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ORIGINAL ARTICLE

DORA: 48-week weight and metabolic changes in Black women with HIV, in a phase IIIb switch study from dolutegravir- or efavirenz- to doravirine-based first-line antiretroviral therapy

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Abstract

Objectives: Treatment-related weight gain and metabolic complications with antiretroviral integrase-based regimens, especially among Black women, suggest the need for alternative options.

Methods: We conducted a 48-week, open-label, single-arm, single-centre, phase IIIb switch study to evaluate the tolerability, safety and efficacy of switching from stable efavirenz- or dolutegravir-based antiretroviral therapy to doravirine/lamivudine/tenofovir disoproxil fumarate in Black women.

Results: The 101 participants enrolled (median age 35 years; interquartile range 31–40) were on efavirenz ($n = 46$; mean duration on therapy 1.7 years) or dolutegravir-based ($n = 55$; mean duration 1.5 years) antiretrovirals at screening. Retention at 48 weeks was 92/101 participants, and viral suppression was >90% throughout the study, with a single case of doravirine resistance (106 M, V108I and H221Y mutations). The mean weight percentage change at week 48 was 4.7% (95% confidence interval [CI] 3.0–6.5; $p < 0.001$), and the adjusted mean change was 2.7 kg (95% CI 1.50–3.98; $p < 0.001$); for efavirenz, the percentage change was 5.0% (95% CI 2.9–7.1; $p < 0.001$), and the adjusted weight gain was 3.5 kg (95% CI 1.93–5.13); for dolutegravir, the percentage change was 4.5% (95% CI 1.8–7.3; $p < 0.001$), and the adjusted weight gain was 2.1 kg (95% CI 0.26–3.90). Statistically significant decreases in lipid panel percent mean to week 48 included: total cholesterol −8.4% (95% CI −11.3 to −5.5; $p < 0.001$), triglycerides −10.4% (95% CI −16.4 to −4.4; $p < 0.001$) and high-density lipoprotein −14.8% (95% CI −18.5 to −11.2%; $p < 0.001$), with

minor differences when disaggregating the mean percent change in lipids between previous efavirenz/dolutegravir regimens. Adverse events due to doravirine were few and mild.

Conclusions: Our findings suggest that a switch to doravirine from efavirenz or dolutegravir is safe and effective in Black women, with significant improvement in lipid profiles, but does not arrest progressive weight gain.

KEYWORDS

antiretroviral, black, doravirine, female, metabolic

INTRODUCTION

Globally, nearly 30 million people are on antiretroviral treatment (ART), 5.5 million of whom reside in South Africa [1]. South Africa introduced tenofovir disoproxil fumarate/lamivudine/dolutegravir (TLD) as the preferred first-line regimen in 2019 [2]. This transition, replacing efavirenz with dolutegravir, was due to rising resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs), a better side-effect profile, and alignment with World Health Organization recommendations [3].

However, concerns regarding the integrase strand transfer inhibitor (INSTI) class have emerged. INSTI-based ART has been associated with increases in body weight and development of clinical obesity, changes in lipid profiles, new cardiovascular events and new incidence of hypertension [4–7]. Furthermore, increases in body weight on tenofovir prodrugs in combination with dolutegravir appear to be progressive in Black women [7, 8]. The Joint United Nations Programme on HIV/AIDS estimates that ~4.8 million women aged ≥15 years are living with HIV in South Africa, representing 63% of people living with HIV [9], with Black women having a country-wide HIV prevalence of around 24% [9, 10].

Switching to efavirenz-based regimens, although plausibly associated with weight mitigation in efavirenz slow-metabolizers, is accompanied by metabolic, organ and neuropsychiatric side effects, which may be severe, in those likely to experience weight loss [11].

Doravirine, a second-generation NNRTI, may be an alternative to INSTIs or older NNRTIs, with virological suppression comparable to that of ritonavir-boosted darunavir and efavirenz [12, 13]. The efficacy, safety and tolerability of doravirine in treatment-naïve participants has been demonstrated in clinical trials, including DRIVE-FORWARD and DRIVE-AHEAD, where it demonstrated a favourable lipid profile and tolerability over 48 weeks compared with ritonavir-boosted darunavir and efavirenz, respectively, and demonstrated a superior neuropsychiatric profile compared with efavirenz [12, 13]. DRIVE-SHIFT showed comparable virological suppression when switching from efavirenz-based ART to TLD, with fewer discontinuations due to adverse events (AEs) [14]. Network meta-analysis affirmed the non-inferiority of doravirine-based regimens in virological suppression compared with traditional first-line regimens [15].

Experience with doravirine-based ART is limited in globally representative populations of people with HIV because of the relatively small numbers of women and Black participants in previous studies [12–14]. We investigated doravirine as a potential alternative in first-line ART among Black women on stable efavirenz- or dolutegravir-containing ART.

MATERIALS AND METHODS

Study design and participants

The DORA trial was an open-label, single-arm, single-centre, phase IIIb study in virologically suppressed women with HIV on first-line ART switching to a doravirine-based regimen. The trial enrolled medically stable women with HIV-1 with virological suppression at study baseline (HIV RNA <50 copies per mL) on ART comprising efavirenz or dolutegravir (with an NRTI backbone of emtricitabine/lamivudine and tenofovir disoproxil fumarate, respectively) from primary healthcare facilities in Johannesburg metro (South Africa). Inclusion criteria included age ≥18 years, weight ≥40 kg and creatinine clearance >50 mL/min. Exclusion criteria included pregnancy, pregnancy gestation >28 weeks in the last 2 years, active tuberculosis and history of virological failure on previous ART regimens. We had no targeted approach to participant selection and no quota regarding the efavirenz or dolutegravir pre-existing regimen; participants were selected at participating health facilities and screened if they met all the inclusion criteria.

Procedures

The trial drug used was a fixed-dose formulation of doravirine 100 mg, lamivudine 300 mg and tenofovir disoproxil fumarate 300 mg (TLD) donated by Merck Sharp & Dohme. After providing written consent, participants were switched to TLD and followed up for 48 weeks, with post-trial access for 2 years. After enrolment, participants were seen for follow-up at 4 weeks, 12 weeks and subsequently every 12 weeks until week 48. Infants were followed up to 6 months.

Outcomes

The study's primary outcome was to evaluate the 48-week safety of once-daily oral TLD on weight, metabolic and neuropsychiatric outcomes among women (and outcomes on their infants). Secondary outcomes included the evaluation of 48-week virological suppression, CD4+ count changes, tolerability and overall safety and efficacy of TLD.

Neuropsychiatric and metabolic outcomes of the study drug among women included the proportion of participants with neuropsychiatric AEs in three pre-specified categories (dizziness, sleep disorders/ disturbances and altered sensorium), changes in fasting lipids and glucose and changes in weight and body mass index (BMI) from baseline to week 48. Women who become pregnant during the study were retained in the final analysis.

Secondary outcome measures included the proportion of participants with detectable plasma HIV-1 RNA levels (≥50 copies per mL) at weeks 24 and 48, the proportion of participants with neuropsychiatric AEs at week 24, changes in fasting lipids and glucose from baseline to week 24, changes in weight and BMI from baseline to week 24, changes in quality of life from baseline, median adherence by each adherence measure at weeks 24 and 48 and any emergence of antiretroviral resistance mutations in participants with virological failure. Although pregnancy and breastfeeding were study exclusion criteria, the infants of any women who fell pregnant while part of the trial were evaluated for HIV-positive status using an HIV DNA polymerase chain reaction test, congenital abnormalities and growth and development up to 6 months post-birth.

Throughout the trial, data were collected on AEs, vital sign measurements, symptom-directed physical examinations, laboratory assessments and questionnaires (adherence and modified ACTG Quality of Life). Demographic characteristics, laboratory tests, concomitant medications and pre-existing clinical conditions were captured at enrolment (baseline), and parameters of interest, both laboratory and clinical, were measured at follow-up visits.

