Increases in lipid profile after switch from TDF to TAF-based HAART regimens in a cohort of HIV positive patients: Is it clinically relevant?

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BACKGROUND

- HIV positive patients are at increased risk of cardiovascular disease, due to the HIV-related early aging process.
- Cardiovascular risk monitoring and introduction of preventive strategy/therapy are part of the clinical management of HIV positive patients
- The HAART-scenario has been recently modified by the switch from TDF-based to TAF-based regimens, this change has been demonstrated to affect lipid profile

AIM

Aim of our study is to evaluate whether the change in lipid profile after switch from TDF to TAF-based regimens is clinically relevant and results in an increased frequency of patients out of target-LDL, according to their CV risk score.

STUDY DESIGN AND METHODS

- Retrospective observational analysis.
- All HIV patients switching from TDF to TAF, with no changes of the third drug, and plasma lipids available within 6 months before and after the switch, were included. Ongoing therapy with statin was an exclusion criteria.
- Patients' demographics, HIV-related parameters, CV risk factors and lipid profile on TDF and on TAF were collected.
- For each patient the CV risk SCORE and the target of LDL for each SCORE strata were calculated according to 2016 ESC/EAS Guidelines for the management of Dyslipidaemias.
- Modifications in lipid profiles and in the frequency of patients out-of-target-LDL were evaluated after switch to TAF.
- The Odds Ratio of having out-of-target LDL in the TAF-era, as compared to TDF, was evaluated by univariate analysis, according to the third drug.

RESULTS

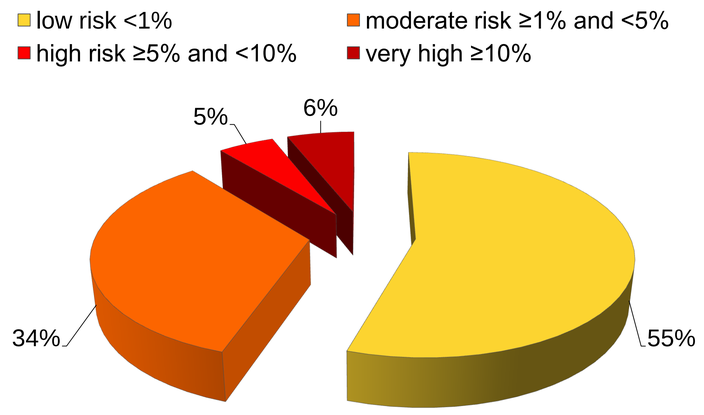
- A total of 221 patients were included (Table 1).

Table1: Main characteristics of the study population at baseline (on TDF-based HAART).

	Patients (N=221)
Age, median (IQR)	45y (38-52)
Female, n (%)	47 (21.3%)
CD4 cell/mm3, median (IQR)	640 (493 -849)
Patients with HIV-RNA <40cp/mL, n(%)	216 (98%)
3rd drug in HAART regimen:	
-NNRTI	96 (43.3%)
-INSTI	11 (5%)
-INSTI/cobi	101(45.7%)
-PI/cobi	13 (6%)
CVD risk factors:	
-hypertension	29 (13.1%)
-smoking	79 (35.7%)
-diabetes	7 (3.2%)
-previous evidence of plaque	8 (3.1%)
-previous CV event	7 (3.1%)

- Distribution of patients according to their ESC/EAS cardiovascular risk score are represented in Figure 1

Figure 1: Distribution of patients according to ESC/EAS SCORE strata



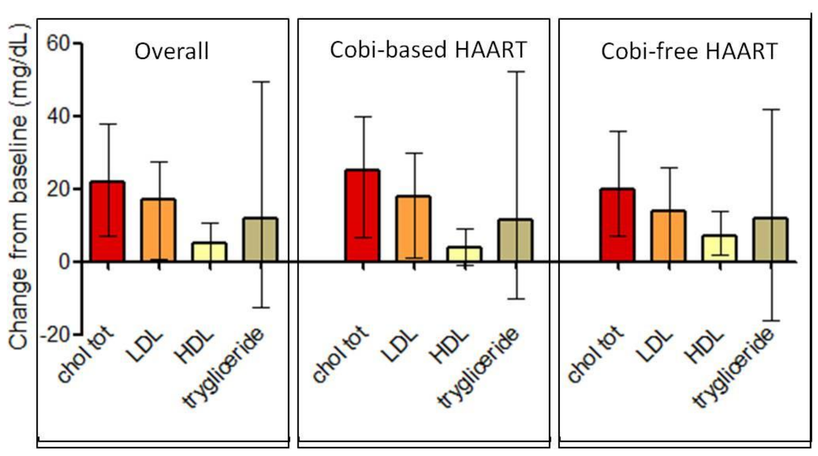
- Median plasma levels of lipids at baseline, on TDF-based HAART regimens, are represented in Table 2.
- Patients on cobi-based HAART regimens displayed higher levels of total cholesterol, as compared to patients on cobi-free HAART [median tot chol: cobi-based 184mg/dL (166-205) vs cobi-free 166mg/dL (144-186), p<0.0001]; higher level of LDL [median LDL: cobi-based 109mg/dL (94-128) vs cobi-free 98mg/dL (79-117), p=0.002] and of tryglicerides [median trygl: cobi-based 118mg/dL (89-59) vs cobi-free 90mg/dL (72-127), p=0.003]; no difference in HDL cholesterol was observed.
- After switch from TDF to TAF-based regimens, an increase in all lipid classes has been observed, indepently by the third drug and by the presence of cobi in the HAART regimen (Table 2 and Figure 2).

