Received: 3 February 2022 | Accepted: 14 July 2022

DOI: 10.1111/hiv.13373

ORIGINAL ARTICLE

Efficacy, durability, and tolerability of dolutegravir/lamivudine and dolutegravir/rilpivirine for the treatment of HIV in a real-world setting in Belgium

Rakan Nasreddine[1] | Jean Cyr Yombi[2] | Gilles Darcis[3] | Eric Florence[4] | Sabine D. Allard[5] | Marie-Angélique De Scheerder[6] | Sophie Henrard[7] | Rémy Demeester[8] | Peter Messiaen[9] | Nathalie Ausselet[10] | Matthias Loeckx[11] | Marc Delforge[1] | Stéphane De Wit[1] | on behalf of the Belgian Research on AIDS and HIV Consortium (BREACH)

[1]Saint-Pierre University Hospital, Brussels, Belgium

[2]Cliniques Universitaires Saint-Luc, Brussels, Belgium

[3]Liège University Hospital, Liège, Belgium

[4]Institute of Tropical Medicine, Antwerp, Belgium

[5]Universitair Ziekenhuis Brussel, Brussels, Belgium

[6]Ghent University Hospital, Ghent, Belgium

[7]University Clinics of Brussels – Erasme Hospital, Brussels, Belgium

[8]University Hospital of Charleroi, Lodelinsart, Belgium

[9]Jessa Hospital, Hasselt, Belgium

[10]UCL University Hospital Namur-Godinne, Yvoir, Belgium

[11]ViiV Healthcare, Belgium

Correspondence
Rakan Nasreddine, Division of Infectious Diseases, Saint-Pierre University Hospital, Rue Haute 322, 1000 Brussels, Belgium.
Email: rakan.nasreddine@stpierre-bru.be

Funding information
ViiV Healthcare

[Correction added on 13 March 2023, after first online publication: 'patient' and 'patients' were changed to 'person' and 'people' or 'participant/s' throughout the article to adhere to journal policy to support the use of people-first language.]

Abstract

Objectives: A paradigm shift from three-drug regimens to two-drug regimens (2DRs) is currently taking place in real-world clinical practice. This study aimed to describe the efficacy, durability, and tolerability of dolutegravir (DTG)/lamivudine (3TC) and DTG/rilpivirine (RPV) in a real-world setting.

Methods: This was a retrospective, observational, multicentre (ten centres in Belgium) study involving adult treatment-naïve and treatment-experienced people living with HIV on DTG/3TC or DTG/RPV between 1 January 2019 and 30 September 2020. The primary endpoint was rate of virological suppression (VS; plasma HIV-1 viral load [VL] <50 copies/ml) using an on-treatment analysis. Main secondary endpoints included the proportion of people that experienced loss of VS (LVS; defined as two consecutive HIV-1 VLs of >200 copies/ml after initially achieving VS) and a resistance analysis at the time of LVS; rate, incidence, and reasons for discontinuation of treatment (stopping treatment or changing any component of the 2DR); and change in weight, along with the proportion of people reporting a >10% weight gain. Ordinal logistic regression analysis examined associations between baseline variables and >10% on-treatment weight gain.

Results: Overall, 948 people were included, of whom 734 (77%) were on DTG/3TC and 214 (23%) were on DTG/RPV. Baseline characteristics included 54% aged ≥50 years, 31% female, 31% Black sub-Saharan African, 95% treatment-experienced, and 8% with HIV-1 VL ≥50 copies/ml. Through 48 weeks, the rate of VS for the overall cohort was 98.3% (99.1% with 3TC; 96.2% with RPV). LVS was observed in 0.5% ($n = 5$) of the overall population ($n = 1$ [3TC group], $n = 4$ [RPV group]). There were 40 treatment discontinuations (4.2%, $n = 27$ [3TC group]; $n = 13$ [RPV group]), corresponding to an incidence of 4.7 per 100 patient-years. The most common reason for discontinuation was an adverse event (1.4%), with neurotoxicity the most frequent (0.5%). Median on-treatment weight gain at week 48 was 1 kg (interquartile range [IQR] −1–3) overall, 1 kg

(IQR −1–3) in the 3TC group, and 2 kg (IQR 0–4) in the RPV group. A >10% weight increase was observed in 6.3% of people. Regression analysis showed that being on a tenofovir disoproxil fumarate-based regimen prior to 2DR initiation was the only variable associated with a >10% increase in weight from baseline (odds ratio 3.48; 95% confidence interval 1.13–10.68; $p = 0.038$).

Conclusion: In this real-world analysis, the 2DRs analysed were effective, durable, and safe for those who were treatment-naive and treatment-experienced. A slight increase in weight was associated with these regimens.

KEYWORDS

dolutegravir/lamivudine, dolutegravir/rilpivirine, HIV, real-world data, virological suppression

INTRODUCTION

Current international guidelines recommend the use of a three-drug combined antiretroviral therapy (cART) regimen for the treatment of most people living with HIV-1 [1–4]. However, these guidelines now also recommend the use of dolutegravir (DTG)-based two-drug regimens (2DRs) for treatment-naïve people (DTG + lamivudine [3TC]) and as a switch option for virologically suppressed people (DTG + 3TC or rilpivirine [RPV]) [1–3]. Support for the use of DTG-based 2DRs has come from several clinical trials that have shown these regimens to be as tolerable and effective as three-drug regimens (3DRs) in achieving and maintaining virological suppression [5–7]. As such, a paradigm shift from 3DRs to 2DRs is currently taking place in real-world clinical practice. However, one of the main concerns with 2DRs is the potential for a lower resistance barrier among those with poorer treatment compliance [8]. Adherence is frequently ≥95% in the clinical setting but <80% in the real world [9]. Furthermore, strict inclusion criteria for HIV drug trials can sometimes lead to certain groups of people being underrepresented, such as women and people with diverse ethnic/racial backgrounds. As such, there is a vital need for real-world data on DTG-based 2DRs to be able to evaluate virological outcomes and describe emerging side effects that were not described in clinical trials. The goal of this study was to describe the efficacy, durability, and tolerability of DTG/3TC and DTG/RPV in various sub-populations of people with HIV in a real-world setting in Belgium.

