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Biktarvy® (BIC/FTC/TAF) BICSTaR Study

This document is in response to your request for information regarding Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) and available data from the BICSTaR real-world cohort study.

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The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.

Summary

BICSTaR: Real-World Data on BIC/FTC/TAF in PWH

BICSTaR is an ongoing, real-world, multicountry, observational cohort study of BIC/FTC/TAF in ARV-naive and TE participants that has demonstrated high rates of virologic suppression through 5 years of treatment (including in subgroup analyses of females, older adults, and late presenters) and 85% treatment persistence through 36 months. Over 5 years of treatment, there were low rates of D/C due to DRAEs.[1-5] PRO assessments were also evaluated at 12 months, 24 months, 4 years, and 5 years.[4-7]

BICSTaR: Real-World Data on BIC/FTC/TAF in PWH

Study Design[1]

BICSTaR is a large, ongoing, multicountry, prospective, observational cohort study in PWH that is evaluating the efficacy, safety, and tolerability of BIC/FTC/TAF in clinical practice. The study includes ARV-naive and TE participants from France, Germany, Ireland, Italy, the Netherlands, Spain, Turkey, UK, Canada, Israel, Singapore, South Korea, Taiwan, and Japan. The study outcomes include virologic suppression (HIV-1 RNA <50 c/mL); changes from BL in CD4 counts and CD4/8 ratios; treatment persistence, resistance status; AEs, SAEs, and DRAEs; and changes in weight, BMI, lipid levels, and renal function.

Pooled Analysis of 12-Month Data

A pooled analysis included data from 1509 participants across all participating countries who started BIC/FTC/TAF between June 2018 and May 2021. The analysis included ARV-naive (n=279) and TE (n=1230) participants who had BL and Month 12 data available and participants who had discontinued the study at the time of data cutoff. The most frequent reason for initiating BIC/FTC/TAF in ARV-naive participants was treatment

according to guidelines (82%), and a majority of TE participants switched to BIC/FTC/TAF to simplify their treatment regimen (58%).[1,8]

Table 1. BL Demographics and Disease Characteristics of Participants Treated With BIC/FTC/TAF for 12 Months (Esser et al)[1]

Key Demographics and Characteristics		ARV-Naive (n=279)	TE (n=1230)
Male, n (%)		251 (90)	1017 (82.7)
Age, median (Q1, Q3), years		38 (30, 47)	49 (39, 56)
≥50 years, n (%)		62 (22.2)	573 (46.6)
Weight, median (Q1, Q3), kg		70 (62, 81)	76 (66, 86)
Race, n (%)	White	193 (69.2)	947 (77)
	Asian	44 (15.8)	49 (4)
	Black	23 (8.2)	173 (14.1)
	American Indian/Alaska native	1 (0.4)	3 (0.2)
	Other	11 (3.9)	44 (3.6)
HIV-1 RNA	Median (Q1, Q3), log_{10} c/mL	4.79 (4.07, 5.29)	1.59 (1.28, 1.59)
	>100,000 c/mL, n (%)	102 (37.1)	8 (0.7)
	<50 c/mL, n (%)	3 (1.1)	996 (92)
CD4 count, median (Q1, Q3), cells/mcL		377 (194, 534)	667 (450, 876)
CD4/CD8 ratio, median (Q1, Q3)		0.36 (0.2, 0.6)	0.87 (0.59, 1.22)
Prior ART regimens, median (Q1, Q3), n		–	2 (1, 4)
Prior ART regimen, %	INSTI/NNRTI/PI	–	66.3/18.9/15.7
	TAF based	–	50.5
	TDF based	–	32.3
Time from HIV diagnosis to BIC/FTC/TAF initiation, median (Q1, Q3), days		20 (9, 45)	–
History of prior virologic failure, n (%)		–	141 (11.5)
≥1 preexisting PRM,[a] n (%)		21 (8)	137 (11)
Comorbidities, 1/2/≥3, %		23.8/12.3/15.9	23.9/15.9/31.9

[a]Overall rates of preexisting PRMs were the following: NRTI, 6%; NNRTI, 6%; PI, 3%; INSTI, <1%. The most common PRMs were K103N/S (ARV-naive, 2%; TE, 3%), M184V/I (ARV-naive, 0%; TE, 4%), and M46I/L (ARV-naive, 0%; TE, 1%).

