A retrospective, multicenter study on the efficacy, durability, and tolerability of bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) for the treatment of HIV in a real-world setting in Belgium

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HIV Drug Therapy GLASGOW 2022 | HYBRID 30 YEARS

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Background

- Several RCTs have demonstrated BIC/FTC/TAF to be a first-line option for treatment-naïve and experienced PLWH [1-4].
- Real-world studies provide complementary information to RCTs and ensure that those results can be generalized to broader populations seen in daily practice.
- The aim of this study was to describe the Belgian HIV population treated with BIC/FTC/TAF and to evaluate its efficacy, durability, and tolerability in a real-world setting.

Study Design

- This was an observational, retrospective, multicenter study. Data were gathered from routine practice at 11 participating HIV reference centers in Belgium which work in concert as members of the *Belgium Research on AIDS and HIV Consortium (BREACH)*.
- Inclusion criteria were treatment-naïve and experienced adult (aged ≥18 years) PLWH that received at least 1 dose of BIC/FTC/TAF between January 1, 2019, which corresponds to the date that BIC/FTC/TAF was approved for use in Belgium, and September 30, 2020.
- **The primary outcome** of this study was effectiveness of BIC/FTC/TAF, measured by the proportion of participants with a plasma HIV-1 VL <50 copies/ml at weeks 24 and 48 using an on-treatment analysis (on treatment, in follow-up, and with available data).
- **Secondary endpoints** included:

(i) Proportion of patients that experienced protocol-defined loss of virologic suppression by week 48 (defined as 2 consecutive HIV-1 VL measurements of >200 copies/mL in individuals who had initially achieved virologic suppression) along with an analysis of RAMs at the time of loss of virologic control
(ii) Safety and tolerability of BIC/FTC/TAF as assessed by the rate, incidence, reasons, and time to discontinuation of treatment over the 48-week study period
(iii) Overall change in weight along with the proportion of patients reporting a 5-10% and >10% weight gain at week 48
(iv) Proportion of patients that experienced a viral blip at any time up to week 24 and up to week 48 (defined as one HIV-1 VL measurement between 50 - 200 copies/mL after having initially achieved virologic suppression)
(v) Change in $CD4^+$ cell count and $CD4^+/CD8^+$ ratio at weeks 24 and 48
(vi) Change in lipid and glycemic parameters at weeks 24 and 48

Results

Study population

- A total of 2001 patients met the criteria for inclusion in this study with a median (IQR) follow-up time of 89.3 (65.6 – 110.4) weeks.

Table 1. Baseline characteristics of the study population.

	Overall (N = 2001)
Age (years), n (%)	
<50	1184 (59.2)
≥50	817 (40.8)
Gender, n (%)	
Male	1299 (64.9)
Female	702 (35.1)
Ethnicity, n (%)	
Caucasian	1145 (57.2)
Black Sub-Saharan African	646 (32.3)
Other	146 (7.3)
Unknown	64 (3.2)
Weight (kg)	
Median (IQR)	76 (67 – 87)
Data not available, n (%)	283 (14.1)
Co-morbidities, n (%)	
Diabetes mellitus	76 (3.8)
Coronary heart disease	16 (0.8)
Non-AIDS-defining malignancy	68 (3.4)
Chronic renal disease	3 (0.1)
Data not available	470 (23.5)
Co-infections	
HBV co-infection	93 (4.7)
HCV co-infection	82 (4.1)
Data not available	617 (30.8)
HIV acquisition, n (%)	
MSM	884 (44.2)
Heterosexual	866 (43.3)
Other	80 (4)
Unknown	171 (8.5)
HIV treatment status, n (%)	
Treatment-naïve	408 (20.4)
Treatment-experienced	1593 (79.6)
INSTI-experienced	1108 (55.4)
Prior AIDS defining illness, n (%)	510 (25.5)
Nadir $CD4^+$ T-cell count (cells/µL)	
Median (IQR)	308 (157 – 492)
Data not available, n (%)	51 (2.5)
Total time on cART prior to baseline (years)	
Median (IQR)	6 (0.9 – 12.3)
Number of cART regimens prior to baseline	
Median (IQR)	2 (1 – 4)
ARV resistance data available, n (%)	387 (19.3)
EFV resistance	53 (13.7)
3TC/FTC resistance	39 (10.1)
ABC resistance	37 (9.6)
RPV resistance	34 (8.8)
DRV resistance	24 (6.2)
TDF resistance	18 (4.7)
EVG/RAL resistance	9 (2.3)
Most common cART regimen prior to baseline, n (%)	
EVG/c/FTC/TAF	399 (19.9)
DTG + FTC/TAF	241 (12)
EFV/FTC/TDF	92 (4.6)
DRV/c/FTC/TAF	80 (4)
DTG + FTC/TDF	59 (2.9)
HIV-1 viral load (copies/mL), n (%)	
<50	1363 (68.1)
≥50	638 (31.9)
$CD4^+$ T-cell count (cells/µL)	
Median (IQR)	567 (367 – 793)
$CD4^+$ T-cell count (cells/µL), n (%)	
<350	418 (21)
350 – 499	327 (16.3)
≥500	1063 (53.1)
Data not available	193 (9.6)
$CD4^+/CD8^+$ ratio	
Median (IQR)	0.7 (0.4 – 1.1)
Data not available, n (%)	741 (37)

