Greater Weight Gain in Treatment Naïve Persons Starting Dolutegravir-Based Antiretroviral Therapy

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This is the author's manuscript of the article published in final edited form as:

**Summary of the Article:**

In this paper, we evaluate the differences in weight gain among treatment-naïve persons living with HIV (PLWH) initiating antiretroviral therapy. Our results highlight enhanced weight gain among PLWH starting dolutegravir-based therapy. Additionally, we describe lower weight gain with elvitegravir-based therapy.

**ABSTRACT**

**Background**

Recent studies have reported weight gain in virologically-suppressed persons living with HIV (PLWH) switched from older antiretroviral therapy (ART) to newer integrase strand transfer inhibitor (INSTI)-based regimens. In this study, we investigated whether weight gain differs among treatment-naïve PLWH starting INSTI-based regimens compared to other ART regimens.

**Methods**

Adult, treatment-naïve PLWH in the Vanderbilt Comprehensive Care Clinic cohort initiating INSTI, protease inhibitor (PI), and non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based ART between January 2007 and June 2016 were included. We used multivariable linear mixed effects models to generate marginal predictions of weights over time, adjusting for baseline clinical and demographic characteristics. We used restricted cubic splines to relax linearity assumptions and bootstrapping to generate 95% confidence intervals.
Results

Among 1,152 ART-naïve PLWH, 356 initiated INSTI-based regimens (135 dolutegravir, 157 elvitegravir and 64 raltegravir), 86% were male, and 49% were white. At ART initiation median age was 35 years, BMI was 25.1 kg/m², and CD4+ T-cell count was 318 cells/mm³. Virologic suppression at 18-months was similar between different ART classes. At all examined study time points, weight gain was highest among PLWH starting dolutegravir. At 18 months, PLWH on dolutegravir gained 6.0 kg, compared to 2.6 kg for NNRTI (p<0.05), and 0.5 kg for elvitegravir (p<0.05). PLWH starting dolutegravir also gained more weight at 18 months compared to raltegravir (3.4 kg) and PI (4.1 kg), though these differences were not statistically significant.

Conclusion

Treatment-naïve PLWH starting dolutegravir-based regimens gained significantly more weight at 18 months than those starting NNRTI-based and elvitegravir-based regimens.

Keywords:

1. Integrase Strand Transfer Inhibitors
2. Treatment naïve adults with HIV
3. Weight gain
4. HIV metabolic complications
BACKGROUND

The decrease in morbidity and mortality of persons living with HIV (PLWH) has been associated with a parallel increase in the rate of noncommunicable diseases (NCD), particularly metabolic disorders [1]. In PLWH the traditional metabolic disease risk factors of obesity, sedentary lifestyle and genetic predisposition intersect with HIV-specific risk factors, including metabolic perturbations related to antiretroviral therapy (ART) [2]. The median body mass index (BMI) and prevalence of baseline obesity among PLWH initiating ART has been steadily increasing [3], with greater weight gain in the first year after initiating ART among women, patients with lower CD4+ T-cell count. Short-term weight gain following ART initiation has been associated with increased risk of diabetes [4-7] and cardiovascular disease [5]. This is particularly concerning as nearly half of people in the United States living with diagnosed HIV are currently aged 50 and older [8]. We recently reported that virologically suppressed PLWH on efavirenz-based regimens who switched to integrase strand transfer inhibitor (INSTI)-based regimens experienced significantly more weight gain compared to those who remained on efavirenz, and weight gain was greatest among those who switched to dolutegravir [9]. Several other studies have also investigated the association between INSTI-based regimens and weight gain. In AIDS Clinical Trial Group (ACTG) study A5260, a substudy of A5257, raltegravir was associated with similar changes in lean mass and regional fat at 96-weeks compared to ritonavir-boosted darunavir and ritonavir-boosted atazanavir [10]. However, raltegravir was associated with increased leg and arm, but not truncal fat, when compared to lopinavir/ritonavir in the PROGRESS study [11]. In observational studies, INSTI-based regimens generally [12], and particularly dolutegravir-based regimens [13], have been associated with accelerated weight gain. In a cohort from Brazil, PLWH receiving INSTI-based regimens were noted to be 7-times more likely to develop clinical obesity compared to those receiving non-nucleoside reverse-transcriptase inhibitor (NNRTI)- or PI-based regimens [12]. However, data comparing the weight gain between different INSTI drugs is limited.
In the current study, we sought to evaluate short-term weight gain among treatment-naïve PLWH starting ART. We also aim to explore differences in short-term weight gain between different INSTI drugs and between these drugs and other PI and NNRTI-based regimens.