METHODS

Study design and population

We conducted a retrospective, observational, multicentre study. Electronic data capture collected study variables on people who met the inclusion criteria for this study. Data were gathered from routine practice at ten participating HIV reference centres (HRCs) in Belgium that work in concert as members of the Belgium Research on AIDS and HIV Consortium. This study was conducted in accordance with good clinical practice guidelines and the General Data Protection Regulation 2016/679. Study-specific informed consent was not required, as informed consent for the use of routinely obtained data from each participant had previously been obtained at each participating centre. Furthermore, the principal investigator or designee at each study site ensured that the dataset for each participant underwent coding/de-identification before data extraction. Ethical approval was obtained from a central ethics committee and from site-specific ethics committees before data collection. This method of research has been used repeatedly in the past and represents an accessible and reliable source of data. Moreover, since more than 90% of people living with HIV in Belgium are treated and monitored at these HRCs [10], and given their geographical distribution in various parts of the country, this allowed for an adequate sampling of the Belgian HIV population receiving DTG/3TC and DTG/RPV.

Inclusion criteria were treatment-naïve and treatment-experienced people living with HIV aged ≥18 years, having received at least one dose of DTG/3TC or DTG/RPV, either as a single- or dual-tablet regimen, between 1 January 2019 and 30 September 2020. People who fulfilled these criteria were included in the total population count at baseline. However, if a person did not have an HIV-related laboratory analysis performed at week 24 (a window of tolerance of ±8 weeks was used), then the person was withdrawn from the remainder of the study. If a person received DTG/3TC and/or DTG/RPV on multiple or separate occasions, only data from the first occurrence were included. People receiving a DTG-based 2DR as part of a clinical trial or a medical need programme (defined as a programme in which a

pharmaceutical company provides its medications to a patient at no cost in the context of either off-label use or a potential life-saving measure) were excluded. Data collected included (i) participant characteristics such as age, sex, ethnicity, weight, and co-morbidities; (ii) HIV-related data such as mode of HIV-1 acquisition, existence of a prior AIDS-defining illness, HIV treatment status at baseline, total time on cART prior to baseline, number of cART regimens prior to baseline, integrase strand transfer inhibitor (INSTI) experienced prior to baseline, last cART regimen prior to baseline, antiretroviral resistance profile, $CD4^+$ and $CD8^+$ cell counts, HIV-1 viral load (VL), and discontinuation of 2DR; and (iii) non-HIV-related laboratory data such hepatitis B virus (HBV) serology, lipid panel, and plasma glucose. Baseline was defined as the time at which DTG/3TC or DTG/RPV was initiated, and HIV treatment status was defined as naive (never been treated with cART) or experienced (currently being treated or previously treated with cART).

The primary endpoint of this study was to measure the rate of virological suppression while on DTG/3TC and DTG/RPV (defined as a plasma HIV-1 VL <50 copies/ml) at weeks 24 and 48. Secondary endpoints included (i) proportion of people that experienced protocol-defined loss of virological control by week 48 (defined as two consecutive HIV-1 VL measurements of >200 copies/ml in individuals who had initially experienced virological suppression) along with an analysis of resistance-associated mutations (RAMs) at the time of loss of virological control; (ii) proportion of people that experienced a viral blip at any time up to week 24 and up to week 48 (defined as one HIV-1 VL measurement of ≥50 copies/ml after having initially experienced virological suppression); (iii) rate and incidence of, reasons for, and time to discontinuation of treatment (defined as stopping treatment or changing any component of the 2DR) over the 48-week study period; (iv) the number of newly diagnosed HBV co-infections over the 48-week study period (defined as becoming HBV seropositive after initially being HBV seronegative at 2DR initiation); (v) overall change in weight, along with the proportion of people reporting a 5%–10% and >10% weight gain at week 48; (vi) change in $CD4^+$ cell count and $CD4^+/CD8^+$ ratio at weeks 24 and 48; and (vii) change in lipid and glycaemic parameters at weeks 24 and 48.

Statistical analysis

We used descriptive statistics to describe the overall study population and two pre-defined groups: those on DTG/3TC and those on DTG/RPV. We reported continuous variables as the number of available and missing data, mean, standard deviation (SD), median, and interquartile range (IQR). We conveyed categorical values as the number of available and missing data and as percentages and used a pairwise deletion approach for missing data. We compared continuous variables using the Wilcoxon rank-sum test and evaluated differences between proportions using Fisher's exact test. Two-sided p-values <0.05 were considered statistically significant. Both primary and secondary endpoints were analysed on the overall study population and on both treatment regimens. We also analysed some secondary endpoints on several sub-groups, including age, sex, men who have sex with men (MSM), Black sub-Saharan African (SSA) ethnicity (identified according to the United Nations Statistics Division classification [11]), HIV treatment status, time on cART prior to baseline, cART regimen immediately preceding 2DR initiation, and baseline HIV-1 VL and $CD4^+$ cell count. We used an on-treatment analysis for the primary endpoint and performed an ordinal logistic regression analysis using a stepwise variable selection algorithm to examine associations between baseline variables and discontinuation of treatment and >10% on-treatment weight gain at week 48. All statistical analyses were conducted using Statistical Analysis System (SAS) software v9.4 (SAS Institute, Inc., Cary, North Carolina, USA).

RESULTS

Study population

Overall, 948 people were included, of whom 734 (77.4%) were on DTG/3TC and 214 (22.6%) were on DTG/RPV; median duration of follow-up was 76.1 weeks (IQR 65.1–94.8). Baseline characteristics of the study population are described in Table 1. The median age was 50.9 years (IQR 41.2–59.4), women represented 31.1% of the study cohort, and people were primarily Caucasian (61.1%) followed by SSA (31%). Acquisition of HIV-1 was predominantly through sexual exposure (91.7%), and MSM accounted for 46% of the study cohort. The majority of people (95.3%) were treatment experienced at baseline, 74.3% were INSTI experienced, median time on cART prior to baseline was 8.8 years (IQR 4.1–15.7), and median number of cART regimens prior to baseline was four (IQR 2–6). Regimens received prior to baseline varied greatly; the most common were two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) + one INSTI (60.9%) and two NRTIs +one non-nucleoside reverse transcriptase inhibitor (NNRTI; 11.4%). The most frequent reasons for starting a DTG-based 2DR were treatment simplification/decrease pill burden (46.7%) and toxicity of previous cART regimen (10.7%). Less frequent

