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Effectiveness, safety, and patient-reported outcomes of bictegravir/emtricitabine/tenofovir alafenamide in routine clinical care in Italy: 12-Month results from the BICSTaR cohort

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Abstract

Background: BICSTaR is a multi-national, observational cohort evaluating the effectiveness, safety, and patient-reported outcomes (PROs) in treatment-naïve (TN) and -experienced (TE) people with HIV-1 receiving bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in routine clinical care. We present the 12-month (M12) outcomes of the Italian BICSTaR cohort.

Methods: Participants initiating B/F/TAF in routine care were prospectively followed. Outcomes included virological and immunologic effectiveness, drug-related adverse events (DRAEs), treatment persistence, and PROs using the HIV Symptom Index (HIV-SI) and the HIV Treatment Satisfaction Questionnaires (HIVTSQ).

Results: *N* = 201 were included (29 TN, 172 TE), 83% male, median age 38 years in TN, 48 years in TE. At baseline, 94% of TE had an HIV-1 RNA <50 cp/mL, 92% switched to B/F/TAF for simplification. Overall, 69% reported comorbidities (TN: 59%, TE: 70%). At M12, 88% (23/26) of TN and 96% (152/159) of TE had an HIV-1 RNA <50 cp/mL in the discontinuation = failure analysis (without emergence of resistance to B/F/TAF). Median CD4 count changes were +296 cells/μL (interquartile range [IQR], 118, 383) in TN, and +23 cells/μl (−137, 114) in TE. DRAEs were reported for 5% and led to discontinuation in 1%. M12 persistence on B/F/TAF was 97%. TN had a median HIV-SI bothersome symptom count decrease of −1.5 (IQR, −5.0, 0.0). Median treatment satisfaction change score was +29.0 (21, 30) in TE indicating an improvement.

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Conclusions: In this real-world Italian cohort of mostly treatment-experienced people switching for simplification, B/F/TAF demonstrated high effectiveness and persistence over 12 months and confirmed the favourable safety profile shown in clinical trials.
Trial registration: European cohort: EUPAS22185.

Keywords
HIV-Infection, antiretroviral therapy, bictegravir, tenofovir alafenamide, real-world data

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Background

Given the substantial improvement in health and life expectancy associated with antiretroviral therapy (ART) for people with HIV, as well as the prevention of transmission, it is recommended that ART be initiated as soon as possible after an HIV diagnosis, if feasible.[1] Considering that treatment is likely life-long, drug regimens should be effective with a low risk of resistance, convenient to take, safe and well tolerated and with minimal potential for food and drug interactions.[1,2] With an ageing HIV population, the focus on polypharmacy and interactions between ART and co-medication has become increasingly important.[3–5]

Initial ART as recommended by the European AIDS Clinical Society (EACS) regimens include one or two nucleos(t)ide reverse transcriptase inhibitors (NRTIs) and either an integrase strand transfer inhibitor (INSTI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). The INSTI bictegravir (BIC; B) combined and co-formulated with the NRTIs tenofovir alafenamide (TAF) and emtricitabine (FTC; F) is among these recommended regimens. Additionally, B/F/TAF has a role in switch strategies for people with a suppressed viral load and in certain cases of virologic failure.[1] Non-inferiority, safety, and tolerability of B/F/TAF without development of resistance-associated mutations was demonstrated in Phase 3 studies of B/F/TAF when used as initial treatment in comparison to 3-drug dolutegravir-based regimens and when switched from a boosted protease inhibitor in virally suppressed individuals.[6–9] Clinical trials have further demonstrated the efficacy, safety, tolerability, and high resistance barrier of B/F/TAF in both treatment-naïve (TN) and treatment-experienced (TE) people with HIV.[10–13] Long-term, real-world data are increasing, but still limited.[14–16]

The BICSTaR (Bictegravir Single Tablet Regimen) cohort study is a multinational, prospective, observational study evaluating the effectiveness, safety, adherence, and self-reported quality of life in 2379 TN and TE people with HIV from Europe, Asia, Canada, Israel, and Japan receiving B/F/TAF in routine clinical care. The 12-month data of this pooled cohort demonstrated the high effectiveness and good safety profile of B/F/TAF.[17] We present here the 12-month results from the Italian sub-cohort.

Methods

Study design and study population

BICSTaR is a prospective, multi-national (14 countries), 2-year (in three countries extended to 5 years), observational, non-interventional cohort study in adult TN and TE people with HIV initiating B/F/TAF (50 mg, 200 mg, 25 mg; once daily) between Dec 2019 and Nov 2020. Participating countries are France, Germany, Ireland, Italy, the Netherlands, Spain, UK, Turkey, Taiwan, South Korea, Singapore, Japan, Canada, and Israel.

