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Assessing Real-world Weight Change in the Treatment and Prevention of HIV-1 with a Cabotegravir-containing Regimen

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Abstract:

Background: Initiation of several Integrase Strand-transfer Inhibitors (INSTIs) has been associated with weight gain in clinical trials. However, the data evaluating weight change with cabotegravir, the newest INSTI, is limited.

Objective: The primary objective was to assess the real-world weight change in patients who switched to long-acting injectable (LAI) cabotegravir or cabotegravir-rilpivirine from another antiretroviral regimen.

Methods: In this retrospective study, patients receiving HIV-1 treatment with cabotegravir-rilpivirine, or pre-exposure prophylaxis (PrEP) with cabotegravir, were identified through an Epic-generated report. Patients on a cabotegravir-containing regimen who met inclusion criteria were followed for 12 months from treatment initiation. The primary endpoint was weight change from month 0 of treatment initiation to 3, 6, and 12 months in all patients on cabotegravir-based LAI.

Results: A total of 48 patients were included in the study. At month 3, the mean weight change was 0.3 kg (95% CI, -0.8 to 1.4; p=0.56). At month 6, the mean weight change was 1.1 kg (95% CI, -0.4 to 2.7; p=0.14). At month 12, the mean weight change was 0.0 kg (95% CI, -2.5 to -2.3; p=0.97). Virologic failure was confirmed in 2 patients on cabotegravir-rilpivirine. Adverse events were documented in 28 patients (58%), including injection site pain, nodules at the injection site, and depression, and 10% discontinued therapy because of an adverse event.

Conclusion: Bimonthly injections of cabotegravir and cabotegravir-rilpivirine were not associated with significant weight change. Adverse reactions were common and frequently led to discontinuation of therapy. This real-world data may be used to influence provider clinical decision-making.

Keywords: HIV, PrEP, long-acting injectable, cabotegravir, weight, INSTI, integrase inhibitor, ART.

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1. INTRODUCTION

Human immunodeficiency virus (HIV)-1 remains a serious and life-threatening global public health emergency. In 2022, an estimated 39 million people globally were living with HIV, with about 630,000 people dying from HIV-related causes [1]. With the introduction of modern antiretroviral therapy (ART), the life expectancy of a person living with HIV (PLWH) has been prolonged significantly, with a 51% reduction in HIV-related deaths since 2010 [1]. While safe and efficacious, current combination antiretroviral regimens require lifelong daily oral intake of medication, which can be burdensome for patients and potentially associated with increased risk of non-adherence, treatment failure, and the emergence of drug resistance [2].

Long-acting injectable (LAI) therapy was introduced to help improve patient satisfaction and overcome the challenges associated with other ART regimens [2, 3]. In a recent survey, 73% of patients reported interest in trying LAI therapy, noting less frequent dosing [4]. Cabotegravir, an integrase strand-transfer inhibitor (INSTI), and rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI), were co-formulated into a long-acting parenteral nanosuspension which was approved by the FDA as the first LAI therapy for PLWH in January 2021 [5]. In December 2021, LAI cabotegravir alone was approved by the FDA for pre-exposure prophylaxis (PrEP) against HIV infection [6]. Both agents have a long duration of action, which allows for maintenance dosing of LAI therapy as infrequently as every eight weeks, with no oral background therapy required [5, 6].

One question surrounding the use of INSTIs in LAI therapy is the incidence of adverse events. Several oral INSTIs were found to be associated with weight gain in clinical trials [7-10]. A retrospective, observational study using data obtained from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) found that INSTI-based regimens, primarily dolutegravir- or raltegravir-based, were associated with greater weight gain compared to NNRTI-based regimens, and similar weight change compared to protease inhibitor (PI)-based regimens [7]. Another pooled analysis found similar results, with the magnitude of weight gain being larger in more recent studies with the use of newer ART regimens. Finally, women living with HIV who were switched to an INSTI-based ART regimen experienced a significantly greater increase in body weight, BMI, body circumferences, and percent body fat compared to women on non-INSTI-based ART regimens in a recent analysis [9]. In addition to the female sex, studies have revealed baseline factors of lower CD4 count, higher HIV-1 RNA, and no injection drug use, and Black and Hispanic race were associated with weight gain. However, cabotegravir was not included in these trials [8, 10].

