cardiovascular risk.[12]

Key outcomes were stratified by baseline variables of interest. Participants were categorized according to receipt of prior treatment (TN vs TE), age (<50 vs ≥50 years), late HIV diagnosis (CD4 count <350 cells/μL and/or ≥1 AIDS-defining event vs ≥350 cells/μL), or late diagnosis with advanced HIV disease (CD4 count <200 cells/μL and/or ≥1 AIDS-defining event vs ≥200 cells/μL).[13]

Medication adherence was self-reported using a visual analog scale [VAS] score.[14] Physical and mental health-related quality of life (QoL) was measured with the 36-Item Short Form Survey (SF-36; Version 2). The SF-36 comprises 36 questions that cover eight domains of health. Responses to the questions across these domains contribute to a physical component summary (PCS) score and a mental component summary (MCS) score, with higher scores indicating better health status.[15]

Treatment satisfaction (in TE participants only) was assessed using the HIV Treatment Satisfaction Questionnaire status (HIVTSQs) and change (HIVTSQc) versions. The HIVTSQs is a validated 10-item questionnaire that employs an ordinal scale (Version 2006), where a score of 6 represents high satisfaction and 0 represents low satisfaction.[16] Responses to all questions are summed to yield a total treatment satisfaction score of 0 to 60, with higher scores indicating greater satisfaction. The HIVTSQc is a 10-item measure of relative satisfaction, where all items are rated on a scale wherein +3 means much more satisfied now and –3 means much less satisfied now. Responses to all questions are summed to produce a total treatment satisfaction (change) score of +30 (improvement) to –30 (deterioration). The HIV Symptom Index (HIV-SI) questionnaire was used to assess signs and symptoms associated with HIV, with a recall period of the previous 4 weeks. Responses to the 5-point Likert scale were dichotomized into bothersome (scores: 2–4) or not bothersome (scores: 0–1). The overall bothersome count indicates the number of bothersome symptoms and ranges from 0 to 20.[17]

Results were assigned to the following timepoints based on time elapsed from the start of B/F/TAF treatment to the date of sample collection: baseline, –2 months to Day 0; 3 months, 1.5 to 4.5 months; 6 months, 4.5 to 9 months; 12 months, 9 to 18 months.

Statistical Analysis

The primary endpoint was evaluated based on a missing = excluded (M=E) analysis. Participants who discontinued the study and/or B/F/TAF before the 12-month visit window, and participants still in the study and taking B/F/TAF but without an HIV-1 RNA value available within the visit window, were not considered (no imputation) for the M=E analysis. For participants who discontinued B/F/TAF during study follow-up and remained in the study (as allowed by study protocols), results collected after discontinuation of B/F/TAF were not considered for analysis.

A treatment discontinuation = failure (D=F) analysis was conducted for the primary endpoint at Months 3, 6, and 12. The 12-month D=F analysis included participants with at least one HIV-1 RNA value recorded within the 12-month visit window and those who discontinued B/F/TAF before the lower bound of the 12-month visit window (ie, ≥275 days or 9 months from baseline); in the latter case, HIV-1 RNA was imputed as ≥50 copies/mL. Results from participants who discontinued B/F/TAF during the 12-month visit window were not imputed for the D=F analysis.

Descriptive analyses were used to describe population baseline characteristics. For categorical variables, the numbers and percentages of individuals were reported, including the 95% confidence intervals (CIs). For continuous variables, the mean, standard deviation (SD), minimum, first and third quartiles (Q1, Q3), median, maximum, and 95% CIs were calculated. P-values and/or CIs (95% two-sided) were calculated when appropriate.

Analyses were conducted using SAS software, Version 9.4 (SAS Institute Inc., Cary, NC, USA).

Ethics Approval and Informed Consent

Written informed consent was obtained from all participants before their participation. The study was conducted in accordance with the Declaration of Helsinki, the protocol was approved by the independent ethics committee at each center, and the study was conducted following Ethical Guidelines for Medical and Health Research Involving Human Subjects. Study registration: European cohort: EUPAS22185.

Results

Baseline Characteristics

In total, 249 people with HIV who started treatment with B/F/TAF according to protocol between November 2019 and July 2021 were included in the present analysis (Figure 1): 62 were newly diagnosed (TN) and 187 had been treated previously with other regimens (TE). Of the 62 TN individuals, 57 (92%) were male, the median (Q1, Q3) age was 32.5 (26, 39) years, and 23 (37%) had ongoing comorbidities at baseline (3% neuropsychiatric, 3% hyperlipidemia, 7% hypertension, 3% musculoskeletal). Of the 187 TE individuals, 148 (79%) were male, the median (Q1, Q3) age was 47 (37, 55) years, and 132 (71%) had ongoing comorbidities at baseline (17% neuropsychiatric, 23% hyperlipidemia, 12% hypertension, 14% musculoskeletal). The median (Q1, Q3) number of treatments taken before B/F/TAF in the TE group was 3 (2, 5). In the TE group, the reasons for switching to B/F/TAF were simplification (81/187 [43%]), side effects of prior regimen (36/187 [19%]), and participant preferences (9/187 [5%]). Participant characteristics are listed in Table 1.

The proportion of late HIV diagnoses with advanced HIV disease (CD4 count <200 cells/μL and/or ≥1 AIDS-defining event) in the TN population was 32% (19/59 participants with available data). About 50% (5/10) of TN participants aged ≥50 years and 31% (16/52) of those aged <50 years present at the time of diagnosis had advanced HIV disease.

