Effectiveness of dolutegravir-based antiretroviral therapy in a real-world setting in a belgian cohort of 4101 HIV patients

Running head: Dolutegravir real-world study

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Objective: To describe the treatment outcomes of patients receiving dolutegravir (DTG) in a 'real-world setting' in Belgium.

Design: Retrospective, observational, multicenter cohort.

Methods: Inclusion criteria: HIV-1 patients ≥18 years old having received DTG as part of their combined antiretroviral therapy (cART) between April 1, 2014 and December 1, 2017. Primary endpoint: rate of virologic suppression, defined as plasma HIV-1 viral load (VL) <50 copies/mL, at weeks 24, 48, and 96. Secondary endpoints: (i) durability, expressed as probability of experiencing loss of virologic suppression by week 96 (defined as 2 consecutive HIV-1 VL measurements of ≥200 copies/mL after having initially achieved virologic suppression), (ii) immunological response at weeks 24, 48, and 96, (iii) incidence of and reasons for DTG discontinuation, and (iv) change in weight at week 96.

Results: 4,101 patients were included. Through 96 weeks, virologic suppression rate was 96% (on-treatment analysis), probability of experiencing loss of virologic suppression was 7%, and mean increase in $CD4^+$ cell count was 100 cells/µL (SD 220). There were 785 (19.1%) discontinuations of DTG (8.9 discontinuations per 100 patient-years). The most common cause of discontinuation was an adverse drug reaction (ADR; 9.5%) with neuropsychiatric (NP) toxicity being the most prevalent (5.2%; 2.4 discontinuations per 100 patient-years). By week 96, the median change in weight for the study population was +2.0 kg (IQR -1.0 – 5.0).

Conclusion: In this large cohort, DTG showed excellent virologic efficacy and was generally well tolerated. Whether DTG results in undesirable weight gain or rather statistically significant results, remains a debate.

Keywords: HIV, dolutegravir, virologic suppression, neuropsychiatric toxicity, weight gain, real-world data

Introduction

Current international guidelines recommend dolutegravir (DTG), a second-generation integrase strand transfer inhibitor (INSTI), in combination with other antiretrovirals (ARVs) as a preferred option for the management of treatment-naïve and treatment-experienced HIV-1 patients [1-4]. Most of the available data concerning the use of DTG are based on controlled trials that may sometimes not reflect the everyday patient. As such, there is an increased interest for 'real-world data', gathered from heterogeneous patient populations by means of patient surveys and observational cohort studies [5]. Some 'real-world data' on DTG have been previously reported revealing some intriguing results such as increased neuropsychiatric (NP) and gastrointestinal (GI) toxicity, and excessive weight gain [6,7]. The objective of this study is to describe the treatment outcomes in various sub-populations of patients receiving DTG in a 'real-world setting' in Belgium.

Methods

Study design

We conducted a retrospective, observational, non-interventional, multicenter cohort study. Data were anonymously collected through the databases of six leading HIV reference centers (HRCs) in Belgium, which together with other centers, work in concert as members of the Belgian HIV Research Consortium (BREACH). The geographical distribution of the HRCs in various parts of the country allowed for an adequate sampling of the Belgian patient population receiving DTG. The databases used have a high concordance with pharmacological chart review and have been used repeatedly for population-based research in Belgium. The study was approved by the Ethics Committee of each participating institution and was conducted in accordance with the International Society for Pharmaco-Epidemiology (ISPE) guidelines for good epidemiology practices. The inclusion