IQR, interquartile range; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; INSTI, integrase strand transfer inhibitor; cART, combined antiretroviral therapy; ARV, antiretroviral; EFV, efavirenz; 3TC, lamivudine; FTC, emtricitabine; ABC, abacavir; RPV, rilpivirine; DRV, darunavir; TDF, tenofovir disoproxil fumarate; EVG, elvitegravir; RAL, raltegravir; C, cobicistat; TAF, tenofovir alafenamide; DTG, dolutegravir.

Virologic suppression

- At week 48, 93.5% of the overall cohort maintained virologic suppression (on-treatment analysis).

Table 2. Rates of virologic suppression for the overall study population and various sub-groups at weeks 24 and 48.

	Week 24		Week 48	
	N	Rate of virologic suppression (%)	N	Rate of virologic suppression (%)
All participants	1611	92	1361	93.5
Age (years)				
<50	939	91.7	785	94
≥50	672	92.6	576	92.7
Gender				
Male	1061	91.6	885	93.8
Female	550	92.9	476	92.8
MSM	725	94.3	624	94.7
Black Sub-Saharan African	496	89.5	411	90.8
HIV treatment status				
Naïve	363	87.5	300	94
Experienced	1248	93.4	1061	93.2
INSTI-experienced	918	93.8	734	93.9
Total time on cART prior to baseline (years)				
≤6	1091	91.4	913	93.5
>6	520	93.5	448	93.3
Number of cART regimens prior to baseline				
≤2	693	91.6	566	93.9
>2	918	93.3	795	93.3
Baseline resistance				
EFV resistance	39	94.9	39	89.7
3TC/FTC resistance	33	84.8	30	83.3
ABC resistance	30	90	22	86.4
RPV resistance	32	87.5	26	88.5
DRV resistance	32	96.6	25	88
TDF resistance	17	94.1	14	78.6
EVG/RAL resistance	6	83.3	3	66.7
Regimen prior to baseline				
ABC-containing	195	92.8	153	92.2
TDF-containing	249	88.8	229	91.7
TAF-containing	791	94.6	638	94.5
RPV-containing	63	93.7	60	92.8
EFV-containing	92	89.1	74	89.2
DTG-containing	431	92.6	358	93.6
Baseline HIV-1 viral load (copies/mL)				
<50	1098	97.2	921	96.7
≥50	513	81.1	440	86.6
Baseline $CD4^+$ count (cells/µL)				
<350	379	81.5	308	86.8
350 – 499	264	93.6	222	94.6
≥500	968	95.3	831	95.7

N, number of participants on treatment, in follow-up, and with available data; MSM, men who have sex with men; INSTI, integrase strand transfer inhibitor; cART, combined antiretroviral therapy; EFV, efavirenz; 3TC, lamivudine; FTC, emtricitabine; ABC, abacavir; RPV, rilpivirine; DRV, darunavir; TDF, tenofovir disoproxil fumarate; EVG, elvitegravir; RAL, raltegravir; TAF, tenofovir alafenamide; DTG, dolutegravir.

Viral blips and loss of virologic suppression

- Viral blips were detected in 29 (1.4%) patients over the 48-week study period.
- Fourteen (0.7%) participants met the protocol-defined criteria for loss of virologic suppression and the occurrence of a viral blip prior to loss of virologic control was observed in 3/14 patients overall.
- At the time of loss of virologic suppression, one patient (with HIV subtype CRF06-cpx) had mutations associated with resistance to NRTIs (184V) and INSTIs (263KR), both of which were not present on resistance testing prior to baseline.

Table 3. Characteristics of the 14 participants with loss of virologic suppression by week 48.