Effectiveness at 12 Months

At 12 months, 86% (48/56) and 98% (167/171) of TN and TE participants, respectively, had HIV-1 RNA <50 copies/mL (M=E analysis, Figure 2a). Similar 12-month results were obtained in the D=F analysis (Figure 2b), where 84% (48/62) of TN participants and 94% (167/187) of TE participants achieved HIV-1 RNA <50 copies/mL.

In TE participants, virologic suppression was achieved in 91% (10/11) of individuals with HIV-1 RNA ≥50 copies/mL at baseline. TN participants with a late diagnosis and advanced HIV disease (CD4 count <200 cells/μL and/or ≥1 AIDS-defining event) achieved less virologic suppression (<50 copies/mL): 11/17 (65%) with a late HIV diagnosis compared with 35/37 participants (95%) with no late HIV diagnosis.

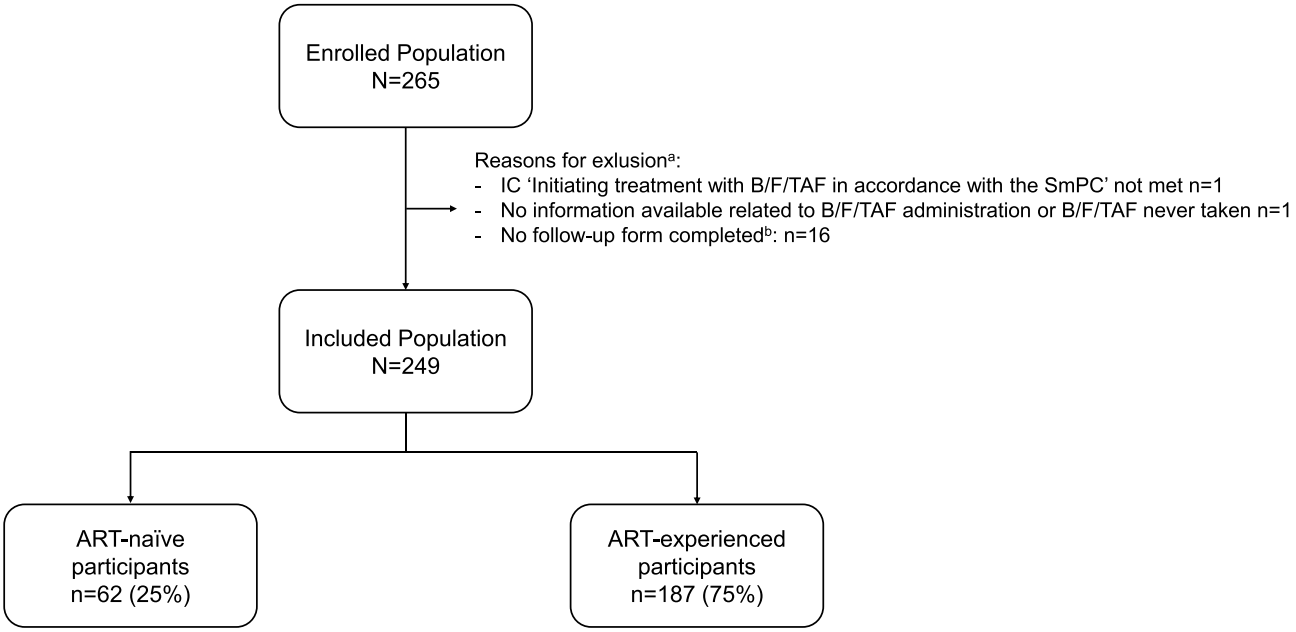

Figure 1 Participant Flow.
Notes: [a]More than one reason may apply for one person. [b]Among 3-month, 6-month, and 12-month follow-up forms.
Abbreviations: ART, antiretroviral therapy; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; IC, inclusion criterion; SmPC, Summary of Product Characteristics.

Table 1 Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	TN (n=62)	TE (n=187)
Male, as defined by participant, n (%)	57 (91.9)	148 (79.1)
Age (years), median (Q1, Q3) <50 years, n (%)	32.5 (26.0, 39.0) 52 (83.9)	47.0 (37.0, 55.0) 106 (56.7)
Weight (kg), median (Q1, Q3)	71.2 (64.0, 81.0)	76.5 (65.2, 85.0)
Age at HIV diagnosis (years), median (Q1, Q3)	32.0 (26.0, 39.0)	32.0 (27.0, 38.0)
Any comorbidities/co-infections ongoing at B/F/TAF initiation, n (%) Neuropsychiatric Hyperlipidemia Hypertension Osteopathic Chronic hepatitis B Chronic hepatitis C	23 (37.1) 2 (3.2) 2 (3.2) 4 (6.5) 2 (3.2) 3 (4.8) 1 (1.6)	132 (70.6) 32 (17.1) 43 (23.0) 23 (12.3) 27 (14.4) 4 (2.1) 6 (3.2)
Receiving concomitant medication, n (%)	17 (27.4)	78 (41.7)
Number of prior regimens, median (Q1, Q3)	–	3.0 (2.0, 5.0)
History of virologic failure on any regimen, n (%)	–	18 (9.6)[a]
HIV RNA viral load (log_{10} copies/mL), median (Q1, Q3) >100,000 copies/mL, n/N (%) <50 copies/mL, n/N (%)	4.71 (3.70, 5.32) 19/61 (31.1) 1/61 (1.6)	1.48 (1.28, 1.69) 0/180 (0) 167/180 (92.8)
CD4 count (cells/μL), median (Q1, Q3)	338.0 (147.0, 490.0)	773.1 (596.5, 954.5)
Late HIV diagnosis, n (%) CD4 <200 cells/μL and/or ≥1 AIDS-defining Event CD4 <350 cells/μL	 17 (27.4) 31 (50.0)	 – –
≥1 primary resistance mutation,[b] n (%)	6 (10.5)[c]	8 (4.3)[d]
Reason for switching to B/F/TAF,[e] n (%) Simplification Participant preferences Side effects of previous ART Other	 – – – –	 81 (43.3) 9 (4.8) 36 (19.3) 70 (37.4)

Notes: [a]12 (6.4%) are unknown. [b]For TN and TE participants, data were not available for 43.9% and 63.1%, respectively. [c]154L/M/V, 184V, V106M/A, K101E/P, M41L, K103N/S. [d]Y188L, G190A/S/E, L90M, M184V/I, L210W, T215Y/F, V106M/A, K101E/P, M41L, K103N/S (a person may have more than one mutation). [e]Participants may have more than one reason for starting treatment with B/F/TAF.