criteria were as follows: male or female patients aged 18 years or above with confirmed HIV-1 infection having received at least one dose of DTG as part of their combined antiretroviral therapy (cART) between April 1, 2014 and December 1, 2017. If a patient was found to have received DTG on multiple or separate occasions, only data from the first occurrence of DTG use were included. Patients receiving DTG as part of a clinical trial or a medical need program (defined as a program in which a pharmaceutical company provides its medication(s) to a patient at no cost in the context of either an off-label use or as a potential life-saving measure) were excluded. Data collected included age, gender, ethnicity, weight, mode of HIV-1 acquisition, HIV treatment status, concomitant ARVs, $CD4^+$ cell count, HIV-1 viral load (VL), prior AIDS defining illnesses, and information concerning discontinuation of DTG including timing and reason. HIV treatment status was defined as: (i) naïve (never been treated with cART); (ii) experienced (currently being treated or has been previously treated with cART); and (iii) highly treatment experienced (HTE; patients with a treatment history of at least 3 core agent switches from at least 3 separate classes of ARVs [protease inhibitors, non-nucleoside reverse transcriptase inhibitors, and INSTIs], i.e. being on their 4th or higher line of treatment).

The primary endpoint of this study was to measure the rate of virologic suppression while on DTG-based cART, defined as plasma HIV-1 VL <50 copies/mL, at weeks 24, 48, and 96. Secondary endpoints included (i) durability of treatment, expressed as a survival probability estimate of experiencing protocol-defined loss of virologic suppression by week 96 (defined as 2 consecutive HIV-1 VL measurements of ≥200 copies/mL in patients who had initially achieved virologic suppression); (ii) immunological response, i.e. increase in $CD4^+$ cell count at weeks 24, 48, and 96; (iii) incidence of and reasons for discontinuation of DTG, defined as a treatment interruption for a

period of at least 90 days and classified according to the data collection on adverse events of anti-HIV drugs (D:A:D) classification; and (iv) change in weight at week 96.

Statistical analysis

Descriptive statistics on demographics were used to describe the overall study population in addition to 2 subsets of patients; men and women. Continuous variables were reported as the number of available and missing data, mean, standard deviation (SD), median, and inter-quartile range (IQR). Categorical values were conveyed as the number of available and missing data and as percentages. Where applicable, a strategy of complete case analysis was adopted for this study in order to take into account the presence of missing data. Analysis of both primary and secondary endpoints was performed on the overall study population in addition to several sub-groups that included men, women, men who have sex with men (MSM), black sub-Saharan African (SSA) patients; identified according to the United Nations Statistics Division classification [8], HIV treatment status, HIV-1 VL, and $CD4^+$ cell count stratified into categories of ≥500, 350-499, 200-349, and <200 cells/μL. The time points used for analysis were baseline (defined as the time at which DTG was initiated for each patient), and weeks 24, 48, and 96. An on-treatment analysis was used for the primary endpoint. The secondary endpoint of durability was evaluated using standard survival analysis by the Kaplan-Meier method and differences in survival probability estimates were analyzed using the log-rank test. Variables were compared using the Wilcoxon rank-sum test, the Kruskal-Wallis test, and the chi-square test. 2-sided p-values < 0.05 were considered statistically significant. Univariable and multivariable logistic regression analyses were performed to examine associations between baseline variables and (i) discontinuation of DTG due to NP toxicity and (ii) weight gain whilst on DTG. Participants' characteristics with $p < 0.05$ in the univariable analyses were considered as potential confounding factors and were included in the multivariable logistic

regression analysis. All statistical analyses were conducted using Statistical Analysis System (SAS®) software v9.4 (SAS® Institute, Inc., Cary, North Carolina, USA).

Results

Study population

We included a total of 4,101 patients with a median follow-up of 120.6 weeks (IQR 72.1 – 154.6). Baseline characteristics of the study participants are summarized in Table 1. A significant proportion of patients were female (32.7%); median age was 46.1 years (IQR 37.2 – 53.8). The two most common ethnicities were Caucasian (57.7%) and SSA (33.9%). Acquisition of HIV-1 was predominantly through sexual exposure (90.2%) with MSM accounting for 43.4% of the study cohort. At baseline, 79.8% of patients were treatment-experienced (of which 8.2% were HTE), 57.4% had a $CD4^+$ cell count ≥500 cells/µL, and 68.6% had an HIV-1 VL <50 copies/mL. The most frequently prescribed concomitant ARV backbones were abacavir/lamivudine (ABC/3TC; 59%) followed by tenofovir disoproxil fumarate/emtricitabine (TDF/FTC; 17.1%). 7.9% of patients did not have a nucleoside/nucleotide reverse-transcriptase inhibitor (NRTI) as their cART backbone and 6.8% received a 2-drug regimen (2DR; DTG with a single companion ARV).

