KINETICS OF HBV RNA AND CORE-RELATED-ANTIGEN LEVELS IN PLWH WITH FUNCTIONAL HBV CURE

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BACKGROUND

- Hepatitis B core-related antigen (HBcrAg) and circulating HBV (hepatitis B virus) RNA correlate with intrahepatic covalently closed circular DNA (cccDNA) levels and cccDNA transcriptional activity.
- Both markers may help identify persons who eventually experience functional HBV cure on therapy.

OBJECTIVE

- To compare long-term kinetics of circulating HBV RNA and HBcrAg levels among persons living with HIV and HBV treated with tenofovir in the Swiss HIV Cohort Study (www.shcs.ch).

METHODS

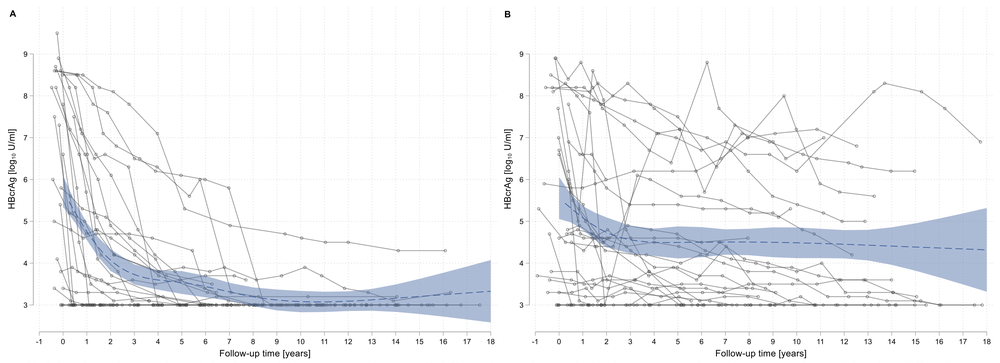
- We included 29 participants with functional HBV cure and 29 participants without functional HBV cure on tenofovir-containing antiretroviral therapy.
- Participants in both groups were matched 1:1 for age (10-year caliper), sex, pretreatment with lamivudine and CD4+ T-cell count category.
- We modeled HBcrAg and HBV RNA levels over time using linear regression, while incorporating time as restricted cubic splines with five knots located at the 5th, 27.5th, 50th, 72.5th and 95th percentile.
- Functional HBV cure was defined as the occurrence of a quantitative hepatitis B surface antigen (qHBsAg) <0.05 IU/ml.
- HBV RNA was quantified by the Roche HBV RNA investigational assay for use on the cobas® 6800 System (lower limit of quantification 10 copies/ml; linearity range 10 to 10^7 copies/ml; lower limit of detection ~3 copies/ml [Scholtès et al., J Clin Virol 2022]).

RESULTS: HBCRAG DECLINE DURING TENOFOVIR THERAPY

- Among participants with HBcrAg >3 $\log_{10}$ U/ml at tenofovir start, 14/22 (64%) with functional HBV cure compared to 8/25 (32%) without functional HBV cure had an HBcrAg decline of ≥1 $\log_{10}$ U/ml after 1 year (p=0.04, Figure 1).
- After 5 years, 18/28 (64%) participants with functional HBV cure had HBcrAg ≤3 $\log_{10}$ U/ml compared to 6/26 (23%) without functional HBV cure (p=0.003).

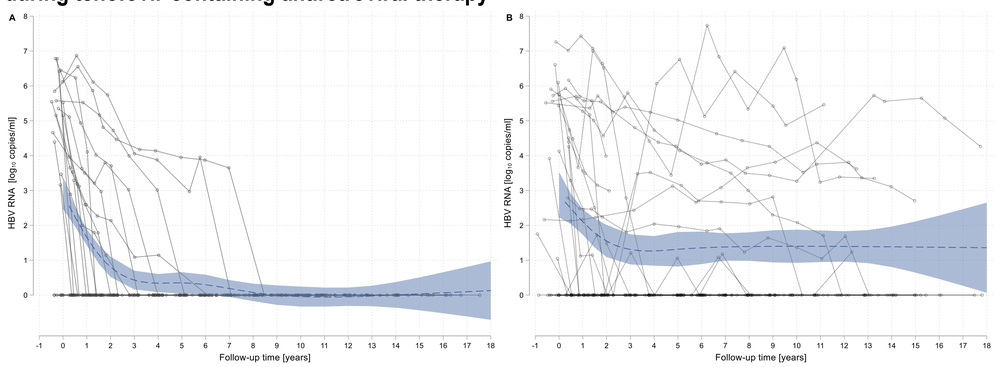
Circulating HBV RNA and HBcrAg levels decreased significantly during the first years of TDF therapy in PLWH who experience functional HBV cure. HBV RNA was undetectable in >90% of those with functional cure within 5 years of TDF therapy.

