Research Article

Efficacy and tolerability of tenofovir alafenamide fumarate prophylaxis in hbv-infected individuals receiving chemo/immunosuppressive therapy

Running title: HBV prophylaxis with TAF in immunosuppressive therapy

Feyza Dilber[1], Serdar Durak[2], Yasemin Unsal[3], Mehmet Demir[4], Abdullah Emre Yildirim[5], Zeynep Melekoglu Ellik[6], Shahin Mehdiyev[1], Haydar Adanir[7], Suna Yapali[8], Coskun Ozer Demirtas[1], Enver Ucbilek[9] Yasemin Balaban[10] Nergis Ekmen[3], Hale Gokcan[6], Elif Sitre Koc[8], Dinc Dincer[7], Orhan Sezgin[9], Halis Simsek[10], Nurdan Tozun[8], Mehmet Arslan[2], Ramazan Idilman[6], and Member of Viral Hepatitis Special Interest Group.

Member of Viral Hepatitis Special Interest Group: Digdem Ozer Etik[11], Pinar Gokcen[12], Derya Ari[13], Kamil Ozdil[12], Meral Akdogan[13], Sedat Boyacioglu[11].

[1] Department of Gastroenterology, Marmara University School of Medicine, Istanbul, Turkiye

[2] Department of Gastroenterology, Karadeniz Technical University School of Medicine, Trabzon, Turkiye

[3] Department of Gastroenterology, School of Medicine, Gazi University, Ankara, Turkiye

[4] Department of Gastroenterology, School of Medicine, Mustafa Kemal University, Hatay, Turkiye

[5] Department of Gastroenterology, School of Medicine, Gaziantep University, Gaziantep, Turkiye

[6] Department of Gastroenterology, School of Medicine, Ankara University, Ankara, Turkiye

[7] Department of Gastroenterology, School of Medicine, Akdeniz University, Antalya, Turkiye

[8]Department of Gastroenterology School of Medicine, Acibadem Mehmet Ali Aydinlar University, Istanbul, Turkiye

[9] Department of Gastroenterology, School of Medicine, Mersin University, Mersin, Turkiye

[10] Department of Gastroenterology, School of Medicine, Hacettepe University, Ankara, Turkiye

Ahead of print

[11] Department of Gastroenterology, School of Medicine, Baskent University, Ankara, Turkiye

[12] Department of Gastroenterology, Health Sciences University, Umraniye Training and Research Hospital, Istanbul, Turkiye

[13] Department of Gastroenterology, Ankara City Hospital, Ankara, Turkiye

Feyza Dilber: https://orcid.org/0000-0003-2901-7044

Serdar Durak: https://orcid.org/0000-0002-8175-9611

Yasemin Unsal: https://orcid.org/0000-0003-2413-7733

Mehmet Demir: https://orcid.org/0000-0001-9348-0848

Abdullah Emre Yildirim: https://orcid.org/0000-0002-4386-9297

Zeynep Melekoglu Ellik: https://orcid.org/0000-0001-8290-7965

Shahin Mehdiyev: https://orcid.org/0009-0006-0664-7034

Haydar Adanir: https://orcid.org/0000-0003-1899-5846

Suna Yapali: https://orcid.org/0000-0001-6069-230X

Coskun Ozer Demirtas: https://orcid.org/0000-0002-0004-2740

Enver Ucbilek: https://orcid.org/0000-0002-2935-5580

Yasemin Balaban: https://orcid.org/0000-0002-0901-9192

Nergis Ekmen: https://orcid.org/0000-0002-7921-3169

Hale Gokcan: https://orcid.org/0000-0001-5663-0683

Elif Sitre Koc: https://orcid.org/0000-0002-6899-0245

Dinc Dincer: https://orcid.org/0000-0001-6769-9344

Orhan Sezgin: https://orcid.org/0000-0002-6704-4716

Halis Simsek: https://orcid.org/0000-0002-9306-557X

Nurdan Tozun: https://orcid.org/0000-0001-6487-2551

Mehmet Arslan: https://orcid.org/0000-0003-0816-4168

Ahead of print

Ramazan Idilman: https://orcid.org/0000-0001-8840-5472

Digdem Ozer Etik: https://orcid.org/0000-0002-4724-0728

Pinar Gokcen: https://orcid.org/0000-0002-6742-6976

Derya Ari: https://orcid.org/0000-0001-8024-781X

Kamil Ozdil: https://orcid.org/0000-0003-2556-3064

Meral Akdogan: https://orcid.org/0000-0003-4624-2542

Sedat Boyacioglu: https://orcid.org/0000-0002-9370-1126

How to cite this article: Dilber F, Durak S, Unsal Y, Demir M, Yildirim AE, Melekoglu Ellik Z, et al. Efficacy and tolerability of tenofovir alafenamide fumarate prophylaxis in HBV-infected individuals receiving chemo/immunosuppressive therapy. Hepatology Forum 2025; 7(1):XX–XX.