Tuberculosis symptom screening, pregnancy testing, weight, height and blood pressure measurements were routinely conducted at all scheduled medical visits. AEs were recorded at every visit and graded according to the Division of AIDS AE grading table (version 2.0, November 2014). Data were captured in real time using an electronic data-capturing system REDCap v.13.5.4 (Vanderbilt University).

No baseline HIV resistance was recorded at screening; however, any two viral loads ≥1000 copies/mL 12 weeks apart were defined as virological failure, and resistance genotyping was done; resistance was managed according to subsequent resistance patterns. Women who became pregnant throughout the study duration could elect to remain in the trial, with infants followed up to 6 months of age.

Sample size calculation and statistical analysis

The original sample size calculation was powered by one of the primary outcome categories of average weight change from baseline at week 48. We regarded a meaningful difference in weight change between prior ART and the switched ART to be approximately 3 kg. To detect a difference in mean change at 90% power and with a two-sided significance level of 0.05, a minimum of 172 individuals were required (86 per group). To account for a ∼10% dropout, we aimed to recruit a total of 190 individuals (95 per group, including males and females). However, drug availability and available funding meant that we selected a sample size of 100 participants, anticipating that data may inform a larger future study.

Proportions and frequencies were used to describe categorical participant characteristics, and means with standard deviations and medians with interquartile ranges (IQRs) were reported for continuous characteristics and outcomes. In addition, proportions of cohort participants with virological suppression, as well as with some reported AEs, were computed. We computed crude changes between baseline measures and follow-up values. Percentage changes were subsequently calculated to provide simple percentage changes in body weight and lipids. We used the linear mixed model to obtain mean changes in the measures (body weight, BMI, blood pressure, glucose and lipids) after adjusting for within- and between-participant variations. Furthermore, we adjusted body weight and BMI changes at scheduled visits for previous ART regimen and duration on ART treatment. All

tests were two-sided, using a 5% significance level. The 95% confidence intervals (CIs) were also reported for each reported change estimate. Furthermore, figures were used to visualize changes in body weight and lipid measures over the follow-up period. The statistical software used was Stata Statistical Software (StataCorp, 2021, release 17; College Station, TX, USA).

RESULTS

Demographic and baseline characteristics

Between December 2020 and March 2022, a total of 191 participants were screened for potential inclusion in the trial. Participant enrolment was finalized by April 2021. However, due to COVID-19-related investigational product (IP) import delays, 32 participants were switched to a non-doravirine-containing regimen (largely TLD) during the study to prevent treatment interruption. This required an additional 32 participants to be recruited (from January to March 2022) to maintain the original sample size. Of the 133 enrolled participants, the final analysis used data from 101 participants who continued IP to study exit. Among screened participants, 58 were deemed ineligible (screen failures: most common cause being unsuppressed viral loads) (Figure 1). The last participant exited the study in March 2023 (date of last data collection). The retention rate throughout the trial was 93% ($n = 92$). Of the eight early withdrawals, two were in violation of the protocol (could not adhere to visit requirements) and six were lost to follow-up.

The median participant age was 35 years (IQR 31–40). All participants were female Black Africans; of 101 participants, 61 were from Zimbabwe and 37 from South Africa. In total, 46 participants switched from efavirenz-based ART and 55 from dolutegravir-based ART. The pre-existing NRTI backbone constituted of lamivudine ($n = 41$) and emtricitabine ($n = 60$). Mean duration on a previous efavirenz-based or dolutegravir-based regimen was 1.7 years and 1.5 years, respectively. At baseline, women had a median body weight of 71.1 kg (IQR 62.4–79.6) and BMI of 27.5 kg/m^2 (IQR 23.8–30.6) (Table 1).

Endpoint changes from baseline

The simple percentage mean body weight change showed an increase from baseline to week 48 (% change = 4.7; 95% CI 3.0–6.5; $p < 0.001$) (Table 2).

The adjusted mean changes for body weight and BMI showed similar increasing patterns (Table 2).

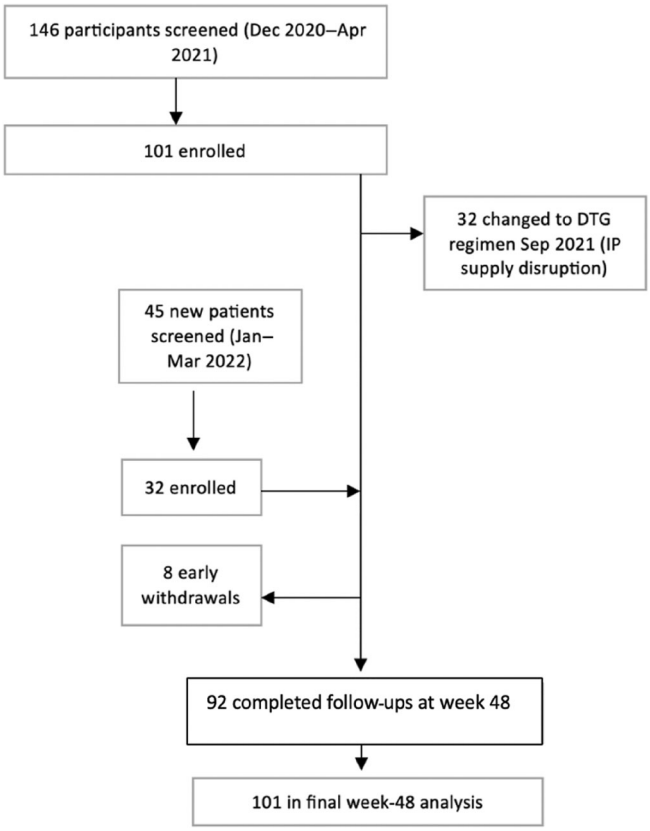

FIGURE 1 Trial profile. DTG, dolutegravir; IP, investigational product.

Participants previously on efavirenz-based ART had a higher starting mean body weight than those on dolutegravir-based ART: for those previously on efavirenz-based ART, the percentage change from baseline to week 48 between the two groups was 5.0% (95% CI 2.9–7.1; $p < 0.001$), and the adjusted weight gain was 3.5 kg (95% CI 1.93–5.13) (Table 3, Figure 2). For those previously on dolutegravir-based ART, the percentage change was 4.5% (95% CI 1.8–7.3; $p < 0.001$) and the adjusted weight gain was 2.1 kg (95% CI 0.26–3.90) (Table 4, Figure 2).

Seven neuropsychiatric AEs were reported between baseline and week 24 (including sleep disturbances, two dizziness and one altered sensorium), but all resolved by week 48.

Systolic and diastolic blood pressure remained stable throughout the trial. There were non-significant differences in glucose change based on previous dolutegravir/efavirenz regimens (Tables 3 and 4). Mean changes in lipids included the following:

- total cholesterol change at 24 weeks (% change −9.7; 95% CI −12.6 to −6.9; $p < 0.001$) and at 48 weeks (% change −8.4; 95% CI −11.3 to −5.5; $p < 0.001$);

TABLE 1 Demographic and baseline clinical characteristics.

Characteristics	Total ($N = 101$)
Age (years)	35.5 ± 6.38
Median	35.0 (31–40)
Minimum, maximum	23, 49
Race	
Black	101 (100.0)
Marital status	
Not married	69 (68.3)
Domestic partnership	19 (18.8)
Other	8 (8.0)
Married	5 (5.0)
Education level	
Primary	5 (5.0)
Secondary	83 (82.2)
Tertiary	13 (12.9)
Employment	
Employed	59 (58.4)
Not employed	28 (27.7)
Self-employed	14 (14.0)
Country of origin	
Zimbabwe	61 (60.4)
South Africa	37 (36.6)
Other	3.0 (3.0)
Previous ART regimen	
DTG based	55 (54.5)
EFV based	46 (45.5)
Previous ART duration (years)	
EFV based	1.7 ± 0.6
DTG based	1.5 ± 0.6
NRTI backbone	
FTC	60 (59.4)
3TC	41 (40.6)

Note: Percentages are based on the value of n/*N*. Data are presented as mean ± standard deviation, n (%) or median (interquartile range) unless otherwise indicated.