METHODS

We conducted a retrospective observational cohort study of adults (age ≥18 years) enrolled in care at the Vanderbilt Comprehensive Care Clinic (VCCC), an outpatient HIV clinic in Nashville, Tennessee. The study cohort included all ART-naïve patients, defined as having no prior history of any antiretroviral agent exposure, who initiated treatment between January 1st, 2007 and June 30th, 2016. Women who were pregnant at the time of ART initiation or became pregnant at any time during the study period were excluded. We also excluded patients who stopped or switched their initial ART regimen within the first 6-months of starting therapy. Patient weight was determined at routine clinic visits using a single measurement on the same mechanical scale. Clinical data were collected from an electronic medical record, which recorded patient encounter data including laboratory results. Research staff systematically extract and validate all laboratory and clinical data, including medication start and stop dates, from the electronic medical record.

Data collected included weight, height, age at ART initiation, sex, race, duration from diagnosis of HIV infection to treatment, year of ART initiation, treatment regimen as well as pre- and post-ART initiation CD4+ T-cell lymphocyte count and plasma HIV-1 RNA measurements. Body weight nearest to ART initiation within the period from 180 days before to 30 days after treatment start was used to calculate baseline weight and BMI (height in meters / weight in kilograms, squared). Similarly, CD4 T-cell count and plasma HIV-1 RNA measurements nearest to ART initiation were used to define baseline levels. The absolute change in weight was defined as the
difference between each subsequent weight measurement and baseline weight. Weight measurements were included from 1 year prior to study start date to 18 months following the predefined study end date.

Prevalence of virologic suppression, defined as having a viral load less than 200 copies/mL, was evaluated for all patients included in the study at 6 weeks, 3-, 6- and 18-months. We assessed whether prevalence of virologic suppression, at these predefined time points, differed by ART class and individual INSTI drugs. Additionally, we evaluated whether virologic failure, defined as having a viral load of more than 1,000 copies/mL after previously achieving virologic suppression, differed by ART classes or INSTI drugs.

The study was approved by Vanderbilt University Institutional Review Board and the requirement for an informed consent was waived. All patient records and pertinent information were de-identified prior to the analysis.

**Statistical Analysis**

We compared patient demographics and baseline clinical characteristics across different ART-regimens, as well as across different INSTI antiretrovirals, using Pearson $\chi^2$, Wilcoxon rank sum, or Kruskal–Wallis tests as appropriate. We used multivariable linear mixed effects models to generate marginal predictions of weight over time, adjusting for age, sex, race, HIV acquisition mode, ART initiation year, and baseline weight, HIV-1 RNA, and CD4 T-cell count. We used restricted cubic splines to relax linearity assumptions for all continuous covariates and bootstrapping with 200 replicates to generate 95% confidence intervals for the marginal predictions. Predicted weights by ART class were reported at 3-month intervals between 6 and 18 months.

Patients who completed at least 6-months of uninterrupted treatment with initial ART regimen were assigned to and analyzed by that class. Records from patients who were initiated on INSTI- based regimens were reviewed to identify any switches between different INSTI drugs.
Furthermore, we evaluated in a multivariable logistic regression model whether different ART regimens were associated with significantly different risk for incident obesity. In this model we only included patients with baseline BMI < 30 kg/m² and evaluated the relative odds of incident obesity (BMI ≥ 30 kg/m²) by regimen class within the follow-up period. The model was adjusted for baseline demographic (age, sex, race, and year of ART initiation) and clinical (baseline CD4 count, baseline viral load, and baseline BMI) variables. NNRTIs were used as the reference group.

All analyses were conducted in R v. 3.4.3 and StataSE 15.