Received: August 22, 2025; **Accepted:** September 12, 2025;

Corresponding author: Ramazan Idilman; Department of Gastroenterology, School of Medicine, Ankara University, Ankara, Turkiye

Phone: +90 533 542 93 17; e-mail: idilman@medicine.ankara.edu.tr

Acknowledgements: We appreciate the TASL Viral Hepatitis Special Interest Group for their contribution in the study design, data collection and preparation of the manuscript.

Author Contributions: Concept –RI; Design –RI, SY, FD, HG; Supervision – RI, SY, FD, HG; Data Collection and/or Processing – SD, YU, MD, AEY, ZME, SM, HA, ESK, EU, YB, DOE, PG, DA; Analysis and/or Interpretation – FD, COD; Literature Search – FD, COD; Writing – FD, COD; Critical Reviews – FD, SD, YU, MD, AEY, ZME, SM, HA, SY, COD,

Ahead of print

EU, YB, NE, HG, ESK, DD, OS, HS, NT, MA, RI, DOE, PG, DA, KO, MA, SB.

Conflict of Interest: All the authors declared no conflict of interest.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: This is an investigator-sponsored Clinical Trial Study investigating the REAL-Life Efficacy and TolerabilitY of Tenofovir Alafenamide Fumarate (TAF) in special groups of Hepatitis B patients (REALITY) which is conducted on behalf of Turkish Association for The Study of Liver (TASL) by the grant of Gilead Sciences, Inc, Foster City CA. (IN-TR-320-5958)

Peer-review: Externally peer-reviewed.

Abbreviations:

Anti HBc: Hepatitis B core antibody

CHB: Chronic hepatitis B

CRF: Electronic case report form

eGFR: Glomerular filtration rates

ETV: Entecavir

HBsAg: Hepatitis B surface antigen

HBV: Hepatitis B virus

HBVr: HBV reactivation

LAM: Lamivudine

LDL: Low-density lipoprotein

NUCs: Nucleos(t)ide analogs

TAF: Tenofovir alafenamide fumarate

TDF: Tenofovir disoproxil fumarate

TG: Triglycerides

Ahead of print

TNF: Tumor-necrosis factor

ABSTRACT

Background and Aim: This study aimed to determine the efficacy and safety of tenofovir alafenamide fumarate (TAF) prophylaxis in hepatitis B virus (HBV)-infected or HBV-experienced individuals with benign and malignant diseases receiving chemo/immunosuppressive or biological modifier therapy.

Materials and Methods: This is a multicenter, observational study in which data from 13 centers were reviewed and entered into a standardized electronic case report form.

Results: A total of 158 individuals who received TAF prophylaxis were included in the analysis. Before starting prophylaxis, 51 individuals were hepatitis B surface antigen positive, while 107 were HBV-experienced. Thirty patients had detectable HBV DNA levels. Twelve of them had abnormal serum alanine aminotransferase levels. Forty patients were switched to TAF. Solid tumors (34%) were the most common primary disease types. The median follow-up period was 17.2 months. From baseline to the end of the follow-up period, none of the patients had clinical, biochemical, or serological evidence of HBV reactivation under TAF prophylaxis. The virological response rate was 87%. HBV suppression was well maintained in the 40 patients who were switched to TAF treatment. All patients maintained their chemo/immunosuppressive therapy without interruption. TAF prophylaxis was well tolerated. No drug discontinuation due to adverse effects was observed. No HBV-related morbidity or mortality was reported during TAF prophylaxis. No significant differences were found in glomerular filtration rate change or hypophosphatemia during TAF prophylaxis, but serum triglyceride levels were significantly increased (p=0.019).

Conclusion: TAF prophylaxis is effective, safe, and tolerable in preventing chemo/immunosuppressive or biological modifier-induced HBV reactivation in HBV-infected or HBV-experienced individuals.

Keywords: Chemotherapy; efficacy; HBV infection; immunosuppressive therapy; prophylaxis; tenofovir alafenamide fumarate; safety.