Abbreviations: B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; Q, quartile; TE, treatment-experienced; TN, treatment-naïve.

Immunologic Outcomes

Median (Q1, Q3) CD4 counts increased by 296 (169, 446) cells/μL (p<0.001) in TN participants and by 12 (–94, 110) cells/μL (p=0.302) in TE participants (Table 2).

Persistence and Adherence

At Month 12, persistence was high, with 236/249 (95%) participants still on B/F/TAF: 61/62 (98%) TN participants and 175/187 (94%) TE participants. Self-reported medication adherence (measured by VAS score among TE participants) was high at baseline (mean [SD]: 95% [15%]; n=158) and remained high at Month 12 (97% [5%]; n=171) (Table 2).

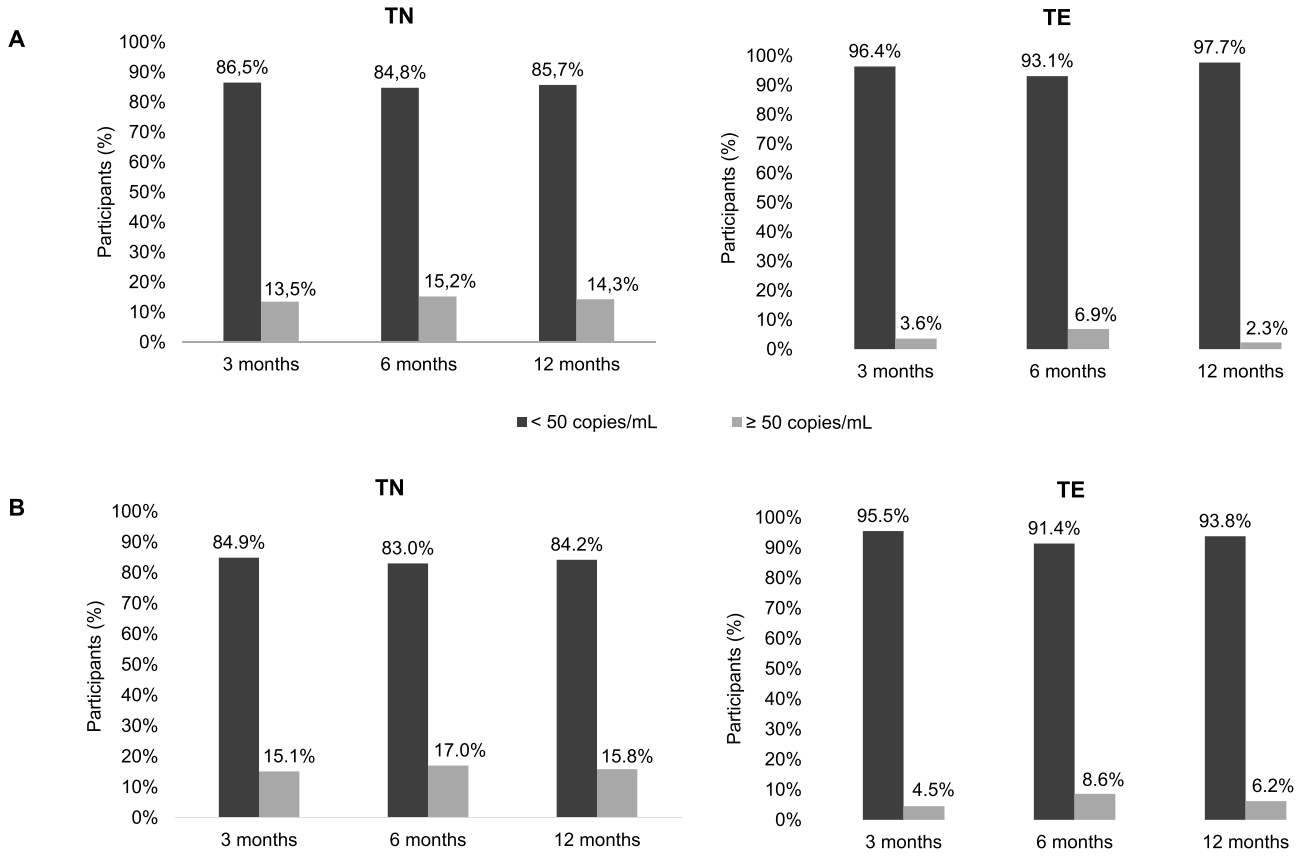

Figure 2 Effectiveness in TN and TE Participants. (**A**) Missing = excluded analysis at 3, 6, and 12 months. (**B**) Treatment discontinuation = failure analysis at 3, 6, and 12 months.
Notes: Window periods were defined as follows: 3 months = 1.5 to 4.5 months; 6 months = 4.5 to 9 months; 12 months = 9 to 18 months.
Abbreviations: TE, treatment-experienced; TN, treatment-naïve.

