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

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Disclosures

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Background

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

David A Wohl, Yazdan Yazdanpanah, Axel Baumgarten, Amanda Clarke, Melanie A Thompson, Cynthia Brinson, Debbie Hagins, Moti N Ramgopal, Andrea Antinori, Xuelian Wei, Rima Acosta, Sean E Collins, Diana Brainard, Hal Martin

Co-formulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial

Hans-Jürgen Stellbrink, José R Arribas, Jeffrey L Stephens, Helmut Albrecht, Paul E Sax, Franco Maggiolo, Catherine Creticos, Claudia T Martorell, Xuelian Wei, Rima Acosta, Sean E Collins, Diana Brainard, Hal Martin

Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380–1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial

Paul E Sax, Anton Pozniak, M Luisa Montes, Ellen Koenig, Edwin DeJesus, Hans-Jürgen Stellbrink, Andrea Antinori, Kimberly Workowski, Jihad Slim, Jacques Reynes, Will Garner, Joseph Custodio, Kirsten White, Devi SenGupta, Andrew Cheng, Erin Quirk

Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial

Joel Gallant, Adriano Lazzarin, Anthony Mills, Chloe Orkin, Daniel Podzamczer, Pablo Tebas, Pierre-Marie Girard, Indira Brar, Eric S Daar, David Wohl, Jürgen Rockstroh, Xuelian Wei, Joseph Custodio, Kirsten White, Hal Martin, Andrew Cheng, Erin Quirk

Efficacy and safety of switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from boosted protease inhibitor-based regimens in virologically suppressed adults with HIV-1: 48 week results of a randomised, open-label, multicentre, phase 3, non-inferiority trial

Eric S Daar, Edwin DeJesus, Peter Ruane, Gordon Crofoot, Godson Oguchi, Catherine Creticos, Jürgen K Rockstroh, Jean-Michel Molina, Ellen Koenig, Ya-Pei Liu, Joseph Custodio, Kristen Andreatta, Hiba Graham, Andrew Cheng, Hal Martin, Erin Quirk

Switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from dolutegravir plus abacavir and lamivudine in virologically suppressed adults with HIV-1: 48 week results of a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial

Jean-Michel Molina, Douglas Ward, Indira Brar, Anthony Mills, Hans-Jürgen Stellbrink, Luis López-Cortés, Peter Ruane, Daniel Podzamczer, Cynthia Brinson, Joseph Custodio, Hui Liu, Kristen Andreatta, Hal Martin, Andrew Cheng, Erin Quirk

Wohl et al. Lancet HIV. 2019; Stellbrink et al. Lancet HIV. 2019; Sax et al. Lancet. 2017; Gallant et al. Lancet 2017; Daar et al. Lancet HIV. 2018; Molina et al. Lancet HIV. 2018.

- However, patients in RCTs are usually carefully selected which can sometimes lead to certain groups of patients being underrepresented such as women and people with diverse ethnic/racial backgrounds
  - Furthermore, participants in the clinical trial setting tend to exhibit higher levels of treatment adherence as compared to the real-world

- Real-world studies provide therefore, complementary information to the data obtained from RCTs and ensure that results from clinical trials can be generalized to broader populations seen in daily clinical practice

- The aim of this study was to describe the baseline characteristics of PLWH in Belgium being treated by BIC/FTC/TAF and to evaluate its' efficacy, durability, and tolerability in a real-world setting

Methodology

- *Study design and population*
  - This was an observational, retrospective, multicenter study (11 HIV reference centers)
  - Inclusion criteria were: (i) 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
  - If a patient had received BIC/FTC/TAF on multiple or separate occasions, only data from the first occurrence was included

- *Study variables*
  - **Patient characteristics** such age, gender, ethnicity/race, weight, and co-morbidities
  - **HIV-related characteristics** such as HIV treatment status at baseline, total time on cART and number of cART regimens prior to baseline, last cART regimen prior to baseline, reasons for BIC/FTC/TAF initiation, antiretroviral (ARV) resistance profile using the Stanford HIV Drug Resistance Database, version 9.0 (an ARV was considered resistant when substitutions conferring low level, intermediate-level, or high-level resistance were present), $CD4^+$ and $CD8^+$ cell counts, HIV-1 VL, and discontinuation of treatment
  - **Non-HIV-related laboratory characteristics** such as current hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infection, lipid panel, and plasma glucose

- *Study outcomes*
  - 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 analysis)
  - Secondary outcomes included:
    - 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 resistance-associated mutations (RAMs) at the time of loss of virologic control
    - Proportion of patients that experienced a viral blip at any time up to week 48 (defined as an HIV-1 VL measurement between 50 - 200 copies/mL after having initially achieved virologic suppression)
    - 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
    - Change in weight along with the proportion of patients reporting a 5-10% and >10% weight gain at week 48
    - Change in $CD4^+$ cell count and $CD4^+/CD8^+$ ratio at week 48
    - Change in lipid and glycemic parameters at week 48

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)	
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)

	Overall *(N = 2001)*
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)
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)

- The most frequent reasons for starting BIC/FTC/TAF were treatment simplification/decrease pill burden (61.1%) and treatment initiation for a naïve patient (20.4%)

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.

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Rates of virologic suppression 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
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.

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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	339300	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

HIV subtype ← CRF06-cpx

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.

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Poster #125

Development of Integrase Inhibitor Resistance Under Firstline Treatment With Bictegravir

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Identification of a treatment-emergent integrase resistance mutation in an HIV late-presenter on first-line therapy

V. Dauny[1], E. Gras[1], L. Levi[1], I. Devred[1], C. Poignon[2], S. Lambert-Niclot[2], E. Bourgogne[3], J. Pacanowski[1], J.-L. Meynard[1], K.

Case Report: Emergent Resistance in a Treatment-Naive Person With Human Immunodeficiency Virus Under Bictegravir-Based Therapy

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Braun et al. HIV Drug Therapy 2022. Poster 125.
Dauny et al. EACS 2021. Poster 209.
Chamberlain et al. Open Forum Infect Dis. 2021.

Reasons, rate, and time to treatment discontinuation over the 48 week study period

	Overall (*N* = 2001)
Total number of discontinuations, (%)	131 (6.5)
Reasons for discontinuation, n (%)	
CNS/psychiatric 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)
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)

CNS, central nervous system; IQR, inter-quartile range.

7.4 discontinuations per 100 patient-years

- The most frequent cART regimens prescribed after treatment discontinuation were dolutegravir/lamivudine (DTG/3TC; 40.5%) and doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF; 25.2%)

Regression analysis did reveal 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)

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Change in weight at week 48 along with the proportion of patients experiencing 5-10% and >10% increase in weight from baseline

	N	Median change in weight (kg) from baseline (IQR)	5-10% increase in weight from baseline (%)	>10% increase in weight 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
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

- Logistic regression analysis using baseline variables did not show age >50 years (p = 0.16), female gender (p = 0.48), or being of SSA origin (p = 0.78) to be associated with a >10% increase in weight
- However, regression analysis 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

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.

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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; 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.
- 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, the most common being CNS/psychiatric and gastrointestinal toxicity.
- On-treatment weight gain was minimal and was significantly associated with being on a TDF-based regimen prior to baseline and having a baseline $CD4^+$ count <350 cells/µL.
- These data support the use of BIC/FTC/TAF in clinical practice, both as a first-line and as a switch treatment option, in a wide variety of PLWH.

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