RESULTS

Baseline Characteristics

A total of 1,152 patients were included in the analysis. Of these, 454 (39%) started PI-based regimens while 347 (31%) started NNRTI-based and 351 (30%) started INSTI-based regimens. Among those starting INSTI-based regimens, 63/351 (18%) patients started raltegravir, while 153/351 (44%) and 135/351 (39%) started elvitegravir and dolutegravir, respectively. The most commonly used ART combinations among PLWH starting NNRTI, PI and INSTI are listed in Supplemental Table 1. Tenofovir disoproxil fumarate and emtricitabine constituted the nucleoside backbone for the majority of NNRTI-, PI-, elvitegravir- and raltegravir-based regimens. Meanwhile, abacavir (ABC) and lamivudine (3TC) were the predominant nucleoside backbone for the dolutegravir-based regimens. Most PI-based regimens were ritonavir-boosted and all the elvitegravir-based regimens were cobicistat-boosted.

Patient demographic and clinical characteristics are shown in Table 1. The majority of patients were men. The median age of ART initiation was significantly lower among patients starting elvitegravir and dolutegravir. A higher proportion of women started PI-based regimens compared to men. The median baseline CD4+ T-cell count at time of ART initiation was higher among patients starting INSTI-based regimens, especially in those starting elvitegravir and dolutegravir. The median baseline HIV-1 RNA at time of ART...
initiation was $4.4 \log_{10}$ copies/mL, with the lowest levels in those starting elvitegravir and the highest in those starting dolutegravir. Patients starting PI-based regimens had significantly lower baseline weight compared to other ART classes. NNRTI and PI-based regimens were more commonly used prior to 2013, while INSTI-based regimens were predominant from 2014 onwards. Among INSTIs, elvitegravir-based combination ART was the most commonly prescribed in 2014 to early 2015, after which it was surpassed by dolutegravir-based combination ART. Regimen distribution by year is shown in Supplemental Figure 1. The variation of baseline BMI and CD4 T-cell count by year of ART initiation are shown in Supplemental Figure 2. Observed baseline BMI (mean ± SD) increased from $25.7 ± 5.7$ kg/m$^2$ in 2007 to $27.7 ± 7.1$ kg/m$^2$ in 2016, with an increase in the prevalence of baseline obesity (defined as BMI $\geq 30$ kg/m$^2$) from 19% in 2007 to 34% in 2016. In contrast, baseline CD4+ T-cell count steadily increased over the study period. Patients with baseline CD4+ T-cell count <200 cells/µL dropped from 54% in 2007 to 19% in 2016.

None of the patients initiated on dolutegravir-, elvitegravir-, or raltegravir-based regimens switched regimen during the study period.

**Virologic Suppression**

Among all PLWH, 350 (30.4%) achieved virologic suppression by 6 weeks, and viral suppression at 3-, 6- and 18-months was 60.2%, 87.2%, and 97.3%, respectively (Supplemental Table 2). Patients starting INSTIs were significantly more likely to be virally suppressed early after treatment initiation (at 6 weeks, 3 months, and 6 months). However, by the end of the study follow-up, the rates of viral suppression were similar across all ART regimens. There was no difference in rates of viral suppression throughout the study period between INSTI-based regimens (Supplemental Table 2).
A total of 74 patients (6.4%) had virologic failure during study follow-up (Supplemental Table 2). Prevalence of virologic failure was significantly higher among PLWH starting a PI (41/145, 9.0%) than NNRTI (13/347, 3.7%) or INSTI (20/351, 5.7%). Proportions with virologic failure were similar across the different INSTI drugs (Supplemental Table 2).