Abbreviations: 3TC, lamivudine; ART, antiretroviral therapy; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; NRTI, nucleoside analogue reverse transcriptase inhibitor.

- high-density lipoprotein (HDL) at 24 weeks (% change −18.3; 95% CI −22.0 to −14.5; $p < 0.001$) and at 48 weeks (% change −14.8; 95% CI −18.5 to −11.2; $p < 0.001$);
- low-density lipoprotein at 24 weeks (% change −2; 95% CI −7.1–3.1; $p = 0.438$) and at 48 weeks (% change −0.8; 95% CI −6.2–4.7; $p = 0.784$);
- triglycerides at 24 weeks (% change −6.1; 95% CI −14.6–2.5; $p = 0.161$) and at 48 weeks (% change −10.4; 95% CI −16.4 to −4.4; $p = 0.001$) (Table 2).

There was no significant change in total cholesterol/HDL ratios from baseline to week 48, at a low-risk ratio of 3.

There were minor differences when disaggregating the mean % change in lipids between previous dolutegravir/efavirenz regimens at week 48 (Tables 3 and 4, Figure 3). The most significant of these was the triglyceride change for those previously on an efavirenz regimen (% change −18.9; 95% CI −26.4 to −11.5; $p < 0.001$) compared with a previous dolutegravir regimen (% change −3.1; 95% CI −11.9–5.8; $p = 0.493$).

At weeks 24 and 48, six (6.7%) and three (3.2%) of the 101 participants had HIV RNA ≥50 copies/mL, respectively; one participant had a viral load >200 copies/mL at both 24 and 48 weeks (Figure 4). Only one participant switched treatment due to virological failure; all the other participants resuppressed.

One participant (previously on an efavirenz-based ART regimen) developed doravirine resistance at week 24 after self-reported poor adherence. The participant's NNRTI resistance profile included V106M, V108I and H221Y mutations. The participant fully resuppressed virologically after switching to a dolutegravir-containing regimen.

There was an increase in individual participant CD4 count change over the 48 weeks of follow-up (% mean change 7.4; 95% CI 2.4–12.3; $p = 0.004$) (Table 5).

AEs due to doravirine were few and mild (grade 1 or 2); there were four grade 3/4 AEs, including two loss of weight, cervical dysplasia and obstructive jaundice (below serious AE). Ten treatment-emergent cardiometabolic-related AEs occurred: six hypertensive, three type 2 diabetes and one dyslipidaemia diagnoses were made during the trial period (Table 6). No clinically significant renal AEs occurred (as measured by creatinine clearance and urinary examinations).

One serious AE was reported in a participant who developed predominantly obstructive jaundice after 8 weeks on IP. The abdominal ultrasound was inconclusive (no obvious obstruction or bile duct abnormalities noted), viral hepatitis tests (hepatitis A, B and C) were negative and transaminases were <100 U/L; however, so as not to contribute to liver dysfunction, the doravirine-containing regimen was discontinued. The participant was referred to a specialist gastroenterology unit for further management, but she relocated to Zimbabwe, missing any further site and tertiary care referral visits. Site attempts to contact the participant further were unsuccessful.

TABLE 2 Mean percentage changes and adjusted changes in body weight, lipids and glucose from baseline to week 48 (total participants switched from efavirenz- OR dolutegravir-based regimens to doravirine).

Variable	Baseline *N* = 101	Week 4 *N* = 99	Week 12 *N* = 98	Week 24 *N* = 95	Week 36 *N* = 93	Week 48 *N* = 92
Body weight (kg)						
Mean ± SD	72.3 ± 15.68	72.6 ± 15.62	73.6 ± 15.67	74.7 ± 15.83	75.2 ± 16.29	75.5 ± 16.53
Median (IQR)	71.1 (62.4–79.6)	70.8 (62.4–81.1)	71.2 (63.2–81.8)	73.4 (64.5–82.1)	74.3 (64.2–83.3)	74.2 (63.8–83.1)
Minimum, maximum	45.8, 154.3	45.8, 155.3	48.6, 155.2	51.4, 156.9	49.8, 158.8	49.1, 156.6
Mean % change (95% CI)	-	0.5 (−0.1–1.2)	1.8 (0.9–2.7)	3.9 (2.7–5.1)	4.2 (2.7–5.6)	4.7 (3.0–6.5)
% change *p*-value	-	0.102	<0.001	<0.001	<0.001	<0.001
LMM change (95% CI)[a]	-	0.26 (−0.21–0.74)	1.13 (0.58–1.67)	2.45 (1.71–3.19)	2.69 (1.71–3.67)	2.74 (1.50–3.98)
p-value[b]	-	0.276	<0.001	<0.001	<0.001	<0.001
Body mass index (kg/m^2)	*N* = 101	*N* = 99	*N* = 98	*N* = 95	*N* = 93	*N* = 92
Mean ± SD	27.6 ± 5.60	27.8 ± 5.60	28.2 ± 5.66	28.6 ± 5.77	28.7 ± 5.88	28.9 ± 5.96
Median (IQR)	27.5 (23.8–30.6)	27.5 (24.0–30.6)	27.6 (24.7–30.7)	28.3 (24.4–31.3)	28.5 (24.8–31.6)	28.6 (24.4–32.2)
Minimum, maximum	18.4, 55.3	18.4, 55.7	19.5, 55.6	20.5, 56.3	19.9, 56.9	19.7, 56.1
Mean % change (95% CI)	-	0.5 (−0.1–1.2)	1.8 (0.9–2.7)	3.9 (2.7–5.1)	4.2 (2.7–5.6)	4.7 (3.0–6.5)
% change *p*-value	-	0.102	<0.001	<0.001	<0.001	<0.001
LMM change (95% CI)[a]	-	0.11 (−0.07–0.29)	0.45 (0.24–0.66)	0.96 (0.68–1.25)	1.04 (0.67–1.41)	1.06 (0.59–1.53)
p-value[b]	-	0.238	<0.001	<0.001	<0.001	<0.001
Glucose (mmol/L)	*N* = 101	-	-	*N* = 98	-	*N* = 90
Mean ± SD	4.9 ± 0.52	-	-	4.8 ± 0.73	-	4.8 ± 0.77
Median (IQR)	4.9 (4.6–5.1)	-	-	4.6 (4.4–5.0)	-	4.7 (4.4–5.1)
Minimum, maximum	2.8, 7.0	-	-	3.2, 8.1	-	3.9, 9.0
Mean % change (95% CI)	-	-	-	−3.3 (−5.6 to −1.1)	-	−2.6 (−4.7 to −0.5)
% change *p*-value	-	-	-	0.004	-	0.018
LMM change (95% CI)[a]	-	-	-	−0.16 (−0.27 to −0.05)	-	−0.14 (−0.26 to −0.01)
p-value[b]	-	-	-	0.003	-	0.030
Total cholesterol (mmol/L)	*N* = 101	-	-	*N* = 97	-	*N* = 93
Mean ± SD	4.2 ± 0.74	-	-	3.8 ± 0.67	-	3.8 ± 0.70
Median (IQR)	4.2 (3.8–4.6)	-	-	3.6 (3.3–4.2)	-	3.7 (3.4–4.1)
Minimum, maximum	2.2, 6.4	-	-	2.0, 5.9	-	2.3, 5.6
Mean % change (95% CI)	-	-	-	−9.7 (−12.6 to −6.9)	-	−8.4 (−11.3 to −5.5)
% change *p*-value	-	-	-	<0.001	-	<0.001

TABLE 2 (Continued)

