Hepatitis B Infection or Reactivation After Switch to 2-Drug Antiretroviral Therapy: A Case Series, Literature Review, and Management Discussion

Shilpa Vasishta, MD,[a] Douglas Dieterich, MD,[b] Michael Mullen, MD,[a] and Judith Aberg, MD[a]

Background: Two-drug antiretroviral therapy (ART) without hepatitis B virus (HBV) activity is prescribed for persons with HIV as simplified or salvage therapy. Although two-drug regimens are not recommended for persons with chronic HBV infection, guidelines do not address their use in those with HBV susceptibility and/or core antibody reactivity. We present a case series of individuals with HBV infection or reactivation following switch to two-drug, non-HBV-active ART.

Setting: HIV primary care clinics of an academic medical center in New York, NY.

Methods: Case surveillance was conducted to identify persons with HBV surface antigenemia and viremia following two-drug ART switch. Clinical characteristics and outcomes were ascertained through chart review.

Results: Four individuals with HBV infection or reactivation after ART switch were identified. Two had HBV susceptibility, 1 had core antibody reactivity, and 1 had surface antigen reactivity preswitch. All eligible persons had received HBV vaccination: 2 with low-level antibody response and 1 with persistent nonresponse. Two presented with fulminant hepatitis, with 1 required liver transplantation.

Conclusion: Two-drug ART switch may pose risk of HBV infection or reactivation. We propose careful patient selection and monitoring through the following: (1) assessment of HBV serologies before switch and periodically thereafter, (2) vaccination and confirmation of immunity before switch, (3) risk stratification and counseling about HBV reactivation for those with core antibody, (4) preemptive HBV DNA monitoring for those at the risk of reactivation, (5) continuation of HBV-active prophylaxis when above measures are not feasible, and (6) continuation of HBV-active therapy and surveillance for chronic HBV infection.

Key Words: HIV/hepatitis B coinfection, hepatitis B screening, hepatitis B vaccination, antiretroviral therapy switch

(*J Acquir Immune Defic Syndr* 2023;94:160–164)

INTRODUCTION

Two-drug antiretroviral therapy (ART) without hepatitis B virus (HBV) activity is prescribed for persons with HIV (PWH) for simplification following virologic suppression or salvage following virologic failure. Single-tablet regimens, including dolutegravir (DTG)-rilpivirine (RPV) and DTG-lamivudine (3TC), and long-acting injectable cabotegravir (CAB)-RPV, are approved for switch following virologic suppression to minimize pill burden, drug interactions, and toxicities of prolonged nucleoside reverse transcriptase inhibitor (NRTI) therapy.[1–3] Regimens consisting of 2 highly active agents, such as an integrase strand transfer inhibitor and boosted protease inhibitor, are recommended as salvage following virologic failure on NRTI-based regimens.[4–6]

Discontinuing HBV-active ART may increase the risk of new HBV infection in persons who are susceptible (lacking hepatitis B surface antibody, HBsAb).[7] It may also increase the risk of HBV reactivation (reverse seroconversion of hepatitis B surface antigen (HBsAg) or rise in HBV DNA from baseline)[8] in persons with hepatitis B core antibody (HBcAb) or chronic HBV infection.[9] We present 4 cases of HBV infection or reactivation following switch to two-drug ART without HBV activity. We discuss guidelines for HBV prevention and treatment among PWH and explore measures to reduce complications during two-drug ART switch. This report is approved by the Mount Sinai Institutional Review Board (#22-01548).

CASE REPORTS

Case 1

A 65-year-old man presented with HIV (CD4 190 cells/mL) diagnosed 20 years ago and virologically suppressed on abacavir (ABC), 3TC, nevirapine, and ritonavir-boosted fosamprenavir (FPV/r) following initial treatment failure.

HBsAg, HBcAb, and HBsAb were nonreactive. He received three 20-μg doses of combined hepatitis A inactivated/HBV recombinant vaccine (Twinrix GlaxoSmithKline, Brentford, United Kingdom) at 0, 1, and 6 months. HBsAb postvaccination was nonreactive. He received 2 additional 20-μg doses of HBV

Received for publication March 3, 2023; accepted June 12, 2023.