**Weight Gain**

All patients had substantial weight gain within the first year of starting ART, after which time the rate of weight gain slowed. The predicted changes in weight over time by treatment regimen from our multivariable model are shown in Figure 1 and Supplemental Table 3. Overall, the adjusted average weight gain was 2.4 kg (95% CI 1.0 – 3.7) at 6 months and 3.9 kg (95% CI 2.4 – 5.4) at 18-months. Among INSTI drugs, adjusted average weight gain varied by individual drug, with patients on dolutegravir gaining more weight than those on elvitegravir or raltegravir (Figure 2). Dolutegravir-based regimens were associated with adjusted average weight gain of 2.9 kg and 6.0 kg at 6- and 18-months, respectively, which was significantly higher than the adjusted average weight gain associated with elvitegravir at these time points (0.6 kg and 0.5 kg, respectively). The adjusted average weight gain associated with raltegravir-based regimens at 6- and 18-months (3.0 kg and 3.4 kg, respectively) was significantly higher than that with elvitegravir, but not significantly different than the adjusted average weight gain associated with dolutegravir (Figure 2 and Supplemental Table 3).

At 6- and 18-months, NNRTI-based regimens were associated with adjusted average weight gains of 1.1 kg and 2.6 kg, respectively; at 18 months, weight gain on NNRTI-based regimens was significantly lower compared to dolutegravir-based regimens (Figure 3 and Supplemental Table 3). The adjusted average weight gain associated with NNRTI-based regimens was not significantly different compared to elvitegravir-based regimens (Figure 4 and Supplemental Table 3).

In comparison, PI-based regimens were associated with 2.6 kg and 4.1 kg weight gains at 6- and 18-months, respectively. PI-based regimens were associated with significantly higher weight gain compared to that seen with elvitegravir-based regimens (Figure 4 and
Supplemental Table 3). While PI-based regimens were associated with lower weight gain compared to dolutegravir-based regimens, the difference was not statistically significant (Figure 3 and Supplemental Table 3).

Moreover, neither sex nor race had a significant effect on weight gain. In our adjusted models, weight gain among women was, on average, 0.4 kgs (95% CI: -2.1 – 1.4) lower than that among men. Additionally, weight gain among black patients was, on average, 0.1 kg (95% CI: -1.1 – 1.3) higher than weight gain among non-blacks.

Among PLWH with BMI < 30kg/m², the odds of incident obesity during study follow-up did not differ by ART regimen. Nevertheless, dolutegravir-based regimens were associated with the highest, albeit non-statistically significant, odds of incident obesity [odds ratio (OR): 1.6, 95% CI: 0.6 – 4.4].

DISCUSSION

Our observational analysis is the first to explore differences in short-term weight gain following treatment initiation among different INSTI drugs and between INSTI-, PI-, and NNRTI-based regimens. Our findings highlight the variation in short-term weight gain among ART-naïve PLWH starting INSTI-based regimens according to the INSTI drug used. We observed that PLWH starting dolutegravir- and raltegravir-based regimens gained significantly more weight compared to persons starting elvitegravir-based regimens. Additionally, PLWH starting dolutegravir-based regimens gained significantly more weight at 18-months compared to persons starting NNRTI-based regimens. Those on dolutegravir-based regimens also gained more weight than persons initiating PI-based regimens, but the difference was not statistically significant. In contrast, elvitegravir-based regimens were associated with the least short-term weight gain. PLWH starting elvitegravir-based regimens gained significantly less weight than persons starting PI-, dolutegravir-, and raltegravir-based regimens.
Initiation of ART among treatment-naïve PLWH is often associated with a short period of weight gain, especially among patients with low baseline BMI, those with profound depletion of CD4 T-cells, and high baseline HIV-1 RNA viral load [10, 14-16]. In the early ART era, weight gain among PLWH was associated with improved immunologic recovery and better survival [14, 17-20]. Therefore, early in the clinical experience of treating PLWH when untreated patients suffered from cachexia and wasting, weight gain following ART initiation was seen as part of the “return to health” phenomenon. This phenomenon was thought to be a direct result of successfully suppressing viral replication, controlling inflammation and normalizing resting energy expenditure [21]. However, obesity is increasingly prevalent among PLWH initiating ART [3]. By 2016, one-third of the patients starting ART in our study were obese and over half had a BMI higher than normal (≥ 25 kg/m²). In the context of higher pre-treatment BMI among patients starting ART in the current era, short term weight gain after ART initiation may represent an undesirable effect that is placing patients at higher risk for cardiovascular and metabolic complications. In a recent study, short-term gain in BMI following ART initiation appeared to increase the longer-term risk of cardiovascular disease and diabetes compared to HIV-negative persons [5, 6]. Additionally, weight gain following ART initiation has been associated with worsening of two key risk factors for cardiovascular disease among overweight and obese patients: dyslipidemia [22] and systemic inflammation [23]. This is especially concerning since PLWH are already at a higher risk of hypertension [24], myocardial infarction [24-28] peripheral arterial disease [24, 29] and impaired renal function [24, 30] compared to the general population.