INTRODUCTION

Hepatitis B virus (HBV) infection is a global public health problem affecting approximately 300 million people worldwide, with 1.5 million new infections each year.[1] A significant proportion of these individuals develop chronic hepatitis, cirrhosis, and hepatocellular carcinoma, which are associated with an increased risk of liver-related morbidity and mortality.[2] In 2019, HBV resulted in an estimated 820,000 deaths.[1] Despite a successful HBV vaccination program and efforts to reduce transmission and prevention in Turkey, HBV infection remains a major public health problem, especially in the adult population. In 2009, an epidemiologic study determined that hepatitis B surface antigen (HBsAg) positivity was around 4%, and hepatitis B core antibody (anti-HBc) positivity was 31% in Turkiye.[3]

HBV reactivation (HBVr) is a well-recognized complication of chemo/immunosuppressive and biological modifier therapies in HBV-infected or HBV-experienced individuals.[4] HBVr is characterized by the emergence of HBV particles in patients with previously resolved HBV or an increase in HBV viremia in patients with chronic HBV infection.[5] Reactivation can

Ahead of Print

occur spontaneously, but it is generally triggered by immunosuppressive therapy. HBVr is a serious event that can result in hepatic decompensation, acute liver failure, and death.[6]

Several risk factors, such as host factors (male gender, older age, severity of liver disease), virological factors (HBV DNA levels), primary disease (lymphoma, stem cell transplantation), and the type and degree of immunosuppressive agent, are associated with HBVr.[6,7] There is a rapid expansion of new immunosuppressive agents, such as monoclonal antibodies, immune checkpoint inhibitors, and tyrosine kinase inhibitors, which are used in the treatment of various autoimmune, dermatologic, and rheumatologic diseases, as well as many cancers. It has been demonstrated that a risk gradient of immunosuppressive drugs could affect HBVr [8]. Thus, these drugs have been categorized into low-, moderate-, and high-risk groups based on their estimated risk of HBVr.

HBVr can be preventable when at-risk individuals are identified through screening and started on antiviral prophylaxis if indicated. Antiviral prophylaxis with potent nucleos(t)ide analogs (NUCs) is strongly recommended for HBV-infected patients or HBV-experienced individuals who are considered high-risk for HBVr while undergoing chemo/immunosuppressive and biological modifier therapies.[8] Previous studies have shown that antiviral prophylaxis is associated with an 87% relative risk reduction in HBVr and an 84% relative risk reduction in HBV-associated hepatitis flares.[9]

Lamivudine (LAM), entecavir (ETV), and tenofovir disoproxil fumarate (TDF) may be used in the prevention of HBVr in patients undergoing chemo/immunosuppressive therapy. As high long-term antiviral efficacy leading to undetectable HBV DNA levels is necessary, clinical guidelines recommend the use of potent NUCs with high genetic barriers, such as ETV or TDF, over LAM prophylaxis in such patients.[9,10]

More recent antiviral agents, such as tenofovir alafenamide fumarate (TAF), a prodrug that is proven to be non-inferior to TDF by providing a more stable plasma concentration of tenofovir, have also been proposed to offer some benefits, such as reduced drug exposure to bone and kidneys.[11] Little data have been gathered on the efficacy and tolerability of TAF prophylaxis in HBV-infected patients undergoing chemo/immunosuppressive and biological modifier therapies. Thus, the aim of this study was to determine the efficacy and tolerability of TAF prophylaxis in HBV-infected or HBV-experienced individuals undergoing chemo/immunosuppressive and biological modifier therapies.

Materials And Methods

Patients

Between January 2019 and June 2021, a total of 326 HBV-infected or HBV-experienced patients who were candidates for chemo/immunosuppressive and/or biological modifier therapies were enrolled in this investigation. TAF was administered at a dose of 25 mg/day at the initiation of chemo/immunosuppressive therapy. A specific electronic case report form (CRF) was designed for data collection and recording. Each center entered the relevant data into the CRF. This study was approved by the local ethics committee of the XXX Medical School (09.2020/698), and written informed consent was waived due to the retrospective nature of the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in a priori approval by the institution's human research committee.

Ahead of print

The laboratory investigations conducted included serum alanine aminotransferase (ALT), aspartate aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase, bilirubin, creatinine, fasting glucose levels, lipid profile, and prothrombin time. Complete blood cell counts were obtained using the local central laboratory of each unit. HBsAg, anti-HBs antibody, HBeAg, anti-HBe antibody, anti-HBc IgM and IgG antibodies, and anti-delta antibody were performed. HBV DNA levels were measured using the Roche COBAS TaqMan assay (lower limit of quantitation: 20 IU/mL).