Adult participants could be enrolled in this study after the physician had independently decided to treat them with B/F/TAF (50/25/200 mg once daily) in accordance with the approved indication label in Europe and with the participants' written informed consent. Data were collected prospectively from electronic medical records or using patient questionnaires. Detailed methodology of the BICSTaR study has been described previously.[17]

The present month 12 (M12) analysis includes those TN and TE people with HIV receiving B/F/TAF in routine clinical care in Italy as part of BICSTaR with at least one follow-up visit.

Study endpoints

The primary endpoint of the BICSTaR cohort was the proportion of participants in the overall cohort with viral suppression at M12 after initiating B/F/TAF.

Secondary endpoints included the change in CD4 cell count from baseline to M12, CD4/CD8 cell ratio at baseline and M12, selection of resistance mutations after treatment failure, and the cumulative incidence of drug-related adverse events (DRAEs) and drug-related serious adverse events (DRSAEs) at M12.

Additional factors evaluated were reasons for switching to B/F/TAF (TE participants), persistence on B/F/TAF and reasons for any discontinuations, metabolic assessment (total cholesterol, high-density lipoprotein [HDL], low-density lipoprotein [LDL] and triglycerides), renal assessment (creatinine and estimated glomerular filtration rate [eGFR]), weight, and BMI. Patient-reported outcomes (PROs) focused on treatment satisfaction and HIV Symptom Index.

Outcome measures

Virologic effectiveness was defined as plasma HIV-1 RNA level <50 cp/mL. Analyses were performed using two approaches, a missing/discontinuation/loss-to-follow-up-as-excluded (M = E) approach (considering only HIV-1 RNA data collected during the M12 time window while on

study treatment) and a discontinuation-equals-failure (D = F) approach (with imputation for participants who discontinued B/F/TAF before the M12 time window).

Safety parameters included adverse events and serious adverse events, including those considered related to B/F/TAF as well as changes in body weight and change in laboratory parameters. All medical events were coded using MedDRA (Medical Dictionary for Regulatory Activities) SOC (systems organ classes) and preferred terms (PT).[18] Concomitant medication was classified using the 2nd ATC (Anatomical Therapeutic Chemical Classification) level.[19] The eGFR was calculated using the Cockcroft-Gault formula.[20]

Standardized questionnaires were used to evaluate HIV symptom burden and treatment satisfaction using the 20-item HIV Symptom Index (HIV-SI) questionnaire[21] and the HIV Treatment Satisfaction Questionnaire (HIVTSQ),[22,23] respectively. The total HIV-Symptom score ranges from 0 to 20 with higher scores indicating more (bothersome) symptoms. The HIV Treatment Satisfaction Questionnaire encompasses both a status (HIVTSQs, scores 0 to 60 with higher scores indicating greater treatment satisfaction, as well as a change (HIVTSQc, scores −30 to +30 with positive scores indicating improvement in treatment satisfaction) version and provides insight into how participants rate their satisfaction with current treatment in comparison to their previous treatment.

Statistical analysis

All analyses were carried out for the full analysis set and stratified by TN or TE participants. The analyses were performed in a descriptive manner based on observed data (with missing data imputation applied only for the D = F effectiveness analysis) using the software package SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Numbers and percentages of participants were reported for categorical variables. Data of continuous variables are expressed as median (interquartile range, IQR, expressed as Q1 (quartile 1) and Q3) if not otherwise specified.

Testing for statistical significance using two-sided p-values and/or 95% confidence intervals [CIs]) was only performed for explorative reasons, that is when considered relevant (and only in case of ≥20 observations). To account for multiple testing, Bonferroni correction has been applied. The alpha level for statistical testing was <0.05.

Regulatory requirements, ethics, and quality control

Approval of the ethics committees and competent authorities was obtained prior to study initiation according to the local regulations in Italy. All participants provided written informed consent prior to study enrolment and following the physicians' independent decision to treat with B/F/TAF. Quality control of data entries in the electronic case report forms involved programmed plausibility checks, electronic queries, and remote monitoring.

Results

Study population

Between December 2019 and November 2020, 208 people with HIV were enrolled in ten leading HIV centers in Italy. Of these, seven people were not included due to missing follow-up data after enrolment, giving a final study population of 201 (29 TN, 172 TE participants).

Baseline characteristics are shown in Table 1.