In our study, weight gain varied between ART regimens after controlling for several baseline clinical and demographic characteristics that have been previously associated with higher BMI gain following treatment initiation (i.e., sex, baseline BMI, CD4+ T-cell count and HIV-1 viral load) [10, 14, 16]. One variable we did not adjust for was the nucleoside reverse transcriptase inhibitor (NRTI) backbone. In our cohort, most patients who received dolutegravir had abacavir/lamivudine as the NRTI backbone while tenofovir disoproxil fumarate/emtricitabine was the NRTI backbone used with the majority of other INSTI, NNRTI, and PI medications. However, in light of
previously published studies, we do not expect for the NRTI backbone to have significant effects on weight gain. In the ACTG study A5224s, a substudy of A5202, changes in weight, BMI, and lean body mass were not statistically different between PLWH receiving ART with abacavir/lamivudine NRTI-backbone, compared to those receiving ART with tenofovir disoproxil fumarate/emtricitabine NRTI-backbone [31]. Moreover, changes in insulin-resistance were also similar among ART-naive patients randomized to tenofovir disoproxil fumarate/emtricitabine vs. abacavir/lamivudine-based regimen [32].

The mechanism explaining the difference noted in weight gain among INSTI- based regimens and between these regimens and NNRTI- or PI- based regimens is unknown. One possible explanation is the rapid drop in viral load seen with INSTI-based regimens and the correlation of virologic suppression with lower energy expenditure [33]. However, we did not observe a marked difference in rates of virologic suppression between dolutegravir and elvitegravir- based regimens at the time points examined. Another possible mechanistic explanation is differences in inflammatory biomarkers, and potentially related catabolic processes, between regimens. As an example, switching from PI- based regimens to a raltegravir-based regimen has been associated with statistically significant decline in soluble CD14 [34], a monocyte activation marker, as well as a decrease in levels of other systemic inflammatory biomarkers (high sensitivity C-reactive protein, interleukin-6, tumor necrosis factor alpha and D-dimer) [35]. However, this hypothesis falls short of explaining the difference in weight gain noted between raltegravir and dolutegravir when compared to elvitegravir, especially in that the latter has also been associated with decrease in plasma levels of systemic, vascular, and monocyte activation biomarkers [36]. Other plausible hypotheses include possible differential effects of ART-regimens on systems regulating energy homeostasis, food intake and on insulin resistance. For example, in vitro dolutegravir has been shown to affect the activity of melanocyte-stimulating hormone, a family of peptide hormones and neuropeptides involved in appetite control. Therefore, increased appetite with dolutegravir could be a plausible explanation for the higher weight gain noted with this drug [37]. Moreover, further studies are needed to evaluate whether
secondary-effects of cobicistat, the pharmacologic enhancer used with all the elvitegravir-based regimens, could explain the lower weight gain seen with this regimen.

Our study had several limitations. It was a retrospective analysis of a predominantly male cohort from a single center in the southeastern United States; the results may therefore not be generalizable to other populations. Based on the recent Federal Drug and Food Administration (FDA) approval of dolutegravir in August 2014, we limited our analysis window to 18-months to reduce data sparseness over a longer time period. Additionally, patients who initiated and completed 6 months of therapy with a treatment regimen were assigned and analyzed to that class without accounting for the possibility of regimen switches during the 18-month follow-up. However, as mentioned in the results, none of the patients who were assigned and analyzed in either the raltegravir, elvitegravir or dolutegravir groups had switched classes during the study period. Moreover, we did not have data regarding patients’ caloric intake or physical activity levels. We also did not account for concomitant medication usage that may have caused weight changes (i.e. metformin, psychiatric medications). Furthermore, to ensure adequate follow-up, we limited our study to patients who initiated antiretroviral therapy prior to July 1st, 2016 and therefore did not include any patients on bictegravir, approved by FDA in February 2018, or tenofovir alafenamide, approved in November 2016.