Little data exists on whether treatment with cabotegravir is associated with weight gain. The HIV Prevention Trials Network Study 077 (HPTN 077) analyzed weight gain in participants receiving at least one injection of cabotegravir or placebo (134 vs 43 participants) for HIV prevention in low-risk, uninfected individuals. This phase 2b study revealed no significant differences in weight change between the two arms over a 41-week period, prompting further investigation [10, 11]. The ATLAS and FLAIR trials were two phase 3, randomized, open-label trials assessing the efficacy of cabotegravir-rilpivirine in maintaining HIV-1 viral suppression [2, 12]. A 48-week pooled analysis of these two trials reported a weight change of 2.34 kg in the LAI arm and 1.17 kg in the current ART arm from baseline to week 48 [13]. However, the ATLAS and FLAIR trials included predominantly white males (73%), which is not representative of the patient population we see at our institution's infectious disease clinics [2, 12]. The pathogenesis of weight gain in PLWH is poorly understood and may lead to serious comorbidities, including diabetes mellitus and cardiovascular disease, making early identification of these effects a priority [10, 14]. Hence, the primary objective of this study is to assess the real-world weight change in patients who switched to LAI cabotegravir or cabotegravir-rilpivirine from another anti-retroviral regimen.

2. MATERIALS AND METHODS

2.1. Study Design and Participants

This was a retrospective, single-center study of patients at our institution's infectious disease clinics: Burgdorf Health Center and Saint Francis Hospital Gengras Clinic. Prior to starting LAI therapy, our patients received oral lead-in therapy with 30 mg cabotegravir ± 25 mg rilpivirine for approximately 28 days. On the last day of oral lead-in therapy, patients returned to the clinic to receive their first injection at a loading dose of 600 mg cabotegravir ± 900 mg rilpivirine administered into the gluteal muscle at two separate injection sites. Patients returned to the clinic 4 weeks later for their second injection at a maintenance dose of 400 mg cabotegravir + 600 mg rilpivirine for HIV-1 treatment or 600 mg cabotegravir for PrEP. Following this dose, maintenance doses were administered every 8 weeks. An Epic report was generated to identify all patients from Saint Francis Hospital Gengras Clinic and Burgdorf Health Center that were treated with a cabotegravir-based regimen between January 1, 2021, and May 31, 2023. Patients were included if they were male or female, aged 18 to 89 years old, completed oral lead-in therapy, and received at least one injection of cabotegravir or cabotegravir-rilpivirine during the study period. Pregnant patients were excluded. Patients were followed for 12 months from the start of oral lead-in therapy. Given the design of this study, patients were not actively recruited or randomized. Since this was a retrospective study, informed consent was waived.

2.2. End Points

At each clinic visit, our clinicians conducted a physical exam, recorded patient vital signs, assessed for adverse events, and administered each injection. HIV-1 RNA viral load was routinely obtained every 3-6 months. The primary

end point was weight change from month 0 of treatment initiation to 3, 6, and 12 months in all patients on cabotegravir-based LAI. Secondary endpoints included weight change from month 0 of treatment initiation to 3, 6, and 12 months in patients on LAI cabotegravir alone, weight change from month 0 of treatment initiation to 3, 6, and 12 months in patients on LAI cabotegravir-rilpivirine, and proportion of patients remaining virally suppressed or HIV negative at 3, 6, and 12 months. HIV viral suppression was defined as plasma HIV-1 RNA viral load of less than 50 copies/ml. Patients were deemed to have confirmed virologic failure if they had two consecutive HIV-1 RNA viral loads greater than or equal to 200 copies/ml.