TABLE 1 Baseline characteristics of the study population

Characteristics	Overall ($n = 948$)	DTG + 3TC ($n = 734$)	DTG + RPV ($n = 214$)	p-value[a]
Age (years)				0.02
<50	439 (46.3)	355 (48.4)	84 (39.3)	
≥50	509 (53.7)	379 (51.6)	130 (60.7)	
Sex				0.402
Male	653 (68.9)	511 (69.6)	142 (66.4)	
Female	295 (31.1)	223 (30.4)	72 (33.6)	
Ethnicity				0.132
Caucasian	579 (61.1)	453 (61.7)	126 (58.9)	
Black Sub-Saharan African	294 (31)	221 (30.1)	73 (34.1)	
Other	54 (5.7)	40 (5.5)	14 (6.5)	
Unknown	21 (2.2)	20 (2.7)	1 (0.5)	
Weight (kg)	76 (68–85.5)	77 (68–86)	75 (66.5–83)	0.053
Co-morbidities				0.156
Diabetes mellitus	56 (5.9)	50 (9.6)	6 (4.4)	
Coronary heart disease	32 (3.4)	25 (3.4)	7 (3.3)	
NADM	27 (2.8)	23 (3.1)	4 (1.9)	
Cerebrovascular disease	12 (1.3)	9 (1.2)	3 (1.4)	
Chronic renal disease	7 (0.7)	6 (1.2)	1 (0.7)	
Data not available	292 (30.8)	215 (29.3)	77 (36)	
HIV acquisition				0.669
Heterosexual	433 (45.7)	333 (45.4)	100 (46.7)	
MSM	436 (46)	343 (46.7)	93 (43.5)	
Other	20 (2.1)	14 (1.9)	6 (2.8)	
Unknown	59 (6.2)	44 (6)	15 (7)	
HIV treatment status				0.357
Treatment-naïve	44 (4.6)	37 (5)	7 (3.3)	
Treatment-experienced	904 (95.4)	697 (95)	207 (96.7)	
INSTI-experienced	704 (74.3)	556 (75.7)	148 (69.2)	
DTG-experienced	601 (63.4)	491 (66.9)	110 (51.4)	
Prior AIDS-defining illness	136 (14.4)	90 (12.3)	46 (21.5)	0.001
Nadir $CD4^+$ T-cell count (cells/μl)	343 ± 243	355 ± 252	301 ± 204	0.006
Data not available	11 (1.2)	8 (1.1)	3 (1.4)	
Time on cART (years)	8.8 (4.1–15.7)	8.6 (4–14.2)	11 (4.9–20.6)	0.0001
Number of previous cART regimens	4 (2–6)	3 (2–5)	4 (2–6)	0.0003
cART regimen prior to baseline				0.001
2 NRTIs + 1 INSTI	577 (60.9)	488 (66.5)	89 (41.6)	
2 NRTIs + 1 NNRTI	108 (11.3)	75 (10.2)	33 (15.4)	
2 NRTIs +1 PI	48 (5.1)	32 (4.4)	16 (7.5)	
1 INSTI + 1 PI	18 (1.9)	11 (1.5)	7 (3.3)	
1 PI	18 (1.9)	12 (1.6)	6 (2.8)	
Other/not receiving treatment	179 (18.9)	116 (15.8)	63 (29.4)	
HIV-1 viral load (copies/ml)				0.178

TABLE 1 (Continued)

Characteristics	Overall ($n = 948$)	DTG + 3TC ($n = 734$)	DTG + RPV ($n = 214$)	p-value[a]
<50	871 (91.9)	677 (92.2)	194 (90.7)	
50–200	19 (2)	17 (2.3)	2 (0.9)	
201–499 999	56 (5.9)	39 (5.3)	17 (7.9)	
≥500 000	2 (0.2)	1 (0.2)	1 (0.5)	
$CD4^+$ T-cell count (cells/μl)				0.341
<200	21 (2.2)	13 (1.8)	8 (3.7)	
200–349	58 (6.1)	45 (6.1)	13 (6.1)	
350–499	120 (12.7)	96 (13.1)	24 (11.2)	
≥500	692 (73)	539 (73.4)	153 (71.5)	
Data not available	57 (6)	41 (5.6)	16 (7.5)	
$CD4^+/CD8^+$ ratio	1 ± 0.5	1 ± 0.5	0.8 ± 0.4	0.002

Abbreviations: 3TC, lamivudine; cART, combined antiretroviral therapy; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NADM, non-AIDS-defining malignancy; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; RPV, rilpivirine.

[a]Comparison of 3TC group versus RPV group.

Data are presented as n (%), mean ± standard deviation, or median (interquartile range) unless otherwise indicated.

reasons included treatment initiation for a treatment-naïve patient (4.6%), drug–drug interactions (0.6%), and virological failure of previous cART regimen (0.5%). At baseline, the median $CD4^+$ cell count was 705 cells/μl (IQR 523–902), and 91.9% were virologically suppressed (<50 copies/ml).

Virological suppression

The rate of virological suppression at weeks 24 and 48 for the overall population and for the various subgroups is shown in Table 2. At week 48, the virological suppression rate for the overall cohort was 98.3%. Similar suppression rates were observed in the DTG/3TC group (99.1%) and in the DTG/RPV group (96.2%), including for occurrences of off-label use of these 2DRs (DTG/3TC in a person with an HIV-1 VL ≥500 000 copies/ml; DTG/RPV in treatment-naïve and virologically non-suppressed switch people). Compared with the overall study population, a lower but statistically nonsignificant rate was seen in those with a baseline HIV-1 VL of 201–499 999 copies/ml (92.3%) and in those with a baseline $CD4^+$ cell count <200 cells/μl (92.9%). Furthermore, minor but nonsignificant differences in virological suppression rates among the two treatment regimens were observed in certain sub-populations, including SSA people (97.7% [3TC group] vs. 92.9% [RPV group]). No viral blips were detected over the first 24 weeks of the study period; however, by week 48, seven viral blips were observed overall (three in the 3TC group; four in the RPV group). The proportion of people experiencing loss of virological control by week 48 was 0.5% ($n = 5$) for the overall population, 0.1% ($n = 1$) for the 3TC group, and 1.9% ($n = 4$) for the RPV group (Table S1). A viral blip prior to loss of virological control was observed in one of the five people overall, and only one person had novel RAMs at the time of loss of virological control (one person had a VL at the time of loss of virological control below the required minimum to accurately perform resistance testing). Median HIV-1 VL at confirmation of loss of virological control was 3080 copies/ml (IQR 450–3860).

