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Metabolic effects of switching to tenofovir alafenamide/emtricitabine/ bictegravir (B/F/TAF) from tenofovir difumarate (TDF) or tenofovir alafenamide (TAF) sparing regimens. (METABIC Study)

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Background and aim

- Cardiovascular disease is the leading cause of death in the general population and a frequent comorbidity in people with HIV (PWH), in fact PWH have a 2-fold higher risk for cardiovascular disease than negative controls.
- Most of the published studies switching from TDF-based regimens to TAF-based regimens raise concern about a worse metabolic profile (weight gain, higher lipids, and liver steatosis) in PWH. Few studies have explored the metabolic impact of B/F/TAF when switching from a previous regimen without TDF or TAF.
- We aim to assess changes in lipid fractions, glucose, and triglyceride to glucose ratio (TyG) after switching from a TDF/TAF sparing regimen to B/F/TAF at 6 and 12 months.

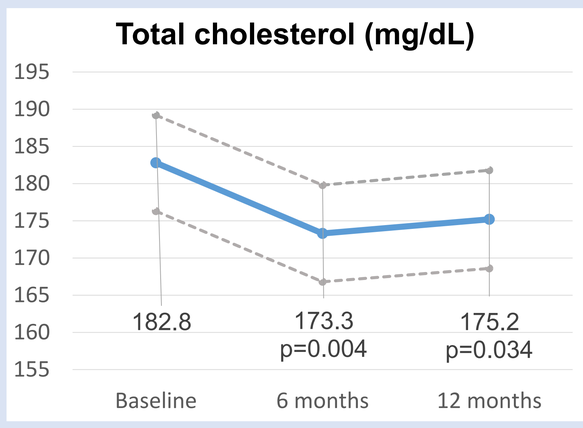
Patients and Methods

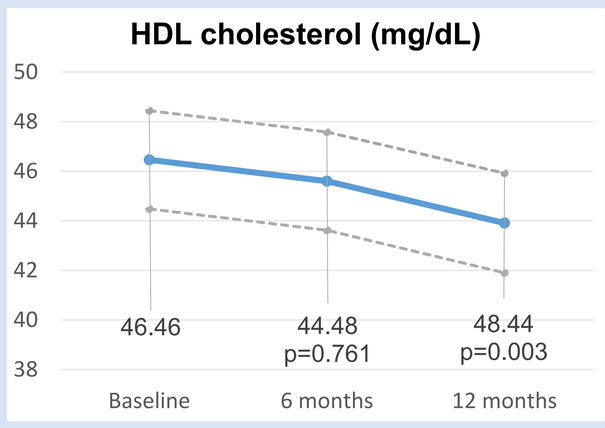
- A retrospective observational study of PWH who switched to B/F/TAF from ART regimens without TDF or TAF.
- We included participants who started B/F/TAF from January 2019 to May 2022, with at least six months of follow-up, and at least two blood samples in the period.
- The primary endpoint was the absolute change in lipid fractions at six months.
- Secondary outcomes were changes in lipid fractions at 12 months and other metabolic parameters (glucose, creatinine, and the serum marker for hepatic steatosis triglycerides to glucose ratio (TyG) with a cut-off (> 8.36) at 6 and 12 months.
- Mixed Linear Regression models with random intercept and time as a fixed effect were used to analyse these changes.

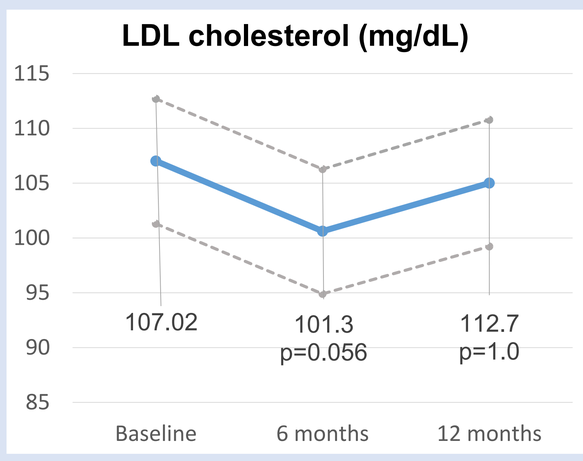
Table 1: Changes in metabolic and renal parameters *