From the [a]Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; and [b]Division of Gastroenterology and Liver Medicine, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY.

D.D. has received financial compensation as a consultant for Gilead Sciences and Abbvie. The remaining authors have no disclosures. This work was previously presented at Digestive Diseases Week, Chicago, IL, May 8, 2023.

Correspondence to: Shilpa Vasishta, MD, Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, One Gustave Levy Place, Box 1090, New York, NY 10029 (e-mail: shilpa.vasishta@mssm.edu).

recombinant vaccine (Engerix-B, GlaxoSmithKline) at 0 and 3 months. HBsAb remained nonreactive.

The patient expressed interest in single-tablet ART. HIV genotype revealed M184V, M41L, L210L, and T215T mutations, although preserved nonnucleoside reverse transcriptase inhibitor susceptibility. He was switched to DTG-RPV.

He presented 5 months later with alanine aminotransferase (ALT) value of 570 IU/mL from normal baseline. HBsAg was newly reactive; HBV DNA was 1.75 million IU/mL. He denied recent sexual or needle-borne exposures.

Tenofovir disoproxil fumarate (TDF)-emtricitabine (FTC) were initiated. HBV DNA suppression and ALT normalization were achieved after 10 months of therapy and maintained for 6 months before the patient expired from unrelated causes.

Case 2

A 33-year-old man presented with HIV, initially suppressed on tenofovir alafenamide (TAF)-FTC-RPV but subsequently with virologic failure. CD4 was 300 cells per milliliter and HIV viral load (VL) was 30,000 copies per milliliter despite treatment adherence.

HBsAg, HBcAb, and HBsAb were nonreactive. He received three 20-mcg doses of Engerix-B at 0, 8, and 11 months. Three months later, HBsAb was 41 mIU/mL. Hepatitis C virus (HCV) infection was diagnosed with HCV VL of 386,000 IU/mL. HIV genotype revealed M184V, K65R, K103N, and E138Q mutations, prompting switch to DTG and ritonavir-boosted darunavir (DRV/r).

The patient presented 4 months later with acute liver failure (ALT: 2640 U/L, bilirubin: 17 mg/dL, international normalized ratio [INR]: 3.1, from normal baselines). HBsAg and HBcAb IgM were newly reactive; HBV DNA was 380 million IU/mL. HIV and HCV VL were undetectable. The patient reported multiple potential HBV exposures.

The patient was treated with TAF and evaluated for transplant given fulminant liver failure but recovered and was discharged 2 weeks later. On 6-month follow-up, HBV DNA was suppressed, and ART was simplified to TAF-FTC-bictegravir and doravirine with continued follow-up.

Case 3

A 67-year-old woman presented with HIV (CD4 525 cells/mL) diagnosed 20 years prior and suppressed on TDF-FTC and ritonavir-boosted atazanavir (ATV/r). She had untreated HCV and isolated HBcAb reactivity.

She received 2 of 3 doses of HBV recombinant vaccine (unknown formulation) at 0 and 1 month. HBsAb was reactive 1 year after this partial series. HCV was treated with elbasvir-grazoprevir. HBsAb was sustained at 86 mIU/mL after HCV treatment and 4 years after vaccination.

The patient developed adherence difficulties related to substance use and re-presented with CD4 of 30 cells/mL and HIV VL exceeding 500,000 copies milliliter. She had progressive renal dysfunction and was switched to tenofovir-sparing therapy with DTG and cobicistat-boosted darunavir (DRV/c).

She presented 5 months later in acute renal failure. ALT was 155 IU/mL (from normal baseline). HBsAg was newly reactive with HBV DNA of 141 million IU/mL; HBsAb remained reactive at 79 mIU/mL.

Therapy was switched to TAF-FTC-bictegravir. Subsequent outcomes are unavailable due to the loss of follow-up.

