**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 nucleotide/tyde 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 (antiHBsV).1,3,4
- However, loss of HBsAg in PLWH, with or without seroconversion to anti-HBs antibodies (HBsAb), could be due to ART containing drugs active against both viruses.3,5
- Furthermore, HBV reactivation has been described in individuals with isolated antiHBc and, in case of severe immunosuppression, with antiHBc and HBsAb.1,3,4,5

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

**METHODS**

- Cohort study on PLWH with antiHBc (isolated or with HBsAb) who switched from NA-containing regimens to antiHBsV (dolutegravir/riplavipin (DTG/RPV) or cabotegravir/riplavipin long-acting (CAB/RPV/ALA)). Follow-up accrued from the date of regimen switch (baseline (BL)) to the date of antiHBsV 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 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] 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 SciOhLART 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 antiHBsV (Table 1).
- Median follow-up after switch to antiHBsV: 8.91 months ([IQR 6.78 - 24.14] in PLWH with HBsAbs 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 antiHBsV according to the presence or absence of anti-HBsAg**

<table>
<thead>
<tr>
<th>BL Characteristics</th>
<th>Overall (n=41)</th>
<th>antiHBc positive (n=7)</th>
<th>antiHBc HBsAb positive (n=34)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.1 (50.2 - 62.2)</td>
<td>57.8 (43.2 - 70.2)</td>
<td>54.4 (50.2 - 61.5)</td>
<td>0.690</td>
</tr>
<tr>
<td>Male sex</td>
<td>41 (100%)</td>
<td>7 (100%)</td>
<td>34 (100%)</td>
<td>-</td>
</tr>
<tr>
<td>Years of HIV infection</td>
<td>15.4 (9.5 - 20.4)</td>
<td>15.5 (10.1 - 26.4)</td>
<td>15.3 (8.9 - 19.7)</td>
<td>0.533</td>
</tr>
<tr>
<td>HIV-RNA</td>
<td>&lt;50 copies/mL</td>
<td>40 (97.6%)*</td>
<td>1 (2.4%)*</td>
<td>0.611</td>
</tr>
<tr>
<td>50-200 copies/mL</td>
<td>7 (100%)</td>
<td>0 (0%)</td>
<td>33 (96.8%)*</td>
<td>3 (3.2%)*</td>
</tr>
<tr>
<td>CD4+ cells count (cells/mm³)</td>
<td>607 (460 - 772)</td>
<td>693 (485 - 867)</td>
<td>603 (459 - 772)</td>
<td>0.726</td>
</tr>
<tr>
<td>AntihBVsr</td>
<td>DTG/RPV/CAB/RPV/ALA</td>
<td>15 (36.6%)</td>
<td>3 (42.9%)</td>
<td>12 (35.3%)</td>
</tr>
<tr>
<td>HBV-DNA &lt;10 IU/mL (available in 26 PLWH)</td>
<td>26 (100%)</td>
<td>5 (100%)</td>
<td>21 (100%)</td>
<td>-</td>
</tr>
<tr>
<td>ALT levels (IU/L)</td>
<td>27.5 (21 - 32)</td>
<td>28 (20 - 32)</td>
<td>27 (21 - 39)</td>
<td>0.763</td>
</tr>
</tbody>
</table>

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

**CONCLUSIONS**

- 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 (HBcAg) 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.

- HBV reactivation after switching to antiHBVs 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 antiHBsV.

**REFERENCES**


**CONTACT INFORMATION**

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