Treatment discontinuation

There were 40 (4.2%) discontinuations of treatment over the 48-week study period, corresponding to an incidence of 4.7 discontinuations per 100 patient-years (Table S2). There were 27 (3.7%) discontinuations in the 3TC group and 13 (6.1%) in the RPV group ($p = 0.126$). Logistic regression analysis showed no significant association between baseline variables and discontinuation of treatment (data not shown). The most common reasons for discontinuation of 2DR were an adverse event (AE; 1.4%, 1.5 discontinuations per 100-patient years) and a newly diagnosed HBV co-infection (0.8%, 0.9 discontinuations per 100-patient years). Of the eight people with HIV-HBV co-infection, six (75%) were on a tenofovir-based 3DR directly prior to 2DR initiation, and the remaining two were treatment-naïve people who were started on DTG/3TC. Less common causes of treatment discontinuation included patient/physician decision (0.4%), drug–drug interactions (0.2%), and pregnancy (0.1%). The

TABLE 2 Rates of virological suppression and number of viral blips for the overall study population and various sub-groups at weeks 24 and 48

Population and sub-groups	Overall W24 $N = 766$	DTG/3TC W24 $N = 590$	DTG/RPV W24 $N = 176$	Overall W48 $N = 586$	DTG/3TC W48 $N = 429$	DTG/RPV W48 $N = 157$
All people (%)	97.9	98.1	97.2	98.3	99.1	96.2
Age (%)						
≥50	97.9	98.4	96.3	98.6	99.6	96.2
<50	98	97.8	98.5	97.9	98.3	96.2
Sex (%)						
Male	98.1	98.3	97.5	98.5	99.7	95.3
Female	97.4	97.7	96.6	97.8	97.7	98
MSM (%)	98.3	98.9	96.1	99.3	99.5	98.5
Black SSA (%)	96.5	96.5	96.7	96.2	97.7	92.9
HIV treatment status (%)						
Naïve	94.3	92.9	100[a]	100	100	100[b]
Experienced	98.1	98.4	97	98.2	99	96
INSTI-experienced	97.6	98	96	98	98.8	95.4
Baseline HIV-1 VL (copies/ml), (%)						
<50	98.6	98.9	97.5	98.6	99.3	96.6
50–200	86.7	92.3	50[c]	100	100[b]	100[c]
201–499 999	90.9	86.7	100	92.3	93.8	90
≥500 000[d]	100	100	100	100	100	100
Baseline $CD4^+$ count (cells/μl), (%)						
<200	83.3	75	100[b]	92.9	85.7[a]	100[a]
200–349	95.9	94.6	100	96.6	100	85.7[a]
350–499	96.6	96.1	100	96.1	100	85
≥500	98.6	99.3	96.1	99	99	99.1
Viral blips (copies/ml), *n*						
VL 50–200	0	0	0	4	1	3
VL >200	0	0	0	3	2	1

Abbreviations: 3TC, lamivudine; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; *N*, number of participants with available data; RPV, rilpivirine; SSA, sub-Saharan African; VL, viral load; W, week.

[a]Data only available for seven people in this sub-group.

[b]Data only available for six people in this sub-group.

[c]Data only available for two people in this sub-group.

[d]Data only available for two people in this category, one in each treatment group.

most frequent AE resulting in discontinuation of treatment was neurotoxicity (0.5%; 0.6 discontinuations per 100-patient years) followed by gastrointestinal toxicity (0.3%; 0.4 discontinuations per 100-patient years). For the overall population, median time to discontinuation for any reason was 20.1 weeks (11.5–31.7), and the median time was longer in the RPV group than in the 3TC group (25.6 vs. 17.1 weeks; $p = 0.189$). Among those who discontinued DTG/3TC, the most common cART regimen prescribed after discontinuation was bictegravir/emtricitabine/tenofovir alafenamide (29.6%), whereas the most commonly prescribed cART regimen after DTG/RPV discontinuation was DTG/3TC (61.5%).

Change in weight

Median on-treatment weight gain at week 48 was 1 kg (IQR −1 to 3) for the overall study population, 1 kg (IQR −1 to 3) for the 3TC group, and 2 kg (IQR 0–4) for the

TABLE 3 Change in weight (kg) at week 48, along with the proportion of people experiencing 5%–10% and >10% increase in weight from baseline for the study cohort and various sub-groups

	DTG/3TC			DTG/RPV		
Baseline variable	**Median (IQR)**	**5%–10% increase from baseline**	**>10% increase from baseline**	**Median (IQR)**	**5%–10% increase from baseline**	**>10% increase from baseline**
All people	1 (−1–3)	14.8	5.4	2 (0–4)	22.2	9.5
Age (years)						
<50	2 (−1–4)	17.4	6.5	2 (−0.5–4)	20.8	8.3
≥50	1 (−1–3)	11.6	4.1	2 (0–4)	22.6	9.8
Sex						
Male	1 (−1–3)	15.2	4.5	1.5 (−1–4)	23.7	7.9
Female	1 (−2–3)	13.1	6	2 (0–4)	18.5	11.1
MSM	1 (−1–3)	14.7	3.7	1 (−0.5–4)	29.2	7.2
SSA	1 (−1–3)	11.1	6.2	2 (0–4)	21.4	7.1
HIV treatment status						
Naïve	1 (−2–2)	15.6	5.8	4[a] (2.5–5.5)	75[a]	0[a]
Experienced	1 (−1–3)	14.8	5.2	2 (0–4)	18	9.8
INSTI-experienced	1 (−1–3)	14.4	5.1	1 (−1–3)	17.7	9.8
Time on cART						
≥10 years	0 (−2–3)	13.7	2.8	2 (0–4)	20.5	7.7
<10 years	1 (−1–3)	15.1	6.8	2.5 (−1–4)	23.1	11.5
Regimen prior to baseline						
ABC-based	2 (−1–4)	14.6	7.3	2 (−1–4)	33.3	6.7
TDF-based	3 (0–7)	20	13.3	2 (0–4)	15	15.8
TAF-based	1 (−1.5–3)	14.7	2.6	1.5 (0–4)	12.5	5.1
$CD4^+$ count (cells/μl)						
<350	2 (−2–4)	13.3	6.7	3.5 (0.5–5)	14.3	10
350–499	1 (−1–3)	12.8	2.6	0 (−1–2)	11.1	0
≥500	1 (−2–3)	14.6	4.9	2 (0–4)	24.5	8.2
HIV-1 VL (copies/ml)						
<50	1 (−1–3)	14.3	4.8	2 (−1–4)	18.6	8.5
≥50	1 (−1–4)	15.9	8.3	4[b] (3–7)	28.9[b]	12.7[b]

Abbreviations: 3TC, lamivudine; ABC, abacavir; cART, combined antiretroviral therapy; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; MSM, men who have sex with men; RPV, rilpivirine; SSA, black Sub-Saharan African; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; VL, viral load.