Variable	Baseline $N = 101$	Week 4 $N = 99$	Week 12 $N = 98$	Week 24 $N = 95$	Week 36 $N = 93$	Week 48 $N = 92$
LMM change[a] (95% CI)	-	-	-	−0.45 (−0.56 to −0.34)	-	−0.38 (−0.50 to −0.26)
p-value[b]	-	-	-	<0.001	-	<0.001
High-density lipoprotein (mmol/L)	$N = 101$	-	-	$N = 97$	-	$N = 93$
Mean ± SD	1.4 ± 0.38	-	-	1.2 ± 0.32	-	1.2 ± 0.31
Median (IQR)	1.4 (1.2–1.6)	-	-	1.1 (1.0–1.3)	-	1.1 (1.0–1.4)
Minimum, maximum	0.6, 2.8	-	-	0.2, 2.0	-	0.7, 2.5
Mean % change (95% CI)	-	-	-	−18.3 (−22.0 to −14.5)	-	−14.8 (−18.5 to −11.2)
% change *p*-value	-	-	-	<0.001	-	<0.001
LMM change (95% CI)[a]	-	-	-	−0.28 (−0.34 to −0.23)	-	−0.24 (−0.30 to −0.18)
p-value[b]	-	-	-	<0.001	-	<0.001
Low-density lipoprotein (mmol/L)	$N = 101$	-	-	$N = 94$	-	$N = 93$
Mean ± SD	2.3 ± 0.67	-	-	2.2 ± 0.61	-	2.2 ± 0.60
Median (IQR)	2.3 (1.9–2.7)	-	-	2.1 (1.8–2.6)	-	2.2 (1.9–2.7)
Minimum, maximum	0.5, 4.4	-	-	1.0, 3.6	-	0.8, 3.8
Mean % change (95% CI)	-	-	-	−2.0 (−7.1 to 3.1)	-	−0.8 (−6.2 to 4.7)
% change *p*-value	-	-	-	0.438	-	0.784
LMM change (95% CI)[a]	-	-	-	−0.13 (−0.22 to −0.04)	-	−0.10 (−0.20 to −0.00)
p-value[b]	-	-	-	0.005	-	0.042
Triglyceride (mmol/L)	$N = 101$	-	-	$N = 97$	-	$N = 93$
Mean ± SD	1.0 ± 0.38	-	-	0.9 ± 0.59	-	0.8 ± 0.32
Median (IQR)	0.9 (0.7–1.1)	-	-	0.8 (0.6–1.1)	-	0.8 (0.6–1.0)
Minimum, maximum	0.4, 2.5	-	-	0.3, 5.6	-	0.4, 1.8
Mean % change (95% CI)	-	-	-	−6.1 (−14.6 to 2.5)	-	−10.4 (−16.4 to −4.4)
% change *p*-value	-	-	-	0.161	-	0.001
LMM change (95% CI)[a]	-	-	-	−0.09 (−0.17 to −0.00)	-	−0.12 (−0.21 to −0.03)
p-value[b]	-	-	-	0.047	-	0.008

Note: Height is stable; percentage change in body mass index is equal to percentage change in body weight.

[a]Average change in the patient parameters from baseline adjusted for between and within variation using LMM.

[b]*p*-value from the LMM model assessing significance of change from baseline to the follow-up time point.

Abbreviations: CI, confidence interval; IQR, interquartile range; LMM, linear mixed model; SD, standard deviation.

TABLE 3 Mean percentage changes in body weight, glucose and lipids for participants switched from an efavirenz-based regimen to doravirine.

Characteristics	Baseline ($N = 46$)	Week 24 ($N = 44$)	Week 48 ($N = 43$)
Body weight (kg)			
Mean ± SD	74.8 ± 18.85	78.8 ± 19.09	78.9 ± 19.46
Median (IQR)	71.2 (63.0–81.5)	76.0 (65.7–87.6)	75.7 (66.2–89.4)
Minimum, maximum	45.8, 154.3	51.4, 156.9	49.1, 156.6
Mean % change (95% CI)	-	4.9 (3.2–6.6)	5.0 (2.9–7.1)
% change *p*-value	-	<0.001	<0.001
LMM change (95% CI)[a]	-	3.22 (2.23–4.22)	3.53 (1.93–5.13)
p-value[b]	-	<0.001	<0.001
Body mass index (kg/m^2)			
Mean ± SD	28.7 ± 6.61	30.3 ± 6.75	30.4 ± 6.80
Median (IQR)	28.2 (24.0–31.0)	29.9 (25.4–32.8)	29.9 (25.1–33.6)
Minimum, maximum	18.4, 55.3	20.9, 56.3	19.7, 56.1
Mean % change (95% CI)	-	4.9 (3.2–6.6)	5.0 (2.9–7.1)
% change *p*-value	-	<0.001	<0.001
LMM change (95% CI)[a]	-	1.27 (0.89–1.66)	1.37 (0.74–2.00)
p-value[b]	-	<0.001	<0.001
Glucose, fasting (mmol/L)			
Mean ± SD	4.9 ± 0.59	4.8 ± 0.74	4.9 ± 0.82
Median (IQR)	4.9 (4.6–5.1)	4.6 (4.4–4.8)	4.7 (4.5–5.2)
Minimum, maximum	2.8, 7.0	3.8, 7.8	3.9, 9.0
Mean % change (95% CI)	-	−4.4 (−7.2 to −1.6)	−2.4 (−5.1–0.3)
% change *p*-value	-	0.003	0.082
LMM change (95% CI)[a]	-	−0.21 (−0.35 to −0.07)	−0.12 (−0.28–0.04)
p-value[b]	-	0.003	0.155
Total cholesterol (mmol/L)			
Mean ± SD	4.3 ± 0.69	3.8 ± 0.64	3.9 ± 0.65
Median (IQR)	4.3 (3.9–4.7)	3.6 (3.4–4.1)	3.8 (3.5–4.1)
Minimum, maximum	2.9, 6.4	2.5, 5.9	2.3, 5.4
Mean % change (95% CI)	-	−12.9 (−16.9 to −9.0)	−10.5 (−14.8 to −6.1)
% change *p*-value	-	<0.001	<0.001
LMM change (95% CI)[a]	-	−0.59 (−0.74 to −0.44)	−0.51 (−0.69 to −0.33)
p-value[b]	-	<0.001	<0.001
High-density lipoprotein (mmol/L)			
Mean ± SD	1.6 ± 0.37	1.2 ± 0.31	1.2 ± 0.27
Median (IQR)	1.5 (1.3–1.9)	1.1 (1.0–1.4)	1.2 (1.0–1.4)
Minimum, maximum	0.9, 2.3	0.7, 2.0	0.7, 2.0
Mean % change (95% CI)	-	−20.6 (−26.1 to −15.2)	−18.4 (−23.9 to −12.9)
% change *p*-value	-	<0.001	<0.001
LMM change (95% CI)[a]	-	−0.35 (−0.43 to −0.27)	−0.33 (−0.42 to −0.24)
p-value[b]	-	<0.001	<0.001

TABLE 3 (Continued)

Characteristics	Baseline ($N = 46$)	Week 24 ($N = 44$)	Week 48 ($N = 43$)
Low-density lipoprotein (mmol/L)			
Mean ± SD	2.3 ± 0.65	2.2 ± 0.62	2.2 ± 0.60
Median (IQR)	2.2 (1.9–2.5)	2.1 (1.7–2.6)	2.2 (1.9–2.7)
Minimum, maximum	0.7, 4.4	1.0, 3.6	0.8, 3.6
Mean % change (95% CI)	-	−3.6 (−10.2–3.1)	(−8.0–5.7)
% change *p*-value	-	0.285	0.743
LMM change (95% CI)[a]	-	−0.15 (−0.28 to −0.02)	−0.10 (−0.25–0.06)
p-value[b]	-	0.021	0.216
Triglyceride (mmol/L), *n*			
Mean ± SD	1.0 ± 0.37	0.9 ± 0.36	0.8 ± 0.34
Median (IQR)	1.0 (0.8–1.2)	0.8 (0.6–1.1)	0.8 (0.6–1.1)
Minimum, maximum	0.4, 1.9	0.3, 2.0	0.4, 1.6
Mean % change (95% CI)	-	−16.3 (−24.9 to −7.6)	−18.9 (−26.4 to −11.5)
% change *p*-value	-	<0.001	<0.001
LMM change (95% CI)[a]	-	−0.20 (−0.28 to −0.12)	−0.21 (−0.30 to −0.13)
p-value[b]	-	<0.001	<0.001

[a]Average change in the patient parameters from baseline adjusted for between and within variation using LMM.
[b]*p*-value from the LMM model assessing significance of change from baseline to the follow-up time point.
Abbreviations: CI, confidence interval; IQR, interquartile range; LMM, linear mixed model; SD, standard deviation.

