HBV Reactivation Post-switch to HBV-inactive ART: A Scoping Review

771

Kyle Ring[1,2], Chloe Orkin[1,2], Miłosz Parczewski[3], Marta Boffito[4], Federico Garcia[5], Anna Maria Geretti[6–8]

[1]SHARE Collaborative, Blizard Institute, Queen Mary University of London, London, UK; [2]Barts Health NHS Trust, London, UK
[3]Pomeranian Medical University, Szczecin, Poland; [4]Chelsea and Westminster Hospital NHS Trust, London, UK
[5]Hospital Clinico Universitario San Cecilio, Granada, Spain; [6]University of Rome Tor Vergata, Rome, Italy
[7]Royal Free London NHS Foundation Trust, London, UK; [8]King's College London, London, UK

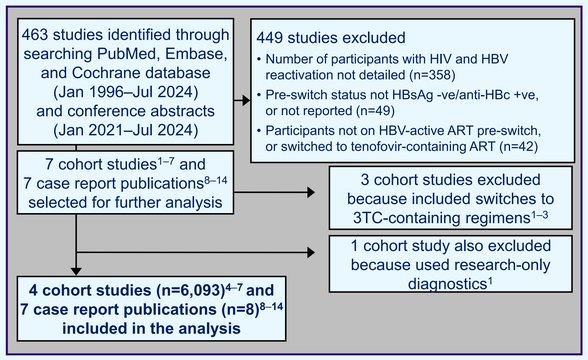
AIMS

- To summarise available evidence on reactivation risk after switching to HBV-inactive ART and identify predictors that may guide clinical practice

DEFINITION OF REACTIVATION

- HBsAg and/or HBV DNA detection by routine diagnostics in individuals who tested HBsAg negative and anti-HBc positive before switching to tenofovir-free regimens (ART interruption excluded)

DATA SOURCE AND RESULTS



- Six cohort studies described 133 reactivations among 11,731 switches (1.1%) in 11,507 individuals, with two US cohorts contributing most data;[2–7] 2,854/11,731 allowed post-switch 3TC/FTC use[2,3] and only one reported accordingly,[3] noting no reactivations over 144 weeks of DTG/3TC (n=71)
- In four cohorts, there were 99 reactivations among 6,093 participants switching to fully HBV-inactive ART **(1.6%; 95% CI: 1.3, 2.0)** (**Table 1**)[4–7]
- The earliest HBsAg and/or HBV DNA detection post-switch ranged from 3 weeks to 14 months
- Reactivations occurred across a range of CD4 counts and HIV RNA loads, were typically less common with pre-switch anti-HBs ≥10 IU/L (range 0–11%) than with anti-HBs lack or loss (range 3.2–14%), and were variably associated with ALT increases, including severe hepatic flares
- Hepatic flares resolved after re-introduction of HBV-active agents, with HBsAg loss documented within 2–5 months

Table 1. Cohort studies reporting on HBV reactivation after switching to fully HBV-inactive ART