2.3. Statistical Analysis

The primary and secondary analyses included all patients according to intention-to-treat principles. The sample size was determined to be a maximum of 60 patients based on clinic administration records since the FDA approval of each agent. Weight change at each time point was reported as the mean and a paired t-test was used to assess for differences at each point. Categorical data were analyzed using a chi-square test and reported as percentages. A histogram and Q-Q plot were used to ensure normal distribution of data. A two-sided 95% confidence interval was calculated to assess for statistically significant differences between groups. Subgroup analyses were performed to assess for confounders.

3. RESULTS

3.1. Participants

A total of 58 patients were screened for inclusion. Of the 58 patients, 4 had not yet received their first injection, 3 reported not starting oral lead-in therapy, 2 transitioned back to previous therapy due to insurance denial, and 1 self-discontinued oral lead-in therapy, with the remaining 48 patients meeting inclusion criteria. Participants included a median of 46 years of age, with 63% male and 93% black or Hispanic Table **1**. A total of 40 patients had a confirmed diagnosis of HIV-1, and 8 patients were receiving therapy for PrEP. Of those with HIV-1, 98% had an HIV-1 RNA viral load of <50 copies/ml at baseline, and all patients receiving therapy for PrEP were HIV-negative at baseline. Approximately, 79% were overweight (BMI $\geq$ 25 kg/m^2) or obese (BMI $\geq$ 30 kg/m^2), and 79% were on an INSTI prior to initiation of LAI.

Table 1. Demographic and baseline characteristics of the participants at baseline.

Characteristic	All LAI Patients (N=48)	LAI Cabotegravir-rilpivirine (N=40)	LAI Cabotegravir (N=8)
Median age (IQR) – yr	46 (38-57)	49 (37-59)	43 (40-51)
Sex – no. (%)			
Male	30 (63)	24 (60)	6 (75)
Female	18 (38)	16 (40)	2 (25)
Race – no. (%)			
White	3 (6)	2 (5)	1 (13)
Black	29 (60)	25 (63)	4 (50)
Hispanic	16 (33)	13 (33)	3 (38)
BMI class – no. (%)			
Underweight	0 (0)	0 (0)	0 (0)
Normal weight	10 (21)	7 (18)	3 (38)
Overweight	17 (35)	15 (38)	2 (25)
Obese	21 (44)	18 (45)	3 (38)
Median weight (IQR) – kg	87.8 (75.2-102.9)	87.8 (75.2-102.2)	88.9 (75.5-103.1)
HIV-1 RNA viral load – no. (%)			
Detectable	1 (2)	1 (2)	0 (0)
Undetectable	47 (98)	39 (98)	8 (100)
Last used HIV medication class – no. (%)			
NRTI	42 (88)	34 (85)	8 (100)
NNRTI	8 (17)	8 (20)	0 (0)
INSTI	38 (79)	37 (93)	1 (13)
PI	0 (0)	0 (0)	0 (0)
Comorbidities – no. (%)			
Prediabetes	11 (23)	9 (23)	2 (25)
Type 2 diabetes	6 (13)	6 (15)	0 (0)
ASCVD	2 (4)	2 (5)	0 (0)
Dyslipidemia	19 (40)	18 (45)	1 (13)
Confounding medications – no. (%)			
Weight gain	19 (40)	19 (48)	0 (0)
Weight loss	4 (8)	4 (10)	0 (0)

3.2. Primary and Secondary EndPoints

For the primary outcome of weight change from month 0 of treatment initiation to 3, 6, and 12 months in all patients on cabotegravir-based LAI, the mean weight change from baseline to 3 months was 0.3 kg (95% confidence interval [CI], -0.8 to 0.4; p=0.56). From baseline to 6 months, the mean weight change was 1.1 kg (95% CI, -0.4 to 2.7; p=0.14). From baseline to 12 months, the mean weight change was 0.0 kg (95% CI, -2.5 to 2.3; p=0.97). The median weight for each time point is shown in Table 2.

For the secondary outcome of weight change from month 0 of treatment initiation to 3, 6, and 12 months in patients on LAI cabotegravir-rilpivirine, the mean weight change from baseline to 3 months was 0.7 kg (95% CI, -0.5 to 1.8; p=0.67). From baseline to 6 months, the mean weight change was 1.3 kg (95% CI, -0.3 to 3.0; p=0.11). From baseline to 12 months, the mean weight change was -0.3 kg (95% CI, -2.9 to 2.4; p=0.84).