At baseline, the majority (94%) of TE participants presented with viral suppression (HIV-1 RNA <50 copies/mL). In the TN group, median HIV-1 RNA level was 5.3 $\log_{10}$ cp/mL (4.9, 5.8). Median CD4 cell counts at baseline were 225 cells/µl for TN and 719 cells/µL for TE participants; Median CD4/CD8 ratios were 0.27 and 0.90, respectively. (Table 1).

Antiretroviral treatment history and reason for B/F/TAF initiation

Median time from diagnosis to treatment was 22 days (IQR, 15, 38; n = 21).

The antiretroviral treatment history was available for 170 of the 172 TE participants. Prior to switching to B/F/TAF, TE participants were treated with a median of 3 (2, 5) ART regimens. Fifteen percent had taken one previous regimen, 29% two regimens, 20% had taken three, and 35% more than three previous regimens (1% unknown). Among the 170 TE with a known ART history, 68% had been exposed to INSTIs, 55% to PIs, 38% to NNRTIs, and 97% to NRTIs; 79% had a history of prior TDF use. Past virological failure was documented in 14%.

The most common regimen immediately prior to the B/F/TAF in the 172 TE participants was elvitegravir/cobicistat/F/TAF (47%). Another 34% had been on F/TAF combined with (boosted) atazanavir, boosted darunavir, dolutegravir, raltegravir, or rilpivirine. (Figure 1). Fifteen percent of participants had previously been on a regimen that included a boosted PI. Prior to B/F/TAF 5% of the participants had received a TDF-based regimen.

Most TE participants reported simplification of ART as a reason for switching to B/F/TAF (92%); side effects of the previous ART regimen were documented as a reason in 3% of participants. Using the VAS as a measure of adherence to the ART regimen just prior to B/F/TAF, 117/144 (85%) self-reported adherence of ≥95% (131/144, 96% reported adherence ≥80%).

HIV drug resistance at baseline and during follow-up

At baseline, resistance testing was available for 21 TN and 104 TE participants. Pre-existing major or minor resistance-associated mutations (RAMs) were identified for 16 of

Table 1. Baseline characteristics and comorbidities/comedications.

	All (n = 201)	TN (n = 29)	TE (n = 172)
Demographics			
Male sex*, n (%)	166 (83)	24 (83)	142 (83)
Female sex*, n (%)	35 (17)	5 (17)	30 (17)
Age, years	47 (36, 56)	38 (33, 56)	48 (38, 57)
Age ≥50 years, n (%)	88 (44)	9 (31)	79 (46)
White, n (%)	192 (96)	28 (97)	164 (95)
HIV-related characteristics			
Number of previous ART regimens		—	3 (2, 5)
HIV-1 RNA, $\log_{10}$ cp/mL	1.3 (1.3, 1.6)	5.3 (4.9, 5.8)	1.3 (1.3, 1.5)
HIV-1 RNA >100,000 cp/mL, n (%)	20 (12)	19 (66)	1 (1)
HIV-1 RNA <50 cp/mL, n (%)	135 (78)	0	135 (94)
CD4 count, cells/μL	653 (425, 868)	225 (49, 452)	719 (542, 922)
CD4 count <200 cells/μL, n (%)	21 (10)	14 (48)	7 (5)
CD4 count ≥200 and <350 cells/μL, n (%)	8 (5)	1 (3)	7 (5)
CD4 count ≥350 and <500 cells/μL, n (%)	23 (14)	8 (28)	15 (11)
CD4 count ≥500 cells/μL, n (%)	116 (69)	6 (21)	110 (79)
CD4/CD8 ratio	0.78 (0.47, 1.20)	0.27 (0.08, 0.60)	0.90 (0.59, 1.30)
CDC stage C (AIDS), n (%)	41 (20)	9 (31)	32 (19)
History of virological failure, n (%)		—	24 (14)
Comorbidities/comedication			
Any comorbidity, n (%)	137 (68)	17 (59)	120 (70)
None	64 (32)	12 (41)	52 (30)
1–2	76 (38)	12 (41)	64 (37)
≥3	61 (30)	5 (17)	56 (33)
Category (in ≥5% participants)			
Hyperlipidemia	55 (27)	1 (3)	54 (31)
Hypertension	34 (17)	3 (10)	31 (18)
Musculoskeletal disorders	27 (13)	1 (3)	26 (15)
Cardiovascular illness	19 (9)	1 (3)	18 (10)
Neuropsychiatric disorders	19 (9)	0 (0)	19 (11)
Chronic hepatitis C	17 (8)	1 (3)	16 (9)
Chronic hepatitis B	11 (5)	2 (7)	9 (5)
Any comedication, n (%)	103 (51)	16 (55)	87 (51)

*Sex was defined by the individual; continuous variables are summarized as median and interquartile rage, that is IQR expressed as (Quartile 1, Quartile 3).