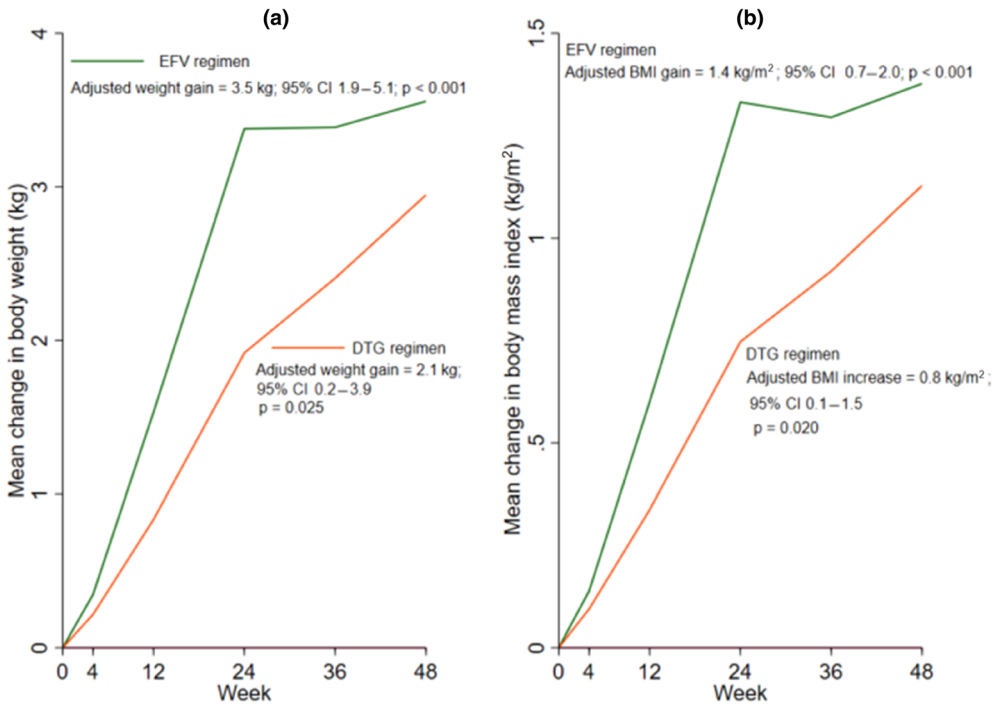

FIGURE 2 Changes in body weight (a) and body mass index (b) by previous antiretroviral therapy, with standard error bars at each measurement week. BMI, body mass index; CI, confidence interval; DTG, dolutegravir; EFV, efavirenz.

In total, 90 (89%) of 101 participants reported not missing any IP doses in the previous 4 days, with 84 (83%) keeping to the prescribed medication schedule on self-reported adherence measures at week 48. Two participants became pregnant during the study; both infants had normal post-partum foetal outcomes with no

TABLE 4 Mean percentage changes in body weight, glucose and lipids for participants switched from a dolutegravir-based regimen to doravirine.

Characteristics	Baseline ($N = 55$)	Week 24 ($N = 53$)	Week 48 ($N = 50$)
Body weight (kg)			
Mean ± SD	70.1 ± 12.20	71.4 ± 11.87	72.5 ± 12.90
Median (IQR)	69.4 (60.6–78.6)	71.5 (62.4–79.5)	72.2 (62.2–79.9)
Minimum, maximum	49.1, 97.5	52.3, 100.9	49.8, 101.8
Mean % change (95% CI)	-	3.1 (1.4–4.8)	4.5 (1.8–7.3)
% change *p*-value	-	0.001	0.002
LMM change (95% CI)[a]	-	1.82 (0.76–2.88)	2.08 (0.26–3.90)
p-value[b]	-	0.001	0.042
Body mass index (kg/m^2)			
Mean ± SD	26.7 ± 4.44	27.3 ± 4.48	27.6 ± 4.84
Median (IQR)	26.4 (22.5–29.9)	26.7 (23.5–30.0)	28.0 (23.3–30.8)
Minimum, maximum	19.7, 39.6	20.5, 40.9	19.9, 41.3
Mean % change (95% CI)	-	3.1 (1.4–4.8)	4.5 (1.8–7.3)
% change *p*-value	-	0.001	0.002
LMM change (95% CI)[a]	-	1.27 (0.89–1.66)	0.81 (0.13–1.49)
p-value[b]	-	<0.001	0.02
Glucose, fasting (mmol/L)			
Mean ± SD	4.9 ± 0.46	4.8 ± 0.73	4.8 ± 0.72
Median (IQR)	4.8 (4.6–5.2)	4.6 (4.4–5.0)	4.8 (4.3–5.0)
Minimum, maximum	4.3, 6.9	3.2, 8.1	4.0, 8.6
Mean % change (95% CI)	-	−2.5 (−5.9–1.0)	−2.8 (−6.1–0.6)
% change *p*-value	-	0.153	0.102
LMM change (95% CI)[a]	-	−0.13 (−0.30–0.03)	−0.17 (−0.36–0.02)
p-value[b]	-	0.103	0.076
Total cholesterol (mmol/L)			
Mean ± SD	4.1 ± 0.78	3.7 ± 0.70	3.8 ± 0.74
Median (IQR)	4.0 (3.5–4.6)	3.7 (3.3–4.3)	3.6 (3.3–4.2)
Minimum, maximum	2.2, 6.4	2.0, 5.2	2.5, 5.6
Mean % change (95% CI)	-	−7.1 (−11.1 to −3.1)	−6.7 (−10.7 to −2.7)
% change *p*-value	-	0.001	0.001
LMM change (95% CI)[a]	-	−0.33 (−0.48 to −0.18)	−0.28 (−0.44 to −0.12)
p-value[b]	-	<0.001	0.001
High-density lipoprotein (mmol/L)			
Mean ± SD	1.3 ± 0.36	1.1 ± 0.32	1.2 ± 0.34
Median (IQR)	1.3 (1.2–1.4)	1.1 (0.9–1.3)	1.1 (1.0–1.3)
Minimum, maximum	0.6, 2.8	0.2, 1.9	0.7, 2.5
Mean % change (95% CI)	-	−16.3 (−21.6 to −11.0)	−11.8 (−16.7 to −6.8)
% change *p*-value	-	<0.001	<0.001
LMM change (95% CI)[a]	-	−0.23 (−0.29 to −0.17)	−0.17 (−0.24 to −0.10)
p-value[b]	-	<0.001	<0.001

TABLE 4 (Continued)

Characteristics	Baseline ($N = 55$)	Week 24 ($N = 53$)	Week 48 ($N = 50$)
Low-density lipoprotein (mmol/L)			
Mean ± SD	2.3 ± 0.70	2.2 ± 0.60	2.3 ± 0.59
Median (IQR)	2.4 (1.8–2.8)	2.1 (1.8–2.7)	2.3 (1.8–2.7)
Minimum, maximum	0.5, 3.8	1.1, 3.6	1.2, 3.8
Mean % change (95% CI)	-	−0.8 (−8.5–6.9)	(−8.9–8.0)
% change *p*-value	-	0.835	0.918
LMM change (95% CI)[a]	-	−0.12 (−0.24–0.01)	−0.11 (−0.24–0.02)
p-value[b]	-	0.067	0.097
Triglycerides (mmol/L)			
Mean ± SD	0.9 ± 0.37	0.9 ± 0.73	0.8 ± 0.30
Median (IQR)	0.9 (0.6–1.0)	0.7 (0.6–1.1)	0.8 (0.6–1.0)
Minimum, maximum	0.5, 2.5	0.4, 5.6	0.4, 1.8
Mean % change (95% CI)	-	2.4 (−11.3–16.1)	−3.1 (−11.9–5.8)
% change *p*-value	-	0.729	0.493
LMM change (95% CI)[a]	-	0.01 (−0.14–0.16)	0.05 (−0.21–0.31)
p-value[b]	-	0.892	0.698

[a]Average change in the patient parameters from baseline adjusted for between and within variation using LMM.
[b]*p*-value from the LMM model assessing significance of change from baseline to the follow-up time point.
Abbreviations: CI, confidence interval; IQR, interquartile range; LMM, linear mixed model; SD, standard deviation.

congenital abnormalities and negative birth (and subsequent) HIV polymerase chain reaction test results.