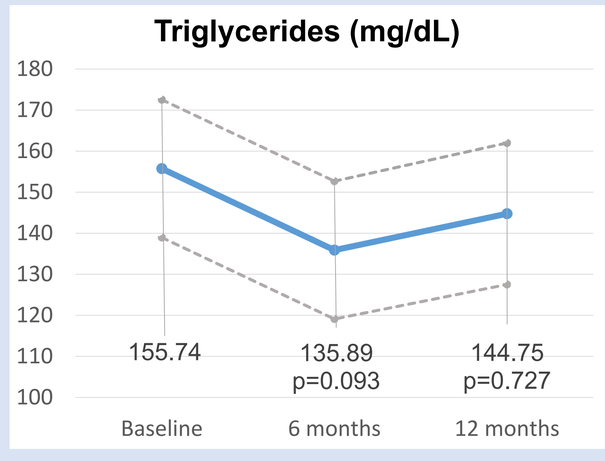
Parameter	Baseline N= 147	6 months N= 146	12 months N=137
Total Cholesterol mg/dl			
Mean (95% CI)	182.8 (176.3,189.2)	173.3 (166.8, 179.8)	175.2 (168.6-181.8)
Change from baseline, (95% CI); p-value		-9.45 (-16.43, -2.48); p=0.004	-7.54 (-14.67, -0.41); p=0.034
LDL cholesterol mg/dl			
Mean (95% CI)	107.02 (101.3, 112.7)	100.62 (94.9, 106.28)	105.01 (99.23, 110.78)
Change from baseline, (95% CI); p-value		-6.39 (-12.9, 0.12); p=0.056	-2.01 (-8.67, 4.65); p=1.0
HDL cholesterol mg/dl			
Mean (95% CI)	46.46 (44.48, 48,44)	45.60 (43.62, 47.58)	43.91 (41.90, 45.92)
Change from baseline, (95% CI); p-value		-0.855 (-2.65, 0.94); p=0.761	-2.55 (-4.39, -0.70); p =0.003
Triglycerides mg/dl			
Mean (95% CI)	155.74 (138.95, 172.53)	135.89 (119.10, 152.68)	144.75 (127.51, 161.99)
Change from baseline, (95% CI); p-value		-19.85 (-41.92, 2.22); p=0.093	-10.98 (-33.58, 11.60); p=0.727
TC: HDL ratio			
Mean (95% CI)	4.12 (3.93, 4.30)	3.89 (3.71, 4.08)	4.14 (3.95, 4.33)
Change from baseline, (95% CI); p-value		-0.22 (-0.44, -0.001);p=0.048	0.02 (-0.20, 0.24); p=1.0
Glucose mg/dl			
Mean (95% CI)	99.23 (94.80, 103.67)	101.56 (97.13, 105.99)	102.86 (98.37, 107.34)
Change from baseline, (95% CI); p-value		2.32 (-6.37, 1.72); p=0.50	3.62 (-7.76, 0.52); p =0.1088
Creatinine mg/dl			
Mean (95% CI)	0.93 (0.89, 0.96)	0.96 (0.92, 0.99)	0.96 (0.93, 1.0)
Change from baseline, (95% CI); p-value		0.03 (0.009, 0.05); p=0.0025	0.03 (0.013, 0.06); p< 0.001
CKD-EPI mg/min			
Mean (95% CI)	85.71 (83.60, 87.82)	83.84 (81.73, 85.95)	82.97 (80.84, 85.10)
Change from baseline, (95% CI); p-value		-1.87 (-3.62, -0.11); p=0.0319	-2.73 (-4.52, -0.95); p< 0.001
TyG ratio			
Mean (95% CI)	8.79 (8.69, 8.89)	8.64 (8.55, 8.74)	8.74 (8.64, 8.84)
Change from baseline, (95% CI); p-value		-0.147 (-0.25, -0.04); p=0.0023	-0.005 (-0.158, 0.005); p=0.7387