21 TN (76%) and 60 of 104 TE (58%) participants. Major (primary) RAMs were detected in 3 TN and 23 TE participants at baseline (including M184 V/I [n = 9], no K65 R; and one INSTI-RAM [T97 A (n = 1)]. During follow-up, five resistance tests were performed (3 in TN, 2 in TE), without detection of any INSTI or NRTI RAMs.

Comorbidities and comedication

At baseline, comorbidities or co-infections were present in 68% of participants (59% TN, 70% TE). (Table 1).

Almost one-half of the participants (51%; 55% TN, 51% TE) were receiving concomitant medication and/or supplements at baseline. The most common were vitamins (20%), followed by agents acting on the renin-angiotensin system (14%) and analgesics (13%). The use (by >5%) of the following drug classes was exclusively observed in the TE group and reflected the documented comorbidities: lipid-modifying agents (15%), agents acting on the renin-angiotensin system (15%), analgesics (14%), psycholeptics (9%), antithrombotic agents (9%), β-blockers (7%), drugs for acid related disorders (6%), proton-pump inhibitors (6%), and urologicals (6%).

Virologic outcomes

In the M = E analysis, 92% [23/25] TN and 98% [152/155] TE had an HIV-1 RNA of <50 cp/mL at M12 (Figure 2(a)).

In the D = F analysis, M12 suppression rate was 88% (23/26) in TN and 96% (152/159) in TE participants. Three (out of 159) TE and two (out of 26) participants had an HIV-1 RNA ≥50 cp/mL at M12 (discontinuers: TE 4/159; TN 1/26).

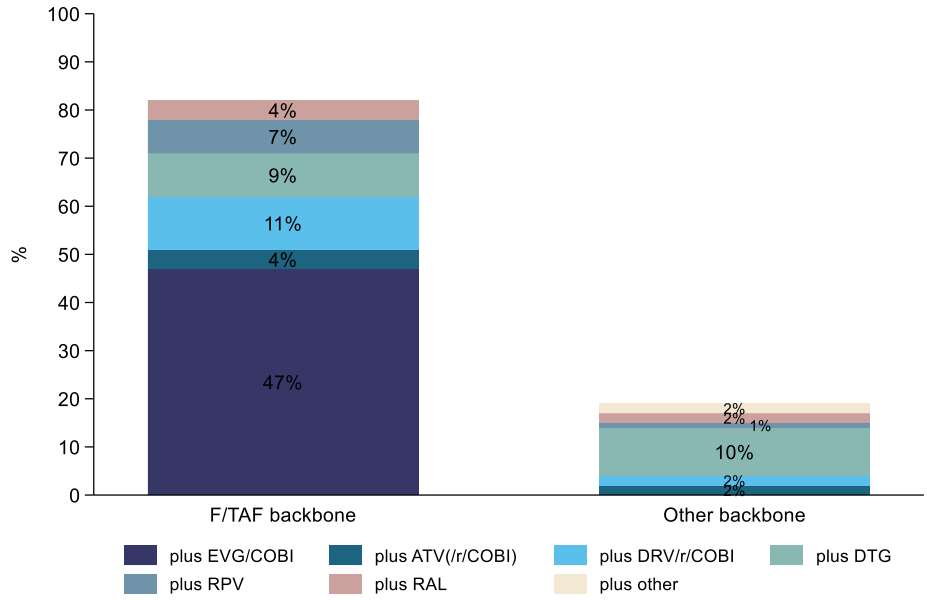

Figure 1. ART regimens immediately prior to B/F/TAF (n = 88). F = emtricitabine; TAF = tenofovir alafenamide; EVG = elvitegravir; COBI = cobicistat; ATV = atazanavir; r = ritonavir as booster; DRV = darunavir; DTG = dolutegravir; RPV = rilpivirine; RAL = raltegravir. Additional information: 5% receiving F/TDF.

Treatment persistence and discontinuations

Persistence on B/F/TAF was high through M12 with only 3% (1/29) of TN and 3% (6/172) of TE participants discontinuing B/F/TAF within 12 months of initiation of treatment (Figure 2(b)). In seven cases, six in the treatment-experienced arm, B/F/TAF was discontinued after a median time of 7.3 (6.4, 12.2) months. The reasons were drug-related adverse events (three; see below), investigator's decision (three), and one death. There was no treatment discontinuation due to virological failure.

