Weight Gain after Initiation of Anti-Retroviral Therapy in Acute HIV-1

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Introduction

- Initiation of antiretroviral therapy (ART) has been associated with weight gain.
- Newer ART medications, specifically integrase strand inhibitor (INSTI)-based regimens, have been associated with more weight gain in comparison to non INSTI-based regimens in people with chronic HIV-1.
- We aimed to explore if acute weight gain was associated with INSTI use in comparison to non-INSTI regimens in people with acute HIV-1 (AHI), and to determine any ensuing metabolic complications.

Methods

- A retrospective, single center, chart review analysis of 108 ART-naïve people diagnosed with AHI (Feibig stage 1-5) was conducted.
- 61 people met inclusion criteria (age>18, longitudinal follow up of at least 48 weeks [+/-12 weeks], diagnosed before June 30, 2019) and their data were extracted from the electronic medical record (Epic).
- Changes in weight, body mass index (BMI) and metabolic parameters between people started on INSTI- vs non-INSTI regimens were compared.
- In subgroup analyses, elvitegravir (EVG) vs non-EVG and tenofovir alafenamide (TAF) vs non-TAF were compared.
- Chi-square, Mann-Whitney U test, or Wilcoxon Rank Sum test were used, when appropriate.

Results

Baseline characteristics and ART regimen distributions are listed in Tables 1 and 2.

Weight change.

- People initiating ART during AHI had a median (IQR) weight change of 4.53 kg (1.22-8.36; P<0.0001) and median BMI change 1.60 kg/m^2 (0.50-2.70; P<0.0001) (Figure 1)**.**
- Median weight changes on different ART regimens, including INSTI vs non-INSTI, as well as subgroup analysis of within-INSTI regimens were performed and are shown in Table 3.
- Lower baseline CD4$^+$ T cell count correlated with greater weight gain (P= 0.012).
- No association between weight gain and race (P= 0.930) or gender (P= 0.379) was noted.

Table 1: Baseline characteristics of participants.

	Total	INSTI-based regimen	Non-INSTI based regimen	Elvitegravir	Non-Elvitegravir INSTI-based regimen
No of participants	61	58	3	41	17
Age, median (IQR)	37 (32-46)	36.50 (31-46)	41 (37-49)	37 (28-43)	36 (35-50)
Race					
Black	25 (40.9)	24 (41.4)	1 (33.3)	15 (36.5)	9 (52.9)
White	35 (57.3)	33 (56.9)	2 (66.6)	25 (60.9)	8 (47.1)
Other	1 (1.6)	1 (1.7)	0 (0.0)	1 (2.4)	0 (0.0)
Ethnicity					
Hispanic	36 (59.0)	34 (58.6)	2 (66.7)	26 (63.4)	8 (47.1)
Non-Hispanic	25 (40.9)	24 (41.4)	1 (33.3)	15 (36.6)	9 (52.9)
Sex at Birth					
Male	49 (80.3)	46 (79.3)	3 (100.0)	34 (82.9)	12 (70.6)
Female	12 (19.7)	12 (20.7)	0 (0.0)	7 (17.1)	5 (29.4)
Baseline CD4 T-cell count, cells/µL	272 (172-392)	267.50 (168-392)	305 (276-547)	272 (172-543)	205 (151-332)
Baseline HIV RNA, copies/ml	1,740,000 (901,000 -10,000,001)	2,215,000 (1,062,500 -10,000,001)	543,000 (402,500 -4,491,500)	1,740,000 (901,000 -10,000,001)	3,190,000 (1,510,000 -10,000,001)

Note: Data are presented as median (IQR) or no (%). The EVG and Non-EVG subgroup analysis only includes patients on an INSTI-based regimen

Table 2: Baseline weight and metabolic components.

	Total	INSTI-based regimen	Non-INSTI based regimen	Elvitegravir	Non-Elvitegravir INSTI-based regimen
No of participants	61	58	3	41	17
Baseline weight, kg	71.7 (64.6-87.4)	72.7 (64.7-87.5)	66.4 (63.4-67.5)	75.4 (64.9-90.7)	69.9 (63.5-79.8)
Baseline BMI, kg/m^2	25.5 (22.7-30.4)	25.9 (22.8-30.7)	23.6 (22.9-24.4)	26.3 (22.7-30.9)	25.5 (23.6-27.6)
Baseline Metabolic components					
Blood Glucose, mg/dL	99 (86-121)	98.50 (86-122)	99 (85-109)	95 (86-119)	103 (93-124)
HDL, mg/dL	41 (30-46)	41 (30-46)	27 (17-40)	41.5 (32-46)	41 (30-50)
LDL, mg/dL	86 (51-106)	88 (52-105)	57 (43-114)	93.50 (50.5-113)	70 (52-89)
Total cholesterol, mg/dL	155 (116.3-181)	157 (120.5-182.5)	130 (114-156.5)	165.5 (129.3-200.5)	143 (112-161)
Triglycerides, mg/dL	149.5 (105.8-193.5)	147 (99-190)	189 (168-209)	154.5 (116.3-198.5)	121 (67-185)
Baseline HSI	38. 1 (31.3-42.6)	38.7 (31.9-42.8)	29.9 (29.4-33.8)	39.3 (32.9-44.3)	36.1 (30.9-39)

Data are presented as median (IQR). The EVG and Non-EVG subgroup analysis only includes participants on the INSTI-based regimen. Of note, longitudinal data for lipid panel was only available for 49 participants. LDL (INSTI group) includes one fewer participant as TG level was too high to calculate LDL.
Abbreviations: HDL (high density lipoprotein), LDL (low density lipoprotein), HSI (Hepatic steatosis index): 8 x (ALT/AST ratio)+BMI (+2, if female, +2, if diabetes mellitus)

Table 3: Median weight change amongst different anti-retroviral therapy regimens.

