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With or Without TAF? What is the difference? Data from a real-life setting

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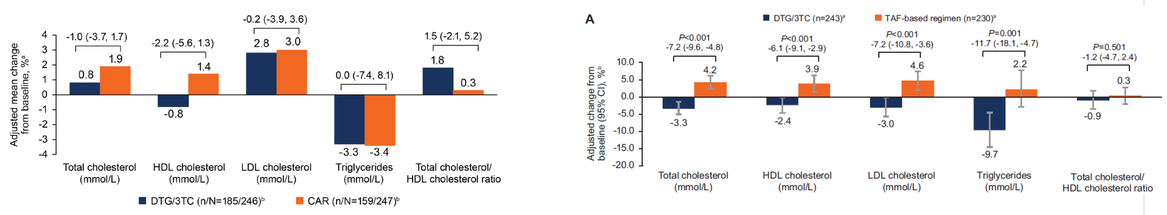
Introduction

- Conflicting results are reported in literature about metabolic impact switching to two-drug regimen (2DR) vs Emtricitabine/Tenofovir Alafenamide (FTC/TAF) based regimen (1-2).
- Salsa study (1) reported only minimal changes in lipid profile after 48 weeks (see figure 1) while Tango trial (2) observed a more favourable lipid asset in people switching to 2 DR (see figure 1) .
- In Tango study transaminase increase was observed in <1% of the sample with no differences between the 2DR and FTC/TAF-based regimens (TAF-BR) (2).
- Our aim was to investigate the role of switching from FTC/TAF based regimen to a dolutegravir (DTG) containing 2DR vs continuing TAF-BR on metabolic and parameters and liver enzymes.

Figure 1 Changes in lipids in SALSA and TANGO studies



Methods

- Consecutive people living with HIV infection (PLWH) enrolled in a multicenter observational cohort (SCOLTA) project, on a stable FTC/TAF-based regimen with an HIV-RNA<50 copies/ml were included.
- HBsAg positive PLWH were excluded.
- Changes from baseline (T0) to follow-up (T1, week 24) were analyzed.

Table 1. Patients'characteristics

Variables at enrollment	2DR N=104 Mean SD or N (%) or Median (IQR)	TAF-based N=253 Mean SD or N (%) or Median (IQR)	P
Age, years	48.5 ± 13.2	48.4 ± 11.5	0.96
Sex M	80 (76.9%)	187 (73.9%)	0.55
BMI Kg/m²	25.4 ± 3.9	26.0 ± 6.0	0.35
Weight, Kg	75.8 ± 13.7	75.2 ± 14.3	0.74
Caucasian	94 (90.4%)	219 (86.6%)	0.32
Risk factor for HIV acquisition			
Sexual	95 (91.4%)	174 (68.8%)	
IDU	6 (5.6%)	40 (15.8%)	
Other/ND	3 (2.9%)	39 (15.4%)	<0.0001
HCV coinfection (n=107/329)	7 (6.9%)	55 (23.2%)	0.0004
Previous ART			
PI	7 (6.7%)	38 (15.0%)	0.03
INI	61 (58.6%)	199 (78.7%)	<0.0001
NNRTI	36 (34.6%)	14 (5.5%)	<0.0001
COBI	37 (35.6%)	161 (63.6%)	<0.0001
Current regimen			
3TC/DTG	84 (80.8)	0	
RPV/DTG	20 (19.2)	0	
FTC/TAF/BIC	0	243 (96.0)	
FTC/TAF/DTG	0	10 (4.0)	
CDC Stage			
A	80 (76.9%)	129 (51.2%)	
B	19 (18.3%)	78 (31.0%)	
C	5 (4.8%)	45 (17.9%)	<0.0001
CD4, cells/mm3	738 (614-926)	645 (490-838)	0.0002
Total cholesterol, mg/dL	197 ± 37	196 ± 41	0.91
HDL-cholesterol, mg/dL	51 ± 14	52 ± 17	0.45
LDL-cholesterol, mg/dL	119 ± 32	116 ± 36	0.35
Triglycerides, mg/dL	108 (80-154)	115 (85-163)	0.33
Blood glucose, mg/dL (nondiabetics, n=99/232)	88 ± 12	93 ± 15	0.004
Blood glucose, mg/dL (diabetics, n=5/21)	117 ± 40	163 ± 69	0.17
On lipid-lowering drugs	8 (7.7%)	42 (16.6%)	0.03
AST, UI/dL	21 (17-25)	21 (18-26)	0.23
ALT, UI/dL	21 (16-27)	21 (16-29)	0.44

Legend to table 1: SD, Standard Deviation; IQR, Inter Quartile Range; CI, Confidence Interval; M, Male; BMI, Body Mass Index, LDL, Low Density Lipoprotein; HDL, High Density Lipoprotei; eGFR, estimated Glomerular Filtration Rate; IU, International Unit; AST, aspartate aminotransferase; ALT, aspartate aminotransferase; IDU, Intravenous Drug User; HCV, Hepatitis C Virus; PI, Protease Inhibitors; INI, Integrase Inhibitors; NNRTI , Non – nucleoside Reverse Transcriptase Inhibitors