Immunologic outcomes

After 12 months, median absolute CD4 cell count was 508 cells/µl (293, 865) for TN (n = 23) and 699 cells/µl (508, 928) for TE (n = 150) with data at M12. The median absolute CD4 change from baseline in participants remaining on B/F/TAF with baseline and M12 data available was +296 cells/µl (118, 383) for TN (n = 23) and +23 cells/µl (−137, +114) for TE (n = 122). At M12, 52% of TN and 77% of TE had a CD4 cell count of ≥500 cells/µL. Relative CD4 changes were +82% (+38, +513) for TN and +5% (−17, +19) for TE.

At M12, the CD4/CD8 ratio was 0.58 (0.25, 0.92) for TN (n = 23) and 0.81 (0.60, 1.24) for TE (n = 150).

Safety

Within the 12-month observation period, adverse events were reported by 84/201 (42%) of participants (11/201 [5%] considered related to B/F/TAF), of which 7/201 (3%) were considered serious adverse events.

Adverse events related to B/F/TAF are depicted in Table 2 (most common psychiatric, nervous system, and gastrointestinal disorders), none of which were serious.

Three (1%) participants (1 TN, 2 TE) discontinued B/F/TAF due to drug-related adverse events (n = 7 events as per MedDRA preferred terms, i.e. affect lability, anxiety, and loss of libido, hypersensitivity, amnesia, headache and alopecia). There was no discontinuation due to weight increase, renal or bone adverse events related to B/F/TAF during follow-up.

Laboratory parameters

Small changes in the lipid profile and in renal function were detected at M12. Slight increases in lipids and creatinine as well a decrease in eGFR (median [IQR] change, −17.78 mg/dL [-41.12, −4.84] [n = 20]), were found in the TN group. Reductions from baseline were observed for total cholesterol and LDL in the TE group A small reduction was also seen in the eGFR level (consistent with the known inhibitory effect of bictegravir on renal tubular secretion of creatinine) (Figure 3).

Body weight changes

Body weight changes and body mass index changes throughout the course of the observation period were assessed for 137/201 (68%) (20/29 [69%] TN, 117/172 [68%]