Efficacy, resistance, and persistence[1]

Using an M=E analysis at Month 12, 94% of ARV-naive participants (221/236) and 97% of TE participants (977/1008) were virologically suppressed (HIV-1 RNA <50 c/mL). Rates of virologic suppression were high across all specified subgroups of ARV-naive and TE participants, including those who were female (100% and 97%, respectively), aged ≥50 years (89.4% and 96%), Black (100% and 96.4%), and had any BL PRM, including M184V/I (77.8% and 99%). Among ARV-naive participants, there was a significant difference in the rates of virological suppression between participants with a late HIV diagnosis and CD4 <200 cells/mcL vs CD4 ≥200 cells/mcL (85.5% vs 96.4%, respectively; *P*=0.006), as well as between participants with and without comorbidities at BL (89.8% vs 99%, respectively; *P*=0.017). Among TE participants, there was a significant difference in virologic suppression rates between participants with and without a history of neuropsychiatric symptoms at BL (94.6% vs 97.8%; *P*=0.008). No treatment-emergent resistance to the components of BIC/FTC/TAF was reported.

From BL to Month 12, median CD4 counts increased by 214 cells/mcL in ARV-naive participants (*P*<0.001) and by 13 cells/mcL in TE participants (*P*=0.014); median CD4/CD8 ratios increased by 0.3 and 0.03, respectively (each, *P*<0.001).

Treatment persistence was high: 97% of all ARV-naive participants (258/265) and 95% of all TE participants (1137/1201) continued to receive BIC/FTC/TAF treatment at Month 12.

Key safety parameters

From BL to 12 months, DRAEs were reported in 12.5% of ARV-naive participants (35/279) and 13% of TE participants (160/1230); overall, most DRAEs (94%) were mild to moderate in severity. The most frequently reported DRAEs in ARV-naive and TE participants were weight increased (10 [3.6%] and 42 [3.4%], respectively), headache (4 [1.4%] and 14 [1.1%]), nausea (3 [1.1%] and 9 [0.7%]), depression (1 [0.4%] and 11 [0.9%]), and fatigue (1 [0.4%] and 9 [0.7%]). Drug-related SAEs were reported in no ARV-naive participants and in 2 TE participants (0.2%). Through 12 months, 10 deaths were reported (ARV-naive, n=1; TE, n=9); none were considered to be treatment related. D/Cs due to DRAEs were reported in 11 ARV-naive participants (3.9%) and 73 TE participants (5.9%); the most common reasons for D/C were weight increased (1.7%), headache (0.6%), depression (0.5%), and fatigue (0.5%).[1]

From BL to Month 12, there were statistically significant increases in median body weight in both ARV-naive participants (3 kg; $P<0.001$) and TE participants (1 kg; $P<0.001$). An increase of >10% body weight was reported in 39 ARV-naive participants (26.5%) and 36 TE participants (5.3%). A decrease of >10% body weight was reported in 1 ARV-naive participant (0.7%) and 16 TE (2.3%) participants.[1]

Statistically significant increases in TC, LDL, and HDL (each, $P\leq0.001$) in the ARV-naive cohort and statistically significant reductions in TC, LDL, and triglycerides (each, $P<0.05$) in the TE cohort were reported. Significant decreases in median eGFR from BL to Month 12 were reported in both cohorts (ARV-naive, 9.24 mL/min/1.73m^2; TE, 3.11 mL/min/1.73m^2; each, $P<0.001$).[1,8]

PROs[1,8]

Treatment satisfaction scores, as measured by the HIVTSQs and HIVTSQc, were high at BL and improved from BL to Month 6 and Month 12 (Table 2).