For the secondary outcome of weight change from month 0 of treatment initiation to 3, 6, and 12 months in patients on LAI cabotegravir only, mean weight change from baseline to 3 months was -1.6 kg (95% CI, -4.7 to 1.4; p=0.23). From baseline to 6 months, the mean weight change was -0.1 kg (95% CI, -5.1 to 5.1; p=0.98). From baseline to 12 months, the mean weight change was 1.6 kg (95% CI, -6.2 to 9.4; p=0.63).

Table 2. Weight change from baseline to 3, 6, and 12 months.

Characteristic	Median Weight (IQR) – kg	Mean Weight Change from Baseline - kg (95% CI)	P-Value
Primary End Point			
All patients on LAI	-	-	-
Baseline, n=48	87.8 (75.2-102.9)	-	-
3 months, n=46	89.8 (76.4-100.8)	0.3 (-0.8 to 1.4)	0.56
6 months, n=41	90.5 (78.0-100.4)	1.1 (-0.4 to 2.7)	0.14
12 months, n=36	88.2 (72.5-100.1)	0.0 (-2.5 to 2.3)	0.97
Secondary End Points			
Patients on cabotegravir-rilpivirine	-	-	-
Baseline, n=40	87.8 (75.2-102.2)	-	-
3 months, n=39	89.8 (76.7-103.2)	0.7 (-0.5 to 1.8)	0.67
6 months, n=35	91.3 (78.9-99.8)	1.3 (-0.3 to 3.0)	0.11
12 months, n=30	87.7 (71.4-99.3)	-0.3 (-2.9 to 2.4)	0.84
Patients on cabotegravir only	-	-	-
Baseline, n=8	88.9 (75.5-103.1)	-	-
3 months, n=7	82.1 (75.2-93.2)	-1.6 (-4.7 to 1.4)	0.23
6 months, n=6	87.2 (75.4-97.8)	-0.1 (-5.1 to 5.1)	0.98
12 months, n=6	90.6 (79.5-100.9)	1.6 (-6.2 to 9.4)	0.63

Table 3. HIV viral load from baseline to 3, 6, and 12 months.

Characteristic	HIV-1 RNA Viral Load Undetectable or HIV-1 Negative – No./total No. (%)	HIV-1 RNA Viral Load Detectable or HIV-1 Positive – No. (%)
Secondary End Point		
All patients on LAI	-	-
Baseline	47/48 (98)	1/48 (2)
3 months	37/38 (97)	1/38 (3)
6 months	38/40 (95)	2/40 (5)
12 months	32/33 (97)	1/33 (3)
Patients on cabotegravir-rilpivirine	-	-
Baseline	39/40 (98)	1/40 (3)
3 months	31/32 (97)	1/32 (3)
6 months	32/34 (94)	2/34 (6)
12 months	26/27 (96)	1/27 (4)
Patients on cabotegravir only	-	-
Baseline	8/8 (100)	0/8 (0)
3 months	6/6 (100)	0/6 (0)
6 months	6/6 (100)	0/6 (0)
12 months	6/6 (100)	0/6 (0)

For viral suppression, 98% of patients on cabotegravir-rilpivirine for HIV-1 treatment were virally suppressed at baseline. At 3 months, 97% remained virally suppressed, followed by 94% at 6 months and 96% at 12 months, respectively (Table **3**). Two patients on cabotegravir-rilpivirine had confirmed virologic failure, resulting in discontinuation of therapy. All patients on cabotegravir for PrEP remained HIV-negative on LAI for the first 12 months.

3.3. Subgroup Analysis

To account for the presence of potential confounders, a subgroup analysis was conducted to assess the effect of sex, race, baseline BMI, weight change in the year prior to LAI initiation, INSTI use, comorbidities, and use of concurrent medications known to cause weight change, on weight at 3, 6, and 12 months (Table **4**). All subgroups mirrored the results of the primary analysis at the 3- and 12-month endpoints ($p > 0.05$). At 6 months only, there was a significant weight increase from baseline in patients who were overweight prior to initiation of LAI therapy, were on concurrent medications known to cause weight gain, and in patients who achieved clinically significant weight loss in the year prior to initiation of LAI therapy ($p < 0.05$).