[a]Data only available for four people in this sub-group.

[b]Data only available for five people in this sub-group.

RPV group. Change in weight from baseline for various sub-groups of people is shown in Table 3. At week 48, a >10% increase in weight was observed in 5.4% of people on DTG/3TC and in 9.5% of people on DTG/RPV. The lowest proportion of people experiencing a >10% weight increase were those on a tenofovir alafenamide fumarate-based cART regimen prior to 2DR initiation (2.6% [3TC group]; 5.1% [RPV group]). Logistic regression analysis using baseline variables described in Table 3 revealed that the only factor significantly associated with a >10% increase in weight from baseline was being on a tenofovir disoproxil fumarate (TDF)-based cART regimen directly prior to 2DR initiation (odds ratio 3.48; 95% confidence interval 1.13–10.68; $p = 0.038$).

Laboratory analyses

Mean ± SD increase in $CD4^+$ cell count in the DTG/3TC group was 5 ± 199 and 14 ± 184 cells/μl at weeks 24 and

48, respectively, whereas in the DTG/RPV group, it was 7 ± 161 and 22 ± 177 cells/μl at weeks 24 and 48, respectively (Table S3). However, there was no change in the $CD4^+/CD8^+$ ratio over the course of the study period. At week 48, there were no statistically significant differences in the mean change from baseline of lipid parameters and fasting glucose in both treatment regimens.

DISCUSSION

In this multicentre, retrospective trial of treatment-naïve and treatment-experienced people in a real-world setting, DTG/3TC and DTG/RPV provided durable virological suppression and were well tolerated. Indeed, despite several differences in baseline characteristics among the two groups and a few occurrences of off-label use of these 2DRs, factors that could have potentially influenced endpoints such as virological and immunologic response, these regimens achieved a rate of virological suppression close to 100% (week 48 on-treatment analysis) for both treatment-naïve and treatment-experienced people. Furthermore, impressive virological suppression rates were observed across various pre-defined sub-groups, including those aged ≥50 years, women, and those from SSA. Slightly lower, but statistically nonsignificant, rates of virological suppression were observed in people with baseline $CD4^+$ cell count <200 cells/μl (93%) or baseline HIV-1 VL of 201–499 999 copies/ml (92%). The overall virological efficacy observed in our study is quite similar to the 48-week results reported in clinical trials and generally higher than what is classically reported in real-world studies. In the ASPIRE randomized controlled trial (RCT) of DTG/3TC in treatment-experienced people, the rate of virological suppression was 91% [12]. The GEMINI-1 and -2 studies, both phase III RCTs evaluating DTG/3TC in treatment-naïve people, reported a 91% virological suppression rate in the pooled population [5], and the TANGO trial of DTG/3TC in treatment-experienced people demonstrated a virological efficacy of 93% [6]. In the SWORD-1 and SWORD-2 studies, which were phase III studies involving treatment-experienced people treated with DTG/RPV, pooled analysis showed the rate of virological suppression to be 94% [7]. However, in real-world studies, the week-48 rates of virological suppression varied between 84% and 100% [13–21]. Potential factors that may explain the discrepant rates of virological efficacy observed include the difference in study populations (heterogeneous in real-world studies vs. pre-selected [including prior treatments, virological failures, and prior RAMs] in clinical trials) and that real-world studies usually employ a retrospective, observational design using an on-treatment analysis (such as in this study), whereas clinical trials tend to use a snapshot algorithm in an intention-to-treat-exposed population. Overall, there were five (0.5%) cases of loss of virological control in our study population. Resistance analysis at the time of loss of virological control showed that three of those instances were mutation free and, although sub-optimal adherence cannot be excluded, it is reassuring that the future treatment options for those participants were not compromised. However, one person who was on DTG/RPV had RAMs for both NNRTIs and INSTIs, and one person had a VL at the time of loss of virological control below the required threshold to accurately perform resistance testing. None of the people who experienced loss of virological control had any RAMs prior to 2DR initiation. These findings, which are in line with those of both clinical and real-world trials [5–7, 12–21], show that loss of virological control with DTG-based 2DRs is extremely rare in both treatment-naïve and treatment-experienced people and that the development of resistance to either DTG, 3TC, and RPV is equally rare. Despite seven people experiencing a viral blip over the study period, only one of those people experienced loss of virological control. Reports as to the clinical significance of viral blips are conflicting. Similar to this study, some trials have reported that viral blips were not associated with either virological failure or the development of drug resistance [22–24], whereas others have reported an association [25–28].

DTG/3TC and DTG/RPV were well tolerated, with 4.2% of people discontinuing their treatment. No significant difference was observed in the overall discontinuation rates among the two treatment regimens. Interestingly, participants in both groups had the same rate of discontinuation due to an AE (1.4%; most common cause of discontinuation). Rate of discontinuation due to an AE were 1%–2% in the investigational trials GEMINI 1 and 2 and TANGO [5, 6] and 3% in the SWORD-1 and -2 studies [7]. In several observational studies, the discontinuation rate due to an AE ranged between 2% and 8% for DTG/3TC [17, 29–32] and 2%–11% for DTG/RPV [13, 21, 33]. The most frequent AE leading to discontinuation in our study was neurotoxicity; once again, the same rate was observed in both treatment regimens (0.5%). Real-world data have reported neurotoxicity discontinuation rates of 1%–3% for DTG/3TC [17, 29–31] and 2%–3% for DTG/RPV [33, 34]. Given that the observation period of our study was comparable to all the abovementioned reports and that our study population was, in many cases, larger than in those studies, the difference in discontinuation rates observed can most likely be explained by the differences in study populations. Indeed, the majority of the people in our study were treatment experienced (95%), and a significant proportion was INSTI (74%) and DTG experienced (63%).