Definitions

HBVr was defined as the presence of abnormal serum ALT levels (>1.3-fold increase above the upper limit of normal), detection of HBV DNA in individuals with previously undetectable HBV DNA levels, or a ≥2 log increase in HBV DNA level from baseline, or seroreversion of HBsAg in HBsAg-negative individuals.

Hypophosphatemia was defined as a serum phosphate level of less than 2.5 mg/dL.

The primary endpoint of the study was to determine the incidence of HBVr and hepatitis flare during TAF prophylaxis. The secondary endpoint was to determine the tolerability and adverse effects of TAF in such patients.

Safety

Safety and tolerability analyses were assessed during TAF prophylaxis. Adverse events (AEs), serious AEs, laboratory abnormalities, drug discontinuation due to AEs, and deaths were evaluated. Serum creatinine levels and estimated glomerular filtration rates (eGFR) were assessed. eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) formula.

Follow-up

All patients were seen at three- or six-month intervals in the outpatient clinic after antiviral prophylaxis was started. A physical examination was performed, and vital signs and patient compliance were assessed. Blood was drawn to determine the metabolic, biochemical, and serological parameters. HBsAg and HBeAg loss and seroconversion were monitored.

Statistical Analysis

Means and standard deviations, medians, ranges and interquartile ranges, and frequencies and percentages were used in descriptive statistics. For categorical variables, differences between groups were assessed using the chi-squared test or Fisher's exact test, as appropriate. GLMMs (Generalized Linear Mixed Models) were conducted for comparisons versus baseline values. R version 2.15.3 software (R Core Team, 2013) was used for data analyses. P-values of less than 0.05 were considered statistically significant.

Results

A total of 158 HBV-infected or HBV-experienced individuals with benign and malignant diseases who received TAF prophylaxis were included in the analysis. The remaining 168 patients who were lost to follow-up (n=78), had short-term (<6 months) follow-up (n = 63), or died (n=27) due to primary disease were excluded (Fig. 1). The mean age of the included patients was 59.5±12.2 years, and the majority were male (52.5%).

Ahead of print

Before starting TAF prophylaxis, 51 individuals (32.3%) had HBsAg positivity, while the remaining 107 individuals (67.7%) were HBV-experienced (anti-HBs positivity and anti-HBc IgG positivity). Thirty patients had a detectable HBV DNA level: 27 were HBsAg-positive, and the remaining three were only anti-HBc IgG positive, consistent with occult hepatitis B infection. Twelve of these 30 patients had abnormal serum ALT levels (>40 U/L). Overall, only eight patients (8/158, 5%) were HBeAg-positive.

Before TAF prophylaxis, 118 patients were treatment-naive. Forty patients were initially treated with TDF (n=24), ETV (n = 9), or LAM (n=7) and were switched to TAF due to older age (>60 years), renal dysfunction, or osteoporosis. The characteristics of the patients are summarized in Table 1.

Solid tumors (33.5%) were the most common primary disease types, followed by rheumatologic/autoimmune diseases (32.9%) and myeloproliferative diseases (32.2%). Overall, 48% of the patients received cytotoxic chemotherapy, 17% received B-cell depleting therapy, 13% received anti-TNF therapy, 8% received glucocorticoid therapy, and 12% received biological modifier therapies (imatinib, revlimid, ocrelizumab, bevacizumab, or ibrutinib). The characteristics of the primary diseases and chemo/immunosuppressive and/or biological modifier therapies are presented in Table 1. The median follow-up period was 17.2 months (range, 9.4–25 months).

During and after the administration of chemo/immunosuppressive and/or biological modifier therapies, none of the patients showed clinical, biochemical, or serological evidence of HBVr during TAF prophylaxis. From baseline to the end of the follow-up period, the virological response rate was 87%. Serum ALT levels significantly improved in patients with abnormal ALT levels from baseline to the end of the follow-up period (p=0.04). HBV suppression was well maintained in the 40 patients who were switched to TAF treatment.

Safety

TAF prophylaxis was well tolerated. Headache, nausea, and fatigue were the most common adverse effects. No drug discontinuation due to adverse effects was observed. No HBV-related morbidity or mortality occurred. All patients continued their chemo/immunosuppressive therapy without interruption. No significant clinical side effects or serious AEs were reported during TAF prophylaxis.