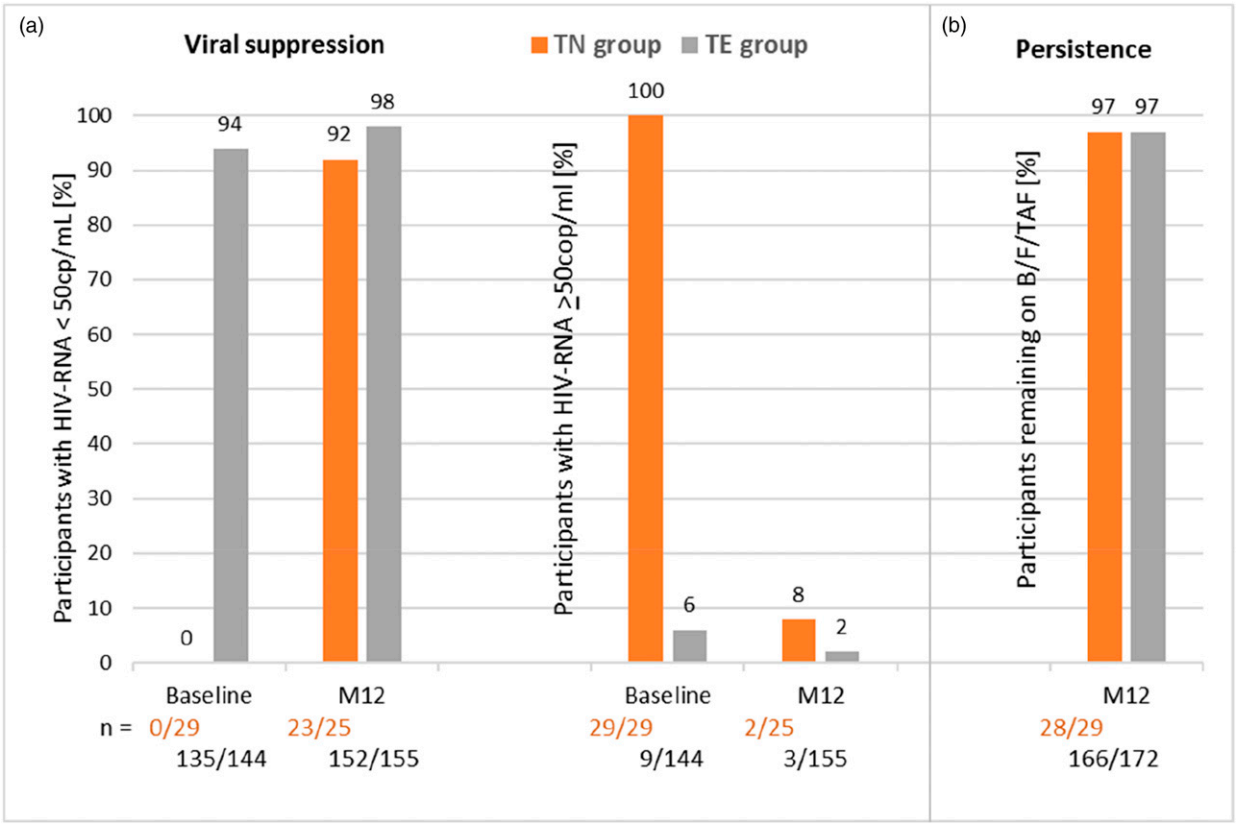

Figure 2. a&b. Virologic outcomes (HIV-1 RNA <50 copies/mL, M = E analyses) and persistence at M12. M = E, missing = excluded analysis: only values available within the time windows are analyzed. Time window is as follows: M12 (month 12) = 9–18 months; TN = treatment-naive; TE = treatment experienced.

TE) participants remaining on B/F/TAF and with data available at baseline and at M12. At M12, a median absolute weight change of +1.0 kg (−1.5, 8.5) was observed in TN participants. Overall, weight in TE remained stable with a median weight change of +0.0 kg (−2.0, 3.0) (p = .153, signed rank test). In 7/20 (35%) TN and 22/117 (19%) TE participants, relative weight gain was >5%. A >10% relative weight gain was documented for 5/20 (25%) TN participants and 7/117 (6%) TE participants. A weight loss of >5% was observed in 3/20 (15%) TN and in 15/117 (13%) TE participants; 2/117 (2%) TE participants experienced a >10% weight loss.

At M12, a median absolute BMI change of +0.4 kg/m^2 (−0.5, 2.7) was observed in TN participants. Overall, BMI in TE remained stable with a median weight change of +0.0 kg/m^2 (−0.6, 1.0) (p = .125, signed rank test).

Patient-related outcomes (PROs)

HIV Symptom Index (HIV-SI) questionnaire

Sixteen TN (55%) and 120 TE participants (70%) completed the HIV-SI questionnaire at baseline and M12. At baseline, median bothersome counts were 5.0 (1.5, 8.0) in TN and 2.0 (1.0, 4.0) in TE participants. At M12, the median change in bothersome symptoms was −1.5 (−5.0, 0.0) (p = not available) for TN and 0.0 (−1.0, 1.0) (p = .591, signed rank test) for TE participants. For the item "changes in the way your body looks such as fat deposits or weight gain", median change in bothersome symptom was +1.5 (+1.0, +2.0) for TN and −1.0 (−2.0, +1.0, p = 1.0) for TE participants.

Treatment satisfaction: HIVTSQ in TE

Overall, 160/172 (93%) and 124/172 (72%) TE participants responded to the HIVTSQ status questionnaire at baseline and to the HIVTSQ change questionnaire at M12, respectively. The median treatment satisfaction status score was 58.0 (51.0, 60.0) at baseline. The median treatment satisfaction change score at M12 was +28.5 (+21.0, +30.0).

Discussion

In the Italian BICStaR cohort, reflecting routine clinical care, B/F/TAF showed high effectiveness with respect to the primary endpoint of viral suppression. After 12 months, HIV-1 RNA was <50 copies/mL in 95% of mostly treatment-experienced participants in the D = F analysis confirming the high persistence and virologic efficacy observed in clinical studies.[11]

Table 2. B/F/TAF-related adverse events.

DRAEs (SOC and PT)	Participants[a] (*n* = 11/201)	Events (*n* = 16)
Psychiatric disorders / nervous system disorders	4 (2.0%) / 4 (2.0%)	10
Insomnia	2 (1.0%)	2
Hypersomnia	1 (0.5%)	1
Affect lability	1 (0.5%)	1
Anxiety	1 (0.5%)	1
Loss of libido	1 (0.5%)	1
Amnesia	1 (0.5%)	1
Headache	1 (0.5%)	1
Paraesthesia	1 (0.5%)	1
Somnolence	1 (0.5%)	1
Gastrointestinal disorders	4 (2.0%)	4
Diarrhoea	1 (0.5%)	1
Nausea	1 (0.5%)	1
Tongue disorder	1 (0.5%)	1
Vomiting	1 (0.5%)	1
Skin and subcutaneous tissue disorders	2 (1.0%)	2
Alopecia	1 (0.5%)	1
Hyperhidrosis	1 (0.5%)	1

DRAE: drug-related adverse event; SOC: system organ class; PT: preferred term.