Furthermore, the median time on cART prior to 2DR initiation was 8.8 years (IQR 4.1–15.7) with a median of four (IQR 2–6) cART regimens. As such, our study population had been greatly exposed to antiretrovirals prior to study inclusion and are therefore either less likely to experience AEs or more likely to tolerate AEs, thereby leading to fewer treatment discontinuations. It is important to note that the AEs described in this study were aligned with those reported in the aforementioned trials, and all the AEs observed were already recognized. In addition, the incidence of neurotoxicity leading to discontinuation observed in this study is consistent with what has been described for each of the individual components (DTG and RPV), which argues against the notion of an additive or synergistic effect of 2DRs when it comes to AEs [35]. Eight participants were newly diagnosed with HBV over the course of the study period. Six of those eight were on a tenofovir-based 3DR prior to 2DR initiation. Furthermore, seven participants were newly diagnosed with HBV despite being on 3TC at the time of their diagnosis, a result most likely explained by a combination of the following factors: an incubating HBV (indeed, two of these people were treatment naïve at baseline), poor treatment adherence, and infection with a 3TC-resistant HBV. These findings highlight the importance of ensuring people are immunized against HBV at the time of 2DR initiation and that those who are not are advised to do so.

Several laboratory parameters were assessed over the 48-week study period. A slight increase in the overall mean $CD4^+$ cell count was observed, with those in the RPV group experiencing the greatest increase (22 cells/μl). However, we did not observe a change in the mean $CD4^+/CD8^+$ ratio in either treatment regimen. The $CD4^+/CD8^+$ ratio is a marker of immune activation, and a low value acts as a predictor of non-AIDS-related complications [36]. Reports on whether this ratio is improved while on treatment with a 2DR [17] or whether 2DR initiation has a negative impact on the $CD4^+/CD8^+$ ratio are conflicting [37]. In terms of changes in lipid profiles, we observed a modest reduction in triglycerides for both treatment groups and a generally neutral effect on the other serum lipids. It is important to note that 37% of the study cohort were on a TDF-based cART regimen prior to 2DR initiation; since TDF has been reported to be a lipid-friendly drug [38], it would be expected that a similar proportion of participants would experience some worsening of their lipid parameters after switching away from TDF. However, we did not observe this in our study. We propose two possible explanations for this finding. First, Belgian Ministry of Health regulations stipulate that the management of people living with HIV occur at designated HRCs and that these people be followed by a multi-disciplinary team that includes a dietitian. As such, people regularly receive dietary recommendations as part of their follow-up. Second, the environment surrounding participants in this study may be more health-conscious than other settings, and this can influence the participant's dietary and exercise habits.

The issue of weight gain in people treated with INSTIs, and specifically DTG, has become a concern for clinicians and the people they provide care to [39–41]. In this real-world study, the median on-treatment weight gain at week 48 for DTG/3TC and DTG/RPV was 1 kg (IQR −1 to 3) and 2 kg (IQR 0–4), respectively. Data on weight gain associated with 2DRs are limited; however, our findings are consistent with what has been reported. Median weight gain at week 48 reported for DTG/3TC ranged between 0.8 and 4.5 kg [32, 42–44], whereas—for DTG/RPV—one study reported a median weight gain at week 48 of 1.8 kg [45] and another study reported a gain of 1.4 kg [46]. These differences may reflect the heterogeneity of the populations studied, including treatment status (treatment naïve or experienced) and the number of regimens and duration of treatment prior to inclusion. We also observed that 5.4% of people on DTG/3TC and 9.5% of those on DTG/RPV experienced a >10% increase in weight at week 48. Studies have associated certain characteristics with the greatest weight gain in patients on INSTI-based 3DRs, including female sex, Black race, older age, lower baseline $CD4^+$ cell counts, and higher HIV-1 VLs [47, 48]. Our data show that, for both treatment regimens, the only characteristic associated with a >10% weight gain at week 48 was being on a TDF-based regimen prior to 2DR initiation. This finding, which probably reflects loss of the weight-suppressant effect of TDF, has been previously reported [49, 50].

This study has some limitations. The single-arm analysis implies the lack of a control group. In addition, because of its retrospective and multicentre design, a proportion of data was missing for some of the variables included. Similarly, only AEs leading to treatment discontinuation were described, and it was not possible to report on the seriousness and severity of the various AEs; nor was it possible to characterize them in detail. Furthermore, it was not possible to account for the presence of any psychological or social factors that may have influenced certain endpoints, such as neuropsychiatric toxicity and weight gain. Lastly, the instances of loss of virological control were minimal, making it impossible to explore for associations with potential predictors. However, the main strength of this multicentre study is its observational nature. The lack of restrictions on the inclusion criteria allowed for an evaluation of the 2DRs in various patient populations, some of which are typically excluded from RCTs but are, in fact, representative of a real-world setting. This in turn makes the results of our study

applicable to people with HIV in clinical practice. Additional strengths include the large sample size, which comprised a significant proportion of women and people from SSA, and the substantial amount of data collected.

CONCLUSION

Our findings indicate that treatment with DTG/3TC or DTG/RPV in clinical practice results in a high rate of virological suppression, a low rate of loss of virological control, and rare occurrence of treatment-emergent resistance. In addition, viral suppression was maintained across various populations, including women, those from SSA, those who are treatment-naive, and those simplifying their treatment from a 3DR to a 2DR. Both regimens were well tolerated, and the rates of AE-induced and neurotoxicity-induced treatment discontinuations were low. Instances of newly diagnosed HBV co-infection while on 2DR were few. Overall, >10% weight gain was observed in a small proportion of people, whereas the reported changes in weight were similar between the two treatment regimens. Furthermore, being on a TDF-based regimen directly prior to 2DR initiation was associated with the greatest weight gain. Data presented here should provide reassurance to clinicians that treatment with DTG/3TC or DTG/RPV is effective in a diverse set of people living with HIV. [Correction added on 13 March 2023, after first online publication: the preceding sentence has been modified.]

AUTHOR CONTRIBUTIONS

Rakan Nasreddine and Stéphane De Wit conceptualized and designed the study. Jean Cyr Yombi, Gilles Darcis, Eric Florence, Sabine D. Allard, Marie-Angélique De Scheerder, Sophie Henrard, Rémy Demeester, Peter Messiaen, Nathalie Ausselet, and Stéphane De Wit participated in data acquisition. Marc Delforge and Rakan Nasreddine performed the statistical analyses. Rakan Nasreddine drafted the first manuscript. All authors provided feedback on manuscript drafts and approved the final manuscript.

ACKNOWLEDGEMENTS

This study was supported by ViiV Healthcare.