Safety

AEs were reported in 21/62 (34%) and 88/187 (47%) of TN and TE participants, respectively, while 1/62 (2%) of TN participants and 15/187 (8%) of TE participants reported DRAEs (Table 2). All DRAEs were considered mild or moderate. Five TE participants (3%) experienced DRAEs that led to discontinuation of B/F/TAF. The reasons for discontinuation are shown in Table 3.

There were small changes in fasting lipids from baseline, with small reductions in the TC/HDL-C ratio. In TN participants, all lipid fractions increased, which were statistically significant for TC (+0.73, p<0.001), LDL (+0.35, p<0.001), and HDL (+0.26, p<0.001). In TE participants, statistically significant decreases were observed TC (−0.21, p<0.012), LDL (−0.26, p=0.007), and triglycerides (−0.14, p=0.009) (Figure 3).

Median (Q1, Q3) weight increase at 12 months was 2.9 (0.5, 5.6) kg for TN participants (n=49, p<0.001) and 1.0 (–1.0, 3.0) kg for TE participants (n=126, p<0.001) (Table 2). Weight gain of >5% relative to baseline occurred in 22 TN (45%) and 23 TE (18%) participants; weight gain of >10% occurred in 10 TN (20%) and 4 TE (3%) participants. Two TN (4%) and 14 TE (11%) participants lost >5% of their weight relative to baseline.

Patient-Reported Outcomes

At baseline, SF-36 PCS scores were high and did not change significantly after 12 months. Changes in the SF-36 MCS score showed statistically significant improvement from baseline in the TN group after 12 months, with a median (Q1, Q3) increase of 8.4 (1.4, 12.4; p<0.001) (Table 4). In the TE group, the MCS score remained stable.

Table 2 Summary of Outcomes at 12 Months

	TN (n=62)	TE (n=187)
CD4 change from baseline (cells/μL), median (Q1, Q3)	296 (169, 446)	12 (–94, 110)
Adherence to B/F/TAF: VAS score (%), mean (SD)	97 (6)	98 (5)
Weight change from baseline (kg), median (Q1, Q3)	2.9 (0.5, 5.6)	1.0 (–1.0, 3.0)
Summary of AEs through 12 months, n (%)		
Participants with ≥1 AE	21 (33.9)	88 (47.1)
Participants with ≥1 DRAE	1 (1.6)	15 (8.0)
Mild AE	1 (1.6)	11 (5.9)
Moderate AE	0 (0.0)	4 (2.1)
SAE[a]	0 (0.0)	0 (0.0)
DRAEs in >1% of participants		
Weight gain	1 (1.6)	3 (1.6)
Headache	0 (0.0)	3 (1.6)

Notes: [a]Seriousness criteria: led to death, life-threatening, initial/prolonged hospitalization, persistent or significant disability, or other significant medical event.
Abbreviations: AE, adverse event; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DRAE, drug-related adverse event; SAE, serious adverse event; TE, treatment-experienced; TN, treatment-naïve; VAS, visual analog scale.

Table 3 Reasons for B/F/TAF Discontinuation Through 12 Months

	TN (n=62)	TE (n=187)
Any discontinuations	1 (1.6)	12 (6.4)
DRAE[a]	0 (0.0)	5 (2.7)
Participant decision	0 (0.0)	3 (1.6)
Death	0 (0.0)	1 (0.5)
Investigator's decision	1 (1.6)	1 (0.5)
Lack of efficacy	0 (0.0)	1 (0.5)
Data missing	0 (0.0)	1 (0.5)

Notes: Data are presented as n (%). If several events with the same preferred term have been reported for the same person, they are counted once for that term. [a]Asthenia (n=1), fatigue (n=1), weight gain (n=2), headache (n=1).
Abbreviations: B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DRAE, drug-related adverse event; TE, treatment-experienced; TN, treatment-naïve.

Overall bothersome symptom count decreased in TN participants, from a median (Q1, Q3) of 4.0 (2.0, 8.0) at baseline by –1.0 (–5.0, 1.0; p=0.047) at 12 months, but did not change significantly in TE participants (Table 4).

In TE participants, the median (Q1, Q3) HIVTSQs score (for which the total score ranges from 0 to 66) was 55.0 (50.0, 59.0) at baseline, indicating high treatment satisfaction. Treatment satisfaction improved after switching to B/F/TAF compared with prior treatment, with a median (Q1, Q3) HIVTSQc score (for which total score ranges from −33 to +33) of +26.0 (18.0, 30.0) (Table 4).