P	Age	Gender/ Ethnicity	cART directly prior to baseline	RAMs prior to baseline	VL at baseline (copies/mL)	Number of viral blips prior to LVS, (copies/mL)	Time to LVS (weeks)	VL at time of LVS (copies/mL)	RAMs at LVS
1	51	M/C	DRV/c/FTC/TAF	NDA	101	Once, 168	36	218	NDA[a]
2	34	F/SSA	FTC/TAF + NVP	NDA	<50	None	48	397	NRTI: 67N, 70R, 184V
3	27	M/SSA	DTG/ABC/3TC	NDA	15300	None	48	1188	None
4	22	M/SSA	Naïve	None	<50	None	48	588000	NDA
5	33	F/SSA	DRV/c/FTC/TAF	None	1080	None	48	21000	NDA
6	46	F/C	DTG/ABC/3TC	NDA	12600	None	16	418	None
7	45	M/SSA	DRV/c/FTC/TAF	None	<50	None	27	385	NDA
8	55	F/SSA	ABC/3TC + DRV/r	NRTI: 184V INSTI: 66A, 92G	<50	None	32	578	NDA
9	51	M/SSA	Naïve	None	5152	None	17	2154	None
10	55	M/SSA	DTG + FTC/TAF	None	<50	Once, 77	37	457	None
11	31	M/C	Naïve	None	30233	None	42	11130	NDA
12	52	M/C	DTG + FTC/TAF	None	<50	None	48	22700	None
13	34	M/SSA	DRV/c/FTC/TAF	None	<50	None	48	89200	None
14	42	M/SSA	Naïve	None	932	Once, 182	48	836	NRTI: 184V; INSTI: 263KR

P, patient; cART, combined antiretroviral therapy; RAMs, resistance-associated mutations; VL, viral load; LVS, loss of virologic suppression; M, male; C, Caucasian; DRV/c, darunavir/cobicistat; FTC/TAF, emtricitabine/tenofovir alafenamide; NDA, no data available; F, female; SSA, black Sub-Saharan African; NVP, nevirapine; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; DTG, dolutegravir; ABC/3TC, abacavir/lamivudine; DRV/r, darunavir/ritonavir; INSTI, integrase strand transfer inhibitor.
[a]Viral load was below the required minimum to accurately perform resistance testing.

Treatment discontinuation

- Overall, 131 (6.5%) participants discontinued their treatment over the 48-week study period corresponding to an incidence of 7.4 discontinuations per 100 patient-years.
- Multivariable logistic regression analysis using baseline variables described in Table 1 showed that CNS/psychiatric toxicity resulting in the discontinuation of a previous cART regimen was significantly associated with discontinuation of BIC/FTC/TAF due to CNS/psychiatric toxicity (odds ratio [OR] 4.64; 95% confidence interval [CI] 1.24 – 17.38, p = 0.03).

Table 4. Reasons and time to treatment discontinuation over the 48-week study period.

Total number of discontinuations, (%)	131 (6.5)
Reasons for discontinuation, n (%)	
Neuropsychiatric adverse event	8 (0.4)
Gastrointestinal adverse event	8 (0.4)
Other adverse events	32 (1.6)
Switch to a two-drug regimen	26 (1.3)
Pregnancy (existing or intended)	7 (0.3)
Loss of virologic suppression	3 (0.1)
Other causes	19 (0.9)
Data not available	28 (1.4)
Time to discontinuation due to any reason (weeks)	
Median (IQR)	24.9 (8.4 – 35.1)
Time to discontinuation due to an adverse event (weeks)	
Median (IQR)	22.5 (4.7 – 35.3)
Time to discontinuation due to neuropsychiatric toxicity (weeks)	
Median (IQR)	18.1 (4.3 – 26.6)

IQR, inter-quartile range.

Change in weight

- At week 48, the median (IQR) on-treatment weight gain was 2 kg (-1 – 5) for the overall study population, which corresponds to a median percent change from baseline of 2.6%.
- Logistic regression analysis using variables described in Table 1 revealed that being on a TDF-based regimen prior to BIC/FTC/TAF initiation (odds ratio [OR] 2.29; 95% confidence interval [CI] 1.31 – 4, p = 0.006) and having a baseline $CD4^+$ count <350 cells/µL (OR 6.12; 95% CI 3.48 – 10.77, p < 0.001) were associated with a >10% weight gain.

Table 5. Change in weight at week 48 along with the proportion of patients experiencing 5-10% and >10% increase in weight from baseline for the study cohort and various sub-groups.