CONFLICT OF INTEREST

No conflict of interest declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Rakan Nasreddine https://orcid.org/0000-0002-1265-1500

Gilles Darcis https://orcid.org/0000-0001-8192-1351

REFERENCES

1. Department of Health and Human Services. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Accessed September 6, 2021. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf
2. European AIDS Clinical Society. Guidelines version 11, October 2021. Accessed November 2, 2021. https://www.eacsociety.org/files/guidelines-10.1_finaljan2021_1.pdf
3. Saag MS, Gandhi RT, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2020 recommendations of the international antiviral society-USA panel. *JAMA*. 2020;324:1651-1669.
4. World Health Organization. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidance, 2018. Accessed November 2, 2021. https://www.who.int/hiv/pub/guidelines/ARV2018update/en
5. Cahn P, Madero JS, Arribas JR, et al. Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. *Lancet*. 2019;393(10167):143-155.
6. Wyk JV, Ajana F, Bisshop F, et al. Switching to DTG/3TC fixed-dose combination (FDC) is non-inferior to continuing a TAF-based regimen in maintaining virologic suppression through 48 weeks (TANGO study, Oral Presentation). Presented at the 10th International AIDS Society Conference on HIV Science, July 2019, Mexico City, Mexico.
7. Llibre JM, Hung C-C, Brinson C, et al. Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies. *Lancet*. 2018;391(10123):839-849.
8. Sutton S, Magagnoli J, Hardin J. Odds of viral suppression by single-tablet regimens, multiple tablet regimens, an adherence level in HIV/AIDS patients receiving antiretroviral therapy. *Pharmacotherapy*. 2017;37(2):204-213.
9. Parienti J, Barrail-Tran A, Duval X, et al. Adherence profiles and therapeutic responses of treatment-naive HIV-infected patients starting boosted atazanavir-based therapy in the ANRS 134-COPHAR 3 trial. *Antimicrob Agents Chemother*. 2013;57(5):2265-2271.
10. Sciensano. Epidémiologie du sida et de l'infection à VIH en Belgique: situation au 31 décembre 2020. Accessed September 8, 2021. https://www.sciensano.be/en/biblio/epidemiologie-du-sida-et-de-linfection-a-vih-en-belgique-situation-au-31-decembre-2020
11. United Nations Statistics Division. Composition of macro geographical (continental) regions, geographical sub-regions, and

selected economic other groupings. Accessed June 22, 2021. https://unstats.un.org/unsd/mi/africa.htm
12. Taiwo BO, Marconi VC, Berzins B, et al. Dolutegravir plus lamivudine maintains human immunodeficiency Virus-1 suppression through week 48 in a pilot randomized trial. *Clin Infect Dis*. 2018;66(11):1794-1797.
13. Noe S, Ummard-Berger K, Hillenbrand H, et al. 12-month outcome of Dolutegravir/Rilpivirine in virologically suppressed HIV-infected patients:real-world data from the German JUNGLE cohort (poster). Presented at HIV Drug Therapy 2020, October 2020, Virtual.
14. Capetti AF, Sterrantino G, Cossu MV, et al. Switch to Dolutegravir plus Rilpivirine dual therapy in cART-experienced subjects: an observational cohort. *PLoS One*. 2016;11(10):e0164753.
15. Maggiolo F, Gulminetti R, Pagnucco L, et al. Lamivudine/dolutegravir dual therapy in HIV-infected, virologically suppressed patients. *BMC Infect Dis*. 2017;17(1):215.
16. Joly V, Burdet C, Landman R, et al. Dolutegravir and lamivudine maintenance therapy in HIV-1 virologically suppressed patients: results of the ANRS 167 trial (LAMIDOL). *J Antimicrob Chemother*. 2019;74(3):739-745.
17. Hidalgo-Tenorio C, Cortés LL, Gutiérrez A, et al. DOLAMA study: effectiveness, safety and pharmacoeconomic analysis of dual therapy with dolutegravir and lamivudine in virologically suppressed HIV-1 patients. *Medicine (Baltimore)*. 2019 Aug; 98(32):e16813.
18. Galizzi N, Poli A, Galli L, et al. Retrospective study on the outcome of two-drug regimens based on dolutegravir plus one reverse transcriptase inhibitor in virologically-suppressed HIV-infected patients. *Int J Antimicrob Agents*. 2020;55: 105893.
19. Deschanvres C, Raffi F, Reynes J, et al. Virologic failure and resistance in dolutegravir-based maintenance dual regimens. (poster). Presented at the Conference on Retroviruses and Opportunistic Infections 2020, March 2020, Boston, MA.
20. Gagliardini R, Lorenzini P, Cozzi-Lepri A, et al. Effect of past virological failure on dolutegravir+lamivudine as maintenance regimen (poster). Presented at the Conference on Retroviruses and Opportunistic Infections 2020, March 2020, Boston, MA.
21. Diaz A, Casado JL, Dronda F et al. Dolutegravir plus rilpivirine in suppressed heavily pre-treated HIV-infected patients [abstract tupdb0 106]. Presented at the 21st International AIDS Conference, July 2016, Durban, South Africa.
22. Garcia-Gasco P, Maida I, Blanco F, et al. Episodes of low-level viral rebound in HIV-infected patients on antiretroviral therapy: frequency, predictors and outcome. *J Antimicrob Chemother*. 2008;61(3):699-704.
23. Nettles RE, Kieffer TL, Kwon P, et al. Intermittent HIV-1 viremia (blips) and drug resistance in patients receiving HAART. *Jama*. 2005;293(7):817-829.
24. Podsadecki TJ, Vrijens BC, Tousset EP, Rode RA, Hannaet GJ, et al. Decreased adherence to antiretroviral therapy observed prior to transient human immunodeficiency virus type 1 viremia. *J Infect Dis*. 2007;196(12):1773-1778.
25. Grennan JT, Loutfy MR, Su D, et al. Magnitude of virologic blips is associated with a higher risk for virologic rebound in HIV-infected individuals: a recurrent events analysis. *J Infect Dis*. 2012;205(8):1230-1238.
26. Sorstedt E, Nilsson S, Blaxhult A, et al. Viral blips during suppressive antiretroviral treatment are associated with high baseline HIV-1 RNA levels. *BMC Infect Dis*. 2016;16:305.
27. Cohen Stuart JW, Wensing AM, Kovacs C, et al. Transient relapses ("blips") of plasma HIV RNA levels during HAART are associated with drug resistance. *J Acquir Immune Defic Syndr*. 2001;28(2):105-113.
28. Macias J, Palomares JC, Mira JA, et al. Transient rebounds of HIV plasma viremia are associated with the emergence of drug resistance mutations in patients on highly active antiretroviral therapy. *J Infect*. 2005;51(3):195-200.
29. Baldin G, Ciccullo A, Rusconi S, et al. Long-term data on the efficacy and tolerability of lamivudine plus dolutegravir as a switch strategy in a multicenter cohort of HIV-1-infected, virologically suppressed patients. *Int J Antimicrob Agents*. 2019;54: 728-734.
30. Maggiolo F, Comi L, Gulminetti R, et al. Dolutegravir? Lamivudine in patients with suppressed HIV-RNA: long term virologic and immunologic results of a multicenter cohort (poster). Presented at HIV Drug Therapy Glasgow 2018, October 2018, Glasgow, Scotland.
31. Bravo J, Martinez O, Martinez-Alfaro E, et al. Multicenter study to evaluate the effectiveness and safety of dolutegravir and lamivudine dual therapy in real life (poster). Presented at the XI Congreso Nacional GeSIDA, December 2019, Toledo, Spain.
32. Postel N, Schneeweiss S, Wyen C, et al. Real-world data from the prospective URBAN cohort study on the use of dolutegravir (DTG) + lamivudine (3TC) in ART-naïve and pre-treated people living with HIV in Germany (Oral presentation). Presented at HIV Drug Therapy Glasgow 2020, October 2020, Virtual.
33. Bonijoly T, Cabié A, Cheret A, et al. Week-48 efficacy and safety of dolutegravir + rilpivirine dual therapy as a switch strategy in a real-life cohort study (Oral presentation). Presented at the 16th European AIDS Conference, October 2017, Milan, Italy.
34. Casado JL, Monsalvo M, Fontecha M, et al. Dolutegravir plus rilpivirine as dual regimen in virologically suppressed HIV-1 infected patients in a clinical setting. *HIV Res Clin Pract*. 2019 Apr;20(2):64-72.
35. Reeves AA, Fuentes AV, Caballero J, Thomas JE, Mosley JF, Harrington C. Neurotoxicities in the treatment of HIV between dolutegravir, rilpivirine and dolutegravir/rilpivirine: a meta-analysis. *Sex Transm Infect*. 2021;97(4):261-267.
36. Jenks JD, Hoenigl MJ. CD4:CD8 ratio and CD8+ cell count for prognosticating mortality in HIV-infected patients on antiretroviral therapy. *Lab Precis Med*. 2018;3:8.
37. Masia M, Padilla S, Barber X, et al. Comparative impact of suppressive antiretroviral regimens on the CD4/CD8 T-cell ratio: a cohort study. *Medicine (Baltimore)*. 2016;95(11):e3108.
38. Santos JR, Saumoy M, Curran A, et al. The lipid-lowering effect of tenofovir/emtricitabine: a randomized, crossover, double-blind, placebo-controlled trial. *Clin Infect Dis*. 2015;61(3):403-408.
39. Menard A, Meddeb L, Tissot-Dupont H, et al. Dolutegravir and weight gain: an unexpected bothering side-effect. *Aids*. 2017;31: 1499-1500.
40. Bourgi K, Jenkins CA, Rebeiro PF, et al. Weight gain among treatment-naïve persons with HIV starting integrase inhibitors compared to non-nucleoside reverse transcriptase inhibitors or