Study setting & design[a] Reference	Pre-switch HIV RNA and CD4	Pre-switch HBV tests	HBV reactivations	Reactivation markers[b]	Notes
Cameroon (n=60) Retrospective RCT analysis Abdullahi[4]	VS 100% Median CD4 423 (338–568)	36 (60%) anti-HBs+ 0 HBV DNA+	6/60 (10%) over 48 wks Anti-HBs+ 4/36 (11%) Anti-HBs- 2/24 (8.3%)	HBsAg/HBV DNA Timing: earliest Week 12 ALT ↑ 3/6 (max. 102 U/L)	Switch ART: DRV/r monotherapy
USA (n=38) Retrospective cohort Welford[5]	Only reported for reactivations: VS, CD4 677, anti-HBs-, HBV DNA- VS, CD4 351, anti-HBs-, HBV DNA- VL 110 cps/mL, CD4 432, anti-HBs+		3/38 (7.9%) over 3–6 months	HBV DNA Timing: earliest Week 4 ALT ↑ 0/3	Switch ART: CAB+RPV
USA (n=5,954) Retrospective cohort Denyer[6]	VS 61% CD4 >500 40% CD4 <200 15%	4,543 (76%) anti-HBs+ 0 HBV DNA+[c]	89/5,954 (1.5%) Anti-HBs+ 44/4,543 (1.0%) Anti-HBs- 45/1,411 (3.2%)	HBsAg/HBV DNA Timing: median 10 months (5–27) ALT ↑ 12/37 >100 U/L	Switch ART: Multiple HIV viremia ↑ reactivation risk
Italy (n=41) Retrospective cohort Morsica[7]	VS 98% Median CD4 607 (460–772)	34 (83%) anti-HBs+ 0 HBV DNA+[c]	1/41 (2.4%) Anti-HBs+ 0/34 (0%) Anti-HBs- 1/7 (14%)	HBsAg/HBV DNA Timing: earliest Week 12 ALT ↑ 1/1 (max. 3,100 U/L)	Switch ART: DTG/RPV or CAB/RPV

[a]n= Number of HBsAg -ve/anti-HBc +ve participants; [b]Denominators= Individuals with available data; [c]Incomplete data; ↑ = ALT increase from baseline, >35 U/L, or >ULN

Table 2. Case reports reporting on HBV reactivation after switching to fully HBV-inactive ART

Reference Country Age & Sex	ART history	Pre-switch HIV RNA & CD4	Pre-switch HBV		Reactivation parameters				Follow-up & outcome
			Anti-HBs	HBV DNA	Reactivation markers	HBV DNA (max. IU/mL)	ALT ↑ (max. U/L)	Acute hepatitis clinically	
Altfeld[8] Germany 46 M	AZT/3TC/IDV to d4T/ddi/IDV **3 weeks prior**	Viremic CD4 120	Lost during reactivation	Neg.	HBsAg & HBV DNA	>170 million	Yes 1,000 U/L	No	Switch to AZT/3TC/NFV Resolution within 3 months with HBsAg & HBV DNA loss and anti-HBs development
De Monte[9] France 53 M	TDF-containing ART to RAL/ETR/DRV/r **14 months prior**[a]	VS CD4 >500	Neg.	Neg.	HBV DNA → HBsAg	960 million	Yes 1,026 U/L	Yes	TDF reintroduced Resolution within 2 weeks with HBsAg loss
Palmore[10] USA 46 M	3TC-containing ART to ABC/EFV/APV/r **16 weeks prior**	Possibly viremic CD4 770	Neg.	Neg.	HBsAg, HBeAg, & HBV DNA	220 million	Yes 2,911 U/L	Yes	3TC reintroduced Resolution with HBV DNA suppression (HBsAg NR)
Seang[11] France 60 M	TDF/FTC DRV/r to RAL DRV/r **1 month prior**	VS CD4 >500	Low +	NR	HBV DNA → HBsAg & HBeAg	>100 million	Yes 2,474 U/L	No	TDF/FTC reintroduced Resolution within 4 months with HBsAg loss
Bloquel[12] France 25 F	TDF/FTC/LPV/r/T20 to RAL/ETR/DRV/r **2 months prior**	VS CD4 ~300	Neg.	Neg.	HBV DNA → HBsAg	123 million	Yes 868 U/L	Yes	TDF/FTC reintroduced Resolution within 2 months with HBsAg loss
Bloquel[12] France 42 M	ABC/3TC/FPV/r/T20 to RAL/ETR/DRV/r **1 month prior**	VS CD4 433	Lost	NR	HBV DNA only (HBsAg neg.)	1,786	No	No	Continued same ART with VS HBV DNA neg. within 2 months
Katlama[13] France[b]	ABC/3TC/ATV to RAL/MVC **16 weeks prior**	VS CD4 716	Neg.	NR	NR	NR	Yes >~800 U/L	NR	NR
Vasishta[14] USA 67 F	TDF/FTC/ATV/r to DTG/DRV/c **5 months prior**	Viremic CD4 30	+[c] (86 IU/L 4 years prior)	NR	HBsAg & HBV DNA (anti-HBs 79 U/L)	141 million	Yes 155 U/L	No	Switch to BIC/FTC/TAF Lost to follow-up