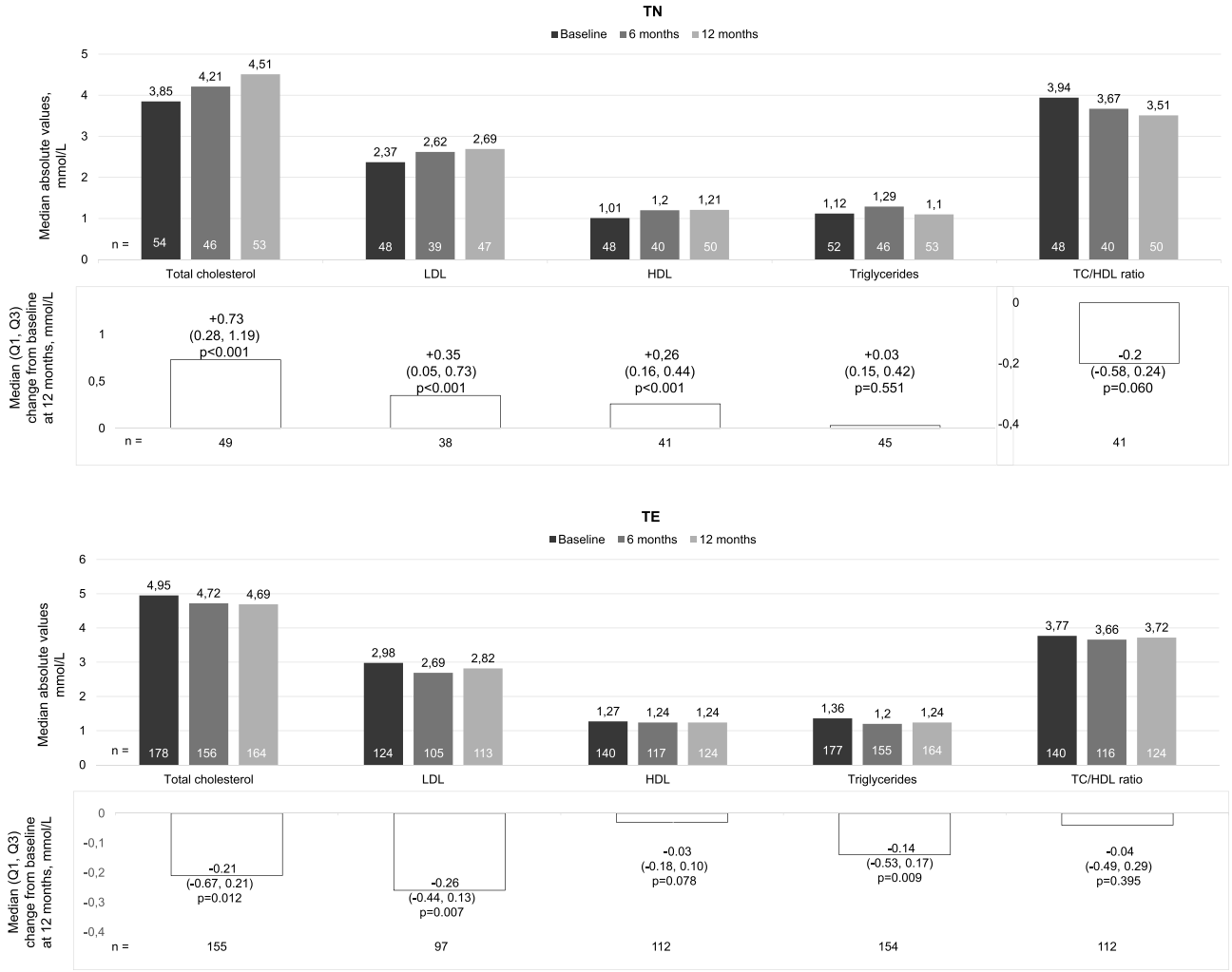

Figure 3 Absolute Values and Change in Lipid Fractions During the Treatment Period With B/F/TAF in TN and TE Participants.
Notes: N = number of participants with available data at baseline and within the follow-up time window. For people who discontinued B/F/TAF during study follow-up and remained in the study, results collected after discontinuation of B/F/TAF were not considered for analysis. P-values were calculated using Sign tests.
Abbreviations: B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NA, not available; TC, total cholesterol; TE, treatment-experienced; TN, treatment-naïve; Q, quartile.

Discussion

Our study contributes to the growing body of real-world evidence on the effectiveness and safety of the antiretroviral regimen B/F/TAF in people with HIV. This research highlights critical clinical outcomes by analyzing data from 249 people with HIV in Spain, including virologic suppression, comorbidity prevalence, and QoL improvements.

As would be expected (given the age difference), a higher prevalence of comorbidities was observed in the TE group. This difference in baseline health status could affect treatment outcomes and highlights the need for tailored treatment approaches.[18,19] These observational cohort data provide further evidence supporting the use of B/F/TAF in clinical practice.

The results presented for the subpopulation of Spanish centers from the BICSTaR study showed similar results to the global pooled BICSTaR population.[11] The high rates of virologic suppression at 12 months observed in our analysis (86% of TN and 98% of TE participants) are in line with rates of 94% and 97%, respectively, in the pooled analysis.[11] Additionally, the effectiveness of B/F/TAF has been evaluated in a systematic review and meta-analysis confirming the results reported from randomized clinical trials, showing virologic suppression rates of 80% (95% CI: 0.72–0.86%) in TN participants at Week 24 and 95% (95% CI 0.93–0.97%) in TE participants at Week 48.[20]

Table 4 Patient-Reported Outcomes at Baseline and 12 Months

	TN			
	n	**Baseline**	**12-Month Change**	**P-value**
SF-36[a] PCS score	37	57.4 (54.7, 59.4)	–0.1 (–4.3, 4.9)	1.000
SF-36[a] MCS score	37	44.0 (38.2, 52.6)	8.4 (1.4, 12.4)	<0.001
HIV-SI[b] overall bothersome symptom count	47	4.0 (2.0, 8.0)	–1.0 (–5.0, 1.0)	0.047
HIVTSQ	-	-	-	-
	TE			
	n	**Baseline**	**12-Month Change**	**P-value**
SF-36[a] PCS score	102	55.9 (50.9, 59.0)	–0.1 (–4.2, 2.8)	1.000
SF-36[a] MCS score	102	48.1 (39.7, 55.4)	0.4 (–6.8, 4.7)	0.767
HIV-SI[b] overall bothersome symptom count	146	5.0 (1.0, 7.0)	0.0 (–3.0, 2.0)	0.149
HIVTSQ	-	55.0 (50.0, 59.0)[n=183; HIVTSQs[c]]	+26.0 (18.0, 30.0)[n=141; HIVTSQc[d]]	-

Notes: Score values are shown as median (Q1, Q3). [a]SF-36: median scores >50 indicate better-than-average function; increased change scores indicate improvement. [b]HIV-SI: indicates the number of bothersome symptoms and is ranged from 0 to 20. [c]HIVTSQs: ranges from 0 to 60 (baseline); the higher the score, the greater the satisfaction with treatment. [d]HIVTSQc: ranges from −30 to +30 (12 months); the higher the score, the greater the improvement in satisfaction with treatment; the lower the score, the greater the deterioration in satisfaction with treatment; a score of 0 represents no change.