[a]if several events with the same preferred term were reported for the same patient, s/he is counted once for that term; the same rule applies for results by system organ class. All events experienced within 548 days (= upper bound of the 12-month time window) after B/F/TAF initiation and up to 30 days after B/F/TAF discontinuation were considered.

Adverse events observed in this cohort are consistent with those previously described for INSTIs and TAF.[24] Adverse events related to B/F/TAF were reported in 5% of participants, namely psychiatric disorders, nervous system disorders and gastrointestinal disorders, which led to discontinuation in three individuals only (1%). The discontinuation rate due to adverse events was low in the Italian BICStaR cohort. It was similar to that in clinical studies (occurrence ≤1%) and lower in number than that observed in a retrospective cohort study by Hoffmann et al. where B/F/TAF was discontinued by 3.3% of individuals after approximately 6 months due to adverse events, including neuropsychiatric effects.[6,7,25]

Reductions in the lipid parameters (TC and LDL) were detected in the treatment-experienced arm. Since the majority of TE participants (81%) were on a F/TAF-based ART prior to treatment with B/F/TAF, the observed decreases may be attributable to the change in the third agent, including boosted EVG or a boosted PI. Overall, TC/HDL ratio remained stable. A decrease in LDL and TC after 48 weeks on B/F/TAF was also observed by Lazzaro, et al. in a treatment-experienced population.[15]

The observed decreases in eGFR, primarily in the TN participants, are consistent with the known inhibitory effect of bictegravir (and other antiretroviral agents) on renal tubular secretion of creatinine mediated inhibition of two protein transporters, that is OCT-2 (organic cation transporter (2) and MATE-1 (multidrug and toxin extrusion protein 1), with no effect on actual glomerular filtration rate.[24,26]

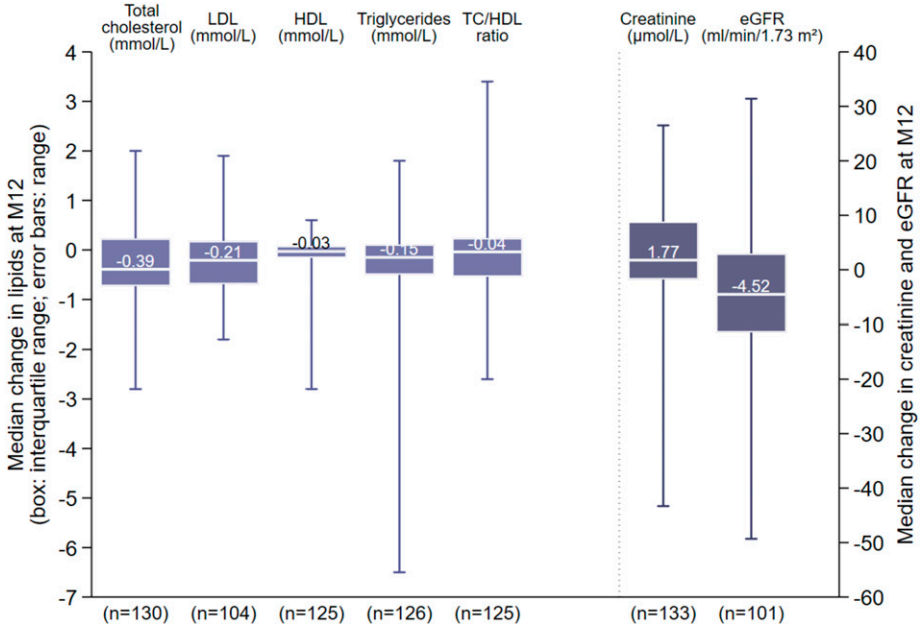

Figure 3. Change in laboratory parameters in TE participants from baseline to M12. Changes in the TN participants are not shown due to the small sample size.

Although often a multifactorial phenomenon, weight change associated with antiretroviral therapy has been a topic of research and discussion in recent years.[24] In the treatment-naïve group of the Italian BICSTaR cohort, a median weight gain of 1.0 kg was observed, with five out of 20 participants (25%) gaining >10%. Weight gain is expected in this patient population due to the "return to health" phenomenon associated with initial treatment of HIV, and it's notable that one-third of the TN participants in this cohort presented with an AIDS-defining condition. The SARS-CoV2 pandemic may also have had an influence on weight change in both TN and TE participants.[27] In the TE cohort, weight remained relatively stable during 12 months of treatment with B/F/TAF.