Changes in laboratory values during the follow-up period in treatment-naive and TDF-experienced patients are presented in Table 2a and Table 2b. In the treatment-naive group, the mean eGFR change from baseline to the end of the follow-up period during TAF prophylaxis was generally stable (82.9 mL/min to 91.5 mL/min). Serum phosphorus levels remained stable in 87% of patients, temporarily decreased in 8.5%, and decreased in 4.6% during TAF prophylaxis. At baseline, hypophosphatemia (<2.5 mg/dL) was found in seven patients. At the end of the follow-up period, hypophosphatemia improved in six of these seven patients. No differences were found in eGFR change and hypophosphatemia during follow-up in patients with TDF experience.

Serum triglyceride (TG) levels were significantly increased from baseline to the end of the follow-up period in antiviral treatment-naive patients (p = 0.019). Serum fasting glucose levels increased at 48 weeks (p = 0.033) but improved at 96 weeks in these patients. However, serum fasting low-density lipoprotein cholesterol (LDL) levels were only slightly increased

Ahead of print

(mean from 125.8 ± 43.8 mg/dL to 140.5 ± 91.3 mg/dL, p = 0.877) (Table 2a). Serum fasting glucose levels and lipid profiles did not significantly change during follow-up in patients with TDF experience.

Overall, 27 patients died due to the progression of primary diseases.

Discussion

This is the first multicenter observational study with a large sample to determine the efficacy and tolerability of TAF prophylaxis in HBV-infected or HBV-experienced individuals receiving chemo/immunosuppressive and/or biological modifier therapies. No HBVr or HBV-related morbidity or mortality was observed during TAF prophylaxis. TAF prophylaxis also enabled the patients treated with these agents to complete their treatment protocol without interruption due to HBVr. Two single-center studies have recently reported that TAF prophylaxis is effective against HBV infection in HBV-infected patients undergoing chemotherapy.[12,13] This result indicates that TAF prophylaxis in HBV-infected or HBV-experienced individuals receiving chemo/immunosuppressive and/or biological modifier therapies prevents chemo/immunosuppressive therapy-induced HBVr.

Current HBV clinical practice guidelines recommend ETV, TDF, and TAF as first-line treatment options in patients with chronic hepatitis B (CHB).[14,15] Real-world studies have shown that TAF is effective and tolerable without the emergence of drug resistance in patients with CHB.[16-18] Therefore, TAF should be preferred over TDF or ETV in patients of older age (>60 years), with renal dysfunction, bone disease (osteopenia/osteoporosis), or prior NUC experience.[14,15,19] TAF does not require renal dose adjustment in patients with chronic kidney disease (CKD) and is not affected by food digestion.[20] Taking advantage of these benefits, TAF has been widely used in patients with CHB in clinical practice. However, limited data report the efficacy and tolerability of TAF prophylaxis in HBV-infected or HBV-experienced individuals receiving chemo/immunosuppressive and/or biological modifier therapies for preventing chemo/immunosuppressive therapy-induced HBVr.

The present study shows that TAF treatment has a high virological response rate, comparable with a previous study demonstrating a virological response rate of 96% more than one year after starting TAF prophylaxis.[13] Notably, all patients who switched from other NUC treatments to TAF had a similarly high virological response rate after switching.

Minimal renal dysfunction has been reported during long-term NUC therapy, but the nephrotoxic potential is higher with TDF treatment than with ETV or TAFç.[14] In addition, fluctuations in renal function tests have been frequently described, and a significant proportion of patients may experience acute kidney injury (AKI) and CKD stage migration during chemo/immunosuppressive therapies.[21,22] AKI is associated with increased morbidity and mortality during this therapy. AKI may also lead to an interruption of the treatment protocol. Chemotherapeutic agents such as cisplatin, higher baseline serum creatinine, bilirubin levels, and hypoalbuminemia are independent risk factors for the development of AKI in such individuals.

Lee et al.[13] found no significant difference in the incidence of renal events among the ETV, TDF, and TAF groups receiving chemo/immunosuppressive therapy. In the present study, no significant changes were found in the mean eGFR and serum creatinine levels from baseline to the end of the follow-up period during TAF prophylaxis. No major renal-related adverse

Ahead of print

effects were observed. The serum phosphate levels were stable in most of the patients. It should be noted that hypophosphatemia improved in six of the seven patients during TAF prophylaxis.