Virologic suppression

The rate of virologic suppression at weeks 24, 48, and 96 for the overall study population and for the various sub-groups are shown on Table 2. At 96 weeks, virologic suppression rate was 96% for the overall cohort with similar rates observed across the various sub-groups. Compared to the overall study population, a lower but statistically non-significant rate of virologic suppression was seen in SSA patients (93%), in patients with baseline $CD4^+$ cell count <350 cells/µL (93%), and in patients with baseline HIV-1 VL ≥50 copies/mL (92%).

Durability of DTG-based therapy

Probability of experiencing loss of virologic suppression by week 96 was 7%, with no significant differences amongst gender, ethnicity, or HIV treatment status. However, the probability of experiencing loss of virologic suppression was higher when comparing non-MSM vs. MSM sub-groups (8% vs. 6%; $p = 0.01$) and in patients with baseline $CD4^+$ cell count <200 vs. ≥200 cells/µL (17% vs. 6%; $p < 0.0001$). No INSTI resistance associated mutations were detected amongst patients experiencing loss of virologic suppression. Overall, the median HIV-1 VL at confirmation of loss of virologic suppression was 591 copies/mL (IQR 219 – 905).

Immunological response

An increase in $CD4^+$ cell count was observed across all sub-groups with a mean increase of 76 (SD 186), 89 (SD 205), and 100 (SD 220) cells/µL for the overall study population at weeks 24, 48, and 96 respectively. As expected, mean increase in $CD4^+$ cell count at week 96 was higher in cART-naïve patients (289 cells/µL; SD 233) than in cART-experienced patients (60 cells/µL; SD 195).

Discontinuation and adverse drug reactions

Over the course of the study period, there were 785 (19.1%) discontinuations of DTG corresponding to an incidence of 8.9 discontinuations per 100 patient-years. The most common cause of discontinuation was an adverse drug reaction (ADR; 9.5%) followed by patient's request (2.3%). Other causes included treatment simplification (1.3%), pregnancy or intention to become pregnant (1.2%), non-compliance (0.5%), and drug-drug interactions (0.1%), amongst others. The most frequent ADRs resulting in discontinuation were NP toxicity (5.2%; 2.4 discontinuations per 100 patient-years) and GI toxicity (1.4%; 0.64 discontinuations per 100 patient-years). Other causes, each representing less than 1%, included hypersensitivity reaction, liver, and renal toxicity.

In the multivariable logistic regression analysis, age ≥50 years (odds ratio [OR] 1.45; 95% confidence interval [CI] 1.04 – 2.04, p = 0.031), being SSA (OR 1.68; 95% CI 1.17 – 2.42, p = 0.005), baseline $CD4^+$ cell count <350 cells/µL (OR 1.62; 95% CI 1.03 – 2.57, p = 0.038), and a backbone of ABC/3TC (OR 1.52; 95% CI 1.07 – 2.15, p = 0.019) were associated with DTG discontinuation due to NP toxicity (Table 3).

Change in weight

By week 96, median weight gain for the overall study population was 2.0 kg (IQR -1.0 – 5.0) with the lowest weight gain being observed in the HTE sub-group and the largest in patients with baseline $CD4^+$ cell count <200 cells/µL (Figure 1). The cut-off used for multivariable logistic regression analysis of on-treatment weight gain was ≥5 kg (≥75th percentile). Being cART-naïve at baseline (OR 2.60; 95% CI 1.62 – 4.19, p < 0.0001), baseline HIV-1 VL ≥50 copies/mL (OR 2.58; 95% CI 1.83 – 3.70, p = 0.001), and baseline $CD4^+$ cell count <200 cells/µL (OR 3.15; 95% CI 1.77 – 5.61, p = 0.0001) were associated with a ≥5 kg on-treatment weight gain (Table 4).