Table 2: Lipids plasma levels (mg/dL) on TDF and change after switch to TAF are represented according to the 3rd drug.

		TDF	TAF	Δ	p
PI/c	total cholesterol	198 (184-219)	209 (204-236)	+19 (+5 +37)	0.02
	LDL	122 (96-133)	129 (115-152)	+15 (-9 +25)	0.06
	HDL	47 (33-56)	50 (42-66)	+7 (+1 +10)	0.04
	tryglicerides	121 (90-187)	134 (95-159)	+9 (-10 +15)	0.6
INSTI/c	total cholesterol	181 (163-201)	209 (182-228)	+26 (+8 +40)	<0.0001
	LDL	108 (93-126)	124 (109-148)	+18 (+2 +30)	<0.0001
	HDL	46 (38-53)	50 (40-59)	+4 (-1 +8)	<0.0001
	tryglicerides	117 (88-156)	135 (94-186)	+12 (-10 +53)	0.0009
INSTI	total cholesterol	162 (124-201)	195 (153-217)	+34 (+19 +50)	0.003
	LDL	76 (56-115)	100 (83-125)	+25 (+10 +32)	0.04
	HDL	44 (38-51)	51 (48-56)	+4 (+0 +18)	0.1
	tryglicerides	82 (54-127)	98 (83-139)	+21 (+7 +52)	0.09
NNRTI	total cholesterol	167 (146-185)	186 (165-204)	+19 (+6 +34)	<0.0001
	LDL	99 (83-117)	114 (95-131)	+14 (+0 +25)	<0.0001
	HDL	43 (37-50)	49 (40-61)	+7 (+2 +14)	<0.0001
	Tryglicerides	91 (74-127)	111 (82-144)	+7 (-16 +41)	0.04

Median (IQR) lipid plasma value; Δ= difference between lipid plasma value on TAF and on TDF.

Figure 2: Change in plasma lipids after switch from TDF to TAF, data are presented overall and according to the presence of cobicistat in the HAART regimen.



- By analyzing lipid profiles according to CV score, 37.5% of patients on TDF had LDL out of target, this proportion increases to 59.5% after switch to TAF (p<0.0001). By univariate analysis, patients on TAF-based regimens had a double risk of out-of-target-LDL, as compared to TDF-based regimens [OR 2.4 (IC95% 1.6-3.6), p<0.0001].
- By analysing data according to cobicitat, switching TDF to TAF in cobicistat-free regimens results in an increase from 28% to 45% of patients out-of-target-LDL (p=0.01); switching strategy in cobicistat-based regimens increase this frequency from 46% to 73% (p=0.0001). At univariate analysis, patients switching to TAF in cobicistat-free regimens had a double risk of out-of-target-LDL, as compared to TDF [OR 2.1 (IC95% 1.2 -3.8), p=0.01], this relative risk increased to 3.1 (IC95% 1.8-5.9, p<0.0001) in cobicistat-based regimens.

Figure 3: Prevalence of patients with out-of-target LDL on TDF-based regimens and after switch to TAF.

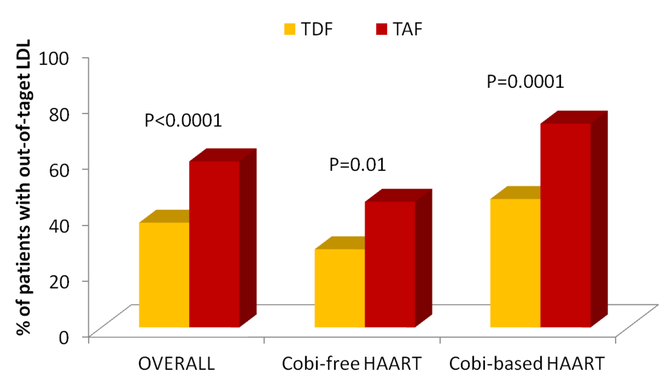


Table 4: Odds ratio of having out-of-taget LDL on TAF-based HAART regimens as compared to TDF-based.

	OR (IC95%)	p
TAF-based HAART	2.4 (1.6-3.6)	<0.0001
TAF-based/cobi-free HAART	2.1 (1.2-3.8)	0.01
TAF-based/cobi-based HAART	3.1 (1.8-5.9)	<0.0001

CONCLUSIONS

- Switching strategy from TDF to TAF worsens the lipid profile in HIV positive patients, leading to an increasing proportion of patients having LDL over their CV-related target.
- This effect is more evident in regimens containing cobicistat.
- Population intervention on lifestyle and increased prescription of therapeutic intervention has to be considered in the TAF era.

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