Table 4. Subgroup analysis.

Subgroup	Mean Weight Change from Baseline - kg (95% CI)	P-Value
Sex	-	-
Male	-	-
3 months	0.3 (-1.2 to 1.7)	0.71
6 months	1.4 (-0.4 to 3.2)	0.21
12 months	0.1 (-2.6 to 2.9)	0.91
Female	-	-
3 months	0.4 (-1.3 to 2.1)	0.62
6 months	0.7 (-2.5 to 3.8)	0.66
12 months	-0.1 (-5.3 to 5.1)	0.95
Race	-	-
White	-	-
3 months	2.1 (-1.4 to 5.7)	0.12
6 months	4.0 (-8.1 to 16.0)	0.29
12 months	2.9 (-105.1 to 110.9)	0.79
Black	-	-
3 months	0.5 (-1.0 to 2.1)	0.49
6 months	1.0 (-1.3 to 3.2)	0.39
12 months	-0.1 (-3.4 to 3.2)	0.96
Hispanic	-	-
3 months	-0.5 (-2.0 to 1.1)	0.53
6 months	0.8 (-0.8 to 2.4)	0.29
12 months	-0.2 (-4.2 to 3.7)	0.9
Baseline BMI	-	-
Normal weight	-	-
3 months	0.3 (-0.5 to 1.2)	0.41
6 months	1.7 (-0.7 to 4.0)	0.14
12 months	1.9 (-2.4 to 6.2)	0.34
Overweight	-	-
3 months	1.4 (-0.6 to 3.3)	0.15
6 months	3.2 (1.1 to 5.4)	0.006
12 months	2.4 (-1.0 to 5.7)	0.15
Obese	-	-
3 months	-0.6 (-2.6 to 1.4)	0.51
6 months	-1.2 (-4.2 to 1.7)	0.38
12 months	-3.7 (-8.7 to 1.2)	0.12
Weight change in the year prior to LAI initiation	-	-
Loss	-	-
3 months	1.8 (-1.1 to 4.7)	0.17
6 months	3.5 (0.2 to 6.7)	0.04
12 months	-0.1 (-6.3 to 6.2)	0.98
Gain	-	-

(Table 4) contd.....

Subgroup	Mean Weight Change from Baseline - kg (95% CI)	P-Value
3 months	1.0 (-23.4 to 25.6)	0.93
6 months	0.5 (-23.2 to 24.3)	0.96
12 months	1.0 (-22.6 to 24.7)	0.92
Neutral	-	-
3 months	-0.6 (-1.8 to 0.6)	0.29
6 months	0.1 (-1.6 to 1.9)	0.89
12 months	-0.2 (-2.5 to 2.2)	0.87
INSTI use prior to LAI initiation	-	-
Y	-	-
3 months	0.3 (-0.9 to 1.5)	0.62
6 months	1.1 (-0.3 to 2.6)	0.13
12 months	-0.5 (-2.9 to 1.8)	0.65
N	-	-
3 months	0.4 (-2.8 to 3.6)	0.78
6 months	1.1 (-5.0 to 7.2)	0.68
12 months	2.1 (-6.6 to 10.7)	0.59
Comorbidities	-	-
Prediabetes	-	-
3 months	-0.5 (-22.7 to 19.6)	0.88
6 months	-0.1 (-26.3 to 13.5)	0.51
12 months	-2.0 (-34.6 to 7.5)	0.19
Type 2 diabetes	-	-
3 months	1.6 (-41.7 to 44.8)	0.94
6 months	1.2 (-41.7 to 50.7)	0.83
12 months	-3.7 (-46.4 to 50.7)	0.92
Dyslipidemia	-	-
3 months	0.8 (-9.0 to 9.4)	0.96
6 months	1.6 (-7.3 to 11.4)	0.66
12 months	2.1 (-8.5 to 9.3)	0.41
Confounding medications known to influence weight	-	-
Causing weight gain	-	-
3 months	1.5 (-0.2 to 3.1)	0.08
6 months	2.3 (0.2 to 4.4)	0.03
12 months	-0.2 (-5.8 to 5.4)	0.95
Causing weight loss	-	-
3 months	2.2 (-4.0 to 8.4)	0.34
6 months	1.9 (-4.9 to 8.7)	0.44
12 months	-4.8 (-34.4 to 24.7)	0.56