According to previous reports, switching from TDF to TAF appears to be associated with body weight gain, increased cardiovascular risk scores, and altered lipid profiles with higher LDL and TG levels.[23-32] In the present study, prophylactic TAF treatment was shown to be associated with higher fasting glucose levels at 48 weeks and higher TG levels at 96 weeks. However, the clinical importance of these effects is not yet clearly understood.

Our study has several limitations. As described in the Materials and Methods section, this study aimed to collect data on patients receiving prophylactic TAF. Unfortunately, there was no control group to compare the virological response rate and safety profile among groups. TAF has been demonstrated to lead to a greater extent of serum HBsAg level reduction compared with ETV.[17] Several automated assays have been developed to quantify serum HBsAg levels. The Architect HBsAg QT assay (Abbott Diagnostics, Abbott Park, IL, USA) and the Elecsys HBsAg II assay (Roche Diagnostics, Indianapolis, IN, USA) are the most widely used. However, a standard HBsAg quantification assay was not routinely used in the clinical practice of Turkiye.

Bone mineral density at the hip and spine decreases during both TDF and TAF treatments. However, this study did not include data regarding body weight or bone mineral density during prophylactic TAF treatment.

Conclusion

TAF prophylaxis prevents chemo/immunosuppressive therapy-induced HBVr in HBV-infected or HBV-experienced individuals receiving chemo/immunosuppressive and/or biological modifier therapies. Prophylactic TAF treatment is safe and tolerable in such individuals.

Ahead of print

References

1. Organization WH. Hepatitis B: WHO; 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b Accessed on Oct 24, 2025.
2. McMahon BJ. The natural history of chronic hepatitis B virus infection. Hepatology. 2009;49(Suppl 5):S45-S55. [CrossRef]
3. Tozun N, Ozdogan O, Cakaloglu Y, Idilman R, Karasu Z, Akarca U, et al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clin Microbiol Infect 2015;21(11):1020-1026. [CrossRef]

4. Aygen B, Demir AM, Gumus M, Karabay O, Kaymakoglu S, Koksal AS, et al. Immunosuppressive therapy and the risk of hepatitis B reactivation: Consensus report. Turk J Gastroenterol 2018;29(3):259-269. [CrossRef]
5. Myint A, Tong MJ, Beaven SW. Reactivation of hepatitis B virus: A review of clinical guidelines. Clin Liver Dis (Hoboken) 2020;15(4):162-167. [CrossRef]
6. Smalls DJ, Kiger RE, Norris LB, Bennett CL, Love BL. Hepatitis B virus reactivation: Risk factors and current management strategies. pharmacotherapy. 2019;39(12):1190-1203. [CrossRef]
7. 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(6):1297-1309. [CrossRef]
8. 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(1):221-244 e3. [CrossRef]
9. Reddy KR, Beavers KL, Hammond SP, Lim JK, Falck-Ytter YT; American Gastroenterological Association Institute. American Gastroenterological Association Institute guideline on the prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. Gastroenterology 2015;148(1):215-219; quiz e16-e17. [CrossRef]
10. Lau G, Yu ML, Wong G, Thompson A, Ghazinian H, Hou JL, et al. APASL clinical practice guideline on hepatitis B reactivation related to the use of immunosuppressive therapy. Hepatol Int 2021;15(5):1031-1048. [CrossRef]
11. Lee WA, He GX, Eisenberg E, Cihlar T, Swaminathan S, Mulato A, et al. Selective intracellular activation of a novel prodrug of the human immunodeficiency virus reverse transcriptase inhibitor tenofovir leads to preferential distribution and accumulation in lymphatic tissue. Antimicrob Agents Chemother 2005;49(5):1898-1906. [CrossRef]
12. Inada K, Kaneko S, Kurosaki M, Yamashita K, Kirino S, Osawa L, et al. Tenofovir alafenamide for prevention and treatment of hepatitis B virus reactivation and de novo hepatitis. JGH Open 2021;5(9):1085-1091. [CrossRef]
13. Lee IC, Lan KH, Su CW, Li CP, Chao Y, Lin HC, et al. Efficacy and renal safety of prophylactic tenofovir alafenamide for HBV-infected cancer patients undergoing chemotherapy. Int J Mol Sci 2022;23(19):11335. [CrossRef]
14. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol 2017;67(2):370-398. [CrossRef]
15. Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology 2018;67(4):1560-1599. [CrossRef]
16. Lampertico P, Buti M, Fung S, Ahn SH, Chuang WL, Tak WY, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in virologically suppressed patients with chronic hepatitis B: A randomised, double-blind, phase 3, multicentre non-inferiority study. Lancet Gastroenterol Hepatol 2020;5(5):441-453. [CrossRef]
17. Uchida Y, Nakao M, Yamada S, Tsuji S, Uemura H, Kouyama JI, et al. Superiority of tenofovir alafenamide fumarate over entecavir for serum HBsAg level reduction in patients with chronic HBV infection: A 144-week outcome study after switching of the nucleos(t)ide analog. PLoS One 2022;17(2):e0262764. [CrossRef]