Case 4

A 66-year-old man presented with HIV-HBV coinfection, diagnosed 30 years earlier with cirrhosis, which had regressed on 3TC-based ART. He had experienced treatment failure on sequential NRTI monotherapy but subsequently maintained suppression on TAF-FTC-DRV/r and DTG. CD4 was 732 cells per milliliter. HBsAg was reactive, HBV DNA was undetectable, hepatitis B e antigen (HBeAg) and e antibody (HBeAb) were nonreactive, and liver enzymes and imaging were unremarkable.

The patient transferred to a new HIV physician, and 8 months later expressed interest in single-tablet therapy. The physician, overlooking the patient's known history of HBV infection and noting multiple NRTI resistance mutations (M184V, M41L, L210L, T215T), prescribed a switch to DTG-RPV.

Three months later, HIV VL remained suppressed, whereas ALT was newly elevated to 75 U/mL. There was no further documentation until 6 months after ART switch when the patient presented in fulminant liver failure (ALT 680 U/L, bilirubin 21 mg/dL, INR 4.7; imaging with hepatomegaly and gastric varices). HBV DNA was 24.6 million IU/mL.

The patient had progressive liver failure despite HBV-active therapy and ultimately required liver transplantation. He received TDF-FTC and DTG-RPV posttransplant and achieved normalization of liver enzymes, suppression of HBV DNA, and seroconversion of HBsAg at 2 months, all sustained at 1 year. He will continue lifelong immunosuppression.

DISCUSSION

We present 4 cases of HBV infection or reactivation after switch to 2-drug ART without HBV activity (Table 1). These occurred over 1 year during which 332 PWH were prescribed 2-drug ART in our health system. We review recommendations for HBV prevention and treatment among PWH and propose careful patient selection and monitoring during ART switch.

Among PWH worldwide, up to 20% have HBV coinfection, whereas many more have prior infection (ie, HBcAb) or risk of exposure.[10] HIV/HBV coinfection confers increased risk of cirrhosis and hepatocellular carcinoma (HCC) and up to 18-fold greater liver-related mortality than HBV monoinfection.[11] Therefore, vaccination is universally recommended for PWH susceptible to HBV, and treatment is universally recommended for PWH with HBV coinfection.[9,12]

Although vaccination is central to HBV prevention, HBV vaccine response is suboptimal among PWH, ranging 20%–70% among standard vaccine formulations (Twinrix, Engerix-B, Recombivax HB; Merck, Rahway, NJ).[13] Strategies to improve immunogenicity include double-dose vaccination, which is a recommended primary strategy among PWH,[9,14] repeated vaccination with a booster or three-dose series,[15] or adjuvants such as granulocyte-macrophage colony-stimulating factor.[16] Studies of cytosine phosphoguanine-conjugated vaccine (Heplisav; Dynavax, Emeryville, CA) among PWH have shown responses up to 86% with 2-dose series[17,18] and up to 100% with 3-dose series.[19] Although the HIV Medicine Association and US Department of Health and Human Services endorse Heplisav for PWH,[9,20] this vaccine remains costly with limited global access, and further studies in PWH are underway. Persistent vaccine nonresponse after 2 appropriately dosed series remains a global challenge.[15] Case #1 highlights the risk of HBV infection in persons with vaccine nonresponse, which may be heightened after discontinuing