Results

- 357 PLWH met the inclusion criteria, 267 (74.8357 PLWH met the inclusion criteria, 267 (74.8%) were males, 313 (87.7) Caucasians. 104 switched to 2DR, 253 continued TAF-BR. 26 PLWH had diabetes.
- The main characteristics at baseline were shown in table 1 Comparing 2DR and TAF-BR, we observed no differences in blood lipids modifications and weight (see table 2).
- Splitting by previous regimens with vs without cobicistat (COBI), total cholesterol (TC),LDL-cholesterol (LDL-C) and triglycerides (TGL) showed a significant decrease in patients switching from COBI-containing regimens on overall sample (mean change for TC -18 mg/dL vs -10 mg/dL; LDL-c -12 mg/dL vs -7 mg/dL; TGL -22 mg/dL vs -18 mg/dL for 2 DR vs TAF-BR, p<0.05 for each) .
- Including current regimen and previous COBI in a general linear model, we confirmed the association between decreased blood lipids and COBI.
- Repeating the analyses on PLWH who did not take lipid-lowering drugs at T0, we confirmed our results. Three patients began lipid-lowering drugs during the follow-up (one in 2DR and two in the TAF group).
- In PLWH who continued TAF-BR, both with and without previous COBI, we observed a statistically significant increase in the ALT level (+4 UI/dL, P<0.0001), when ALT at T0 was ≤40 UI/dL and within normal ranges value.

Table 2. Change from baseline in lipid profile and weight

All PLWH	T0 mean ± SD or median (IQR)			T1 mean ± SE		
	2DR n=104	FTC/TAF n=253	P	2DR n=104	FTC/TAF n=253	P
Weight (Kg)	75.8 ± 13.7	75.2 ± 14.3	0.74	-0.2 ± 0.3	0.3 ± 0.3	0.36
TC (mg/dL)	197 ± 37	196 ± 41	0.91	-3.5 ± 3.1	-5.1 ± 2.2	0.67
LDL-c (mg/dL)	120 ± 32	116 ± 36	0.35	-2.4 ± 2.7	-2.7 ± 2.0	0.95
TGL (mg/dL)	108 (80-154)	115 (85-163)	0.33	-6.9 ± 5.8	-12.3 ± 5.2	0.54
No COBI in previous regimen	2DR n=67	FTC/TAF n=92	P	2DR n=67	FTC/TAF n=92	P
Weight (Kg)	76.6 ± 13.5	75.2 ± 12.5	0.52	-0.2 ± 0.3	0.3 ± 0.5	0.48
TC (mg/dL)	191 ± 34	189 ± 43	0.80	4.8 ± 2.8	2.6 ± 4.5	0.71
LDL-c (mg/dL)	116 ± 32	110 ± 38	0.30	3.2 ± 2.8	5.3 ± 3.9	0.68
TGL (mg/dL)	107 (79-134)	113 (80-162)	0.37	1.5 ± 6.8	-3.2 ± 8.7	0.69
COBI in previous regimen	2DR n=37	FTC/TAF n=161	P	2DR n=17	FTC/TAF n=104	P
Weight (Kg)	74.3 ± 14.1	75.2 ± 14.8	0.74	-0.1 ± 0.6	0.3 ± 0.4	0.59
TC (mg/dL)	208 ± 39	200 ± 39	0.30	-17.9 ± 6.4	-9.8 ± 2.1	0.13
LDL-c (mg/dL)	126 ± 32	119 ± 35	0.29	-12.3 ± 5.0	-7.2 ± 2.1	0.28
TGL (mg/dL)	122 (86-207)	117 (88-165)	0.77	-21.8 ± 10.4	-17.8 ± 6.4	0.77

Legend to table 2; SE, Standard Error; IQR, Inter Quartile Range; LDL-C, Low Density Lipoprotein-Cholesterol; HDL-C, High Density Lipoprotein; TGL, Tryglicerides; COBI, cobicistat

Discussion and Conclusions

- In our study no difference was found in TC, HDL-C, LDL-C, and blood glucose in PLWH continuing an TAF-BR vs those switching to 2DR.
- The reasons for different results in literature about modification in lipid profile could depend on previous regimen before simplification.
- In the two randomized trial (1-2) there is i.e. and important difference in the percentages of PLWH on EVG/COBI. In 2 DR arm 10% and 66% of PLWH were on EVG/COBI respectively in SALSA and TANGO trial.
- This could be an important bias demonstrated by our results that showed switching from a previous COBI-including regimen was associated with a significant decrease in TC, LDL-C, and TGL.
- In the TAF-BR group a minimal but significant ALT increase was observed without differences in weight or lipid profile in the two groups. Anchor drug might contribute to ALT increase.

Reference

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