Table 2. Treatment Satisfaction at BL and Change From BL to Month 6 and Month 12 in TE Participants (Esser et al)[1,8]

HIVTSQ		TE (n=1230)
Baseline	n	1134
	Total score, median (Q1, Q3)	56 (50, 60)
Month 6	n	628
	Change from BL in total score, median (Q1, Q3)	24 (13, 29)
Month 12	n	842
	Change from BL in total score, median (Q1, Q3)	25 (12, 29)

Subanalysis: TE participants with preexisting PRMs[9]

The efficacy and tolerability of 12 months of BIC/FTC/TAF treatment were assessed in TE participants with preexisting PRMs. Of the 996 participants who were virologically suppressed, 555 had no available genotype data and were considered not to have PRMs. Of the 441 participants with available genotype data at BL, 105 (24%) had preexisting PRMs (NRTI, n=66, 15%; NNRTI, n=56, 13%; PI, n=28, 6%; INSTI, n=1, 0.2%). Efficacy results at Month 12 are reported in Table 3.

Table 3. Month 12 Virologic Suppression by BL Status and Preexisting PRMs (M=E Analysis; Trottier et al)[9]

Month 12 Virologic Suppression, n/N (%)	BL Virologic Suppression[a]	BL Viremia[b]
Preexisting PRMs	78/79 (99)	9/9 (100)
Without preexisting PRMs	739/758 (98)	44/52 (85)

[a]HIV-1 RNA <50 c/mL. [b]HIV-1 RNA ≥50 c/mL.

Of the 20 participants with a detectable viral load at Month 12, 19 had no preexisting PRMs, and 1 participant with preexisting PRMs experienced an isolated blip (HIV-1 RNA, 78 c/mL) before becoming resuppressed by the next visit. A total of 130/996 participants (13%) experienced ≥1 DRAE, and 115 participants (12%) discontinued, with 56 D/Cs (6%) due to DRAEs through Month 12. No treatment-emergent PRMs to BIC/FTC/TAF were reported.

Pooled Analysis of 24-Month Data

The efficacy and safety of BIC/FTC/TAF in ARV-naive (n=483) or TE (n=1591) PWH were evaluated in a 24-month pooled analysis of data from clinical sites in all participating countries (data cutoff date of December 20, 2023).[2]

Table 4. BL Demographics and Disease Characteristics of Participants Treated With BIC/FTC/TAF for 24 Months (Trottier et al)[2]

Key Demographics and Characteristics		ARV-Naive (n=483)	TE (n=1591)
Male, n (%)		439 (90.9)	1328 (83.5)
Age, median (Q1, Q3), years		36 (29, 45)	48 (38, 55)
Race, White/Asian/Black, %		73.3/17.2/5	69/16.3/11.4
HIV-1 RNA <50 c/mL, n (%)		4 (0.8)	1259 (92.2)
CD4 count, median (Q1, Q3), cells/mcL		348.5 (182, 503.5)	665 (458, 868)
Weight,[a] median (Q1, Q3), kg		71 (62.7, 81)	74.6 (65, 85)
Comorbidities, 1/2/≥3, %		19.7/11.6/14.3	23.8/16.7/32.2
Prior ART regimen,[b] %	INSTI/NNRTI/PI	–	66.4/19.4/15.2
	TAF based	–	53.7
	TDF based	–	28.5

[a]ARV-naive, n=418; TE, n=1386.
[b]TE, n=1586.

Efficacy, resistance, and persistence[2]

At Month 24, 94% of ARV-naive participants (342/362) and 96% of TE participants (1198/1247) were virologically suppressed in an M=E analysis. In the ARV-naive cohort, high rates of virologic suppression were observed in participants according to sex (male, 94.3%; female, 96.7%), age (<50 years, 95.6%; 50–64 years, 89.1%; ≥65, 88.9%), race (White, 94.1%; Black, 100%; other, 94.8%), preexisting PRMs (yes, 100%; no, 94%), and comorbidities at BL (yes, 94.1%; no, 94.7%). There was a significant difference in the rates of virologic suppression at 24 months between participants with BL HIV-1 RNA ≤100,000 and >100,000 c/mL (96.8% and 92.1%, respectively; *P*=0.048). In the TE cohort, participants treated with BIC/FTC/TAF demonstrated high rates of virologic suppression at 24 months in subgroup analyses according to sex (male, 96.4%; female, 94.4%) age (<50 years, 96.2%; 50–64 years, 95.6%; ≥65, 97.7%), race (White, 96.2%; Black, 93.8%; other, 96.8%) and, preexisting PRM (yes, 96.6%; no, 96%), BL mutations (M184V/I alone, 100%; M184V/I + 1–2 TAMs, 100%; M184V/I + ≥3 TAMs, 83.3%), and comorbidities at BL

(yes, 96.1%; no, 96.1%). There was a significant difference in the rates of virologic suppression at 24 months between participants with BL HIV-1 RNA <50 and ≥50 c/mL (96.3% and 86.7%, respectively; *P*<0.001). No treatment-emergent resistance to the components of BIC/FTC/TAF was reported.