While our results highlight the association between dolutegravir and increased weight gain among treatment naïve patients, the impact of our findings on clinical practice are, as yet, unclear. A central question is whether the increased weight gain on dolutegravir is related to off-target effects of the medication on energy storage and adipose tissue accumulation, as opposed to greater anti-viral efficacy resulting in lower basal energy expenditure in the setting of HIV infection. Similarly, the impact of the increased weight gain on metabolic and cardiovascular outcomes is unclear at this time. Until additional studies can clarify the mechanisms related to differences in weight gain on different ART regimens, the patient characteristics associated with the greatest weight change as well the
impact of the increased weight gain, we believe clinicians should continue utilizing dolutegravir if it represents the best choice for a patient given other factors.

In summary, short-term weight gain following ART initiation varied among the different INSTIs. Patients starting dolutegravir-based regimens were at the highest risk for short-term weight gain, while, in contrast, weight gain was minimal among those starting elvitegravir-based regimens. Future multicenter cohort studies and randomized controlled trials are needed to confirm our findings in addition to evaluating potential mechanisms linking antiretroviral agents and body weight changes.
FUNDING

This work was supported by the Tennessee Center for AIDS Research [P30 AI110527].

CONFLICTS OF INTEREST

*Potential conflicts of interest.* P.R. and J.K. have received grant funding through an investigator-sponsored research grant from Gilead Sciences.

K.B., M.T., J.C., S.R., T.H. and T.S. have no conflicts.
REFERENCES


### TABLE 1.

Distribution of Study Patients by Regimen Class.

<table>
<thead>
<tr>
<th>Factor</th>
<th>All regimens</th>
<th>NNRTI-based regimens</th>
<th>PI-based regimens</th>
<th>INSTI-based regimens</th>
<th>(p)-value&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Raltegravir</th>
<th>Elvitegravir</th>
<th>Dolutegravir</th>
<th>(p)-value&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (%)</strong></td>
<td>1,152</td>
<td>347 (30.5%)</td>
<td>454 (39.4%)</td>
<td>351 (30.1%)</td>
<td></td>
<td>63 (17.9%)</td>
<td>153 (43.6%)</td>
<td>135 (38.5%)</td>
<td></td>
</tr>
<tr>
<td>Age at Time of ART Initiation (\Delta)</td>
<td>35 (27, 44)</td>
<td>38 (29, 45)</td>
<td>36 (26, 44)</td>
<td>33 (26, 43)</td>
<td>(0.002)</td>
<td>38 (28, 46)</td>
<td>32 (25, 40)</td>
<td>33 (25, 45)</td>
<td>(0.01)</td>
</tr>
<tr>
<td>Birth Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>985 (85.5%)</td>
<td>310 (88.3%)</td>
<td>306 (88.2%)</td>
<td>369 (81.3%)</td>
<td>(0.005)</td>
<td>54 (85.7%)</td>
<td>140 (91.5%)</td>
<td>116 (85.9%)</td>
<td>(0.26)</td>
</tr>
<tr>
<td>Female</td>
<td>167 (14.5%)</td>
<td>41 (11.8%)</td>
<td>85 (18.7%)</td>
<td>41 (11.7%)</td>
<td></td>
<td>9 (14.3%)</td>
<td>13 (8.5%)</td>
<td>19 (14.1%)</td>
<td></td>
</tr>
<tr>
<td>Race Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>559 (48.5%)</td>
<td>169 (48.1%)</td>
<td>189 (54.5%)</td>
<td>201 (44.3%)</td>
<td></td>
<td>38 (60.3%)</td>
<td>72 (47.1%)</td>
<td>59 (43.7%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>484 (42.0%)</td>
<td>124 (35.7%)</td>
<td>216 (47.6%)</td>
<td>144 (41.0%)</td>
<td>(0.01)</td>
<td>19 (30.2%)</td>
<td>65 (42.5%)</td>
<td>60 (44.4%)</td>
<td>(0.28)</td>
</tr>
<tr>
<td>Other</td>
<td>109 (9.5%)</td>
<td>34 (9.8%)</td>
<td>37 (8.1%)</td>
<td>38 (10.8%)</td>
<td></td>
<td>6 (9.5%)</td>
<td>16 (10.5%)</td>
<td>16 (11.9%)</td>
<td></td>
</tr>
<tr>
<td>Baseline CD4 T-cell count (cells/µL)&lt;sup&gt;\Delta&lt;/sup&gt;</td>
<td>318 (159, 469)</td>
<td>291 (144, 440)</td>
<td>282 (127, 427)</td>
<td>401 (234, 594)</td>
<td>(&lt;0.001)</td>
<td>302 (117, 451)</td>
<td>453 (288, 657)</td>
<td>380 (241, 591)</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td>Baseline log HIV-RNA (copy/mL)&lt;sup&gt;\Delta&lt;/sup&gt;</td>
<td>4.4 (3.4, 5.0)</td>
<td>4.5 (3.5, 5.0)</td>
<td>4.5 (3.7, 5.1)</td>
<td>4.4 (3.0, 4.9)</td>
<td>(0.002)</td>
<td>4.6 (3.9, 5.1)</td>
<td>4.2 (2.5, 4.7)</td>
<td>4.5 (3.2, 5.0)</td>
<td>(0.006)</td>
</tr>
<tr>
<td>Baseline Weight (kg)&lt;sup&gt;\Delta&lt;/sup&gt;</td>
<td>76.8 (67.1, 87.9)</td>
<td>77.6 (68.0, 88.5)</td>
<td>75.4 (66.4, 86.0)</td>
<td>78.1 (67.3, 91.9)</td>
<td>(0.02)</td>
<td>79.4 (70.2, 86.6)</td>
<td>77.6 (65.8, 92.5)</td>
<td>78.0 (67.2, 96.2)</td>
<td>(0.84)</td>
</tr>
</tbody>
</table>

