WEIGHT LOSS AND METABOLIC CHANGES AFTER SWITCHING FROM TAF/FTC+DTG TO TDF/3TC/DTG

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BACKGROUND

- Use of tenofovir alafenamide (TAF) with emtricitabine (FTC) and integrase inhibitors such as dolutegravir (DTG) has been associated with significant treatment-emergent weight gain and higher risks of metabolic syndrome versus TDF/FTC/EFV
- Weight gain is particularly high for Black women on first-line antiretrovirals.
- Efavirenz (EFV) and tenofovir disoproxil fumarate (TDF) could suppress weight gain.
- It is unclear whether weight gains during first-line treatment are reversible after changes in antiretrovirals.

METHODS

- In the ADVANCE trial, 1053 treatment naïve participants in South Africa were randomized to TAF/FTC+DTG, TDF/FTC+DTG or TDF/FTC/EFV for 192 weeks.
- After Week 192, participants were switched to open-label TDF/3TC/DTG for at least 52 weeks in a follow up trial, CHARACTERISE.
- At follow up, participants were assessed for weight, lipids, fasting glucose, HBA1C and HIV RNA.
- Changes in weight and laboratory parameters during the first 192 weeks of randomized treatment and then after the switch to TDF/3TC/DTG were evaluated in each treatment arm using paired non-parametric tests.

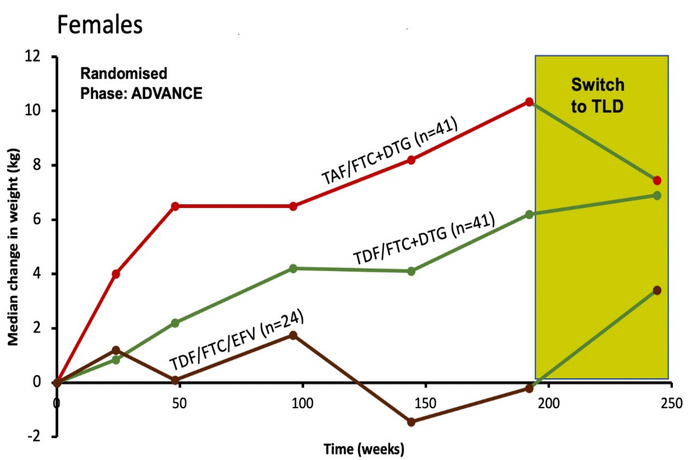

Figure 1: Median weight change for females

After switching from TAF/FTC+DTG to TDF/3TC/DTG for 52 weeks, there were statistically significant reductions in weight, total cholesterol, LDL, triglycerides, fasting glucose and HBA1C (Table 1).

Participants switching from TDF/FTC/EFV to TDF/3TC/DTG showed significant rises in body weight, with reductions in total cholesterol, LDL, HDL, triglycerides and HbA1C (Table 1).

WHO guidelines recommend TDF/3TC/DTG as first line treatment, with TAF only to be used for those with osteoporosis or renal impairment. The results from CHARACTERISE support the WHO guidelines.

Table 1: Baseline characteristics and changes in weight and metabolic parameters from switch to TDF/3TC+DTG by original treatment received. *Note: Continuous variables are displayed as Median and interquartile range (IQR). Count variables are displayed as n/N and %. n.s. = not significant