TABLE 1. Summary of HIV/HBV Case Data

	HIV Parameters at Time of Switch	ART Regimen		Reason for Switch	HBV Vaccination	HBV Studies		Outcomes
		Preswitch	Postswitch			Preswitch	Postswitch	
Case 1 65 yo M	CD4 202 VL <20 Mutations: M184V, M41L, L210L, T215T, D67T, M46I, I54V, V82F	ABC 3TC Nevirapine FPV/r	DTG RPV	Patient preference for single-tablet regimen	Completed 2 series 6 y prior: Time 0, 1, 6 mo 1 y prior: Time 0, 3 mo	HBsAg− HBcAb−HBsAb− (Immediately prior)	HBsAg+ HBcAb+ HBsAb− HBeAg+ HBV DNA 1.75 mil	Peak ALT 570 Recovered on tenofovir
Case 2 33 yo M	CD4 304 VL 30,600 Mutations: M184V, K65R, K103N, E138Q	TAF FTC RPV	DTG DRV/r	NRTI resistance	Completed 1 series 3 y prior: Time 0, 8 mo, 11 mo	HBsAg− HBcAb− HBsAb+ (titer=41) (3 y prior)	HBsAg+ HBcAb− HBsAb− HBeAg+ HBV DNA 380 mil	Peak ALT 2640, Tbili 17, INR 3.3 Hepatomegaly Evaluated for transplant; recovered on tenofovir
Case 3 67 yo F	CD4 13 VL 211,000 No significant mutations	TDF FTC ATV/r	DTG DRV/c	Chronic kidney disease	Completed 1 series 8 y prior: Time 0, 1 mo	HBsAg− HBcAb+ HBsAb+ (titer = 86) (4 y prior)	HBsAg+ HBcAb+ HBsAb+ (titer = 79) HBV DNA 141 mil	Peak ALT 155 Lost to follow-up
Case 4 66 yo M	CD4 716 VL <20 Mutations: M184V, M41L, L210L, T215T, K103N	TAF FTC DRV/r DTG	DTG RPV	Patient preference for single-tablet regimen	Not applicable	HBsAg+ HBsAb− HBV DNA <10 (1 y prior)	HBsAg+ HBcAb+ HBsAb− HBV DNA 24.6 mil	Peak ALT 680, Tbili 21, INR 4.7 Hepatomegaly with gastric varices Required transplantation

CD4 (cells/mL), HIV VL (copies/mL), HBV DNA (IU/mL), HBsAb (mIU/mL), ALT (U/L).
F, female; M, male; mil, million; mo, months; Tbili, total bilirubin (mg/dL); y, years; yo, years old.

HBV-active ART. Occult HBV (detectable viremia without HBsAg reactivity) is another potential etiology of vaccine nonresponse,[21] and it also warrants consideration before stopping HBV-active ART.

Among PWH who respond to vaccination, maintenance of immunity is inconsistent, with up to 50% losing antibodies within 2 years.[22] HBsAb testing is recommended 4 weeks after vaccination, with revaccination if below 10 IU/mL.[9] Some experts recommend annual surveillance and revaccination to maintain protective titers, particularly if exposures are ongoing.[9,12] Studies among PWH have also shown that HBV-active ART reduces the risk of new infection,[7] with greatest protection conferred by tenofovir followed by 3TC.[23,24] This strategy warrants consideration as an adjunct to vaccination. Case #2 highlights the importance of postvaccine surveillance in persons with low antibody titers, which may not be sustained or sufficient to prevent infection, and consideration of maintaining HBV-active ART in those at risk of infection.

HBcAb reactivity is seen in 17%–40% of PWH,[25] signifying prior HBV infection and a lifelong risk of reactivation during immunosuppression.[8] Reactivation may occur in 8%–18% of persons with HBcAb receiving antineoplastic therapies,[12,26] with risk further modified by host factors (eg, age, cirrhosis) and viral factors (eg, baseline HBV DNA).[27] Additional risk factors for HBV reactivation among PWH include low CD4, elevated HIV VL, and withdrawal of HBV-active agents.[28] Individuals with HBcAb receiving immunosuppression are recommended monitoring with HBV DNA every 1–3 months or HBV-active prophylaxis.[9,12] Tenofovir and entecavir (ETV) are preferred prophylaxis given high potency and high barrier to resistance.[12] 3TC also reduces reactivation risk compared with no prophylaxis[29]; however, resistance development is common,[30] and comparative studies have found 3TC less efficacious than ETV.[26,31] Therefore, 3TC monoprophylaxis, as in DTG-3TC, should be considered only when preferred agents cannot be used. Case #3 emphasizes recognition of HBV reactivation risk in persons with HBcAb and providing appropriate monitoring or prophylaxis after ART switch.

