Tenofovir-based antiretroviral therapy in HBV/HIV co-infection: Results from the TREAT Asia HIV Observational Database

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Introduction

The World Health Organisation recommends hepatitis B virus (HBV)/HIV co-infected individuals requiring HBV treatment start ART containing tenofovir. However, there is a lack of clear and feasible criteria to identify those requiring HBV treatment in many parts of Asia. Here we describe predictors of initiating ART with tenofovir and outcomes of ART in co-infected patients from a regional cohort.

Methods

HBV surface antigen positive patients enrolled in the TREAT Asia HIV Observational Database who started ART were included. Follow up was censored at the first change of regimen or last documented clinic visit. ALT upper limits of normal were defined by the local clinic laboratories. Logistic regression adjusted for year of ART initiation was used to determine predictors of receiving tenofovir. Generalised estimating equations adjusted for time on ART were used to evaluate predictors of change in ALT level and CD4 cell count.

Results

There were 548 eligible patients; tenofovir was used by 149 (27.2%). Baseline characteristics are displayed in Table 1.

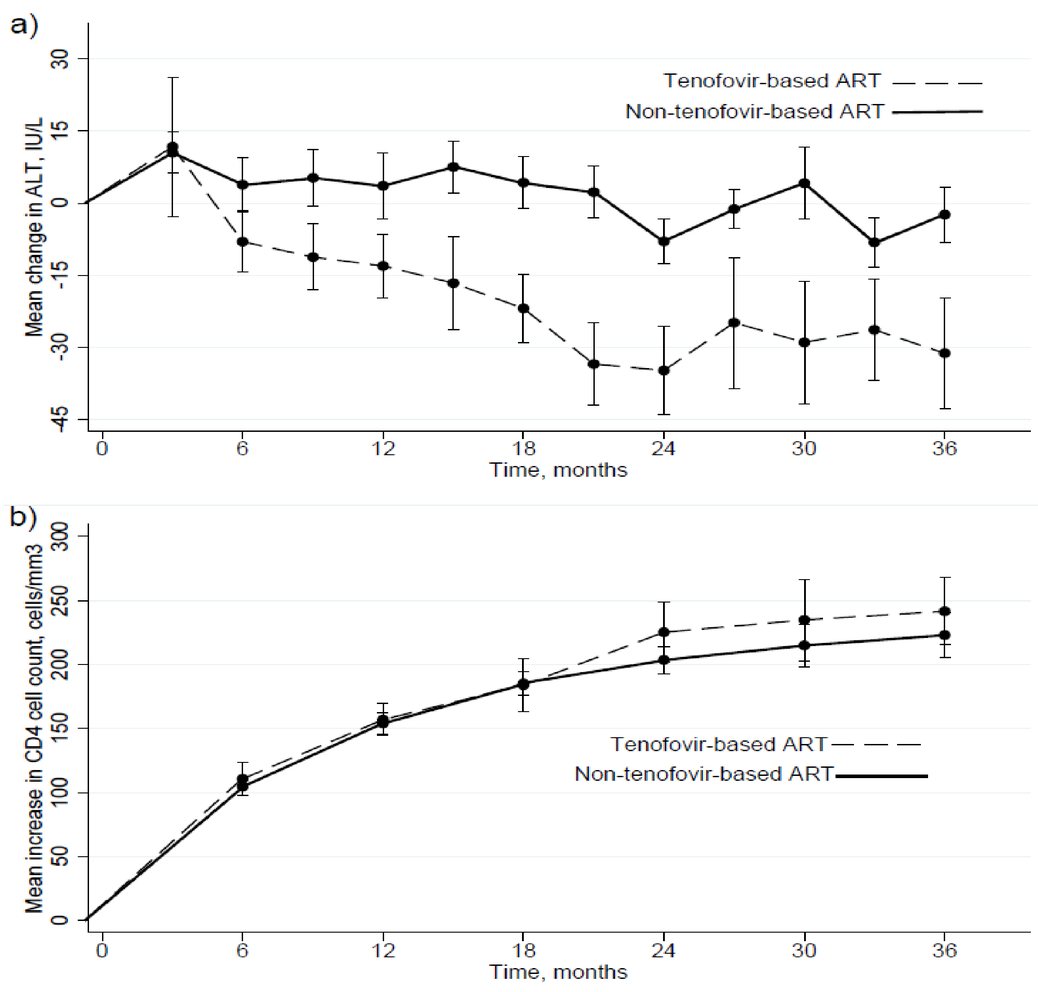
Table 1: Baseline characteristics

	Non-tenofovir (n=399)	Tenofovir (n=149)
Male	306 (76.7)	121 (81.2)
Age in years, median (IQR)	35.1 (29.6 - 41.1)	36.4 (29.9 - 44.3)
HIV exposure		
Heterosexual	238 (59.6)	69 (46.3)
Homosexual	79 (19.8)	62 (41.6)
IDU	57 (14.3)	11 (7.4)
Other	25 (6.3)	7 (4.7)
Hepatitis C antibody-positive, n(%tested)	70 (19.6)	12 (9.8)
ALT > normal, n(%tested)	97 (34.5)	64 (53.8)
Creatinine clearance* in mL/min, median (IQR)	84.7 (70.1-104.0)	89.0 (72.3-109.6)
CD4 cell count in cells/mm^3, median (IQR)	95 (31 - 213)	134 (33 - 245)
HIV viral load in copies/mL, median (IQR)	89,350 (11,793 - 336,274)	61,425 (20,175 - 128,874)
NRTIs in regimen		
3TC/FTC	388 (97.2%)	148 (99.3%)
AZT	165 (41.4%)	6 (4.0%)
d4T	201 (50.4%)	0 (0.0%)
Other	41 (10.3%)	6 (4.0%)
NNRTI/PI/RAL in regimen		
Efavirenz	164 (41.1%)	106 (71.1%)
Nevirapine	198 (49.6%)	7 (4.7%)
PI or RAL	35 (8.8%)	32 (21.5%)
Country income status^		
Low/low-middle	183 (45.9%)	32 (21.5%)
High/high-middle	216 (54.1%)	117 (78.5%)
Year of ART start		
2003 - 2006	165 (41.4%)	8 (5.4%)
2007 - 2009	130 (32.6%)	74 (49.7%)
2010 - 2013	104 (26.1%)	67 (45.0%)