Two-drug regimen sub-population

280 (6.8%) patients received a 2DR at baseline. The majority of patients were male (62.9%), Caucasian (50.4%), and the median age was 50.7 years (IQR 44.7 – 57.3). Most patients (92.5%) were treatment-experienced, 58.4% had a $CD4^+$ cell count ≥500 cells/µL, 8.2% had a $CD4^+$ cell count <200 cells/µL, and 37.6% had an HIV-1 VL ≥50 copies/mL. The most frequent companion ARVs were darunavir/cobicistat (27.9%), darunavir/ritonavir (27.5%), rilpivirine (13.9%), lamivudine (10.4%), and abacavir (7.1%).

At week 96, there was no significant difference in rate of virologic suppression (92%; p = 0.36), immunological response (M = 84 cells/µL; SD 193, p = 0.48), and probability of experiencing loss of virologic suppression (8%; p = 0.38) when compared to patients on triple therapy. The

probability of experiencing loss of virologic suppression was higher when comparing patients with baseline $CD4^+$ cell count <200 vs. ≥200 cells/µL (28% vs. 8%; p = 0.01). The all-cause incidence of DTG discontinuation was lower than those on triple therapy (5.8 vs. 8.9 discontinuations per 100 patient-years; p = 0.002) with ADRs representing the most common cause of discontinuation (6.1%). NP toxicity was the most frequent ADR-induced discontinuation with an incidence of 1.2 discontinuations per 100 patient-years (vs. 2.4 discontinuations per 100 patient-years for patients on triple therapy; p = 0.44). There was no significant difference in median weight gain at week 96 (2.0 kg; IQR 1 – 6, p = 0.3).

Discussion

The landscape of the HIV population in Belgium is continuously changing. New HIV infections diagnosed in 2017 decreased by 2% compared to 2016 and by 27.5% compared to 2012 [9], implying a relative increase in the number of treatment-experienced patients when compared to treatment-naïve patients. This is reflected in our cohort with the majority of participants (79.8%) being treatment-experienced. Furthermore, Belgian guidelines for the management of people living with HIV (PLWH) recommend DTG as a preferred agent for the treatment of both cART-naïve and cART-experienced individuals. As such, the objective of this study was to illustrate the treatment outcomes of DTG-based cART in HIV-1 positive patients in a 'real-world setting', while characterizing the sub-populations receiving such treatment.

The results showed that 96% (on-treatment analysis) of the study population was virologically suppressed at week 96. This finding differs slightly from the data reported in clinical trials which used an intention-to-treat approach when presenting their results. The SINGLE and FLAMINGO trials, both phase 3 studies involving cART-naïve patients, reported a virologic

suppression rate of 88% at week 48 [10] and 80% at week 96 [11]. In the SAILING study, a phase 3 trial involving cART-experienced INSTI-naïve patients, the rate of virologic suppression was 71% at week 48 [12]. Furthermore, our study showed impressive week 96 virologic suppression rates across the various sub-groups including HTE patients (94%). However, we did observe a slightly lower, but statistically non-significant, rate of virologic suppression for patients with baseline $CD4^+$ cell count <350 cells/µL (93%; $p = 0.08$). In addition, patients underwent significant immunological recovery throughout the follow-up period, with treatment-naïve patients experiencing the greatest increase (65.2% over 96 weeks) in $CD4^+$ cell count.

The probability of experiencing loss of virologic suppression at week 96 was significantly higher when comparing patients with baseline $CD4^+$ cell count <200 vs. ≥200 cells/µL ($p < 0.0001$). There are reports concerning the inversely proportional relationship between $CD4^+$ cell counts prior to initiation of cART and the occurrence of virologic failure after having achieved virologic suppression [13,14]. In the study by Miller et al., the authors concluded that lower baseline $CD4^+$ cell counts were associated with an increased risk of viral rebound [15]. Some authors have suggested that the size of the viral reservoir is perhaps the most essential determinant of virologic failure [16,17]. The presence of an inverse correlation between levels of cell-associated HIV DNA and $CD4^+$ nadir has been documented, suggesting that the extent of $CD4^+$ depletion strongly predicts HIV reservoir size and in turn, virologic failure [17].

