Changes in nonalcoholic fatty liver disease spectrum and metabolic markers in people living with HIV after switching to a raltegravir-based regimen

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Background

Nonalcoholic fatty liver disease (NAFLD) is a major comorbidity among people living with HIV (PLWH)(1). In such population, NAFLD is associated with metabolic disorders and exposure to certain antiretroviral therapies (ART)(2). The aggressive nature of hepatic steatosis (HS) in HIV patients, mandates exploring less steatogenic antiretroviral options. The effect of ART, particularly integrase inhibitors (INIs), in such context is not fully investigated.

Objective

We aimed to evaluate the impact of switching to raltegravir (RAL)-based regimen compared to continuing other ART regimens not containing INIs on NAFLD spectrum, body mass index (BMI), and lipids among HIV mono-infected patients with HS.

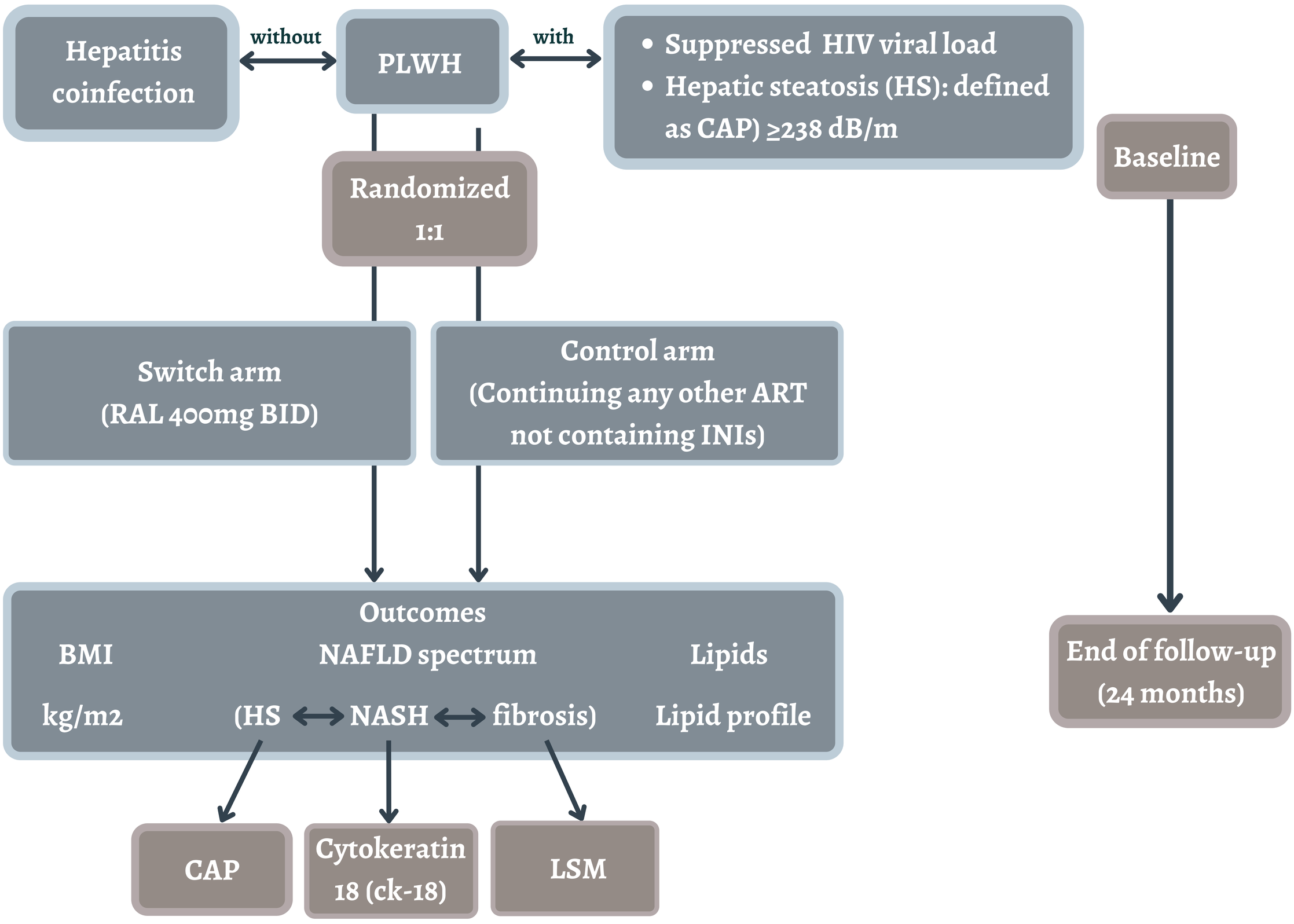
Methods

- This is a phase IV, open–label RCT (ClinicalTrials.gov: NCT02210715). Figure 1. (study design)
- methods used to measure outcomes:

1. NAFLD spectrum; HS by controlled attenuation parameter (CAP), nonalcoholic steatohepatitis (NASH) by cytokeratin 18 (ck-18), and fibrosis through transient elastography (TE) measuring liver stiffness measurement (LSM).
2. Lipids & body mass index (BMI); using serum lipids and anthropometrics measurements.

- Changes in outcomes over time were represented as standardized mean differences (SMD).

Figure 1. Experimental design.



Results

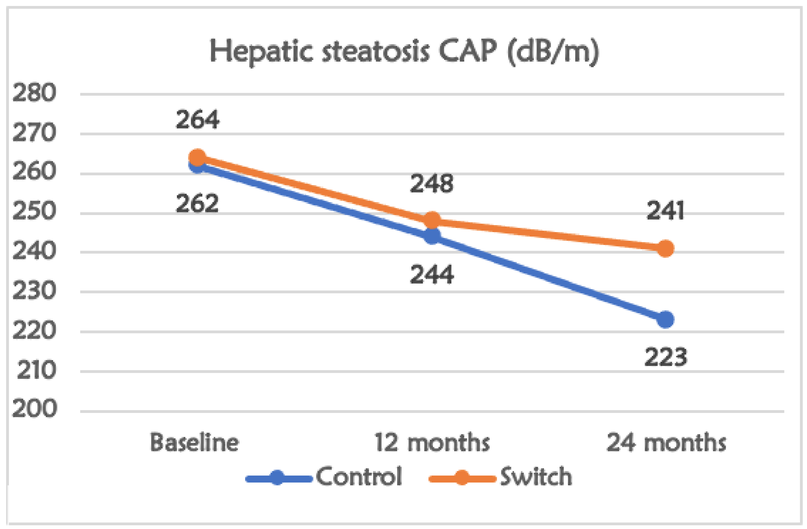
Table 1. Baseline characteristics by switch and control arms.

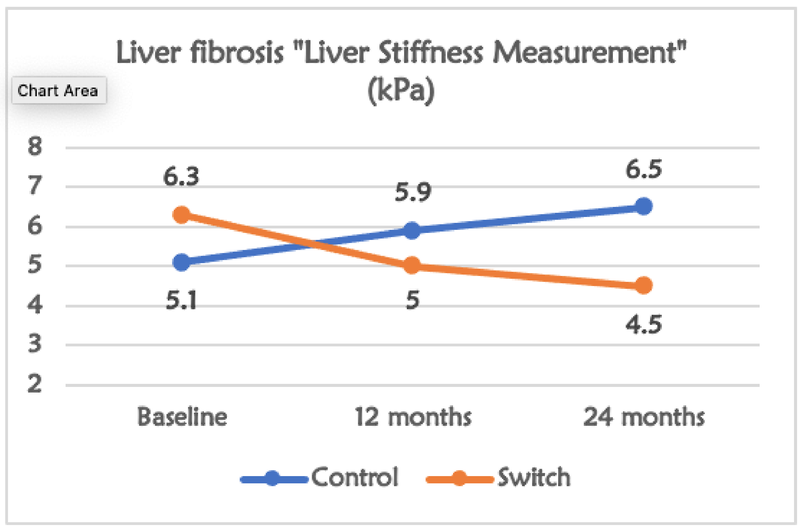
Variables	Randomization		p-value
	Control (n=15)	Switch (n=16)	
Age (y)	49.54 (10)	51.07 (8.6)	0.4504
Age at HIV diagnosis (y)	52.6 (9)	49.36 (8.4)	0.5228
Age at new data (y)	53.7 (9.5)	54.1 (8.9)	0.7553
Male, n (%)*	9 (60)	14 (87.5)	0.0801**
Diabetes mellitus, n (%)*	1 (6.7)	1 (6.7)	1
Hypertension, n (%)*	2 (13.3)	5 (31.3)	0.3898
HIV duration at enrollment (y)	11.7 (4.8)	13.1 (6.8)	0.8365
CD4 count (cell/mL)	630.3 (205.6)	540.4 (212.8)	0.3889
CD8 count (cell/mL)	645.2 (255.5)	672.4 (209.8)	0.7583
BMI (kg/m²)	27.7 (5.1)	26.8 (4.6)	0.8433
Glucose (mmol/L)	5 (1)	5.5 (0.8)	0.2174
Platelet count (x10⁹/L)	203 (44.5)	248.1 (63.1)	0.0965
Creatinine (mg/dL)	79.1 (17)	91.1 (52.4)	0.9509
Triglycerides (mmol/L)	1.5 (1)	1.7 (0.9)	0.4624
T. cholesterol (mmol/L)	4.4 (1)	4.7 (0.9)	0.5623
ALT (U/L)	19.6 (12.3)	29.2 (11.1)	0.0148**
AST (U/L)	17.6 (2.8)	34.2 (23.6)	<0.0001**
CAP (dB/m)	261.6 (34.7)	263.5 (34)	0.8029
LSM (kPa)	5.09 (2.2)	6.31 (4.4)	0.5795
CK–18 (U/L)	68.1 (49.9)	132.2 (122.9)	0.0690
APRI score	0.2 (0.1)	0.3 (0.2)	0.0131**
FIB-4 score	13 (38.8)	15.6 (47.6)	0.8180

