Effect on weight changes upon discontinuation of dolutegravir from antiretroviral regimens among persons with HIV who experienced weight gain

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Background

- Weight gain associated with antiretrovirals (ARV) has emerged as a growing concern for persons with HIV (PWH), particularly second generation integrase strand transfer inhibitors (INSTI) such as dolutegravir (DTG)[1,2]
- Although numerous studies have reported weight gain with INSTI initiation, there is limited data on how to mitigate INSTI-related weight gain and weight changes if switching off INSTIs
- Purpose of this study is to compare weight trends of PWH after switching off a DTG-containing regimen after it was approved in 8/2013

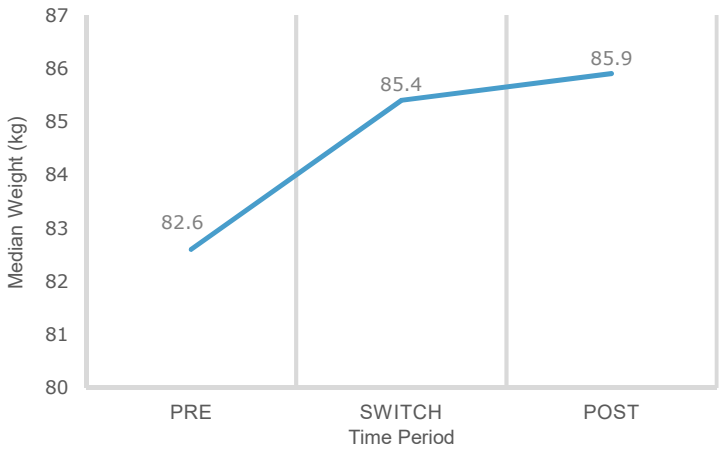
Methods

- Retrospective cohort study among PWH in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) between 1/2010 – 12/2020
- Inclusion criteria:
  - Age ≥ 18 years
  - Receipt of DTG-containing regimen for ≥ 12 months
  - Switched off DTG-containing regimen for ≥ 12 months
  - Experienced any weight gain while on DTG
- Exclusion criteria:
  - Missing weight measurements
- Remaining ARV components were allowed to change at time of switch
- Weight measurements were recorded in 3 month increments and grouped according to the following time points:
  - -12 to -6 months prior to switching off DTG defined as “Pre-switch”
  - -3 months to +3 months defined as “Switch”
  - +6 months to + 12 months defined as “Post-switch”
- Mean weights during each of the 3 defined periods were used for analysis
- Wilcoxon signed rank test was used to compare median weight changes in PWH between “Pre-switch”/”Switch” to “Switch”/”Post-Switch” period
- Comparison of weight change by ARV components were performed using Mann-Whitney U test

Results

- 371 PWH switched off DTG during the study period. Among those, 176 PWH experienced weight gain while on DTG and were included in the analysis
- The mean (SD) age was 48.1 (12.1) years and 72% were male. 85% had a CD4 greater than 200 cells/uL at baseline and 77% were virologically suppressed with a HIV PCR ≤ 200 copies/mL, see Table 1 for more details
- The median duration of DTG exposure prior to switch was 20.2 months
- The most common ARV regimens pre-switch were abacavir (ABC)/lamivudine (3TC)/DTG (38%), tenofovir disoproxil fumarate (TDF)/emtricitamine (FTC)/DTG (23%), TDF/FTC/DTG/darunavir (DRV)/cobicistat (c) (7%)
- The most common ARV regimens post-switch were tenofovir alafenamide (TAF)/FTC/elvitegravir (EVG)/c (43%), TDF/FTC/EVG/c (7%), TAF/FTC/rilpivirine (RPV) (13%), TAF/FTC/DRV/c (9%), TAF/FTC/EVG/c/DRV (9%)
- There was a significant difference in the change in median weight (IQR) between the pre-switch time period 2.7kg (1.3 – 4.8) and the post-switch time period 0.7kg (-1.1 – 3), p<0.001, see Figure 1.
- There were no significant differences in weight change post-switch between those that received non-nucleoside reverse transcriptase inhibitors (NNRTI), protease inhibitors (PI), EVG, TDF or TAF see Table 3 for more details.

- Figure 1: Median Weights in Each Time Period



- Table 1: Baseline Demographics at Time of Study Initiation

	N = 176
Mean Age (years, SD)	48.1 (12.1)
Sex Assigned at Birth (%)	
Male	127 (72.2)
Female	49 (27.8)
Race (%)	
Black	74 (42.0)
White	82 (46.6)
Asian	2 (1.1)
Other/Unknown	18 (10.2)
Ethnicity (%)	
Hispanic	17 (9.7)
Non-Hispanic	134 (76.1)
Unknown	25 (14.2)
Median CD4 at Baseline (cells/uL, %)	
CD4 ≥ 200	149 (84.7)
CD4 < 200	32 (18.2)
Median HIV PCR at Baseline (copies/mL, %)	
HIV PCR > 200	41 (23.3)
HIV PCR ≤ 200	135 (76.7)
Median DTG Duration of Exposure Before Switch (months, IQR)	20.2 (14.2 – 27.4)
Baseline Median Weight (kg, IQR)	82.6 (71.1 – 96.6)
Baseline Median BMI (IQR)	27.5 (24.7 – 31.4)

- Table 2: Change In Weight

	Pre-Switch	Post-Switch	P-value
Median Change in Mean Weights (kg, IQR)	2.7 (1.3 – 4.8)	0.7 (-1.2 – 3)	P<0.001
Median Change in Weight Percentage (%, IQR)	3.1 (1.6 – 5.5)	0.79 (-1.4 – 3.3)	P<0.001

- Table 3: Change in Weight Post-Switch in Various Subgroups

Subgroup	Change in Weight (kg)	N	P-value
Post-switch ARV regimen containing:			
NNRTI	0.8	33	0.99
PI	0.3	50	0.80
EVG	0.6	121	0.26
TDF	0.6	26	0.44
TAF	0.7	137	0.88
Switched off TDF	1.0	57	0.16
Switched to TAF	0.7	126	0.44
Sex assigned at birth			
Female	1.4	49	0.06
Male	0.5	127	
CD4 at baseline < 200	0.7	32	0.36
HIV PCR at baseline			
> 200	1.2	41	0.25
≤ 200	0.6	135	
Black	0.8	74	0.87
BMI <25 at baseline	1.0	48	0.30

Conclusion

- Rate of weight gain after switching off DTG was significantly different when compared to rate of weight gain before switching off DTG
- Although rate of weight gain was significantly different, patients did not lose weight and still had a net gain in weight when compared to the start of the study
- There was a trend towards female patients continuing to experience increases in weight after switching off DTG
- Although not significant, switching off TDF may be associated with weight gain
- Small sample size in subgroup analyses limited statistical power
- Future studies are needed to ascertain effects of contributory factors such as CD4 restoration, underlying body size, optimal time and amount of weight resolution possible

Disclosures

- The authors of this study have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

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