Ahead of print

18. Agarwal K, Brunetto M, Seto WK, Lim YS, Fung S, Marcellin P, et al. 96 weeks treatment of tenofovir alafenamide vs. tenofovir disoproxil fumarate for hepatitis B virus infection. J Hepatol 2018;68(4):672-681. [CrossRef]
19. Sarin SK, Kumar M, Lau GK, Abbas Z, Chan HL, Chen CJ, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: A 2015 update. Hepatol Int 2016;10(1):1-98. [CrossRef]
20. Tamaki N, Kurosaki M, Nakanishi H, Itakura J, Inada K, Kirino S, et al. Comparison of medication adherence and satisfaction between entecavir and tenofovir alafenamide therapy in chronic hepatitis B. J Med Virol 2020;92(8):1355-1358. [CrossRef]
21. Perazella MA, Shirali AC. Nephrotoxicity of cancer immunotherapies: Past, present and future. J Am Soc Nephrol 2018;29(8):2039-2052. [CrossRef]
22. Santos MLC, de Brito BB, da Silva FAF, Botelho A, de Melo FF. Nephrotoxicity in cancer treatment: An overview. World J Clin Oncol 2020;11(4):190-204. [CrossRef]
23. Gomez M, Seybold U, Roider J, Harter G, Bogner JR. A retrospective analysis of weight changes in HIV-positive patients switching from a tenofovir disoproxil fumarate (TDF)- to a tenofovir alafenamide fumarate (TAF)-containing treatment regimen in one German university hospital in 2015-2017. Infection 2019;47(1):95-102. [CrossRef]
24. Kuo PH, Sun HY, Chuang YC, Wu PY, Liu WC, Hung CC. Weight gain and dyslipidemia among virally suppressed HIV-positive patients switching to co-formulated elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide. Int J Infect Dis 2020;92:71-77. [CrossRef]
25. Taramasso L, Berruti M, Briano F, Di Biagio A. The switch from tenofovir disoproxil fumarate to tenofovir alafenamide determines weight gain in patients on rilpivirine-based regimen. AIDS 2020;34(6):877-881. [CrossRef]
26. Mallon PW, Brunet L, Hsu RK, Fusco JS, Mounzer KC, Prajapati G, et al. Weight gain before and after switch from TDF to TAF in a U.S. cohort study. J Int AIDS Soc 2021;24(4):e25702. [CrossRef]
27. Mallon PWG, Brunet L, Fusco JS, Prajapati G, Beyer A, Fusco GP, et al. Lipid changes after switch from TDF to TAF in the OPERA cohort: LDL cholesterol and triglycerides. Open Forum Infect Dis 2022;9(1):ofab621. [CrossRef]
28. Plum PE, Maes N, Sauvage AS, Frippiat F, Meuris C, Uurlings F, et al. Impact of switch from tenofovir disoproxil fumarate-based regimens to tenofovir alafenamide-based regimens on lipid profile, weight gain and cardiovascular risk score in people living with HIV. BMC Infect Dis 2021;21(1):910. [CrossRef]
29. Brunet L, Mallon P, Fusco JS, Wohlfeiler MB, Prajapati G, Beyer A, et al. Switch from tenofovir disoproxil fumarate to tenofovir alafenamide in people living with HIV: Lipid changes and statin underutilization. Clin Drug Investig 2021;41(11):955-965. [CrossRef]
30. Ikeda M, Wakabayashi Y, Okamoto K, Yanagimoto S, Okugawa S, Moriya K. Changing trends in lipid profile and biomarkers of renal function and bone metabolism before and after switching from tenofovir disoproxil fumarate to tenofovir alafenamide: a prospective observational study. AIDS Res Ther 2021;18(1):30. [CrossRef]
31. Kauppinen KJ, Aho I, Sutinen J. Switching from tenofovir alafenamide to tenofovir disoproxil fumarate improves lipid profile and protects from weight gain. AIDS 2022;36(10):1337-1344. [CrossRef]