The rates of DTG discontinuation due to any ADR and to NP toxicity specifically were 9.5% and 5.2% respectively. In the investigational trials SINGLE, FLAMINGO, SAILING, and SPRING-2, the discontinuation rates due to any ADR were 2-3% [10-12,18], whereas in several observational studies, the rates varied between 3.8% and 13.7% [19-24]. In terms of DTG discontinuation due to NP toxicity, the results described in the literature range between 0.7% and 5.6% [19-24]. Potential

factors that may explain the discrepant discontinuation rates between observational studies such as ours and investigational trials include the heterogeneous composition of the study populations, the duration of follow-up, and the observational design. In line with previous reports, our findings showed that age ≥50 years and having an ABC/3TC backbone were significantly associated with DTG discontinuation due to NP toxicity [20-24]. In addition, we found that being SSA and having a baseline $CD4^+$ cell count <350 cells/µL were also significant risk factors. In contrast to previous studies reporting female gender to be significantly associated with DTG discontinuation due to NP toxicity [22-24], our study showed neither gender to be a significant risk factor.

There is growing evidence that the use of INSTIs and specifically DTG could lead to significant increases in weight [25,26]. Consistent with data previously reported, being treatment-naïve at baseline, having a detectable HIV-1 VL at baseline, and baseline $CD4^+$ cell count <200 cells/µL were significantly associated with the most weight gain [26,27]. In contrast to previous studies reporting both gender and ethnicity to be associated with significant weight gain [28, 29], we found neither to be significant risk factors, a result which has been previously described [26]. We put forward two possible explanations for this finding in our cohort. First, Belgian guidelines stipulate that the management of PLWH occur at designated HRCs and that these patients be followed by a multi-disciplinary team that includes a dietitian. As such, patients receive prompt dietary recommendations whenever issues such as weight gain begin to arise. Second, the environment surrounding the participants in this study may be relatively less obesogenic as compared to other settings and this can have an influence on the participant's dietary and exercise habits. Therefore, these aforementioned factors may have affected the extent of weight gain, or lack thereof, observed in our cohort. Nevertheless, there are two aspects to on-treatment weight gain that must be distinguished. First, is the 'return to health' phenomenon, which describes a

desirable weight gain following resolution of a catabolic illness [30]. This phenomenon is observed in patients after treatment initiation and is hypothesized to be due to a reduction in basal metabolic rate following virologic suppression, diminution in the rate of protein turnover, and improved appetite due to a lower inflammatory effect on the hypothalamus [31]. Therefore, it would be expected that the greatest weight gains would occur in patients with advanced and/or untreated HIV infection given that they are in a state of increased catabolism and inflammation at the time of cART initiation [32,33]. Hence, the on-treatment weight gain that these patients experience is in fact partly due to a restoration of their healthy pre-infection weight, which will in turn lead to more effective virologic suppression, higher $CD4^+$ cell counts, slower disease progression, and decreased mortality [34,35]. However, when these patients surpass their target 'return to health' weight or when well-controlled HIV patients experience on-treatment weight gain despite them already being at their respective healthy weight target, this is considered to be an *undesirable* weight gain which may lead to negative outcomes. It is known that PLWH are at higher risk for cardiovascular disease (CVD) [36] and diabetes mellitus (DM) [37], and likewise, it has been demonstrated that disproportionate on-treatment weight gain is a risk factor for CVD and DM [38,39]. In addition, changes to body fat while on cART can be detrimental to self-perception resulting in decreased adherence [40]. It seems therefore, that the requisite for how best to manage on-treatment weight gain lies in the answer to the following fundamental question; where should physicians and patients alike draw the line on how much weight gain should be encouraged and accepted?