Table 5. Adverse events and reasons for discontinuation.

Event	All LAI Patients (N=48) – No. (%)	LAI Cabotegravir-rilpivirine (N=40) – No. (%)	LAI Cabotegravir (N=8) – No. (%)
Adverse Event			-
Any adverse event	28 (58)	24 (60)	4 (50)
Pain at the injection site	21 (44)	18 (45)	3 (38)
Nodule at the injection site	9 (19)	8 (20)	1 (13)
Depression	4 (8)	4 (10)	0 (0)
Fever	3 (6)	2 (5)	1 (13)
Chills	2 (4)	1 (3)	1 (13)
Muscle spasms	2 (4)	2 (5)	0 (0)
Hot flashes	2 (4)	2 (5)	0 (0)
Headaches	1 (2)	1 (3)	0 (0)
Body aches	1 (2)	0 (0)	1 (13)
Leg pain	1 (2)	0 (0)	1 (13)
Bronchospasm	1 (2)	1 (3)	0 (0)

(Table 5) contd.....

Event	All LAI Patients (N=48) – No. (%)	LAI Cabotegravir-rilpivirine (N=40) – No. (%)	LAI Cabotegravir (N=8) – No. (%)
Dizziness	1 (2)	1 (3)	0 (0)
Fatigue	1 (2)	1 (3)	0 (0)
Numbness of extremities	1 (2)	1 (3)	0 (0)
Discontinuation			
Total discontinued	12 (25)	10 (25)	2 (25)
Adverse events	5 (10)	3 (8)	2 (25)
Lost to follow-up	3 (6)	3 (8)	0 (0)
Confirmed virologic failure	2 (4)	2 (5)	0 (0)
Cost	1 (2)	1 (3)	0 (0)
Desired pregnancy	1 (2)	1 (3)	0 (0)

3.4. Adverse Events

At least one adverse event was reported in 28 patients (58%) during the study period. The most reported adverse events were pain at the injection site (44%), nodules at the injection site (19%), and depression (8%). One patient experienced significant bronchospasm and dizziness beginning immediately after injection. This was resolved after about 20 minutes. All other reactions were mild to moderate in nature. The full list of adverse events is listed in Table **5**. Adverse events led to discontinuation of therapy in 5 patients, 2 of which discontinued therapy after the first injection.

4. DISCUSSION

Treatment with LAI therapy has been a focus of research in recent years to improve patient satisfaction and adherence and decrease the negative stigma associated with oral ART therapy. The results of this study suggest that LAI cabotegravir-based regimens can be effective at maintaining HIV-1 viral suppression without significant weight change. Comparing mean weight change from baseline to 3, 6, and 12 months, there was no significant weight change at any time point for the primary and secondary outcomes. However, given the small sample size of this study, there were 3 patients who lost a significant amount of weight due to other causes that may have influenced our results. One patient experienced unexplained weight loss of ~10 kg. During this time, they had an abnormal TSH and were referred for evaluation of their thyroid. Another patient had a prolonged hospital stay >1 month, leading to a weight loss of ~23 kg. A third patient lost ~16 kg after the health decline of a loved one. They stopped eating and began heavily drinking alcohol. While these values can be considered outliners, the primary endpoint was not close to reaching significance at any time point, and we do not believe they affected the outcome of the analysis.