Abbreviations: HIV-SI, HIV Symptom Index; HIVTSQs/c, HIV Treatment Satisfaction Questionnaire: status/change version; MCS, mental component summary; PCS, physical component summary; Q, quartile; SF-36, 36-Item Short Form Survey; TE, treatment-experienced; TN, treatment-naïve.

In the current population, although the proportion of TN participants with a late diagnosis was lower than was seen in other cohorts, we found a higher proportion of participants with a late diagnosis in the subgroup of older participants, consistent with previous studies.[21] The lower suppression rate in late-diagnosed TN in our study, compared to the high rates observed in other BIC/FTC/TAF studies on advanced disease, may be explained by small sample variability, baseline immune status, higher viremia, and adherence.[22] Late HIV diagnosis is associated with increased morbidity, mortality, and healthcare costs.[23,24] Effectiveness at 12 months was higher in participants without a late HIV diagnosis than in those who presented with advanced disease, drawing attention to the importance of early diagnosis and treatment initiation in HIV management.[25]

As expected, CD4 cell count improved with B/F/TAF treatment in TN participants and, to a lesser extent, TE participants. These findings align with the known benefits of ART, indicating restoration of immunologic function.[26,27]

Persistence was high in both TN and TE participants. This is in agreement with a previous analysis, which also showed that participants initiating B/F/TAF were less likely to discontinue their regimen compared with other regimens.[28] It is important to note the potential variability in real-world adherence and management practices that might affect outcomes. Future studies could benefit from a comparative analysis of observational versus controlled trial settings to better understand these dynamics.

No new or unexpected safety findings were reported; AEs or deaths were similar to the pooled BICSTaR population.[11] Our study identified small, non-clinically relevant variations in fasting lipids with respect to baseline, especially among TN participants, with a small improvement in the TC/HDL-C ratio, a cardiovascular risk indicator with greater predictive value than isolated parameters used independently.[29] However, after 12 months of treatment, median values in TN participants remained lower than those observed in TE participants. As expected, changes in lipid parameters were less pronounced in TE than in TN participants. However, we did observe small decreases in all lipid parameters, including a decrease in the TC/HDL-C ratio.

Previous studies have suggested that INSTIs, including bictegravir, are associated with greater weight gain than other antiretroviral agents.[30,31] Additionally, switching from tenofovir disoproxil fumarate (TDF) to TAF has been linked to weight gain in people with HIV.[32] However, recent comprehensive analyses of major clinical trials indicate that TDF-based regimens, particularly when combined with efavirenz (EFV), tend to attenuate weight gain, while dolutegravir,

bictegravir, and TAF can be considered neutral and not a cause of excessive weight gain.[33] It is important to note that no causal relationship between ART and weight gain has been established as the observed weight changes are multifactorial, influenced by the "return to health" effect in TN participants and the weight-suppressing effects of prior ART regimens such as TDF and EFV.[33] Our study data on B/F/TAF align with these recent findings, showing weight gain in both groups, although further studies may be needed to assess whether these changes translate into significant metabolic effects. People with HIV may continue to experience poorer health-related QoL than the general population despite virologic suppression.[34] In our study, the improvement in SF-36 MCS scores on TN participants might reflect the psychological benefits of ART initiation, which reduces anxiety, depressive symptoms, and uncertainty related to untreated HIV (A). Conversely, the stable scores in TE individuals are expected, as most mental health gains occur at treatment start, and long-term ART users generally show limited additional improvement due to already stabilized well-being and persistent comorbid or psychosocial stressors. The decrease in bothersome symptom count in TN participants and the positive change reported in the TE group regarding treatment satisfaction further support the acceptability and QoL benefits of B/F/TAF.

As with all observational cohorts, this study has several limitations, including potential confounding due to its non-randomized design, and, as a single-arm, uncontrolled study, it cannot establish causal associations with B/F/TAF usage. Selection bias may also play a role as clinics were not chosen randomly to participate in the study. The M=E approach for effectiveness analysis may have resulted in an overestimation or underestimation of treatment effects due to systematic differences between participants with and without reported viral loads. While this analysis offered detailed insights into the treatment of HIV in Spain, its findings are constrained by limitations in statistical power given the relatively small study population compared with the overall BICSTaR study population. Reliance on self-reported measures for adherence and treatment satisfaction introduces the possibility of recall bias or social desirability effects. However, data were collected using rigorous, homogeneous, and standardized procedures, reducing the possible reporting biases on a large sample across a broad range of populations. Despite these limitations, the study offers valuable insights into the effectiveness and safety of B/F/TAF in a real-world clinical setting, enhancing our understanding of HIV management in the Spanish population.

Conclusion

This real-world study demonstrated that B/F/TAF is a highly effective and well-tolerated treatment option for both TN and TE participants across diverse groups, and improvements in patient-reported outcomes further support the real-world tolerability and acceptability of B/F/TAF.