protease inhibitors in a large observational cohort in the United States and Canada. *J Int AIDS Soc*. 2020;23(4):e25484.
41. Eckard AR, McComsey GA. Weight gain and integrase inhibitors. *Curr Opin Infect Dis*. 2020;33:10-19.
42. Rolle C-P, Berhe M, Singh T, et al. Feasibility, efficacy, and safety of dolutegravir/lamivudine (DTG/3TC) as a first line regimen in a test and treat setting for newly diagnosed people living with HIV (PLWH): 48 week results of the STAT study (Oral Presentation). Presented at the 11th International AIDS Society Conference on HIV Science; July 2021; Virtual.
43. Calza L, Borderi M, Colangeli V, et al. Short communication: no significant changes in weight and body fat mass in suppressed HIV-infected patients switched to dual combination lamivudine plus Dolutegravir or Raltegravir. *AIDS Res Hum Retroviruses*. 2021;37(3):204-206.
44. Ciccullo A, Dusina A, Lassandro AP, Borghetti A, Baldin G, Di Giambenedetto S. No significant changes in body fat mass in virologically suppressed. *HIV-Positive Patients Switched to Lamivudine-Dolutegravir AIDS*. 2020;34(6):956-957.
45. Vizcarra P, Vivancos MJ, Pérez-Elías MJ, Moreno A, Casado JL. Weight gain in people living with HIV switched to dual therapy: changes in body fat mass. *Aids*. 2020;34(1):155-157.
46. Taramasso L, Bonfanti P, Ricci E, et al. Factors associated with weight gain in people treated with Dolutegravir. *Open Forum Infect Dis*. 2020;7(6):ofaa195.
47. Lake JE, Wu K, Bares SH, et al. Risk factors for weight gain following switch to integrase inhibitor–based antiretroviral therapy. *Clin Infect Dis*. 2020;71(9):e471-e477.
48. Sax PE, Erlandson KM, Lake JE, et al. Weight gain following initiation of antiretroviral therapy: risk factors in randomized comparative clinical trials. *Clin Infect Dis*. 2020;71(6):1379-1389.
49. Lake JE, Trevillyan J. Impact of integrase inhibitors and tenofovir alafenamide on weight gain in people with HIV. *Curr Opin HIV AIDS*. 2021;16(3):148-151.
50. Gomez M, Seybold U, Roider J, Härter G, Bogner JR. A retrospective analysis of weight changes in HIV-positive patients switching from a tenofovir disoproxil fumarate (TDF)- to a tenofovir alafenamide fumarate (TAF)-containing treatment regimen in one German university hospital in 2015-2017. *Infection*. 2019;47(1):95-102.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Nasreddine R, Yombi JC, Darcis G, et al. Efficacy, durability, and tolerability of dolutegravir/lamivudine and dolutegravir/rilpivirine for the treatment of HIV in a real-world setting in Belgium. *HIV Med*. 2023; 24(3):267-278. doi:10.1111/hiv.13373