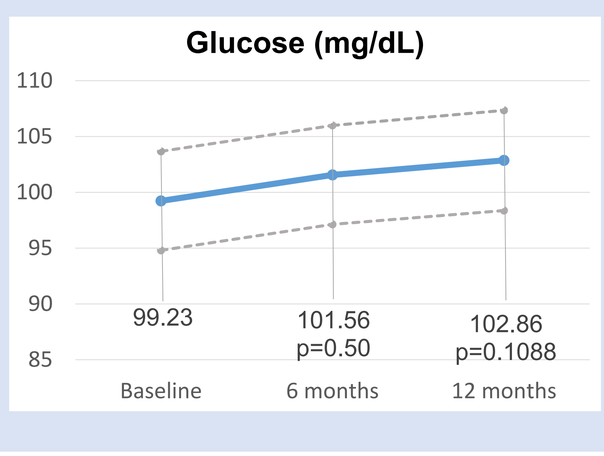
Multiple comparisons adjusted using the Bonferroni Method

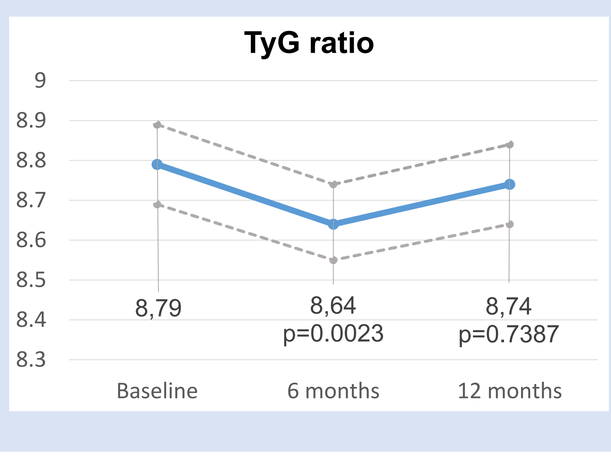












Results

- A total of 147 PWH were included: median (P25-75) age 55 years (46-58), 81% male, 89% Caucasian, CD4+ T cell count 675 cells/mm^3 (449-879), 79.6% HIV-RNA < 50 cp/ml.
- 44 (30%) had hypertension, 72 (49%) dyslipidemia, 24 (16%) diabetes, and 46% had obesity or overweight.
- Most of the participants (97; 66%) switched from integrase inhibitor-based triple therapy (ABC/3TC + dolutegravir or raltegravir), and 28 (19%) received a boosted protease inhibitor (9 patients 3TC +PI, 10 patients PI monotherapy).
- At 6 and 12 months there was a significant reduction in total cholesterol of -9.45 mg/dl (95% CI -16.43, -2.48; p=0.004) and -7.54 mg/dl (95% CI -14.67, -0.41; p=0.034).
- At 6 months there was a significant reduction in the TyG ratio (for hepatic steatosis) of -0.147 (95% CI -0.25, -0.04; p=0.0023). The percentage of patients with TyG > 8.38 at baseline, 6 and 12 months was 75.2, 65.1, and 71.7. These differences were not statistically significant.
- At 6 and 12 months there was a significant reduction in glomerular filtration rate (CPK-EPI): -1.87 ml/min (95% IC -3.62, -0.11; p=0.0319) and -2.73ml/min (-4.52, -0.95; p < 0.001) respectively.

Conclusion

In our real-life cohort, the effect of switching ART regimens without TDF/TAF to triple therapy with B/F/TAF improved total cholesterol at both 6 and 12 months and was neutral for the rest of the metabolic parameters after one year of follow-up.

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