Group	TAF/FTC+DTG (n=70)	TDF/FTC+DTG (n=71)	TDF/FTC/EFV (n=31)
Baseline characteristics*			
Sex (% Female)	41/70 (59%)	41/71 (58%)	24/31 (77%)
Country (% South Africa)	42/70 (60%)	51/71 (72%)	20/31 (64%)
Weight (kg)	81.1 [71.5, 89.1]	72.9 [61.7, 86.3]	74.3 [61.8, 100.5]
BMI (kg/m^2)	28.0 [23.9, 31.8]	25.9 [22.5, 30.6]	25.6 [23.6, 33.1]
HIV RNA <50 copies/mL (%)	66/67 (98%)	62/64 (97%)	23/23 (100%)
CD4 count (cells/uL)	560 [424, 787]	549 [407.5, 743.5]	677 [544, 882]
Cholesterol (mmol/L)	3.9 [3.5, 4.8]	3.7 [3.2, 4.3]	4.5 [3.6, 4.91]
LDL (mmol/L)	2.6 [2.2, 3.1]	2.3 [1.9, 2.9]	2.8 [2.3, 3.27]
HDL (mmol/L)	1.1 [0.9, 1.3]	1.1 [0.9, 1.3]	1.3 [1.0, 1.6]
Triglycerides (mmol/L)	0.9 [0.7, 1.2]	0.8 [0.6, 1.0]	0.9 [0.7, 1.3]
Fasting glucose (mmol/L)	4.9 [4.5, 5.2]	4.9 [4.6, 5.1]	4.7 [4.5, 5.1]
HbA1c (mmol/L)	5.5 [5.1, 5.7]	5.5 [5.2, 5.7]	5.5 [5.2, 5.7]
Systolic blood pressure (mmHg)	127 [119, 134]	122 [117, 132]	118 [113, 126]
Diastolic blood pressure (mmHg)	83 [78, 88]	82 [77.5, 86]	76 [72, 83]
Changes from switch*			
Weight (kg)	-1.2 [-3.8,1], p=0.006	-0.1 [-2.1, 2.2] (n.s.)	+2.9 [-0.7, 4.9], p=0.02
BMI (kg/m^2)	-0.4 [-1.3, 0.3], p=0.005	-0.05 [-0.7, 0.7] (n.s.)	+1.0 [-0.2, 1.9], p=0.022
Total cholesterol (mmol/L)	-0.2 [-0.5, 0.1], p=0.002	+0.2 [-0.1, 0.4], p=0.001	-0.3 [-0.8, 0.01], p=0.011
LDL cholesterol (mmol/L)	-0.3 [-0.6, -0.01], p<0.001	-0.01 [-0.2, 0.2] (n.s.)	-0.3 [-0.5, -0.1], p=0.001
HDL (mmol/L)	-0.03 [-0.2, 0.1] (n.s.)	+0.04 [-0.1, 0.2], p=0.021	-0.1 [-0.3, 0.05], p=0.049
Triglycerides (mmol/L)	-0.1 [-0.3, 0.09], p=0.025	-0.02 [-0.2, 0.2] (n.s.)	-0.1 [-0.3, 0.05], p=0.057
Fasting glucose (mmol/L)	-0.2 [-0.5, 0.1], p<0.001	0 [-0.3, 0.2] (n.s.)	-0.1 [-0.3, 0.1] (n.s.)
HbA1c (mmol/L)	-0.1 [-0.3, 0], p<0.001	-0.1 [-0.3, 0.1] (n.s.)	-0.15 [-0.2, 0], p=0.008
Systolic blood pressure (mmHg)	+1.5 [-6, 14] (n.s.)	+3 [-2.5, 10], p=0.021	+6 [-10, 13] (n.s.)
Diastolic blood pressure (mmHg)	+2 [-4, 6] (n.s.)	+0.5 [-5.5, 4.5] (n.s.)	+2 [-4, 11] (n.s.)
HIV RNA<50 copies/mL at or after week 52 (%)	68/68 (100%)	68/70 (97%)	25/28 (89%)

RESULTS

- Of the 172 participants in the analysis, 106 were female, 100% were Black African with median CD4 count 570.5 cells/uL
- Results from CHARACTERISE are available for 70 of the 351 participants originally in the TAF/FTC+DTG arm at the end of ADVANCE, 71 of the 351 participants in the TDF/FTC+DTG arm and 31 of the 351 participants in the TDF/FTC/EFV arm.
- Table 1 shows changes in weight, lipids, glucose and HBA1C after switch from their original randomized treatment to TDF/3TC/DTG in the CHARACTERISE trial.
- During the 192 weeks of first-line randomized treatment in ADVANCE, participants taking TAF/FTC+DTG showed significantly higher rises in weight and BMI, compared with the TDF/FTC+DTG arm (p<0.001 for both comparisons).

CONCLUSIONS

- After 4 years of weight gain on first-line TAF/FTC+DTG, switching to TDF/3TC/DTG for 52 weeks led to significant weight loss for women (median: -1.6kg, p=0.0125). This change in weight was not significant in men (median: -0.2kg, p=0.2561).
- There were concurrent reductions in total cholesterol, LDL, triglycerides, fasting glucose and HBA1C after switching TAF/FTC+DTG to TDF/3TC/DTG.

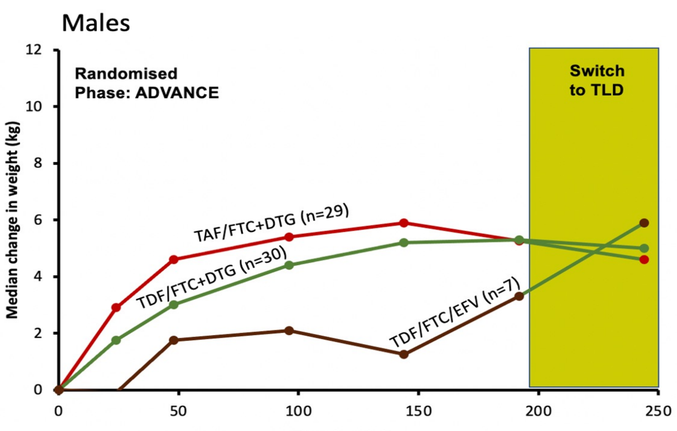

Figure 2: Median weight change for males