When considering patients that were prescribed a 2DR at baseline, rate of virologic suppression, durability, and immunological response were all similar to those on triple therapy, taking into consideration however, that the majority of these patients had a suppressed HIV-1 VL at baseline. It is worthwhile to note that none of the patients that experienced loss of virologic

suppression in this sub-group developed an INSTI associated resistance mutations. This finding is in line with previous reports [41,42] and serves as a reminder of the high genetic barrier of DTG. A statistically significant lower rate of all-cause discontinuations of DTG was observed. Furthermore, lower rates of discontinuation due to any ADR (6.1%) and due to NP toxicity (2.5%) were observed in this sub-group and were similar to those reported in the literature [42]. However, despite these lower incidences of discontinuation, these findings were not found to be statistically significant when compared to patients on triple therapy. The aforementioned results provide further support for the use of a DTG-based 2DR.

The strengths of this study are the substantial amount of data collected from the various HRCs throughout Belgium and the observational nature, which by definition, allows for 'real-world data' to be disclosed without intervention. The study also has some limitations. Due to its retrospective and multi-centered design, a fraction of data was missing for some of the variables included. Similarly, it was not possible to report on the seriousness and severity of the various ADRs nor was it possible to characterize them in detail. Owing to the very low proportion of patients receiving tenofovir alafenamide (TAF) as part of their backbone, it was not possible to include these patients weight gain analysis. Data on each individual's non-ARV medications and the presence of any psychological factors that may have influenced certain endpoints such as NP toxicity and weight gain were not recorded. Furthermore, data concerning the development of metabolic syndrome and other metabolic outcomes while on treatment with DTG in addition to data concerning the presence of pre-existing resistance associated mutations prior to baseline were not uniformly documented across the participating HRCs, rendering the reporting of these results not feasible.

Belgium is currently on the cusp of achieving the UNAIDS 90-90-90 goal with the most recent data from 2017 showing that 89.1% of PLWH knew their HIV status, 98% of all diagnosed PLWH

were receiving sustained cART, and 97% of all people receiving cART had viral suppression [9]. As such, this 'real-world' analysis has proven invaluable in the continuous pursuit of the UNAIDS 90-90-90 goal. The results provide further evidence that DTG has an excellent virologic efficacy in both cART-naïve and cART-experienced patients. The rates of ADR-induced and NP toxicity-induced discontinuations were low, albeit slightly higher than in clinical trials. Whether DTG results in undesirable weight gain or rather just statistically significant results, remains a debate. Given that DTG has taken its place in HIV treatment guidelines as a preferred option and given the existence of an ever-ageing HIV population, further investigation into the mechanism by which DTG may result in weight gain is paramount. Finally, the era of the DTG-based 2DR is upon us and a paradigm shift may be on the horizon. Large observational cohort studies are needed to determine those regimens' overall performance.

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Conflicts of interest

This study was supported by an unrestricted education grant provided by ViiV Healthcare, Belgium.

No potential conflict of interest was reported by the authors.

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Table 1. Baseline characteristics of the study population.

