Incidence of dyslipidemia and modification of atherosclerotic cardiovascular disease (ASCVD) risk in HIV-infected patients who switch away from tenofovir disoproxil fumarate (TDF)-based to TDF-sparing regimens in the Icona Foundation Cohort

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BACKGROUND

Increasing values of total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL) and triglycerides (TG) were observed among HIV patients on combination ART (cART) switching away from TDF–based regimens in randomized trials. However, the impact of these changes in term of modification of ASCVD risk or need for lipid-lowering therapy in clinical practice has not been assessed.

AIMS

This study aimed to characterize changes in lipid profile and atherosclerotic cardiovascular diseases (ASCVD) risk after switching away from a TDF-based to a TDF-sparing cART in a real world setting.

STUDY DESIGN AND METHODS

HIV-positive patients from the ICONA Foundation Cohort, aged 18 years or over, who have started their first line cART regimen with TDF-based backbone plus a 3rd drug from January 1st, 2008 onwards and switched to a TDF-sparing regimen were included in the study.

We analyzed changes of TC, HDL, LDL, non-HDL, TG in patients who discontinued TDF, in the period before [-12; 0] and after [+4; +12] TDF switch. Paired t-test was used to compare two values before and before/after TDF switch and ANCOVA to test the effect on lipid variations of third drug combined with TDF and type of regimen started after.

We calculated the proportion of patients who became eligible for statin treatment within 1 year from TDF discontinuation according to strong/moderate level of recommendation of 2013 ACC/AHA guidelines.

In a subgroup of patients, 10-year ASCVD risk was calculated by Framingham Global Score.

RESULTS

2,543 patients were included in the study (Table 1).

Table 1. Main characteristics of study population at TDF switch

Gender (n,%)		
Male	2127	83.6
Age, median (IQR)	44	36-52
Mode of HIV transmission (n, %)		
Heterosexual	972	38.2
IVDU	161	6.3
MSM	1229	48.3
Other/unknown	181	7.1
CDC stage C (n, %)	297	11.7
HCV Ab (n, %)		
Positive	197	7.8
CD4+ cell/mm^3 (n, %)		
<350	520	20.4
≥350	2018	79.4
HIV-RNA, log$_{10}$ copies/mL, median (IQR)	1.3	0-1.59
Third drug class combined with TDF (n, %)		
NNRTI	719	28.3
PI/b	1007	39.6
INSTI	657	25.8
Other	160	6.3
NRTI started after TDF discontinuation (n, %)		
TAF/FTC	1177	46.3
ABC/3TC	703	27.6
Less drug regimens (dual or monotherapy)	575	22.6
Other	88	3.5
Lipid profile, mg/dl, median (IQR)		
Total cholesterol	176	151-202
HDL	44	36-52
LDL	107	88-130
Non-LDL	132	107-156
Triglycerides	112	81-161
ASCVD risk factors (n, %)		
Smoking	999	39.3
Hypertension	264	10.4
Diabetes	74	2.9
Framingham Global Score, % median (IQR)	4.3	2.4-8.0

Data showed stability before and increase after TDF interruption. TC and non-HDL increased of +19 and +14 mg/dL, respectively (Table 2). No difference in TC and non-HDL was observed according to third drug combined with TDF at switching (NNRTI +18, PI/b +19, INSTI +17, P at ANCOVA=0.932). Receiving PI/b after TDF discontinuing was associated to increase in TC (+28 vs +17, p<.01) and non-HDL (+24 vs +11, p<.01). Conversely, receiving INSTI after TDF switch predicted lower increase in TC (+14 vs +21, p=.02) and in non-HDL (+9 vs +15, p=.03). No difference was observed according to backbone after TDF change (TAF +23, ABC +19, less drug regimen +19, p=0.963). Over 201 subjects, last value of ASCVD risk during TDF was 6.7% and 7.5% after (p<0.01). 22/201 (11.0%) passed from a low (<10%) to intermediate (10-20%) or high (>20%) ASCVD risk or from intermediate to high risk after TDF stop. The proportion of patients who became eligible for statin within 1 y from TDF discontinuation was estimated as 3.8% (95%CI 3.1-4.6).

Legend: TDF, tenofovir disoproxil fumarate; IVDU, intravenous drug use; MSM, men who have sex with men; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI/b, boosted protease inhibitor, INSTI, integrase strand transfer inhibitor; TAF/FTC; tenofovir alafenamide/emtricitabine; ABC/3TC, abacavir/lamivudine; HDL, high-density lipoproteins; LDL, low density lipoproteins; ASCVD, atherosclerotic cardiovascular disease; T Chol, total cholesterol; TG, triglycerides

Table 2. Mean values and differences between two values of lipids before and before-after TDF discontinuation

	Pairs													
	T0-T1 (both pre- TDF)							T1-T2 (pre and post TDF)						
Biomarker	N	Mean1	SD1	Mean2	SD2	Difference	p-value	N	Mean1	SD1	Mean2	SD2	Difference	p-value
LDL	1019	112.7	47.1	110.6	33.0	-2.1	0.178	557	111.5	56.8	121.7	37.1	+10.2	<.01
HDL	1361	44.9	13.2	44.8	13.7	-0.1	0.105	713	43.7	13.3	48.6	15.6	+4.9	<.01
T-Chol	1691	179.2	38.5	178.3	38.6	-0.9	0.550	879	180.4	40.3	199.4	42.8	+19.0	<.01
Non-HDL	1358	134.7	37.8	134.3	36.9	-0.4	0.618	710	137.0	38.0	150.6	41.8	+13.6	<.01
Triglycerides	1484	132.6	96.8	138.0	231.9	-5.4	0.365	866	146.5	85.8	155.7	106.8	+9.2	<.01

CONCLUSIONS

We found evidence for a significant increase in lipids following TDF discontinuation. However, this variation did not appear to have an immediate major impact on the 10-year estimated ASCVD risk.

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References

1. 2013 ACC/AHA Guidelines; 2. 2017 AACE Guidelines; 3. Wohl D, J Acquir Immune Defic Syndr 2016; 4. Sax PE, *Lancet 2015; 5. Arribas JR, J Acquir Immune Defic Syndr 2017; 6. Huhn G, 18th International Workshop on Co-morbidities and Adverse Drug Reactions in HIV, New York, USA, 12-13 September 2016; 7. Lacey A, 16th European AIDS Conference, Milan, Italy 23-25 October 2017.*

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