Adverse events were similar between patients on LAI cabotegravir-rilpivirine versus cabotegravir (60% vs. 50%). Injection site reactions, primarily pain or nodules at the injection site, were common but subsided within a few days after receiving the injection and infrequently led to discontinuation of therapy. One patient experienced significant numbness and tingling of the lower extremities and muscle spasms, which worsened at night, affecting their ability to sleep. This was not believed to be related to cabotegravir-rilpivirine, as symptoms remained despite the eventual discontinuation of therapy. They were later referred to neurology for evaluation for restless leg syndrome and peripheral neuropathy. Another patient reported experiencing headaches on cabotegravir-rilpivirine and discontinued therapy as they believed it was making them sick. Around the same time, the patient had significant uncontrolled hypertension, hypokalemia, and stopped drinking alcohol after previously drinking 2-3 glasses of liquor per day. Therefore, this adverse event may also be unrelated to cabotegravir-rilpivirine.

There were two confirmed cases of virologic failure in patients on cabotegravir-rilpivirine. Studies have shown that mutations associated with rilpivirine (RPV) resistance, HIV-1 subtype A1/A6, BMI $\geq$ 30 kg/m^2, and missed doses or receiving doses outside the treatment window have been associated with increased risk of confirmed virologic failure [3, 15, 16]. In our study, all injections in those with confirmed virologic failure were received within the recommended treatment window. In both cases, the patients were HIV-1 subtype B and obese (BMI $\geq$ 30 kg/m^2) at baseline. The first patient was found to have V90I, K101E, and Y181C mutations on DNA sequencing, resulting in resistance to rilpivirine and other NNRTIs. The second patient was found to have a Q148K mutation, resulting in resistance to cabotegravir and other INSTIs. Both patients were transitioned back to oral ART.

Our population was distinct from the patients in previous trials since our patients were primarily minorities. Pre-specified subgroup analysis showed no difference between race and gender in relation to weight change at 3, 6, or 12 months. This non-significant weight change was generally consistent across other pre-specified subgroups except for patients who were overweight prior to initiation of LAI therapy, were on concurrent medications known to cause weight gain, and in patients who achieved clinically significant weight loss in the year prior to initiation of LAI therapy. Interestingly, the significant weight change in these subgroups was only seen at the 6-month time point, not at 3- or 12-months. This warrants further investigation in future studies.

This study has several limitations. The small sample size and high rate of discontinuation prevent generalizability to other institutions. Given the retrospective design, weights were obtained from the

patient's chart. With injections being given bimonthly, patients often did not have an appointment in the clinic or recorded weight in the chart at each time point. Therefore, the weight collected was defined as the first weight found on chart search recorded immediately after the 3-, 6-, or 12-month endpoint was reached. This allowed us to better capture data for as many patients as possible. If a weight was not recorded at a clinic visit and no other weight was found on the chart search, the weight was recorded as not available, and the patient was not included in the analysis for that specific time point. In this regard, studies conducted with real-time weights may produce additional useful results.

CONCLUSION

In this study, bimonthly LAI cabotegravir and cabotegravir-rilpivirine were not associated with significant weight change from baseline to 12 months. Adverse events were common, but most patients were able to maintain viral suppression or remained HIV-negative throughout 12 months of therapy. This represents real-world data that may be used to influence provider clinical decision-making when selecting a regimen for treatment or prevention of HIV-1.

AUTHORS' CONTRIBUTION

J.B.S and S.J.J.: Study conception and design; N.A.T: Data collection; N.A.T. and J.M.: Analysis and interpretation of results; N.A.T.: Manuscript was written.

LIST OF ABBREVIATIONS

HIV	=	Human immunodeficiency virus
PLWH	=	Persons living with HIV
ART	=	Antiretroviral therapy
LAI	=	Long-acting injectable
INSTI	=	Integrase strand-transfer inhibitor
NNRTI	=	Non-nucleoside reverse transcriptase inhibitor
PrEP	=	Pre-exposure prophylaxis
CI	=	Confidence interval

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by Trinity Health of New England's Institutional Review Board, United States (approval number SFH 23-36).

HUMAN AND ANIMAL RIGHTS

All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committees and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

This was a retrospective study, and informed consent was waived.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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