		Male	Female	Total
Number of participants (%)		2,758 (67.3)	1,343 (32.7)	4,101
Age (years)	Median (IQR)	46.7 (37.4 – 54.3)	44.8 (37 – 52.6)	46.1 (37.2 – 53.8)
Ethnicity, n (%)	Caucasian	2,065 (50.3)	302 (7.4)	2,367 (57.7)
	Black Sub-Saharan African	446 (10.9)	944 (23)	1,390 (33.9)
	Other	171 (4.1)	76 (1.9)	247 (6)
	Unknown	76 (1.9)	21 (0.5)	97 (2.4)
Weight (kg)	Median (IQR)	75 (66 – 84)	72 (61 – 81)	73.5 (64 – 83)
Mode of HIV acquisition, n (%)	Heterosexual	727 (17.8)	1,188 (29)	1,915 (46.8)
	MSM	1,782 (43.4)	—	1,782 (43.4)
	IVDU	47 (1.1)	16 (0.4)	63 (1.5)
	Transfusion related	19 (0.5)	20 (0.5)	39 (1)
	Vertical	26 (0.6)	33 (0.8)	59 (1.4)
	Other/Unknown	157 (3.8)	86 (2.1)	243 (5.9)
HIV treatment status, n (%)	Treatment-naïve	660 (16.1)	168 (4.1)	828 (20.2)
	Treatment-experienced	1,907 (46.5)	1,031 (25.1)	2,938 (71.6)
	HTE	191 (4.7)	144 (3.5)	335 (8.2)
HIV-1 viral load (copies/mL), (%)	≥50	32.2	29.8	31.4
	<50	67.8	70.2	68.6
$CD4^+$ T-cell count (cells/μL), n (%)	N available (missing)	2,204 (554)	1,083 (260)	3,287 (814)
	≥500	1,266 (38.5)	620 (18.9)	1,886 (57.4)
	350-499	487 (14.8)	203 (6.2)	690 (21)
	200-349	279 (8.5)	123 (3.7)	402 (12.2)
	<200	172 (5.2)	137 (4.2)	309 (9.4)
Prior AIDS defining illness, n (%)	Yes	519 (12.7)	328 (8)	847 (20.7)
	No	2,211 (53.9)	1,010 (24.6)	3,221 (78.5)
	Unknown	28 (0.7)	5 (0.1)	33 (0.8)
Concomitant backbone, n (%)	ABC/3TC	1627 (39.7)	794 (19.3)	2421 (59)
	TDF/FTC	496 (12.1)	204 (5)	700 (17.1)
	TAF/FTC	107 (2.6)	55 (1.3)	162 (3.9)
	Other NRTI	322 (7.9)	171 (4.2)	493 (12.1)
	No NRTI	206 (5)	119 (2.9)	325 (7.9)

IQR, interquartile range; MSM, men who have sex with men; IVDU, intravenous drug user; HTE, highly treatment-experienced; ABC, abacavir; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate; FTC, emtricitabine; TAF, tenofovir alafenamide; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor.

Table 2. Rates of virologic suppression (plasma HIV-1 viral load <50 copies/mL) for the overall study population and the various sub-groups at each time point.

	Baseline *N = 4,101*	**Week 24** *N = 3,385*	**Week 48** *N = 3,082*	**Week 96** *N = 2,122*
All study participants	69%	93%	94%	96%
Men	68%	93%	94%	97%
Women	70%	93%	94%	94%
MSM	68%	94%	95%	98%
SSA	70%	93%	94%	93%
Treatment-naïve	0.2%	90%	93%	97%
Treatment-experienced	85%	94%	94%	96%
Highly treatment-experienced	84%	93%	92%	94%
Baseline HIV-1 viral load (copies/mL)				
≥50	—	85%	88%	92%
<50	100%	98%	98%	98%
Baseline $CD4^+$ T-cell count (cells/µL)				
≥500	81%	95%	96%	97%
350-499	62%	94%	92%	96%
200-349	46%	92%	94%	93%
<200	25%	79%	87%	93%

N, number of participants studied; MSM, men who have sex with men; SSA, black sub-saharan african patients.

Table 3. Predictors of DTG discontinuation due to neuropsychiatric toxicity using multivariable logistic regression models.

Variable at baseline	OR (95% CI)	*p*-Value
Age ≥50 years	1.45 (1.04 – 2.04)	**0.031**
Women	0.76 (0.56 – 1.05)	0.1
SSA	1.68 (1.17 – 2.42)	**0.005**
Treatment-naïve	0.95 (0.68 – 1.37)	0.79
Highly treatment-experienced	0.66 (0.31 – 1.43)	0.29
HIV-1 VL ≥50 copies/mL	0.92 (0.67 – 1.27)	0.63
$CD4^+$ T-cell count <350 cells/µL	1.62 (1.03 – 2.57)	**0.038**
Prior AIDS defining illness	0.89 (0.62 – 1.28)	0.60
ABC/3TC	1.52 (1.07 – 2.15)	**0.019**