	Change in weight (kg) from baseline			
	N	Median (IQR)	5-10% increase from baseline	>10% increase from baseline
All patients	741	2 (-1 – 5)	19.2	11.6
Age (years)				
<50	435	2 (0 – 5)	20	13.6
≥50	306	1 (-1 – 4)	18	8.8
Gender				
Male	487	1 (-1 – 3)	17.9	12.2
Female	254	2 (0 – 5)	21.2	10.6
MSM	334	1 (-1 – 5)	20.1	8.7
SSA	250	2 (0 – 5)	19.6	12
HIV treatment status at baseline				
Naïve	160	3 (0 – 8)	21.3	25.6
Experienced	581	1 (-1 – 4)	17.8	7.6
INSTI-experienced	412	1 (-1 – 4)	17.4	7.2
Total time on cART prior to baseline (years)				
≤6	475	2 (0 – 5)	19.6	11.5
>6	266	1 (-1 – 4)	18.4	10.9
Number of cART regimens prior to baseline				
≤2	299	2 (1 – 5)	20.2	13.8
>2	442	1 (0 – 4)	18	9.9
Regimen prior to baseline				
ABC-containing	90	2 (0 – 4)	16.7	8.9
TDF-containing	96	3 (0 – 7)	29.7	20.8
TAF-containing	376	1 (-1 – 3)	16.2	4
RPV-containing	23	1 (-2 – 2)	19.4	11.9
EFV-containing	36	3 (0 – 7)	21.9	13.6
DTG-containing	197	1 (-1 – 4)	16.8	9.6
Baseline HIV-1 VL (copies/mL)				
<50	511	1 (-1 – 4)	17.6	6.5
≥50	230	4 (1 – 8)	22.6	23
Baseline $CD4^+$ count (cells/µL)				
<350	215	4 (1 – 9)	26.1	24.8
350 – 499	126	2 (0 – 5)	24.6	7.1
≥500	400	1 (-1 – 3)	13.2	7.6

N, number of participants on treatment, in follow-up, and with available data; IQR, inter-quartile range; MSM, men who have sex with men; SSA, black Sub-Saharan African; INSTI, integrase strand transfer inhibitor; cART, combined antiretroviral therapy; ABC, abacavir; TDF, tenofovir disoproxil fumarate; TAF, tenofovir alafenamide; RPV, rilpivirine; EFV, efavirenz; DTG, dolutegravir; VL, viral load.

Change in laboratory parameters

- At week 48, the median (IQR) change from baseline in absolute $CD4^+$ cell count and $CD4^+/CD8^+$ ratio was 50 (-50 – 172) cells/µL and 0.1 (0 – 0.2) respectively

Table 6. Change from baseline of laboratory parameters at week 48.

N	Laboratory parameter	Baseline	Change from baseline, median (IQR)	P-value
1303	$CD4^+$ T-cell count (cells/µL)	567 (367 – 793)	50 (-50 – 172)	0.57
898	$CD4^+/CD8^+$ ratio	0.7 (0.4 – 1.1)	0.1 (0 – 0.2)	0.17
805	Total cholesterol (mg/dL)	181 (154 – 208)	2 (-14 – 20)	0.87
769	HDL (mg/dL)	48 (39 – 60)	0 (-6 – 6)	0.69
729	LDL (mg/dL)	104 (82 – 126)	1 (-13 – 12)	0.30
801	Triglycerides (mg/dL)	110 (75 – 161)	-1 (-35 – 30)	0.97
730	FPG (mg/dL)	93 (85 – 102)	2 (-8 – 11)	0.10

N, number of participants on treatment, in follow-up, and with available data for the relevant parameter; IQR, inter-quartile range; HDL, high-density lipoprotein; LDL, low-density lipoprotein; FPG, fasting plasma glucose.

Conclusion

- The data presented in this real-world study show that BIC/FTC/TAF is highly effective at achieving and maintaining virologic suppression in various patient populations, including women, SSA patients, patients aged >50 years, treatment-naïve patients, and those switching from a previous regimen.
- In addition, BIC/FTC/TAF was shown to have a high genetic barrier to resistance with rare occurrence of emergent drug resistance.
- Treatment was well tolerated with infrequent discontinuations due to AEs and a minimal on-treatment weight gain was observed.
- These data support the use of BIC/FTC/TAF in clinical practice in a wide variety of PLWH.

Acknowledgements
We would like to thank everyone who contributed to this study including the study participants and investigators. This study was supported by a grant from Gilead International.

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