The median change from BL to 24 months in CD4 cell count was +257 cells/mcL in the ARV-naive group and +40 cells/mcL in the TE group (each, *P*<0.001); median CD4/CD8 ratios increased by 0.4 and 0.6, respectively (each, *P*<0.001).

At 24 months, 95% of all ARV-naive participants (400/420) and 91% of all TE participants (1346/1483) continued to receive BIC/FTC/TAF.

Subanalysis: adherence patterns among TE participants[10]

A subanalysis was conducted among 1496 TE participants with any VAS/missed doses data through 24 months to identify patterns of treatment adherence in TE participants switching to BIC/FTC/TAF, to identify significant associations between each treatment pattern and BL characteristics, and to determine effectiveness outcomes according to adherence pattern. Self-reported adherence data were collected at BL, 6 months, 12 months, and 24 months using a VAS adherence questionnaire and a report of missed doses in the last 4 and 30 days.

Patterns of adherence identified with GBTM are described in Table 5.

Table 5. BIC/FTC/TAF Adherence Patterns Identified With GBTM (Boffito et al)[10]

Adherence Group	Classification	Mean VAS Score
Group 1 (n=810; 54.1%)	Near-perfect adherence	99.7% at 24 months
Group 2 (n=457; 30.5%)	Consistent high adherence	96.4% at 24 months
Group 3 (n=107; 7.2%)	Moderate adherence	87.9% at 24 months
Group 4 (n=94; 6.3%)	Decreasing adherence	99.7% at BL to 91.4% at 24 months
Group 5 (n=28; 1.9%)	Increasing adherence	16.9% at BL to 89.6% at 24 months

In an M=E analysis at 24 months, virologic suppression was high (92–100%) among all groups, regardless of adherence pattern. Among participants who reported missing ≥4 doses of BIC/FTC/TAF in the last month at 6 months (n=25), 12 months (n=31), and 24 months (n=34), virologic suppression was maintained through 24 months in 92%, 100%, and 94% of participants, respectively.

With Group 1 (near-perfect adherence) as a reference group, participants <65 years of age were more likely to be associated with Group 3 (moderate adherence) than participants aged ≥65 years (aOR, 3.6; 95% CI: 1.5–8.6); participants <50 years of age were more likely to be associated with Group 4 (decreasing adherence) than participants aged ≥50 years (aOR, 2.7; 95% CI: 1.5–4.6); and participants with Black race or CD4 count <350 cells/mcL were more likely to be associated with Group 5 (increasing adherence) than participants of other races (aOR, 6.3; 95% CI: 2.2–18) or those with CD4 counts ≥350 cells/mcL (aOR, 3.39; 95% CI: 1.35–8.5).

Key safety parameters[2]

DRAEs were reported in 11.4% of ARV-naive participants (55/483) and 12.4% of TE participants (197/1591), and drug-related SAEs were reported in no ARV-naive participants and in 2 TE participants (0.1%). BIC/FTC/TAF D/Cs due to DRAEs were reported in 3.1% of ARV-naive participants (15/483) and in 5.6% of TE participants (89/1591), with weight increased (4 [0.8%] and 28 [1.8%], respectively), headache (3 [0.6%] and 7 [0.4%]), and

depression (0 and 11 [0.7%]) as the most frequently reported DRAEs that led to D/C. Deaths were reported in 2 ARV-naive participants and 11 TE participants; none were considered treatment related.

The median weight gain from BL to 24 months was 3.6 kg in the ARV-naive cohort and 1 kg in the TE cohort (each, *P*<0.001); the median changes in BMI were +1.2 and +0.4 kg/m^2, respectively.