Data Sharing Statement

Gilead Sciences shares anonymized individual patient data upon request or as required by law or regulation with qualified external researchers based on submitted curriculum vitae and reflecting non-conflict of interest. The request proposal must also include a statistician. Approval of such requests is at Gilead Sciences' discretion and is dependent on the nature of the request, the merit of the research proposed, the availability of the data, and the intended use of the data. Data requests should be sent to datarequest@gilead.com.

Acknowledgments

We would like to thank all the participants, and investigators involved in the selection and inclusion in this study. We also thank Carla Lluis (Aixial Group), Zita Viegas (Daiichi-Sankyo, Lisbon, Portugal), and Carolina Castillo (Oxford Global Resources, Madrid, Spain) for their contribution in the development of the early drafts of this manuscript, and Anchel González Barriga (Medical Science Consulting, Valencia, Spain) for providing editorial support in the form of medical writing based on authors' detailed directions, collating author comments, copyediting, fact checking, and referencing.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

The BICSTaR program was funded by Gilead Sciences, Inc., Foster City, CA, USA.

Disclosure

AI has received research funding from Gilead Sciences, Janssen-Cilag, GlaxoSmithKline, and ViiV-Healthcare, served on advisory boards for Almirall, Pfizer, AbbVie, and Bayer, and received personal compensation from ViiV-Healthcare.

CM: has received honoraria for advisory meetings from Gilead Sciences and ViiV-Healthcare, for educational meetings material delivery and presentation from Gilead Sciences and ViiV-Healthcare, and conference attendance support from Gilead Sciences.

AS-K has received honoraria for conferences from GSK/ViiV-Healthcare, Gilead Sciences, Janssen-Cilag and Merck Sharp & Dohme.

BR has received honoraria for lectures presentations and travel sponsorship from Merck Sharp & Dohme, Gilead Sciences, Janssen-Cilag and ViiV-Healthcare.

MGD has received research funding from Gilead Sciences and GlaxoSmithKline (all fees paid to the institution) and has participated in conference panels and advisory boards for Gilead Sciences, Janssen-Cilag, and ViiV-Healthcare.

JP has received grants, personal fees and non-financial support from Gilead Sciences, ViiV-Healthcare and Janssen-Cilag.

AA: has participated as an advisor or as a lecturer or as a clinical researcher, in advisory or educational meetings, or in clinical trials, sponsored by Gilead Sciences, Janssen-Cilag, Merck Sharp and Dohme, and ViiV-Healthcare.

MAC-C: has received honoraria for lectures or advisory boards from Gilead Sciences and ViiV-Healthcare.

CdA and JR are employees of Gilead Sciences.

AG-C: has received honoraria for lectures or advisory boards, conference attendance support and grants for her institution from Gilead Sciences, Janssen-Cilag, Merck Sharp & Dohme and ViiV-Healthcare.

JM has received grants, personal fees for conferences and advisory meetings from Gilead Sciences, ViiV-Healthcare, Merck Sharp & Dohme & Janssen-Cilag.

References

1. The urgency of now: AIDS at a crossroads. Geneva: joint United Nations programme on HIV/AIDS; 2024. Licence: CC BY-NC-SA 3.0 IGO.
2. de Sanidad M. VIGILANCIA EPIDEMIOLÓGICA DEL VIH y SIDA EN ESPAÑA 2022. 2023. Available from: https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/vigilancia/docs/Informe_VIH_SIDA_2023.pdf. Accessed March 12, 2023.
3. European Center of Disease Prevention and Control (ECDC). HIV/AIDS surveillance in Europe; 2024. doi: 10.2900/3113714
4. de Sanidad M. Unidad de vigilancia de VIH, ITS y hepatitis B y C. Mortalidad por VIH y sida en España, año 2021. Evolución 1981-2021. 2023. Available from: https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/vigilancia/docs/Mortalidad_por_VIH2021.pdf. Accessed March 16, 2024.
5. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. *Lancet*. 2013;382(9903):1525–1533. doi:10.1016/S0140-6736(13)61809-7
6. Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2022 recommendations of the international antiviral society-USA panel. *JAMA*. 2023;329(1):63–84. doi:10.1001/jama.2022.22246
7. EACS. Guidelines EACS version 12.1. 2024 Available from: https://eacs.sanfordguide.com/. Accessed December 11, 2005.
8. Zhao AV, Crutchley RD, Guduru RC, Ton K, Lam T, Min AC. A clinical review of HIV integrase strand transfer inhibitors (INSTIs) for the prevention and treatment of HIV-1 infection. *Retrovirology*. 2022;19(1):22. doi:10.1186/s12977-022-00608-1
9. Carr A, Mackie NE, Paredes R, Ruxrungtham K. HIV drug resistance in the era of contemporary antiretroviral therapy: a clinical perspective. *Antivir Ther*. 2023;28(5):13596535231201162. doi:10.1177/13596535231201162
10. Sax PE, Arribas JR, Orkin C, et al. Bictegravir/emtricitabine/tenofovir alafenamide as initial treatment for HIV-1: five-year follow-up from two randomized trials. *EClinicalMedicine*. 2023;59:101991. doi:10.1016/j.eclinm.2023.101991