Values are n(%total) unless otherwise specified; *Estimated using Cockcroft-Gault equation; ^As per The World Bank (http://data.worldbank.org/country)

Patients with baseline ALT>normal (OR 4.2 vs. normal, 95%CI 2.4 - 7.2, p<0.01) and those treated in high/high-middle income countries (OR 4.4 vs. low/low-middle, 95%CI 2.6 - 7.4, p<0.01) were more likely to receive tenofovir. Hepatitis C antibody-positive patients (OR 0.4 vs. negative, 95%CI 0.2 - 0.8, p<0.01) were less likely to receive tenofovir.

Figure 1 – Mean change in a) ALT and b) CD4 cell count from baseline



Error bars represent standard error of the mean

After 36 months, the raw mean reduction in ALT was 2.4 IU/L in patients using non-TDF-based ART and 31.3 IU/L in patients using TDF-based ART (Figure 1a). In those starting ART with baseline ALT>normal, the adjusted mean ALT after tenofovir initiation was 11.2 IU/L (95%CI 0.9 - 21.6, p=0.03) lower compared with those using a non-tenofovir-based regimen (Table 2). Tenofovir use was not associated with an improved CD4 response to ART in raw analysis (Figure 1b) or in the final model (6 cells/mm^3 greater for tenofovir vs. non-tenofovir, 95%CI -13 to 25, p=0.54). There were 13 deaths in total and mortality rates on tenofovir- and non-tenofovir-based ART were 0.9 (95%CI 0.3 - 2.7) and 1.6 (95%CI 0.8 - 2.9) per 100 patient-years, respectively.

Table 2: Predictors of ALT change (IU/L) after ART initiation

		Univariate	p	Multivariate	p
Base ALT	**ART**				
Normal	Non-tenofovir	0.0		0.0	
	Tenofovir	-6.2 (-16.3, 3.9)	0.23	-4.7 (-14.7, 5.3)	0.36
>Normal	Non-tenofovir	-21.6 (-29.9, -13.3)	<0.01	-24.1 (-32.4, -15.8)	<0.01
	Tenofovir	-35.1 (-44.5, -25.8)	<0.01	-35.3 (-44.6, -26.0)	<0.01
Hepatitis C antibody					
Negative		0.0		0.0	
Positive		6.8 (-3.6, 17.3)	0.20	12.7 (3.6, 21.8)	<0.01

Values in parentheses represent 95%CI; All models were adjusted for time on ART

Conclusion

HBV/HIV co-infected patients in this Asian cohort were more likely to initiate ART with a tenofovir-based regimen if they had elevated ALT levels, were hepatitis C antibody-negative, and received care in a high/high-middle income country. Compared to other ART, tenofovir-based regimens more effectively reduced liver inflammation in HBV/HIV co-infection but did not result in a superior CD4 response.

The TREAT Asia HIV Observational Database

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