From BL to 24 months, there were statistically significant increases in TC, LDL, HDL, triglycerides, and TC:HDL ratio (each, *P*<0.05) in the ARV-naive cohort and statistically significant reductions in TC, LDL, triglycerides, and TC: HDL ratio (each, *P*<0.05) in the TE cohort; no changes were considered clinically significant. Significant decreases in median eGFR from BL to 24 months were reported in both cohorts (ARV-naive, 11.18 mL/min/1.73m^2; TE, 5.11 mL/min/1.73m^2; each, *P*<0.001).

PROs[11]

A pooled analysis was conducted among TE participants in the BICSTaR Europe, Canada, Israel, Asia, and Japan cohorts, as well as the separate China cohort, to assess changes in QoL and treatment satisfaction after switching to BIC/FTC/TAF. The SF-36 was used to evaluate QoL in 3004 participants and was completed at BL and through Month 12 in the China cohort and through Month 24 in the BICSTaR cohorts. The HIVTSQs/c were used to assess treatment satisfaction at BL (n=3029) and through Month 12 (n=2109) in all cohorts. BL characteristics of participants in this analysis were similar to those in the overall study population. Overall, there were significant improvements in the median MCS and PCS of the SF-36 from BL to Month 6 (+1.3 and +0.6, respectively; each, *P*<0.001) and in the MCS from BL to Month 24 (+0.6; *P*=0.018). Treatment satisfaction was high at BL with a median HIVSQs score of 55/60 and significantly improved at Month 12, with a median HIVTSQc score of +27/+30 (*P*<0.001).

Pooled Analysis of 36-Month Data[3]

A total of 67 ARV-naive and 382 TE PWH in Germany, France, and Canada who completed 24 months of BIC/FTC/TAF participated in the extension phase, with a 36-month data cutoff date of August 12, 2022.

Table 6. BL Demographics and Disease Characteristics of Participants Treated With BIC/FTC/TAF for 36 Months (Sabranski et al)[3]

Key Demographics and Characteristics		ARV Naive (n=67)	TE (n=382)
Male, n (%)		62 (93)	338 (88)
Age, median (Q1, Q3), years		40 (32, 50)	50 (41, 56)
White/Black race, n (%)		59 (91)/4 (6)	318 (84)/34 (9)
HIV-1 RNA >100,000 c/mL, n (%)		22 (33)	1 (<1)
Weight, median (Q1, Q3), kg		72 (67, 83)	78 (67, 87)
BMI, median (Q1, Q3), kg/m^2		24 (22, 27)	25 (22, 28)
Any comorbidity, %		36 (54)	310 (81)
CD4 <350 / <200 cells/mcL and/or ≥1 AIDS-defining event, n (%)		24 (38) / 16 (25)	N/A
≥1 PRM, n (%)		6 (13)	41 (23)
Most common PRMs relevant to BIC/FTC/TAF, n (%)	NRTI overall / M184V/I	1 (2) / 0	23 (12) / 16 (8)
	INSTI overall / T97A	0 / 0	1 (1) / 1 (1)

Key Demographics and Characteristics		ARV Naive (n=67)	TE (n=382)
eGFR, n (%)	<60 mL/min/1.73 m^2	0	21 (7)
	≥60 mL/min/1.73 m^2	59 (100)	284 (93)

Efficacy, resistance, and persistence

According to the results of an M=E analysis, 97% of participants overall maintained virologic suppression at Month 36. In the TE group (n=367), treatment with BIC/FTC/TAF demonstrated high rates of virologic suppression at 36 months in subgroup analyses, including any preexisting PRM at BL (yes, 100%; no, 98%), eGFR at BL (<60 mL/min/1.73 m^2, 100%; ≥60 mL/min/1.73 m^2, 96%), and prior ART regimens (any DTG-based regimen, 97%; EVG/COBI/FTC/TAF, 95%; RPV/FTC/TAF, 100%). In the ARV group (n=60), high rates of virologic suppression were observed in participants with late diagnosis and CD4 count <200 cells/mcL and/or ≥1 AIDS-defining event at BL (yes, 91%; no, 98%), late diagnosis and CD4 count <350 cells/mcL and/or ≥1 AIDS-defining event at BL (yes, 95%; no, 97%), and eGFR ≥60 mL/min/1.73 m^2 (96%). For patients with data available at both BL and Month 36, the median change from BL to 36 months in CD4 cell count was +232 cells/mcL in the ARV-naive group (n=52; *P*<0.001) and +44 cells/mcL in the TE group (n=302; *P*<0.001). The median change from BL to 36 months in CD4/CD8 ratio was +0.5 in the ARV-naive group (n=51; *P*<0.001) and +0.06 in the TE group (n=268; *P*<0.001).