[a]Also started ledipasvir/sofosbuvir for HCV ~8 weeks prior; [b]Age and sex not reported; [c]Post two HBV vaccine doses

REFERENCES

1. Salpini R, et al. EASL 2022. Poster THU-381
2. Dieterich DT, et al. EASL 2024. Poster WED-405
3. Fox D, et al. EMHH 2024. Poster 74
4. Abdullahi A, et al. Open Forum Infect Dis 2018;5:5
5. Welford E, et al. ID Week 2022. Oral 1583
6. Denyer R, et al. IDWeek 2023. Oral 1026
7. Morsica G, et al. CROI 2024. Poster 737
8. Altfeld M, et al. J. Hepatol 1998;29:306–9
9. De Monte A, et al. J Clin Virol 2016;78:27–30
10. Palmore TN, et al. Clin Gastroenterol Hepatol 2009;7:1130–7
11. Seang S, et al. J Infect Chemother 2013;19:987–9
12. Bloquel B, et al. J Med Virol 2010;82:206–12
13. Katlama C, et al. J Antimicrob Chemother 2014;69:1648–52
14. Vasishta S, et al. J Acquir Immune Defic Syndr 2023;94:160–4

KEY FINDINGS

- Low but notable risk of HBV reactivation in people with past HBV infection switching to HBV-inactive ART
- Risk factors: HIV viremia, low CD4 counts, nadir CD4 count <100 cells, HBV DNA detection pre-switch, lack or loss of anti-HBs (alongside any immunosuppression)
- HBsAg and/or HBV DNA detection post-switch signals a heightened risk of hepatic flares, requiring prompt confirmation and management
- Hepatic flares may be severe but typically resolve after re-introducing HBV-active agents

CONCLUSIONS

- Moderate-to-low quality evidence informs estimates of HBV reactivation risk with HBV-inactive ART
- A thorough evaluation of HIV-related and other HBV reactivation risk factors is essential before switching and should continue post-switch
- Standardisation of pre- and post-switch HBV monitoring practices remains a critical need

Correspondence to Geretti@med.uniroma2.it

Author contributions
Concept & design: AMG, CO, KR, MP; Analysis: AMG*; Abstract & poster preparation*: AMG, KR. Abstract & poster review: All authors

Acknowledgements
*Editorial support (searches, data checks, poster drafting) by Ellen Maxwell, PhD, (Ashfield MedComms, an Inizio Company) funded by ViiV Healthcare

Abbreviations
3TC, lamivudine; ABC, abacavir; anti-HBc, hepatitis B core antibody
anti-HBs, hepatitis B surface antibody; HBeAg, hepatitis B e antigen
HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase
APV, amprenavir; ART, antiretroviral therapy; ATV, atazanavir; AZT, zidovudine
BIC, bictegravir; CAB, cabotegravir; c, cobicistat; ddi, didanosine; DRV, darunavir
DTG, dolutegravir; d4T, stavudine; EFV, efavirenz; ETR, etravirine; F, female
FPV, fosamprenavir; FTC, emtricitabine; HBV, hepatitis B virus
HCV, hepatitis C virus; IDV, indinavir; LPV, lopinavir; M, male; MVC, maraviroc
Neg., negative; NFV, nelfinavir; NR, not reported; RAL, raltegravir
RCT, randomised control trial; RPV, rilpivirine; r, ritonavir; T20, enfuvirtide
TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir
ULN, upper limit of normal; VL, viral load; VS, virological suppression

CROI 2025 (March 9–12) San Franscisco, CA, USA