DISCUSSION

In our cohort of Black women living with HIV, drawn from a population where the first major randomized clinical trial findings around weight gain on modern ART were seen, switching to a doravirine-containing regimen had a beneficial impact on lipids and led to a small improvement in fasting glucose, with maintenance of virological suppression and low rates of discontinuation but ongoing weight gain. In the context of modern ART, this is one of the few clinical trials evaluating a switch from a second-generation INSTI to an NNRTI, providing new information regarding weight trajectories and virological/immune-recovery data for a new switch strategy. The major rationale for the study was to find alternative ART agents for people with HIV experiencing weight gain that may slow or reverse the weight gain without adverse metabolic outcomes. This regimen did not appear to make a difference to weight trajectory. We did not have a control arm against which to measure weight gain, but other studies from the same population have shown similar weight trajectories [16].

Participants had a steady increase in weight over the 48-week period, our major endpoint of interest. The weight change was slightly greater in the group previously on efavirenz, with adjusted mean increases in weight (3.5 kg) compared with those previously on dolutegravir (2.1 kg), probably reflecting the reversal of contribution of efavirenz slow metabolizers [11]. In initial doravirine phase III clinical trials, a post hoc pooled analysis of three randomized controlled trials reported that weight gain on doravirine at 96 weeks was 2.4 kg, and the authors cited no significant difference between doravirine/efavirenz/ritonavir-boosted darunavir treatment arms [17]. However, prior trials have associated dolutegravir regimens with weight gain [5, 6, 18–20], and this seems to be greatest in Black women and/or those with lower CD4 counts and associated with an increased risk of up to 10% weight gain over 2 years in this group [19, 21]. Pooled data from ART switch randomized trials by Erlandson et al. [22] showed that median weight gain was 1.6 kg in participants who switched, especially from efavirenz to rilpivirine or elvitegravir/cobicistat and switched from tenofovir disoproxil fumarate to tenofovir alafenamide. They noted that only BMI category and age were associated with greater weight gain (modest gain in those aged <35 years and in non-obese participants). In the

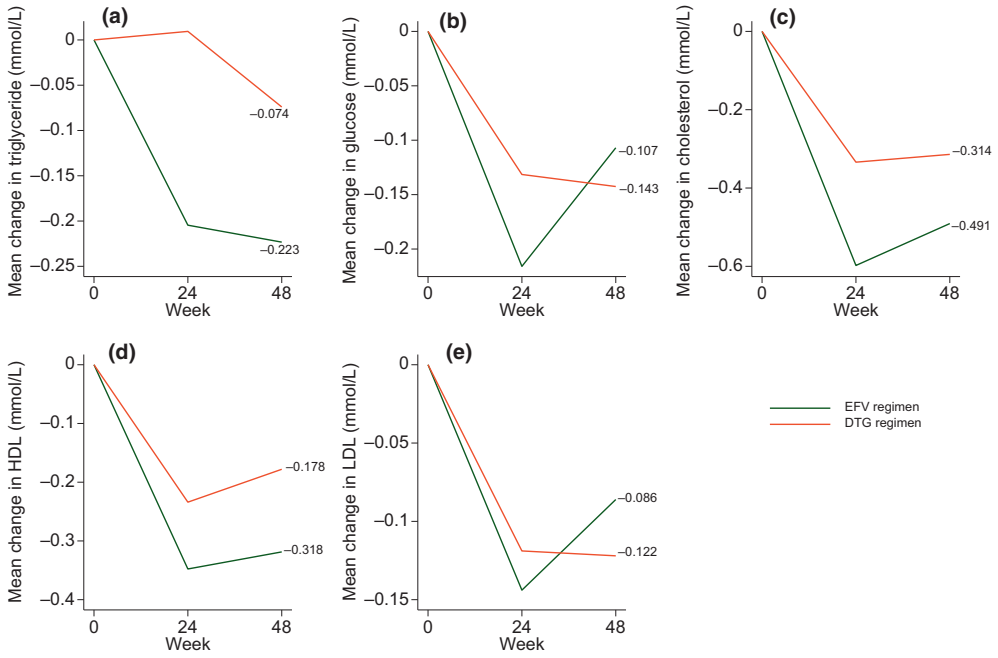

FIGURE 3 Changes in triglycerides (a), glucose (b), total cholesterol (c), high-density lipoprotein (HDL) (d) and low-density lipoprotein (LDL) (e) with associated standard error bars at each measurement week. DTG, dolutegravir; EFV, efavirenz.

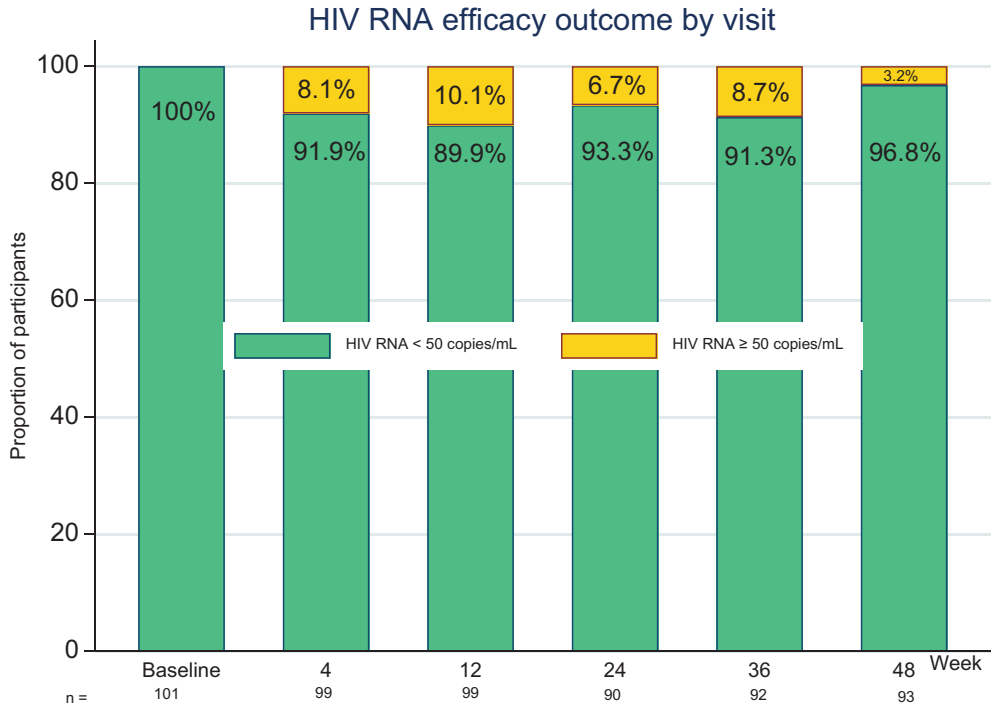

FIGURE 4 HIV RNA suppression proportions at each measurement week.