\(p\)-value <sup>1</sup>: comparing the difference in baseline characteristics by regimen class (INSTI-, NNRTI- and PI-based regimens). \(p\)-value <sup>2</sup>: comparing the difference in baseline characteristics by class of Integrase Inhibitors.
(Raltegravir, Elvitegravir and Dolutegravir). ART: Antiretroviral Therapy; INSTI: Integrase Strand Transfer Inhibitors; NNRTI: Non-nucleoside Reverse-Transcriptase Inhibitors; PI: Protease Inhibitors; $\Delta$ median (Interquartile Range)
**FIGURES**

*Figure Legends.*

**Figure 1.** Changes in weight within 18-months of treatment initiation among persons living with HIV by antiretroviral regimen. DTG: Dolutegravir; RAL: Raltegravir; EVG: Elvitegravir; PI: Protease Inhibitors; NNRTI: Non-nucleoside Reverse-Transcriptase Inhibitors.

**Figure 2.** Panel A: Changes in weight within 18-months of treatment initiation among persons living with HIV starting dolutegravir and elvitegravir. Panel B: Changes in weight within 18-months of treatment initiation among persons living with HIV starting dolutegravir and raltegravir. DTG: Dolutegravir; RAL: Raltegravir; EVG: Elvitegravir.

**Figure 3.** Panel A: Changes in weight within 18-months of treatment initiation among persons living with HIV starting dolutegravir and NNRTI. Panel B: Changes in weight within 18-months of treatment initiation among persons living with HIV starting dolutegravir and PI. DTG: Dolutegravir; PI: Protease Inhibitors; NNRTI: Non-nucleoside Reverse-Transcriptase Inhibitors.

**Figure 4.** Panel A: Changes in weight within 18-months of treatment initiation among persons living with HIV starting elvitegravir and NNRTI. Panel B: Changes in weight within 18-months of treatment initiation among persons living with HIV starting elvitegravir and PI. EVG: Elvitegravir; PI: Protease Inhibitors; NNRTI: Non-nucleoside Reverse-Transcriptase Inhibitor.
Fig 1.