Anti-retroviral therapy regimen	No. of participants	Median weight change (IQR), kg	P value	Between group P value
INSTI-based regimen	58	4.66 (1.22-8.43)	<0.0001	0.33
Non-INSTI-based regimen	3	1.64 (-3.08-6.57)	0.75	
Subgroup analysis within INSTI regimen				
Elvitegravir-based regimen	41	4.40 (0.91-6.71)	<0.0001	0.008
Non-elvitegravir-based regimen	17	7.10 (4.97-13.15)	0.0001	
TAF regimen	33	2.66 (0.81-7.53)	0.002	0.006
Non-TAF regimen	25	5.31 (3.72-9.34)	<0.0001	

Table 3: Subgroup analysis of within-INSTI regimen analysis and weight change reflected less weight gain with EVG based regimen, in comparison to non-EVG regimens.

Figure 1: Weight gain and BMI change with ART initiation using the Wilcoxon Rank Sum test. Left: Overall weight gain seen over 48 weeks. Right: Overall BMI change over 48 weeks.

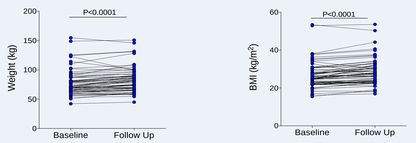
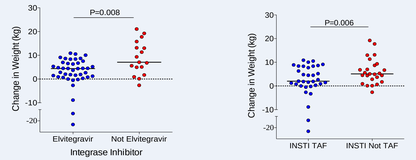


Figure 2: Subgroup analysis within INSTI regimens of change in weight. Left : Weight change on EVG vs non-EVG INSTI-based regimen. Right : Weight change on TAF vs Non-TAF INSTI-based regimen.



BMI Change

- Median BMI change on INSTI was 1.60 kg/m^2 (0.50-2.93) vs non-INSTI regimen was 0.60 kg/m^2 (-0.35-1.55), between group P=0.4331 .

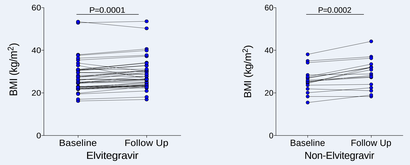


Figure 3: Subgroup analysis of EVG and non-EVG BMI change reflected 1.40 kg/m^2 (0.40-2.30; within group P= 0.0001) and 2.30 kg/m^2 (1.60-5.20; within group P= 0.0002) respectively; between group P= 0.0133

Metabolic Components.

- Overall, ART regimen was not associated with a significant difference in development of hyperlipidemia or incidence of DM.
- Hepatic steatosis index (HSI) was used as a surrogate to determine incidence of non-alcoholic fatty liver disease (NAFLD) in EVG vs non-EVG regimens.
- HSI consistent with NAFLD on EVG was present in 28/41 people at baseline and at follow up. It was present in 10/17 people on non-EVG regimens at baseline and in 12/17 people at follow up.
- Median SBP change from baseline to follow up on EVG and non-EVG was 4 (-3-15) mmHg, (P= 0.0440), and 6 (-4-18) mmHg, (P= 0.1059), respectively (P= 0.6690, between groups).
- Median DBP change from baseline to follow up on EVG was 3 (-5-10) mmHg, (P= 0.1913) and 8 (-5-13) mmHg on non-EVG (P= 0.0594) (P= 0.1974, between groups).

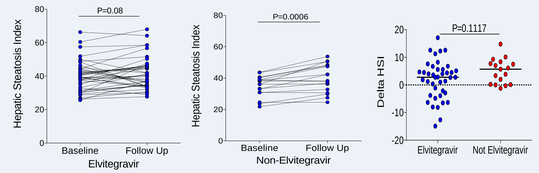


Figure 4: Median HSI (IQR) on EVG was 39.3 (32.9-44.3) at baseline and 40.5 (34.4-46.3) at follow up; and 36.1 (30.9-39) at baseline, and 38.3 (32.8-47.9) at follow up on non-EVG; between group P= 0.1117.

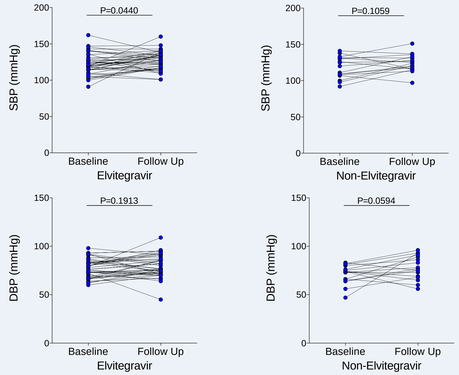


Figure 5: Median SBP and DBP change from baseline to follow up in people on EVG and non-EVG based regimens.

Conclusions

- Initiation of ART during AHI was associated with weight gain, with more weight gain in people on INSTI-based regimens vs non-INSTI regimens; however, this difference was not statistically significant.
- Amongst people on INSTI, less weight gain and less HSI increase was seen in people on EVG-based regimens.
- Changes in metabolic parameters, including hypertension, hyperlipidemia and diabetes mellitus did not reach statistical significance, although limited by small sample size and short duration of follow up.
- While the benefits of starting ART during AHI on immune system preservation and reservoir should not be underestimated, the risk and consequences of weight gain following ART initiation should be discussed when initiating ART during AHI.