DRIVE-SHIFT study, participants who switched from a stable ART regimen to doravirine at baseline (immediate switch group) or at week 24 (delayed switch group) had a mean weight gain of 1.4 kg and 1.2 kg, respectively, at week 144 [23]. However, this study had low participation from Black females.

There are continuing metabolic concerns with virologically suppressed people ageing on ART, with HIV itself contributing to cardiovascular risk factors [24, 25]. In addition, many classes of ART are associated with metabolic disturbances, such as weight gain, lipid abnormalities and impaired glucose metabolism, which all

TABLE 5 CD4 count levels at baseline and weeks 24 and 48 for participants switched to a doravirine-based HIV treatment regimen over 48 weeks of follow-up.

CD4 counts	Baseline $N = 101$	Week 24 $N = 90$	Week 48 $N = 93$
CD4 count (cells/μL)			
Mean ± SD	631 ± 274	NA	638 ± 256
Median (IQR)	600 (437–799)	NA	622 (458–792)
Minimum, maximum	112, 1463	NA	111, 1455
Mean % change (95% CI)	NA	NA	7.4 (2.4–12.3)
% change *p*-value	NA	NA	0.004
CD4 count categories, *n* (%)			
<200	4 (4.0)	NA	4 (4.3)
≥200	97 (96.0)	NA	88 (95.7)

Abbreviations: CI, confidence interval; IQR, interquartile range; NA, not applicable; SD, standard deviation.

TABLE 6 Self-reported adverse events in participants switched to a doravirine-based HIV treatment regimen over 48 weeks of follow-up.

Self-reported AEs	Number (%) of patients with AE ($n = 101$)	Details
Neuropsychiatric AEs	7 (6.9)	
Week 4	3 (42.8)[a]	Dizziness (n=2), severity grade 1; altered sensorium (n=1), severity grade 1
Week 12	2 (28.6)	Sleep disorders/disturbances (n=2), severity grade 1
Week 24	2 (28.6)	Sleep disorders/disturbances (n=2), severity grade 1
Week 36	0	
Week 48	0	
Cardiometabolic-related AEs	10 (9.9)	A total of 10 events; one patient had hypertension and dyslipidaemia
Hypertension	6 (60.0)[a]	Severity grade 1 (n=4), grade 2 (n=2)
Diabetes/hyperglycaemia	3 (30.0)	Severity grade 1 (n=1), grade 2 (n=2)
Dyslipidaemia	1 (10.0)	Severity grade 2 (n=1)
AEs (grade 3/4)	4 (4.0)	
Weight loss	2 (50.0)[a]	Occurred at week 36 (n=2)
Cervical dysplasia	1 (25.0)	Occurred at week 12 (n=1)
Jaundice extrahepatic obstructive	1 (25.0)	Occurred at week 12 (n=1)
Serious AEs	1 (1.0)	Jaundice extrahepatic obstructive; occurred at week 12 (n=1)
AEs possibly related to IP	23 (22.8)	23 AEs were reported as possibly related
AEs related to IP	4 (4.0)	4 AEs were reported as related to study drug
Laboratory abnormalities (grade 3/4)	16 (15.8)	
Haemoglobin	11 (68.8)[a]	
Helper T cells (CD4 count)	4 (25.0)	
Lymphocyte	1	

Note: n = number of subjects with events; % = percentage of subjects enrolled.

[a]Percentage of subjects within subgroup.

Abbreviations: AEs, adverse events; IP, investigational product.

contribute to an increased risk of cardiovascular disease. Efavirenz, along with the protease inhibitors, is known to both increase lipid levels and exacerbate insulin resistance [26, 27]. For example, results from both DRIVE-AHEAD (efficacy of doravirine compared with efavirenz-based regimens) and DRIVE-FORWARD (non-inferiority of doravirine compared with ritonavir-boosted darunavir) showed superior lipid profiles at 96 weeks of follow-up [12, 13]. Furthermore, DRIVE-SHIFT showed a reduction in fasting lipids at 24 weeks after switching to a doravirine-based regimen, maintained to week 144 [14]. Other smaller switch study cohorts have replicated this lipid improvement in real-world settings [28–31]. Our study confirms these lipid changes, with statistically significant decreases in total cholesterol, HDL and triglycerides throughout the study period after a drug switch from prior efavirenz- and dolutegravir-based regimens. Our results for efavirenz were unsurprising, but the data on lipid improvements after a prior dolutegravir-based regimen are the first to show this lipid benefit in first-line participants.

Data on an association between dolutegravir and hypertensive risk, possibly confounded by associated weight gain, are emerging. A recent prospective cohort study showed a 14% increase in the risk of hypertension in those exposed to dolutegravir compared with those who remained on efavirenz [5]. In the RESPOND cohort, the incidence of new hypertensive cases was 23% in participants receiving INSTIs, a higher incidence than with NNRTIs (in both ART-naïve and -experienced participants) [32]. Similarly, in the REPRIEVE cohort, there was an increased odds ratio of 1.4 of hypertension in females on INSTIs [33]. However, only six new hypertensive cases were observed in our study, with blood pressure remaining stable, despite weight gain, and our sample size is far too small to make useful inferences.

Limitations of this study include the single-arm, open-label, single-site design and small sample size. We removed from the analysis participants with disruption to their IP, which may have introduced bias, although the baseline demographics of this group suggest they were similar to those of the overall cohort. As the trial was not randomized to other drug classes, these factors limit our ability to conduct direct comparisons. Strengths include recruitment from routine services, limited inclusion and exclusion criteria and representation of an under-represented study population.

CONCLUSIONS

Our findings suggest that doravirine offers an effective switch first-line ART alternative in Black women, with significant improvement in lipid profiles but does not seem to reverse the progressive weight gain seen with current INSTI or legacy efavirenz-based regimens. Head-to-head comparative randomized and well-powered studies may offer more definitive results.

In conclusion, other options may need to be pursued for weight loss. If weight gain on modern ART is not a function of specific antiretrovirals, interventions may need to consider newer interventions, including specific anti-obesity agents. The finding that switching from dolutegravir to doravirine has beneficial impacts on lipids was unexpected and may merit further exploration.

AUTHOR CONTRIBUTIONS

JW, MM, NC, WDFV and AH conceived and designed the study. SS and WDFV procured the funding. SS led the study, and JW was responsible for methodology and project administration. JW, BB, EB, CK, KM, NM, NT and PM implemented the study and enrolled participants. GA did the statistical analyses. JW, SS and WDFV contributed to the interpretation of the results. JW wrote the original draft, and all authors reviewed and approved the final version of the paper. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. SS, WDFV and KM directly accessed and verified the underlying data reported in the manuscript.

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CONFLICT OF INTEREST STATEMENT

AH has conducted statistical analysis for HIV-related and tuberculosis-related clinical trials for MetaVirology. MM joined ViiV Healthcare, as a full-time employee as Head of Global Medical Directors in August 2020. WDFV's unit (Ezintsha) receives funding from the Bill and Melinda Gates Foundation, SA Medical Research Council, National Institutes for Health, Unitaid, Foundation for Innovative New Diagnostics (FIND), Merck and the Children's Investment Fund Foundation (CIFF); has previously received funding from USAID; and receives drug donations from ViiV Healthcare, Merck, J&J and Gilead Sciences for investigator-led clinical studies. The unit

conducts investigator-led studies for which Merck, J&J and ViiV provide financial support and is conducting commercial drug studies for Merck. The unit performs evaluations of diagnostic devices for multiple biotech companies. Individually, he receives honoraria for educational talks and advisory board membership for Gilead, ViiV, Mylan/Viatris, Merck, Adcock-Ingram, Aspen, Abbott, Roche, J&J, Sanofi and Virology Education.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. Requests for access to the DORA study data should be sent to jwoods@ezintsha.org. De-identified participant data and a data dictionary can be made available and shared under a data transfer agreement.