No treatment-emergent resistance to the components of BIC/FTC/TAF was reported. At 36 months, 86% of all ARV-naive participants (105/122) and 84% of all TE participants (557/659) continued to receive BIC/FTC/TAF (overall population, 85%).

Key safety parameters

Over 36 months, DRAEs were reported in 14% of participants in the overall population (ARV-naive, 16% [19/122]; TE, 14% [89/659]), with 7% of ARV-naive participants and 10% of TE participants experiencing a DRAE in the first 6 months of BIC/FTC/TAF initiation. DRAEs led to BIC/FTC/TAF D/C in 7% (n=54) of the overall population (ARV-naive, 5% [6/122]; TE, 7% [48/659]), with weight increase (ARV naive, 3% [4/122]; TE, 2% [15/659]) and depression (ARV naive, 0; TE, 1% [7/659]) being the most frequently reported DRAEs that led to D/C.

Among participants with available weight at BL and Month 36, the median (Q1, Q3) weight changes from BL were 4.3 (-0.5, 7.3) kg (*P*=0.003) in the ARV-naive group and 1.7 (-1, 4.3) kg (*P*<0.001) in the TE group. Among participants with available BMI data at BL and Month 36, the median (Q1, Q3) change was 1.5 (-0.1, 2.5) kg/m^2 (*P*=0.003) in the ARV-naive group and 0.5 (-0.3, 1.5) kg/m^2 (*P*<0.001) in the TE group. At 36 months, 48% of ARV-naive participants had a normal BMI. The median TC:HDL ratio was stable over 3 years, with a median TC:HDL ratio among ARV-naive participants of 4.18 at BL (n=67) and 4.11 at Year 3 (n=47). Among TE participants, the median TC:HDL ratio was 3.91 at BL (n=366) and 3.99 at Year 3 (n=255).

Pooled Analysis of 4-Year Data[4]

An analysis was conducted among participants from Canada, France, and Germany with ≥4 years of follow-up data (2 years in the main BICSTaR study plus 2 years in the extension phase) to assess the effectiveness and safety outcomes, QoL, and HIV symptom measures (data cutoff, September 1, 2023). The analysis population (N=800) included the

415 participants who had a 4-year visit or discontinued the study having initiated treatment ≥42 months prior to the data cutoff date (lower bound of the 4-year visit window).

Efficacy, resistance, and immunologic outcomes

According to the results of an M=E analysis at 48 months, 98% of the 51 ARV-naive participants and 97% of the 352 TE participants with available data were virologically suppressed (HIV-1 RNA <50 c/mL). No treatment-emergent resistance to the components of BIC/FTC/TAF was reported through 4 years of treatment.

CD4 cell counts and CD4/CD8 ratios improved significantly among all participants with available data through 4 years. The median (IQR) change from BL to 4 years in CD4 cell count was +350 (195–480) cells/mcL in the ARV-naive group (n=45; *P*<0.001) and +96 (-49 to +217) cells/mcL in the TE group (n=274; *P*<0.001). The median (IQR) change in CD4/CD8 ratio among ARV-naive (n=44) and TE participants (n=243) was +0.54 (0.33–0.81) and +0.1 (-0.02 to +0.23), respectively (each, *P*<0.001).

Key safety parameters

A summary of key safety data through 4 years of BIC/FTC/TAF treatment is presented in Table 7.