Among PWH with chronic HBV infection, lifelong HBV treatment is indicated, either with TAF/TDF and 3TC/FTC, or with ETV and a complete HIV regimen.[9] Treatment goals are analogous to those of chronic HBV monoinfection, including HBV suppression, HBsAg seroconversion, and preventive health such as HCC screening.[12] Cessation of HBV-active therapy is strongly discouraged due to the risk of HBV reactivation,[9,32,33] especially for individuals with HBV-associated cirrhosis, in whom the risk of hepatic decompensation during therapy interruptions is especially high.[34,35] Despite the frequency of liver-related complications in HIV-HBV coinfection, studies demonstrate that HIV clinicians may not monitor for HBV complications as frequently as guidelines

recommend.[36–38] Rather, with default inclusion of HBV-active agents in most first-line ART regimens, HBV coinfection is often suppressed and overlooked by clinicians. Case #4 highlights the paramount importance of awareness and surveillance of chronic HBV infection to prevent complications, such as cirrhosis, HCC, and potentially life-threatening decompensation after an elective withdrawal of therapy.

Two-drug ART without HBV activity is commonly prescribed for regimen simplification or salvage; however, little is reported about HBV outcomes after ART switch. HBV infection has been reported after switch to CAB-RPV in the presence of ongoing exposures and vaccine nonresponse.[39] HBV reactivation has also been reported after tenofovir discontinuation in a person with prior HBV infection and low CD4.[40] In addition, HBV viremia is described in 8%–40% of PWH with HBcAb after switch to CAB-RPV or other tenofovir-sparing regimens.[41,42] Our cases provide further support for HBV susceptibility, core antibody, and chronic infection as features of concern in patient selection for two-drug ART.

Although optimal practices during 2-drug ART switch remain to be defined, we propose increased attention to HBV parameters through the following:

a. Reassessment of HBV serologies before switch.
b. Guideline-based vaccination and confirmation of immunity before switch.
c. Annual serologies after switch to ensure sustained immunity and absence of new infection.
d. Counseling about reactivation risk for individuals with HBcAb or concern for occult HBV, considering age, liver disease, and immunologic status.
e. Surveillance of liver enzymes and HBV DNA every 1–3 months after switch for individuals with HBcAb or concern for occult HBV, continued for 1 year or the duration of concurrent immunosuppression.
f. Continuation of HBV-active agents, including TAF, TDF, or ETV, in persons at risk for HBV infection (ie, suboptimal vaccine response, ongoing exposures) or reactivation (ie, HBcAb, especially with advanced age, liver disease, or immunosuppression) when above monitoring strategies are not feasible.3TC alone (as in DTG-3TC) should not be used as treatment for chronic HBV, but it may be used as prophylaxis when preferred agents cannot be used.
g. Continuation of HBV therapy with either TAF/TDF and 3TC/FTC, or ETV with a complete HIV regimen and adherence with guideline-based surveillance in persons with chronic HBV infection.

HBV infection or reactivation may confer significant morbidity and mortality and constitute a preventable complication for PWH on stable HBV-active ART. As NRTI-sparing options continue to expand, we encourage increased scrutiny during ART switches to mitigate HBV-associated complications.