Figure 1: Hepatitis B core-related antigen (HBcrAg) levels in participants with (A) and without (B) functional HBV cure during tenofovir-containing antiretroviral therapy



Individual trajectories (circles with connecting solid lines) and modeled HBcrAg levels over time (dashed line) with 95% confidence intervals (shaded area). Follow-up time refers to time since start of tenofovir therapy.
Abbreviations: HBcrAg, hepatitis B core-related antigen; HBV, hepatitis B virus; U/ml, units per milliliter.

Figure 2: Circulating HBV RNA levels in participants with (A) and without (B) functional HBV cure during tenofovir-containing antiretroviral therapy



Individual trajectories (circles with connecting solid lines) and modeled HBV RNA levels over time (dashed line) with 95% confidence intervals (shaded area). Follow-up time refers to time since start of tenofovir therapy.
Abbreviation: HBV, hepatitis B virus.

Table 1: Characteristics of participants with and without functional HBV cure at start of tenofovir therapy

	Participants without functional HBV cure *N=29*	Participants with functional HBV cure *N=29*
Female sex	6/29 (21%)	6/29 (21%)
Median age [years]	39.0 (36.0-46.0)	42.0 (38.0-46.0)
Median follow-up duration [years]	11.1 (7.9-14.1)	12.3 (10.4-14.1)
European origin	14/29 (48%)	22/29 (76%)
Median BMI [kg/m^2]	22.7 (19.2-26.9)	22.9 (21.0-25.5)
Lamivudine pretreatment	24/29 (83%)	24/29 (83%)
Median duration [years]	6.3 (3.9-7.3)	6.2 (4.8-7.8)
CD4+ T-cell count <200 cells/µl	4/29 (14%)	4/29 (14%)
HIV viral load ≥50 copies/ml	15/29 (52%)	13/29 (45%)
Median HBV DNA [$\log_{10}$ IU/ml]	4.0 (1.5-7.9)	3.0 (1.2-7.5)
Median qHBsAg, [$\log_{10}$ IU/ml]	4.0 (3.5-4.2)	3.4 (2.1-4.5)
Median HBcrAg [$\log_{10}$ U/ml]	5.9 (3.6-7.7)	6.9 (3.9-8.6)
HBcrAg ≤3 $\log_{10}$ U/ml	4/25 (16%)	3/24 (13%)
Median HBV RNA [$\log_{10}$ copies/ml]	3.9 (0.0-5.7)	4.9 (0.0-5.7)
HBV RNA <10 copies/ml	9/25 (36%)	8/24 (33%)
HBeAg positive	10/24 (42%)	13/27 (48%)

Abbreviations: BMI, body mass index; HBcrAg, hepatitis B core-related antigen, HBeAg, hepatitis B e antigen,HBV, hepatitis B virus; IU/ml, international units per milliliter; qHBsAg, quantitative hepatitis B surface antigen; U/ml, units per milliliter.

RESULTS: HBV RNA DECLINE DURING TENOFOVIR THERAPY

- Among participants with detectable HBV RNA levels at tenofovir start, 14/17 (82%) with functional HBV cure compared to 10/18 (56%) without functional HBV cure had an HBV RNA decline of ≥1 $\log_{10}$ copies/ml 1 year after tenofovir start (p=0.15, Figure 2).
- After 5 years, HBV RNA was undetectable among 26/28 (93%) participants with functional HBV cure compared to 17/26 (65%) without functional HBV cure (p=0.02).

CONCLUSIONS

- A decline in circulating HBV RNA and HBcrAg levels during tenofovir therapy is more likely in PLWH with functional HBV cure than in those without cure.
- HBV RNA and HBcrAg may be promising predictive markers of functional HBV cure.

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