

# Weight evolution in patients after stavudine substitution for lipoatrophy in Rwanda: Comparison of zidovudine with tenofovir/abacavir



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## Objectives

In patients manifesting lipoatrophy on stavudine-containing first-line antiretroviral treatment (ART) regimens in Rwanda, to a) assess weight evolution after stavudine substitution and b) verify if there was a significant difference in weight evolution if zidovudine or tenofovir (TDF)/abacavir (ABV) was used for substitution.

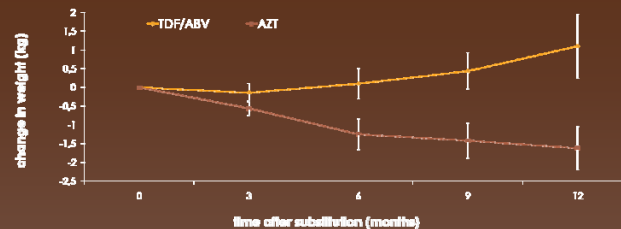
## Analysis

Analysis of ART-outcomes in two urban government health centers (Kinyinya and Kimironko HC) in Kigali. All patients on stavudine-containing first-line regimens for an uninterrupted duration of minimal 6 months and substituting stavudine for lipoatrophy (diagnosed using a Lipodystrophy-Case-Definition-Study-based questionnaire) were included (N=116). The most severe cases replaced stavudine with TDF or ABV (N=40), the remainder with zidovudine (N=76). The weight evolution at 3, 6, 9 and 12 months after stavudine-substitution was recorded. Multivariate linear regression was performed to identify factors associated with the change in weight after substitution.

**Table 1:** Baseline characteristics of patients with lipoatrophy prior to substitution with stavudine

Baseline characteristic	Total (N=116)	TDF/ABV (N=40)	ZDV (N=76)	P-value
Sex				
Male	2 (1.7)	1 (2.5)	1 (1.3)	0.642
Female	114 (98.3)	39 (97.5)	75 (98.7)	0.952
Age (years) <sup>b</sup>	35.7 (32.3-38.6)	36.8 (34.3-39.9)	34.8 (32.1-38.1)	0.074
WHO clinical stage at baseline				
Stage 1	1 (0.9)	0 (0)	1 (1.3)	0.468
Stage 2	14 (12.1)	3 (7.5)	11 (14.5)	0.304
Stage 3	83 (71.5)	31 (77.5)	52 (68.4)	0.582
Stage 4	18 (15.5)	6 (15.0)	12 (15.8)	0.918
CD4 count before substitution (cells/ $\mu$ L) <sup>b,c</sup>	293 (196-370)	289 (222-367)	293 (192-370)	0.751
Time on ART (days) <sup>b</sup>	492 (406-632)	512 (400-596)	490 (417-669)	0.756
NNRTI				
NVP	96 (82.8)	36 (90.0)	60 (78.9)	0.891
EFV	20 (17.2)	4 (10.0)	16 (21.1)	0.305
Body weight at time of substitution (kg) <sup>b</sup>	60 (53-67)	61 (53-72)	60 (53-65)	0.440
Body weight loss prior to substitution (kg) <sup>b</sup>	3.0 (1.9-5.6)	3.3 (2.0-6.0)	3.0 (1.0-5.1)	0.248
Rate of weight loss (g/week) <sup>b</sup>	189 (115-280)	171 (111-326)	201 (125-257)	0.932
Secondary diagnosis of SH/LA				
No	102 (87.9)	31 (77.5)	71 (93.4)	0.385
Yes	14 (12.1)	9 (22.5)	5 (6.6)	0.019
Length of follow-up after substitution (days) <sup>b</sup>	342 (251-434)	398 (265-507)	337 (240-396)	0.018

<sup>a</sup> data represent N (%) unless otherwise stated. <sup>b</sup> median (interquartile range). <sup>c</sup> within 6 months prior to substitution; missing for 5 individuals. TDF: tenofovir; ABV: abacavir; ZDV: zidovudine; WHO: World Health Organisation; ART: antiretroviral treatment; NNRTI: non-nucleoside reverse transcriptase inhibitors; NVP: nevirapine; EFV: efavirenz; SH/LA: symptomatic hyperlactatemia/lactic acidosis



**Figure 1.** Weight evolution after substitution of stavudine for lipoatrophy (N=116). Data presented are the mean weight change and standard error of the mean (SEM).

**Table 3.** Multivariate analysis to assess the independent association of type of drug substitution with weight change<sup>a</sup>

Baseline variables	Univariate analysis		Multivariate analysis	
	Coefficient	P value	Coefficient	P value
NRTI (ZDV vs TDF/ABV)	-1.994	0.010	-2.330	0.002
Time on ART	0.002	0.242	0.002	0.342
Sex	-3.770	0.177	-1.785	0.497
Age	-0.039	0.504	-0.041	0.455
WHO clinical stage (1/2 vs 3/4)	-0.070	0.949	-1.227	0.233
CD4 count before substitution	-0.002	0.441	-0.003	0.204
NNRTI (EFV vs NVP)	-0.857	0.376	-0.727	0.413
Body weight at time of substitution	-0.060	0.101	-0.065	0.083
Body weight loss prior to substitution	0.324	<0.001	0.455	0.002
Rate of weight loss	-0.004	0.086	0.004	0.268
Secondary diagnosis of SH/LA	-2.557	0.059	-2.081	0.132

<sup>a</sup> Excluding 5 individuals with missing CD4 data (N=111);

## Results

For those patients changed to zidovudine, a progressive weight loss was seen (mean loss by 12 months: 1.62 kg; P=0.001). In contrast, those on TDF/ABV displayed stable body weight, with a tendency towards recovery after an initial period of 3 months although this difference did not reach statistical significance. The between-group difference was significant from 6 months on (difference at 12 months: 2.7 kg, P=0.008). In multivariate analysis, substitution with TDF/ABV and pronounced weight loss prior to stavudine-change was significantly associated with weight gain.

## Conclusions

This is the first study in Africa assessing "weight gain" as a proxy of recovery after substitution of stavudine for lipoatrophy. In this regard and although we do not know the metabolic implications of this finding, it might suggest that TDF/ABV is superior to zidovudine. The slow recovery of weight particularly with zidovudine highlights the need of alternatives for stavudine in first-line regimens, and the need of pro-active switching.

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