Table 7. Key Safety Results Through 4 Years of BIC/FTC/TAF Treatment (Analysis Population; Wong et al)[4]

Safety Parameter		ARV-Naive (n=125)	TE (n=675)	Total (N=800)
Any AE, n (%)		98 (78)	513 (76)	611 (76)
Any DRAE, n (%)		21 (17)	96 (14)	117 (15)
Most common DRAEs (≥1 participant), n (%)	Weight increased	9 (7)	25 (4)	34 (4)
	Fatigue	2 (2)	7 (1)	9 (1)
	Depression	1 (1)	11 (2)	12 (2)
	Nausea	1 (1)	8 (1)	9 (1)
	Diarrhea	0	7 (1)	7 (1)
	Flatulence	0	6 (1)	6 (1)
	Sleep disorder	0	6 (1)	6 (1)
	Arthralgia	0	5 (1)	5 (1)
	Headache	0	5 (1)	5 (1)
Serious DRAEs, n (%)		0	2 (<1)	2 (<1)
DRAEs that led to BIC/FTC/TAF D/C,[a] n (%)		6 (5)	52 (8)	58 (7)
BIC/FTC/TAF D/C within 4 years, n (%)		23 (18)	120 (18)	143 (18)
Main study phase (BL to 2 years)		14 (11)	91 (13)	118 (15)
Extension phase (2–4 years)		9 (7)	29 (4)	25 (3)
Time to D/C, median (IQR), months		21.9 (12.6–36.4)	13.5 (6.4–28.1)	14.5 (7.5–32.5)

[a]The most common DRAEs that led to BIC/FTC/TAF D/C were weight increased (n=21), depression (n=7), fatigue (n=6), and sleep disorder (n=5).

The median change in weight at 4 years among ARV-naive participants (n=30) was +4.4 kg from a BL median weight of 70 kg (*P*=0.019); the median change in weight among TE participants (n=295) was +1.6 kg from a BL median weight of 77 kg (*P*<0.001).
BMI increased over 4 years in both groups, with a median change of +1.6 kg/m^2 from a BL BMI of 22.9 kg/m^2 among ARV-naive participants (n=29; *P*=0.022) and +0.5 kg/m^2 from a BL of 24.7 kg/m^2 among TE participants (n=284; *P*<0.001).

PROs

From BL to 4 years, the median change in HIV-SI overall bothersome symptom count was -3 from a BL of 6.5 among ARV-naive participants (n=44; *P*=0.053) and remained stable at the BL median overall bothersome symptom count of 4 among TE participants (n=292; *P*=0.798). Among ARV-naive participants, the incidence of the following symptoms most relevant to the safety profile of BIC/FTC/TAF decreased from BL to 4 years: fatigue or loss of energy (from 69% to 52%), feeling sad/down/depressed (46% to 30%), diarrhea or loose bowel movements (35% to 21%), feeling dizzy or lightheaded (34% to 12%), headache (28% to 26%), and nausea or vomiting (19% to 5%).

QoL scores for the physical and mental health components of the SF-36 remained stable or increased from BL to 4 years among all participants with available data. In ARV-naive participants (n=38), the median PCS increased from 53 to 57 (*P*=1), and the median MCS increased significantly from 46 to 53 (*P*=0.03); in TE participants (n=251), the median PCS remained stable at 56 (*P*=0.569), and the median MCS increased from 48 to 51 (*P*=0.225).

Pooled Analysis of 5-Year Data[5]

An analysis was conducted among participants from Canada, France, and Germany with 5 years of follow-up data (2 years in the main BICSTaR study plus 3 years in the extension phase) to assess the effectiveness and safety outcomes, QoL, and HIV symptom measures (data cutoff, June 24, 2024). The analysis population (N=823) included the 380 participants who had a 5-year visit and those who discontinued the study having initiated treatment ≥54 months prior to the data cutoff date (lower bound of the 60-month visit window).

Efficacy, resistance, and immunologic outcomes

At 5 years, 98% of the 48 ARV-naive participants and 97% of the 316 TE participants were virologically suppressed per an M=E analysis. No treatment-emergent resistance to the components of BIC/FTC/TAF was reported through 5 years of treatment.