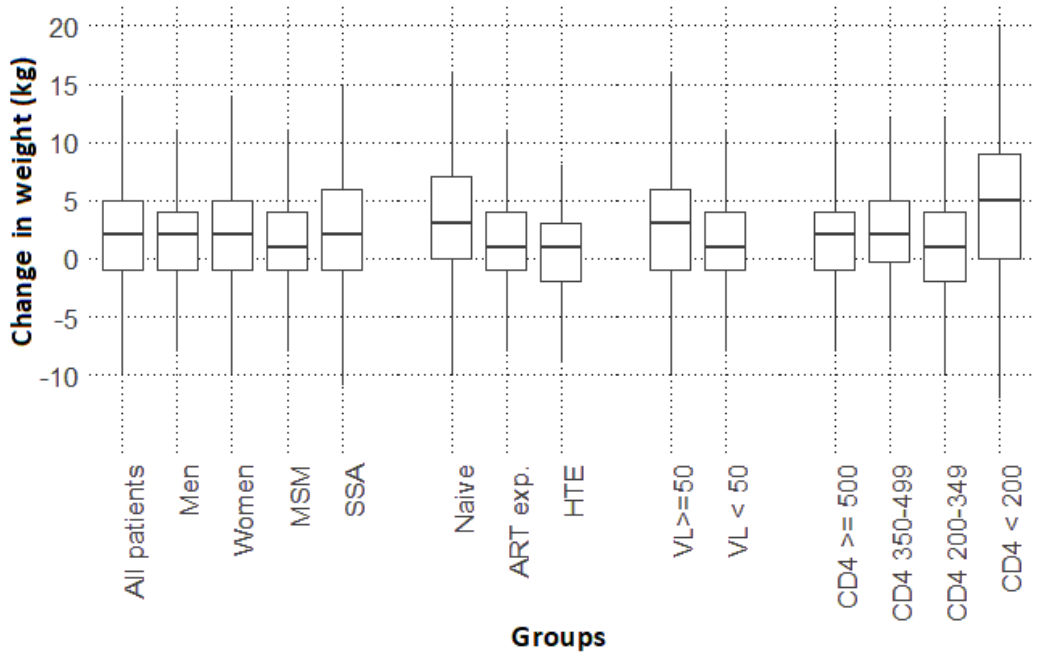
DTG, dolutegravir; OR, odds ratio; CI, confidence interval; SSA, black sub-saharan african patients; VL, viral load; ABC, abacavir; 3TC, lamivudine.

Table 4. Predictors of ≥ 5kg on-treatment weight gain at week 96 using multivariable logistic regression models.

Variable at baseline	OR (95% CI)	*p*-Value
Age, per 10 years older	0.83 (0.60 – 1.17)	0.31
Women	1.54 (0.97 – 2.46)	0.07
SSA	1.18 (0.74 – 1.88)	0.49
Treatment-naïve	2.60 (1.62 – 4.19)	**< 0.0001**
Highly treatment-experienced	0.65 (0.34 – 1.28)	0.23
HIV-1 VL ≥50 copies/mL	2.58 (1.83 – 3.70)	**0.001**
$CD4^+$ T-cell count <200 cells/μL	3.15 (1.77 – 5.61)	**0.0001**
Prior AIDS defining illness	1.57 (1.05 – 2.37)	0.08
ABC/3TC	0.82 (0.59 – 1.17)	0.26
TDF/FTC	0.84 (0.56 – 1.27)	0.45

OR, odds ratio; CI, confidence interval; SSA, black sub-saharan african patients; VL, viral load; ABC, abacavir; 3TC, lamivudine.

Figure 1. Median (range) change in weight at week 96 for the study cohort and for the various sub-groups with the following baseline characteristics.



MSM, men who have sex with men; SSA, black sub-saharan african patients; ART exp, antiretroviral treatment-experienced; HTE, highly treatment-experienced; VL, viral load.