Lipid changes after switch from tenofovir disoproxil fumarate to tenofovir alafenamide: a longitudinal cohort study

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Introduction

Switching from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) has been recommended as strategy to reduce the risk of renal and bone toxicities. However, its effect on lipid profile has not been a main focus of interest.

Methods

This analysis consists of a retrospective data collection on effectively suppressed HIV-positive patients who were switched from TDF to TAF-based antiretroviral treatment (ARVT) due to medical reasons (bone, kidney disease) or as a result of optimization of therapy, in a single site (Center for HIV and Hepatogastroenterology, Düsseldorf). All components of ARVT for all patients whose data were analysed were maintained with the exception of the single substitution of TDF to TAF. Lipid profile was measured before switch and at 12 weeks intervals after initiation of TAF.
For univariate analyses Mann-Whitney-U-test and Wilcoxon test were used. Variables which were significant in the univariate analyses were entered in a multivariate logistic regression model.

Table 1: Demographics at change from TDF to TAF (numbers or median and IQR; n=385 patients)

sex male	345/385 (90%)
ethnicity Caucasian	356/385 (93%)
ethnicity African/ Asian/ na	5%/ 1%/ 1%
age (years)	50 (42 – 56)
BMI (kg/m^2)	23.52 (21.26 – 25.61)
HIV RNA <40 cp/ml	376/385 (98%)
CD4+ cells (/µl)	734 (541 – 914)
CD4+ cells (%)	34 (27 – 39)
CDC stage A/ B/ C	47%/ 27%/ 24%
CD4+ nadir <200/ 200-499/ ≥500 cells/µl	37%/ 44%/ 19%
years since HIV diagnosis	11 (6 – 17)
weeks on TDF	317 (172 – 494)
stable lipid lowering therapy	50/385 (13%)

Table 2: Baseline lipids (mean and standart deviation, n=385)

total cholesterol	186 ± 37 mg/dl
HDL-cholesterol	46 ± 13 mg/dl
LDL-cholesterol	119 ± 34 mg/dl
triglycerides	152 ± 96 mg/dl

Table 3: Comorbidities at change from TDF to TAF n=385 patients

no comorbidities	102/385 (26%)
hypertension	77/385 (20%)
osteopenia/osteoporosis	46/385 (12%)
depression	45/385 (11%)
lipid disorders	39/385 (10%)
COPD, asthma	23/385 (6%)
Diabetes melitus	21/385 (5%)
opioid substitution	16/385 (4%)
coinfection HCV / HBV	2%/ 3%

Results

A total of 385 virologically suppressed patients on stable TDF-containing regimens were included. Baseline demographics at switch from TDF to TAF are listed in **table 1**. Baseline lipids before switch are given in **table 2** and comorbidities are shown in **table 3.**
At baseline total cholesterol >240 mg/dl was measured in 26/385 (7%) of patients and 9/71 (13%) of patients had LDL-cholesterol >160 mg/d. Triglycerides >200 mg/dl were reported in 82/385 (21%) of participants.
At 12 and 24 weeks after switch from TDF to TAF total cholesterol, LDL-cholesterol and triglycerides increased, which is shown in **figure 1.** Differences in mean changes were statistically significant (p<0.001).
Grading of total cholesterol level was unchanged in 242/385 (62%) and increased in 131/385 (34%). Worsening to grade 3 (>240 mg/dl) occurred in 52/385 (14%) of patients **(figure 2)**.
The odds of having total cholesterol >240 mg/dl after switching to TAF was associated with older age (increased by 2% per year; p=0.027), BMI >25 kg/sqm (p=0.020) and elevated baseline LDL cholesterol (p<0.001). In the multivariatle model, age >50 years (OR 1,.58, p<0.01) and BM I>25 kg/sqm (OR 2.08, p< 0.01) remained independently associated with TC >240 mg/dl.

Fig. 1: Lipid changes after switching from TDF to TAF

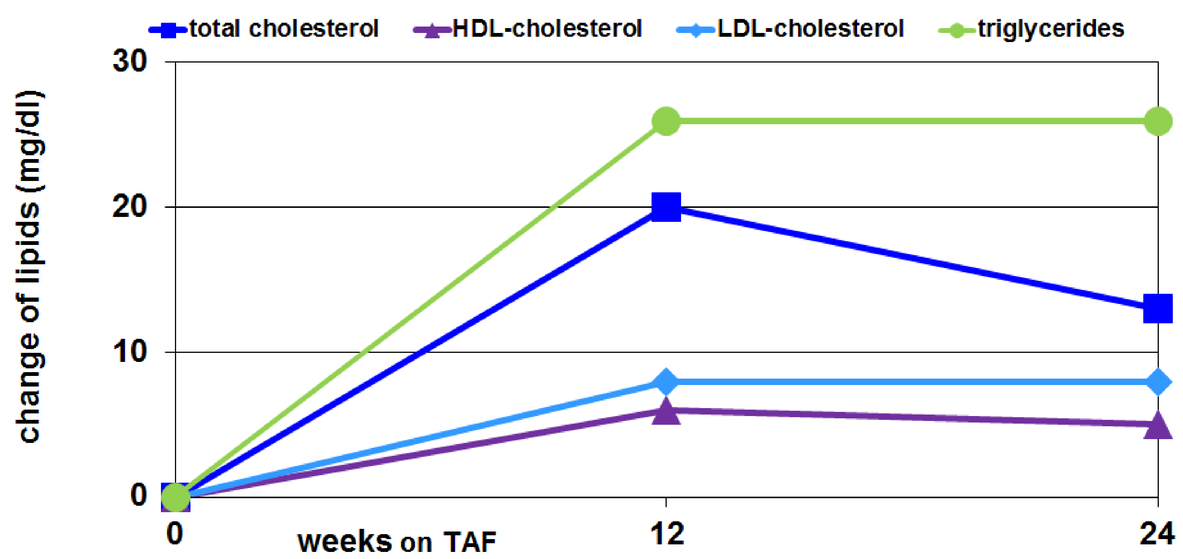

Fig. 2: Change of total cholesterol level after switch TDF to TAF (n=385) Grade: 1: <200 mg/dl; 2: 200-240 mg/dl; 3: >240 mg/dl

	Grade TC 12 – 24 weeks after switch to TAF			
Grade TC before switch		**1**	**2**	**3**
	1	157	79	10
	2	10	61	42
	3	0	2	24

Conclusions

About a third of patients show an increase in total cholesterol after switching from TDF to TAF. Importantly patients with pre-existing higher CV risk are more likely to show increases in lipids after switching from TDF to TAF which may worsen the cardiovascular risk profile. In these patients risk and benefit of switching TDF to TAF should be carefully accessed, taking lipids into consideration.