Bothersome HIV-related symptoms remained stable for those people previously on antiretroviral therapy. This is not surprising, considering that this group was successfully treated. The primary reason for the switch to B/F/TAF was to simplify therapy, with side effects of the previous ART regimen being a secondary reason. The impact of the switch to B/F/TAF may be reflected in the positive HVTSQc score at 12M, which suggests an improvement in treatment satisfaction compared to the previous ART regimen. Though numbers were small, positive changes in bothersome symptoms in the previously ART-naïve group were noted. This has also been shown in earlier studies.[28]

Comparing the 12-month results of the Italian BICSTaR cohort with those of the pooled analysis of the global BICSTaR programme involving 12 countries from Europe, Asia and North America shows that the Italian cohort had similar outcomes to the complete cohort, in particular with regard to the high treatment persistence (>95%) and virologic effectiveness.[17]

Several limitations to the study should be noted. First, the treatment-naïve group in the Italian BICSTaR cohort was quite small, with two thirds having >100,000 HIV-1 RNA copies/mL at baseline. Although impressive, the results cannot be generalised due to the limited sample size. Second, women are underrepresented in the BICSTaR cohort (Italy 17%, overall 16%). In Italy, nearly one-third (29%) of people with HIV are women.[29] Worldwide, girls and women make up more than half of the 37.7 million people living with HIV (UNAIDS 2021 estimates).[30] Third, changes in metabolic variables can only of be of descriptive nature for the national BICSTaR cohorts since outcomes are biased by the heterogeneity in baseline characteristics and treatment history; residual confounding may not be eliminated by statistical adjustment methods.

In conclusion, antiretroviral treatment with B/F/TAF demonstrated high effectiveness and persistence over 12 months in this real-world setting. This was in a population that was mostly treatment-experienced and virologically suppressed and that opted for a simpler regimen. Some of the TE participants had a history of virologic failure with drug resistance mutations. Moreover, B/F/TAF showed a favourable safety profile with few discontinuations due to adverse events.

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Author contributions

AA, GM, VE, SR, DC, EQR, BC, AS, MA and GDP contributed to participant accrual, clinical care, and data recording. All authors reviewed and critically revised the manuscript, approved the final draft, and agree to be accountable for the manuscript's accuracy and integrity.

Declaration of conflicting interests

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Ethics statement

Ethics approval and consent to participate

Approval was obtained from the Comitato Etico Regionale Marche (CERM), Comitato Etico Interregionale (Policlinico di Bari), Comitato Etico Di Brescia, Comitato Etico Milano Area 1, Comitato Etico Dell'Ospedale San Raffaele – Milano, Comitato Etico Milano Area 1, Comitato Etico Dell'Istituto Nazionale Per Le Malattie Infettive Lazzaro Spallanzani, Comitato Etico Indipendente Roma Fondazione PTV - Policlinico Tor Vergata, Comitato Etico Interaziendale Aou Città Della Salute e Della Scienza Di Torino, and Comitato Etico Campania 2.

All participants gave written informed consent.

Consent for publication

Not applicable.

Clinical trial registration

European cohort: EUPAS22185.

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Appendix

List of abbreviations

ART	antiretroviral therapy
B; BIC	bictegravir
BICSTaR	Bictegravir Single Tablet Regimen cohort study
CDC	Centers for Disease Control and Prevention
CI	confidence interval
D = F	discontinuation = failure
DRAE	drug-related adverse event
DRSAE	drug-related serious adverse event
eGFR	estimated glomerular filtration rate
F; FTC	emtricitabine
HDL	high density lipoprotein
HIV	human immunodeficiency virus
HIV-SI	HIV Symptom Index
HIVTSQc	HIV Treatment Satisfaction Questionnaire change
HIVTSQs	HIV Treatment Satisfaction Questionnaire status
HRQoL	health-related quality of life
INSTI	integrase strand transfer inhibitor
IQR	interquartile range
LDL	low density lipoprotein
M	month
M = E −	missing = excluded
MedDRA	Medical Dictionary for Regulatory Acivities
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleos(t)ide reverse transcriptase inhibitors
PLHIV	people living with HIV population
PRO	patient-reported outcome
PT	preferred terms
RAM	resistance-associated mutation
SF-36	Short-Form 36 health survey
SOC	systems organ classes
TAF	tenofovir alafenamide
TE	treatment-experienced
TN	treatment-naïve
VAS	visual analog scale