Hepatitis B Reactivation in PLWH With Anti-Core Antibody After Switch to an Anti-HBV Sparing Regimen

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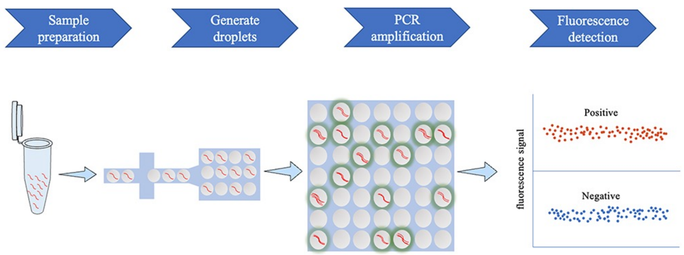
BACKGROUND

- People living with HIV (PLWH) who show the presence of hepatitis B surface antigen (HBsAg) require antiretroviral treatment (ART) regimens containing nucleos(t)ide analogues [(NAs) tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF)], that are active against both HIV and hepatitis B virus (HBV).[1,2]
- Instead, PLWH who are anticore antibody (antiHBc) positive in the absence of HBsAg may have access to antiHBV sparing regimens (antiHBVsr).[1,2]
- However, loss of HBsAg in PLWH, with or without seroconversion to anti-HBsAg antibodies (HBsAb), could be due to ART containing drugs active against both viruses.[3]
- Furthermore, HBV reactivation has been described in individuals with isolated antiHBc and, in case of severe immunosuppression, with antiHBc and HBsAb.[4,5]

We investigated HBV reactivation in PLWH with antiHBc (isolated or with HBsAb) who switched from combination therapy containing drugs active against both viruses to antiHBVsr.

Figure 1. Workflow of ddPCR



Adapted from Fan Y, et al. **Application of Droplet Digital PCR to Detection of Mycobacterium tuberculosis and Mycobacterium leprae Infections: A Narrative Review.** Infect Drug Resist. 2022. doi: 10.2147/IDR.S349607.

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METHODS

- Cohort study on PLWH with antiHBc (isolated or with HBsAb) who switched from NA-containing regimens to antiHBVsr dolutegravir/rilpivirine (DTG/RPV) or cabotegravir/rilpivirine long-acting (CAB/RPVLA). Follow-up accrued from the date of regimen switch [baseline (BL)] to the date of antiHBVsr discontinuation or the freezing date (August 29, 2023).
- HBV reactivation was initially assessed by ALT above the upper limit of normal range (normal value <60 IU/L) and in PLWH with ALT > normal levels by HBV-DNA quantification.
- In case of HBV reactivation and available plasma samples, HBV-DNA and HBV-RNA [as a surrogate marker for covalently closed circular DNA persisting in hepatocytes][6] were determined by highly sensitive digital droplet PCR (ddPCR; Figure 1) and HBV genotype by direct sequencing of the S gene.
- Data extracted from the database of Infectious Diseases, IRCCS San Raffaele Scientific Institute (CSLHIV Cohort) and from the SCohoLART study (single-center, prospective, phase IV, cohort study of people with HIV, treated with long-acting antiretroviral therapy; NCT05663580).

RESULTS

- Overall, 34 PLWH with antiHBc and HBsAb and 7 with isolated antiHBc switched to an antiHBVsr (Table 1).
- Median follow-up after switch to antiHBVsr: 8.91 months [(IQR 6.78 - 24.14); in PLWH with HBsAb 8.96 months (IQR 6.78 - 24.14); in PLWH with isolated antiHBc 6.97 months (IQR 5.56 - 43.22); p=0.742].
- No reactivations in PLWH with antiHBc and HBsAb.

Table 1. Characteristics of PLWH with antiHBc at switch to antiHBVsr according to the presence or absence of anti-HBsAg

BL Characteristics	Overall (n=41)	antiHBc positive (n=7)	antiHBc HBsAb positive (n=34)	p
Age (years)	55.1 (50.2 - 62.2)	57.8 (43.2 - 70.2)	54.4 (50.2 - 61.5)	0.690
Male sex	41 (100%)	7 (100%)	34 (100%)	-
Years of HIV infection	15.4 (9.5 - 20.4)	15.5 (10.1 - 26.4)	15.3 (8.9 - 19.7)	0.533
HIV-RNA				
<50 copies/mL	40 (97.6%)	7 (100%)	33 (96.8%)	0.661
50-200 copies/mL	1 (2.4%)*	0 (0%)	1 (3.2%)*	
CD4$^+$ cells count (cells/mm^3)	607 (460 - 772)	693 (485 - 867)	603 (459 - 772)	0.726
AntiHBVsr				
DTG/RPV	15 (36.6%)	3 (42.9%)	12 (35.3%)	0.693
CAB/RPVLA	26 (63.4%)	4 (57.1%)	22 (64.7%)	
HBV-DNA <10 IU/mL (available in 26 PLWH)	26 (100%)	5 (100%)	21 (100%)	-
ALT levels (IU/L)	27.5 (21 - 32)	28 (20 - 32)	27 (21 - 39)	0.763

*One participant had HIV-RNA >50, <200 copies/mL before switching to DTG/RPV

Of 7 PLWH with **isolated antiHBc**, 1 (14.3%) experienced **HBV reactivation** 3 months after switching to **CAB/RPVLA**

Figure 2. Trend of transaminases in the participant with HBV reactivation

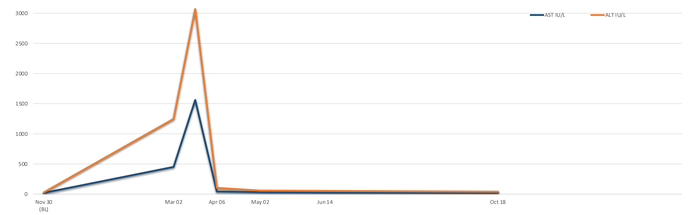
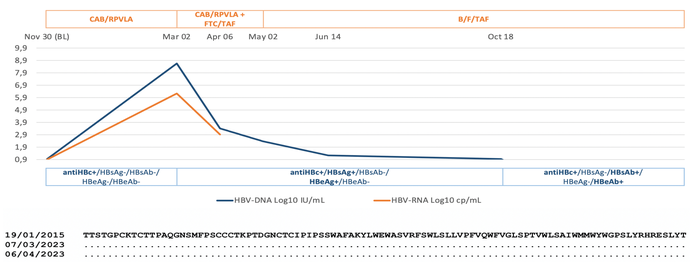


Figure 3. Trend of HBV-DNA, -RNA and serology in the participant with HBV reactivation. Alignment of the partial HBsAg before any ART and during HBV reactivation in the bottom



- In this individual (Figure 2 and Figure 3) we observed:
  - HBV-RNA positive at baseline (8 copies/mL) and very low levels of HBV-DNA (6 copies/mL) by ddPCR assay
  - Overt HBV infection assessed by HBsAg and hepatitis B e antigen (HBeAg) seroreversion and highly increased HBV-DNA
  - HBV genotype A2, with sequence identical to that obtained prior to any ART
  - Progressive decrease in HBV-DNA and normalization of transaminases after receiving emtricitabine/tenofovir alafenamide (FTC)/TAF.

CONCLUSIONS

- HBV reactivation after switching to antiHBVsr is unlikely in PLWH with antiHBc and HBsAb.
- Close monitoring of ALT and possibly HBV-DNA is mandatory in PLWH with isolated antiHBc switching to antiHBVsr.