11. Micán R, de Gea Grela A, Cadiñanos J, et al. Impact of preexisting nucleos(t)ide reverse transcriptase inhibitor resistance on the effectiveness of bictegravir/emtricitabine/tenofovir alafenamide in treatment experience patients. *AIDS*. 2022;36(14):1941–1947. doi:10.1097/QAD.0000000000003311
12. Esser S, Brunetta J, Inciarte A, et al. Twelve-month effectiveness and safety of bictegravir/emtricitabine/tenofovir alafenamide in people with HIV: real-world insights from BICSTaR cohorts. *HIV Med*. 2023;25(4):440–453. doi:10.1111/hiv.13593
13. Calling S, Johansson SE, Wolff M, Sundquist J, Sundquist K. Total cholesterol/HDL-C ratio versus non-HDL-C as predictors for ischemic heart disease: a 17-year follow-up study of women in southern Sweden. *BMC Cardiovasc Disord*. 2021;21(1):163. doi:10.1186/s12872-021-01971-1
14. Croxford S, Stengaard AR, Brännström J, et al. Late diagnosis of HIV: an updated consensus definition. *HIV Med*. 2022;23(11):1202–1208. doi:10.1111/hiv.13425
15. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. *Psychol Med*. 1988;18(4):1007–1019. doi:10.1017/s0033291700009934
16. von der Heyde R. Chapter 6 - Assessment of functional outcomes. In: Cooper C, editor. *Fundamentals of Hand Therapy*. Mosby; 2007:98–113. doi:10.1016/B0-32-303386-5/50009-6
17. Woodcock A, Bradley C. Validation of the HIV treatment satisfaction questionnaire (HIVTSQ). *Qual Life Res*. 2001;10(6):517–531. doi:10.1023/a:1013050904635
18. Akinosoglou K, Antonopoulou S, Katsarolis I, Gogos CA. Patient-reported outcomes in HIV clinical trials evaluating antiretroviral treatment: a systematic review. *AIDS Care*. 2021;33(9):1118–1126. doi:10.1080/09540121.2020.1852160
19. Priest J, Hulbert E, Gilliam BL, Burton T. Characterization of heavily treatment-experienced people with HIV and impact on health care resource utilization in US commercial and medicare advantage health plans. *Open Forum Infect Dis*. 2021;8(12):ofab562. doi:10.1093/ofid/ofab562
20. Garagiola E, Foglia E, Ferrario L, et al. Comorbidities and HCV coinfection in the management of HIV+ patients: evidence from the Italian clinical practice. *Health Econ Rev*. 2020;10(1):27. doi:10.1186/s13561-020-00284-x
21. Chivite I, Berrocal L, de Lazzari E, et al. Effectiveness, safety and discontinuation rates of bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) in people with HIV using real-world data: a systematic review and meta-analysis. *J Antimicrob Chemother*. 2024;79(8):1775–1783. doi:10.1093/jac/dkae138
22. Lauscher P, Hanhoff N, Valbert F, et al. Socio-demographic and psycho-social determinants of HIV late presentation in Germany - results from the FindHIV study. *AIDS Care*. 2023;35(11):1749–1759. doi:10.1080/09540121.2023.2185196
23. Corona D, Pérez-Valero I, Camacho A, et al. Effectiveness and safety of bictegravir/emtricitabine/tenofovir alafenamide in HIV late presenters. *Int J Antimicrob Agents*. 2024;63(1):107016. doi:10.1016/j.ijantimicag.2023.107016
24. Boardman E, Boffito M, Chadwick DR, et al. Tackling late HIV diagnosis: lessons from the UK in the COVID-19 era. *Int J STD AIDS*. 2024;35(4):244–253. doi:10.1177/09564624231202287
25. Sobrino-Vegas P, Moreno S, Rubio R, et al. Impact of late presentation of HIV infection on short-, mid- and long-term mortality and causes of death in a multicenter national cohort: 2004–2013. *J Infect*. 2016;72(5):587–596. doi:10.1016/j.jinf.2016.01.017
26. May MT. Better to know: the importance of early HIV diagnosis. *Lancet Public Heal*. 2017;2(1):e6–e7. doi:10.1016/S2468-2667(16)30038-X
27. Orkin C, DeJesus E, Sax PE, et al. Fixed-dose combination bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir-containing regimens for initial treatment of HIV-1 infection: week 144 results from two randomised, double-blind, multicentre, Phase 3, non-inferiority trials. *Lancet HIV*. 2020;7(6):e389–e400. doi:10.1016/S2352-3018(20)30099-0
28. Wohl DA, Yazdanpanah Y, Baumgarten A, et al. Bictegravir combined with emtricitabine and tenofovir alafenamide versus dolutegravir, Abacavir, and lamivudine for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *Lancet HIV*. 2019;6(6):e355–e363. doi:10.1016/S2352-3018(19)30077-3
29. Mounzer K, Brunet L, Fusco JS, et al. Advanced HIV infection in treatment-naïve individuals: effectiveness and persistence of recommended 3-drug regimens. *Open Forum Infect Dis*. 2022;9(3):ofac018. doi:10.1093/ofid/ofac018
30. Millán J, Pintó X, Muñoz A, et al. Lipoprotein ratios: physiological significance and clinical usefulness in cardiovascular prevention. *Vasc Health Risk Manag*. 2009;5:757–765.
31. Lake JE, Trevillyan J. Impact of Integrase inhibitors and tenofovir alafenamide on weight gain in people with HIV. *Curr Opin HIV AIDS*. 2021;16(3):148–151. doi:10.1097/COH.0000000000000680
32. Sax PE, Erlandson KM, Lake JE, et al. Weight gain following initiation of antiretroviral therapy: risk factors in randomized comparative clinical trials. *Clin Infect Dis*. 2020;71(6):1379–1389. doi:10.1093/cid/ciz999
33. Mallon PW, Brunet L, Hsu RK, et al. Weight gain before and after switch from TDF to TAF in a U.S. cohort study. *J Int AIDS Soc*. 2021;24(4):e25702. doi:10.1002/jia2.25702
34. Wohl DA, Koethe JR, Sax PE, et al. Antiretrovirals and weight change: weighing the evidence. *Clin Infect Dis*. 2024;79(4):999–1005. doi:10.1093/cid/ciae191