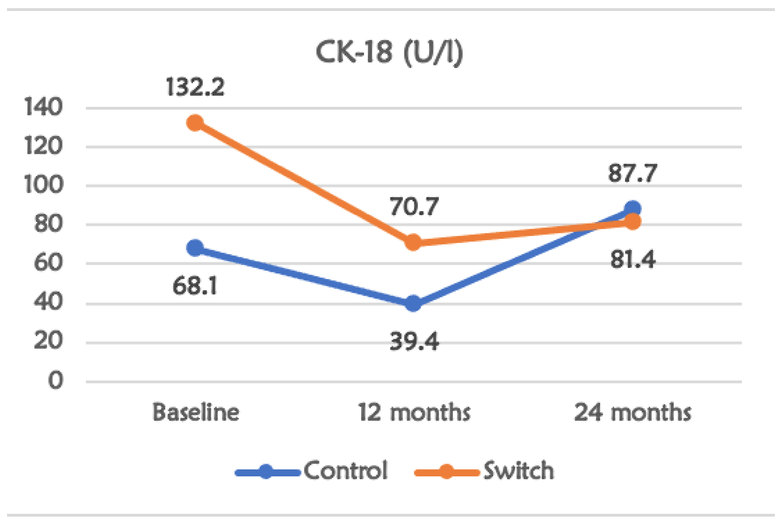
Table 2. Fixed-effect linear regression model comparing control arm to switch counterpart using noninvasive tools for liver steatosis and fibrosis.(CAP=controlled attenuation parameter; LSM=liver stiffness measurement; CK–18=cytokeratin 18; APRI=AST–to–Platelet Ratio Index; FIB–4=fibrosis–4).

Variables	Univariate model		Multivariate model*	
	coefficient	p-value	coefficient	p-value
Δ CAP (24 months – baseline)				
Control group	-0.349	0.6147	-0.641	0.4013
Switch group	-0.729	0.3189	-0.450	0.5547
Difference in slope		0.7110		0.8853
Δ LSM				
Control group	0.117	0.8263	0.063	0.0306
Switch group	-0.050	0.1376	-0.050	0.1376
Difference in slope		0.7279		0.8853
Δ CK–18				
Control group	-0.379	0.6506	-1.242	0.1254
Switch group	-2.394	0.0450	-2.407	0.0649
Difference in slope		0.1995		0.4500
Δ APRI				
Control group	0.002	0.3718	0.0003	0.8792
Switch group	0.0003	0.8377	0.001	0.3418
Difference in slope		0.5362		0.8486
Δ FIB-4				
Control group	-0.232	0.2551	-0.276	0.2563
Switch group	0.0003	0.8377	-0.221	0.3184
Difference in slope		0.9823		0.9735

Figure 2. Changes in HS, NASH, and fibrosis between baseline and end of follow up (24 months).







Conclusions

This study indicated that switching to RAL improves AST. There were changes in HS, NASH, and liver fibrosis. However, these findings were lacking power. Larger interventional studies are needed to confirm or refute such findings.

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