From BL to 5 years of treatment, median (IQR) changes in CD4 cell counts were +363.5 (261–550) cells/mcL in the ARV-naive cohort (n=42; *P*<0.05) and +91 (-67 to 221) cells/mcL in the TE cohort (n=236; *P*<0.05); median (IQR) changes in CD4/CD8 ratios were +0.5 (0.3–0.8) ARV-naive cohort (n=42; *P*<0.05) and +0.1 (0–0.3) in the TE cohort (n=206; *P*<0.05).

Key safety parameters

From BL to 5 years of BIC/FTC/TAF treatment, 42 and 134 DRAEs were reported in ARV-naive and TE participants, respectively. DRAEs reported in ≥1% of ARV-naive and TE participants were weight increase (12 [9.1%] and 25 [3.6%], respectively), fatigue (2 [1.5%] and 8 [1.2%]), nausea (2 [1.5%] and 8 [1.2%]), and depression (1 [0.8%] and 10 [1.4%]). One serious DRAE of depression was reported in a TE participant. DRAEs led to D/C in 7 ARV-naive participants (5%) and 56 TE participants (8%); most of these DRAEs occurred in the first 6 months of BIC/FTC/TAF treatment. Weight increase was the only DRAE that led to BIC/FTC/TAF D/C in ≥1% of participants overall (ARV-naive, n=5 [3.8%]; TE, n=17 [2.5%]).

The median weight gain from BL to 5 years was 4 kg in 36 ARV-naive participants and 2 kg among 240 TE participants with available data (each, *P*<0.05); median changes in BMI were +1.4 and +0.6 kg/m^2, respectively (each, *P*<0.05).

The only statistically significant changes in lipid profiles over 5 years of BIC/FTC/TAF treatment were a median increase of 0.4 mmol/L in LDL levels in the ARV-naive cohort and a median decrease of 0.2 mmol/L in triglycerides (each, $P<0.05$). Among participants with BL eGFR ≥90 mL/min/1.73m^2, significant decreases in median eGFR from BL to 5 years were reported in both cohorts (ARV-naive, 13 mL/min/1.73m^2; TE, 7.5 mL/min/1.73m^2; each, $P<0.05$).

PROs

Among participants with available data at BL and 5 years, the median changes in HIV-SI overall bothersome symptom count reflected significantly fewer symptoms compared with BL in 39 ARV-naive participants (change, -3; $P<0.001$) and no change in 235 TE participants (change, 0; $P=0.331$). Median HIVTSQ treatment satisfaction scores improved significantly, from a score of 57 at 3 months to a score of 58 at 5 years ($P=0.043$) among 36 ARV-naive participants and from a score of 55 at BL to 59 at 5 years among 263 TE participants ($P<0.001$).

The median PCS increased from 52.7 at BL to 58 at 5 years ($P=0.121$), and the MCS increased from 47.5 to 52.3 ($P=0.011$) in 34 ARV-naive participants; among 213 TE participants, the median PCS decreased from 56.2 to 55.5 ($P=0.013$), and the median MCS increased from 48.4 to 51.8 ($P=0.014$).

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Abbreviations

AE=adverse event
aOR=adjusted odds ratio
ART=antiretroviral therapy
ARV=antiretroviral
BIC=bictegravir
BICSTaR=BIC single-tablet regimen
BL=baseline
c/mL=copies per mL
CD4/8=clusters of differentiation 4/8
COBI=cobicistat
D/C=discontinuation
DRAE=drug-related adverse event
EVG=elvitegravir
FTC=emtricitabine
GBTM=group-based joint trajectory modeling
HIV-SI=HIV Symptom Index
HIVTSQ/c=HIV Treatment Satisfaction Questionnaire/change version
INSTI=integrase strand transfer inhibitor
M=E=missing=excluded
MCS=mental component summary
NRTI=nucleos(t)ide reverse transcriptase inhibitor
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
PCS=physical component summary
PI=protease inhibitor
PRM=primary resistance mutation
PRO=patient-reported outcome
PWH-people with HIV
Q=quartile
QoL=quality of life
RPV=rilpivirine
SAE=serious adverse event
SF-36=36-item Short Form Health Survey
TAF=tenofovir alafenamide
TAM=thymidine analog mutation
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TE=treatment-experienced
VAS=visual analog scale

Product Label

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