REFERENCES

1. Llibre JM, Hung CC, Brinson C, et al. Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies. *Lancet*. 2018;391:839–849.
2. Cahn P, Madero JS, Arribas JR, et al. Durable efficacy of dolutegravir plus lamivudine in antiretroviral treatment–naive adults with HIV-1 infection: 96-week results from the GEMINI-1 and GEMINI-2 randomized clinical trials. *J Acquir Immune Defic Syndr*. 2020;83:310.
3. Swindells S, Andrade-Villanueva JF, Richmond GJ, et al. Long-acting cabotegravir and rilpivirine for maintenance of HIV-1 suppression. *N Engl J Med*. 2020;382: 1112–1123.
4. Second-Line Study Group. Ritonavir-boosted lopinavir plus nucleoside or nucleotide reverse transcriptase inhibitors versus ritonavir-boosted lopinavir plus raltegravir for treatment of HIV-1 infection in adults with virological failure of a standard first-line ART regimen (SECOND-LINE): a randomised, open-label, non-inferiority study. *Lancet*. 2013; 381:2091–2099.
5. La Rosa AM, Harrison LJ, Taiwo B, et al. Raltegravir in second-line antiretroviral therapy in resource-limited settings (SELECT): a randomised, phase 3, non-inferiority study. *Lancet HIV*. 2016;3:e247–e258.
6. Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV*. Department of Health and Human Services; 2022. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf.
7. Shilaih M, Marzel A, Scherrer AU, et al. Dually active HIV/HBV antiretrovirals as protection against incident hepatitis B infections: potential for prophylaxis. *J Infect Dis*. 2016;214:599–606.
8. Myint A, Tong MJ, Beaven SW. Reactivation of hepatitis B virus: a review of clinical guidelines. *Clin Liver Dis*. 2020;15: 162–167.
9. Panel on Opportunistic Infections in Adults and Adolescents with HIV. *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV: Recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Hepatitis B Virus*. Available at: https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/. Accessed January 11, 2023.
10. Singh KP, Crane M, Audsley J, et al. HIV-Hepatitis B virus co-infection: epidemiology, pathogenesis and treatment. *AIDS*. 2017;31:2035.
11. Thio CL, Seaberg EC, Skolasky R, et al. HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS). *Lancet*. 2002;360:1921–1926.
12. Terrault NA, Lok AS, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67:1560–1599.
13. Tian Y, Hua W, Wu Y, et al. Immune response to hepatitis B virus vaccine among people living with HIV: a meta-analysis. *Front Immunol*. 2021;12:5538.
14. Lee JH, Hong S, Im JH, et al. Systematic review and meta-analysis of immune response of double dose of hepatitis B vaccination in HIV-infected patients. *Vaccine*. 2020;38:3995–4000.
15. Yanny B, Konyn P, Najarian LM, et al. Management approaches to hepatitis B virus vaccination nonresponse. *Gastroenterol Hepatol*. 2019; 15:93–99.
16. Overton ET, Sungkanuparph S, Klebert M, et al. GM-CSF fails to improve immune responses to booster hepatitis B vaccination in HIV-infected individuals. *Virol J*. 2011;5:109.
17. Khaimova R, Fischetti B, Cope R, et al. Serological response with Heplisav-B® in prior hepatitis B vaccine non-responders living with HIV. *Vaccine*. 2021;39:6529–6534.
18. Schnittman SR, Zepf R, Cocohoba J, et al. Brief report: Heplisav-B seroprotection in people with HIV: a single-center experience. *J Acquir Immune Defic Syndr*. 2021;86:445–449.
19. Marks KM, Kang M, Umbleja T, et al. Immunogenicity and safety of hepatitis B vaccine with a toll-like receptor 9 agonist adjuvant (HEPLISAV-B) in HBV vaccine-naive people with HIV. *Clin Infect Dis*. 2023;ciad201.
20. Thompson MA, Horberg MA, Agwu AL, et al. Primary care guidance for persons with human immunodeficiency virus: 2020 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2021;73:e3572–e3605.
21. Yen YH, Chen CH, Wang JH, et al. Study of hepatitis B (HB) vaccine non-responsiveness among health care workers from an endemic area (Taiwan). *Liver Int.* 2005;25:1162–1168.