ETHICS STATEMENT

The trial received approvals from the Human Research Ethics Committee (ref no. 191108) and the South African Health Products Regulatory Authority (ref no. 20200323). Written informed consent was obtained from participants, including additional consent for participants falling pregnant. The trial adhered to international and local ethical guidelines, with oversight from an independent safety monitoring board. The trial was registered at ClinicalTrials.gov (NCT04433780).

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REFERENCES

1. UNAIDS. FACT SHEET. 2023 [Internet]. [cited 2023 Jul 3]. Available from: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf
2. Voight E. Over 3million people on new HIV drug, but not all smooth sailing. Spotlight [Internet]. 2022 Available from: INSTIs initiation was associated with an early onset, excess incidence of cardiovascular disease in the first 2 years of%0Dexposure, after accounting for known cardiovascular disease risk factors.
3. Clinton Health Access Initiative. 2023 HIV Market Report 2023 [Internet]. [cited 2024 Jan 3]. Available from: https://chai19.wpenginepowered.com/wp-content/uploads/2023/11/2023-HIV-Market-Report_11.2.23.pdf.
4. Neesgaard B, Greenberg L, Miró JM, et al. Associations between integrase strand-transfer inhibitors and cardiovascular disease in people living with HIV: a multicentre prospective study from the RESPOND cohort consortium. *Lancet HIV*. 2022;9:e485.
5. Brennan AT, Nattey C, Kileel EM, et al. Change in body weight and risk of hypertension after switching from efavirenz to dolutegravir in adults living with HIV: evidence from routine care in Johannesburg. *South Africa eClinicalMedicine*. 2023;57:101836.
6. Bai R, Lv S, Wu H, Dai L. Effects of different integrase strand transfer inhibitors on body weight in patients with HIV/AIDS: a network meta-analysis. *BMC Infect Dis*. 2022;22(1):1-8.
7. Venter WDF, Moorhouse M, Sokhela S, et al. Dolutegravir plus two different prodrugs of Tenofovir to treat HIV. *N Engl J Med*. 2019;381(9):803-815.
8. Hill A, Hughes SL, Gotham D, Pozniak AL. Tenofovir alafenamide versus tenofovir disoproxil fumarate: is there a true difference in efficacy and safety? *J Virus Erad*. 2018;4(2):72-79.
9. Geneva: joint United Nations Programme on HIV/AIDS. UNAIDS Data 2022.
10. Mabaso M, Makola L, Naidoo I, Mlangeni LL, Jooste S, Simbayi L. HIV prevalence in South Africa through gender and racial lenses: results from the 2012 population-based national household survey. *Int J Equity Health*. 2019;18(1):167.
11. Maartens G, Sinxadi P, Venter WDF. Weight gain on dolutegravir: association is not the same as causation. *South Afr J HIV Med*. 2023;24(1):1500.
12. Molina JM, Squires K, Sax PE, et al. Doravirine versus ritonavir-boosted darunavir in antiretroviral-naive adults with HIV-1 (DRIVE-FORWARD): 96-week results of a randomised, double-blind, non-inferiority, phase 3 trial. *Lancet HIV*. 2020;7(1):e16-e26.
13. Orkin C, Squires KE, Molina JM, et al. Doravirine/lamivudine/Tenofovir Disoproxil fumarate (TDF) versus Efavirenz/Emtricitabine/TDF in treatment-naive adults with human immunodeficiency virus type 1 infection: week 96 results of the randomized, double-blind, phase 3 DRIVE-AHEAD noninferiority. *Clin Infect Dis*. 2021;73(1):33-42.
14. Johnson M, Kumar P, Molina JM, et al. Switching to Doravirine/lamivudine/Tenofovir Disoproxil fumarate (DOR/3TC/TDF) maintains HIV-1 Virologic suppression through 48 weeks: results of the DRIVE-SHIFT trial. *J Acquir Immune Defic Syndr*. 2019;81(4):463-472.
15. Zhang K, Zhang Y, Zhou J, et al. Comparison of the efficacy and safety of a Doravirine-based, three-drug regimen in treatment-Naïve HIV-1 positive adults: a Bayesian network meta-analysis. *Front Pharmacol*. 2022;13:1-13.
16. Venter WDF, Sokhela S, Simmons B, et al. Dolutegravir with emtricitabine and tenofovir alafenamide or tenofovir disoproxil fumarate versus efavirenz, emtricitabine, and tenofovir disoproxil fumarate for initial treatment of HIV-1 infection (ADVANCE): week 96 results from a randomised, phase 3, non-inferiority trial. *Lancet HIV*. 2020;7(10):e666-e676.
17. Orkin C, Elion R, Thompson M, et al. Changes in weight and BMI with first-line doravirine-based therapy. *Aids*. 2021;35(1):91-99.
18. Kerchberger AM, Sheth AN, Angert CD, et al. Weight gain associated with integrase stand transfer inhibitor use in women. *Clin Infect Dis*. 2020;71(3):593-600.
19. 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:e25484. doi: 10.1002/jia2.25484

20. Wood BR, Huhn GD. Excess weight gain with integrase inhibitors and Tenofovir Alafenamide: what is the mechanism and does it matter? Open forum. *Infect Dis*. 2021;8(12):ofab542.
21. 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.
22. Erlandson KM, Carter CC, Melbourne K, et al. Weight change following antiretroviral therapy switch in people with viral suppression: pooled data from randomized clinical trials. *Clin Infect Dis*. 2021;73(8):1440-1451.
23. Kumar P, Johnson M, Molina JM, et al. Brief report: switching to DOR/3TC/TDF maintains HIV-1 Virologic suppression through week 144 in the DRIVE-SHIFT trial. *J Acquir Immune Defic Syndr*. 2021;87(2):801-805.
24. Feinstein MJ. HIV, subclinical cardiovascular disease, and clinical progression: insights from immunologic heterogeneity. *Jama*. 2022;328(10):931-932.
25. Saad H, Ntusi AB. *N*. HIV-associated cardiovascular disease. In: Okware S, ed. *Advances in HIV and AIDS Control*. IntechOpen; 2018.
26. Vos AG, Venter WDF. Cardiovascular toxicity of contemporary antiretroviral therapy. *Curr Opin HIV AIDS*. 2021;16(6):286-291.
27. Ryom L, Lundgren JD, El-Sadr W, et al. Cardiovascular disease and use of contemporary protease inhibitors: the D:a:D international prospective multicohort study. *Lancet HIV*. 2018;5(6):e291-e300.
28. Iannone V, Passerotto RA, Lamanna F, et al. Changes in metabolic profile in PLWHIV switching to Doravirine-based regimen. *Viruses*. 2023;15(5):1046.
29. Ciccullo A, D'Angelillo A, Iannone V, et al. Real-life safety of Doravirine in treatment-experienced, Virologically suppressed PLWHIV. *J Acquir Immune Defic Syndr*. 2021;88(1):e5-e6.
30. Maggi P, Ricci ED, Cicalini S, et al. Lipids and transaminase elevations in ARV-experienced PLWH switching to a doravirine-based regimen from rilpivirine or other regimens. *BMC Infect Dis*. 2023;23(1):227.
31. Mazzitelli M, Antoni MD, Castelli F, et al. Real-life use of Doravirine in treatment-experienced people living with HIV: a multicenter Italian study. *Medicine (Baltimore)*. 2022;101(30):e29855.
32. Byonanebye DM, Polizzotto MN, Neesgaard B, et al. Incidence of hypertension in people with HIV who are treated with integrase inhibitors versus other antiretroviral regimens in the RESPOND cohort consortium. *HIV Med*. 2022;23(8):895-910.
33. Kileel EM, Lo J, Malvestutto C, et al. Assessment of obesity and Cardiometabolic status by integrase inhibitor use in REPRIEVE: a propensity-weighted analysis of a multinational primary cardiovascular prevention cohort of people with human immunodeficiency virus. Open forum. *Infect Dis*. 2021;8(12):ofab537.

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