22. Kernéis S, Launay O, Turbelin C, et al. Long-term immune responses to vaccination in HIV-infected patients: a systematic review and meta-analysis. *Clin Infect Dis*. 2014;58:1130–1139.
23. Gatanaga H, Hayashida T, Tanuma J, et al. Prophylactic effect of antiretroviral therapy on hepatitis B virus infection. *Clin Infect Dis*. 2013; 56:1812–1819.
24. Heuft MM, Houba SM, van den Berk GE, et al. Protective effect of hepatitis B virus-active antiretroviral therapy against primary hepatitis B virus infection. *AIDS*. 2014;28:999–1005.
25. Chang JJ, Mohtashemi N, Bhattacharya D. Significance and management of isolated hepatitis B core antibody (anti-HBc) in HIV and HCV: strategies in the DAA era. *Curr HIV/AIDS Rep*. 2018;15:172–181.
26. Perrillo RP, Gish R, Falck-Ytter YT. American Gastroenterological Association Institute technical review on prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. *Gastroenterology*. 2015;148:221–244.
27. Loomba R, Liang TJ. Hepatitis B reactivation associated with immune suppressive and biological modifier therapies: current concepts, management strategies, and future directions. *Gastroenterology*. 2017;152:1297–1309.
28. Rouphael NG, Talati NJ, Rimland D. Hepatitis B reverse seroconversion in HIV-positive patients: case series and review of the literature. *AIDS*. 2007;21:771–774.
29. Loomba R, Rowley A, Wesley R, et al. Systematic review: the effect of preventive lamivudine on hepatitis B reactivation during chemotherapy. *Ann Intern Med*. 2008;148:519–528.
30. Kim SJ, Hsu C, Song YQ, et al. Hepatitis B virus reactivation in B-cell lymphoma patients treated with rituximab: analysis from the Asia Lymphoma Study Group. *Eur J Cancer*. 2013;49:3486–3496.
31. Huang H, Li X, Zhu J, et al. Entecavir vs lamivudine for prevention of hepatitis B virus reactivation among patients with untreated diffuse large B-cell lymphoma receiving R-CHOP chemotherapy: a randomized clinical trial. *JAMA*. 2014;312:2521-30.
32. Bellini C, Keiser O, Chave JP, et al. Liver enzyme elevation after lamivudine withdrawal in HIV–hepatitis B virus co-infected patients: the Swiss HIV Cohort Study. *HIV Med*. 2009;10:12–18.
33. Dore GJ, Soriano V, Rockstroh J, et al. Frequent hepatitis B virus (HBV) rebound among HIV–HBV coinfected patients following antiretroviral therapy interruption in the SMART study. *AIDS*. 2010;24:857.
34. Kao JH, Jeng WJ, Ning Q, et al. APASL guidance on stopping nucleos (t) ide analogues in chronic hepatitis B patients. *Hepatol Int*. 2021;15: 833–851.
35. Ghany MG, Feld JJ, Chang KM, et al. Serum alanine aminotransferase flares in chronic hepatitis B infection: the good and the bad. *Lancet Gastroenterol Hepatol*. 2020;5:406–417.
36. Piroth L, Sène D, Pol S, et al. Epidemiology, diagnosis and treatment of chronic hepatitis B in HIV-infected patients (EPIB 2005 STUDY). *AIDS*. 2007;21:1323–1331.
37. Jain MK, Opio CK, Osuagwu CC, et al. Do HIV care providers appropriately manage hepatitis B in coinfected patients treated with antiretroviral therapy? *Clin Infect Dis*. 2007;44:996–1000.
38. Hearn B, Chasan R, Bichoupan K, et al. Low adherence of HIV providers to practice guidelines for hepatocellular carcinoma screening in HIV/hepatitis B coinfection. *Clin Infect Dis*. 2015;61:1742–1748.
39. Pintado C, Delaugerre C, Molina JM. Acute hepatitis B infection after a switch to long-acting cabotegravir and rilpivirine. *Open Forum Infect Dis*. 2020;7:367.
40. Mican R, Vasquez J, Daroca G, et al. Hepatitis B reactivation after tenofovir withdrawal in an HIV-infected patient with history of cured hepatitis B virus infection and poor immunological status. *AIDS*. 2021; 35:1707–1708.
41. Welford E, Yin J, Hill L, et al. 1583. A case series of low-level HBV viremia after switching to long-acting injectable cabotegravir/rilpivirine in patients with HIV, hepatitis B core antibody positivity, and hepatitis B surface antigen negativity. *Open Forum Infect Dis*. 2022;9(suppl 2): 492–106.
42. Salpini R, D'Anna S, Alkhatib M, et al. *Reactivation of Hepatitis B Virus is a Frequent Event in Anti-HBc Positive/HBsAg-Negative HIV-Infected Patients Switching to Tenofovir Sparing Therapy as Revealed by Highly Sensitive HBV Assays*. Presented at: International Conference on Antiviral Research; 2022; Montreal, QC, Canada.