Ahead of print

32. Milinkovic A, Berger F, Arenas-Pinto A, Mauss S. Reversible effect on lipids by switching from tenofovir disoproxil fumarate to tenofovir alafenamide and back. AIDS 2019;33(15):2387-2391. [CrossRef]

Ahead of print

Table 1. Baseline characteristics of patients who received TAF prophylaxis for HBV reactivation

	Whole cohort (n=158)
Age, years, median (min-max)	59.6 (23-85)
Male sex, n (%)	83 (53)
Hypertension, n (%)	62 (41)
Diabetes mellitus, n (%)	37 (24)
Chronic renal failure, n (%)	28 (19)
Osteoporosis, n (%)	27 (32)
Diagnoses requiring IS therapy, n (%) • Solid malignancies • Rheumatologic/autoimmune • Myeloproliferative disease • Stem cell transplantation	 53 (34) 52 (33) 51 (32) 2 (1)
IS treatment type, n (%) • Cytotoxic chemotherapy • B cell suppressing therapies • Anti-TNF • Glucocorticoids • Others	 77 (48) 27 (17) 21 (13) 13 (8) 20 (12)
Previous nucleoside/nucleotide use (%) - Treatment naive - Tenofovir Disoproxil Fumarate - Entecavir - Lamivudine	 118 (75) 24 (15) 9 (6) 7 (4)
Initial HBV status, n (%) -HBs-Ag positive -Anti-HBc positive -HBe-Ag positive -Detectable HBV-DNA	 51 (32) 107 (68) 8 (5) 27
Follow-up period, months	17.2±7.8
Exitus from underlying disease, n (%)	27 (17)
HBV: Hepatitis B virus; IS: Immunosuppressive; TNF: Tumor-necrosis factor.	

Ahead of print

Ahead of print

Table 2. Changes in laboratory values of patients who received TAF prophylaxis

Table 2a. Treatment-naive

Treatment-naive (n=118)	**Baseline (mean±SD)**	**6-months (mean±SD)**	**12-months (mean±SD)**	**18-months (mean±SD)**	**24-months (mean±SD)**	**p value (pairwise comparisons vs baseline)**			
						6-months	**12-months**	**18-months**	**24-months**
Fasting glucose (mg/dL)	110.7±37.1	117.6±37.7	122.9±61.6	112.4±38.1	103.0±22.5	0.095	0.033*	0.147	0.693
Total cholesterol (mg/dL)	200.5±55.1	199.5±50.0	222.3±50.1	236.8±100.0	252.3±92.0	0.322	0.290	0.484	0.187
Triglycerides (mg/dL)	147.5±90.1	179.3±111.7	165.17±106.72	168.9±95.5	168.7±77.7	0.050	0.506	0.083	0.019*
HDL	46.2±14.5	45.6±11.5	53.1±16.3	54.6±20.9	60.1±21.7	0.755	0.165	0.754	0.244

(mg/dL)									
LDL (mg/dL)	125.8±43.8	119.5±35.3	146.6±39.8	149.3±90.7	140.5±91.3	0.788	0.318	0.502	0.877
eGFR (mL/min)	83.2±26.5	84.2±23.7	82.7±26.1	84.1±27.8	91.5±27.3	0.423	0.906	0.126	0.936
Blood phosphate (mg/dL)	3.5±0.8	3.4±0.7	3.3±0.6	3.4±0.6	3.3±0.6	0.061	0.015*	0.069	0.150

Mean ± SD are given.

eGFR: Estimated glomerular filtration rate; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SD: Standard deviation.

Ahead of print

Table 2b. TDF experienced

TDF-experienced (n=24)	**Baseline (mean±SD)**	**6-months (mean±SD)**	**12-months (mean±SD)**	**18-months (mean±SD)**	**24-months (mean±SD)**	**p value (pairwise comparisons vs baseline)**			
						6-months	**12-months**	**18-months**	**24-months**
Fasting glucose (mg/dL)	93.81±13.07	122.89±41.79	105±37.09	107.5±46.48	91.67±17.36	0.039*	0.244	0.263	0.920
Total cholesterol (mg/dL)	203±48.85	199.5±50.2	183.33±29.74	208±0	216.5±12.02	0.998	0.996	0.867	0.652
Triglycerides (mg/dL)	141.44±75.16	142.64±39.55	116.33±30.24	156±0	141.5±20.51	0.976	0.829	0.582	0.999
HDL (mg/dL)	47.63±17.9	46.5±10.33	63.33±22.05	69±0	62.5±9.19	0.758	0.270	0.477	0.377

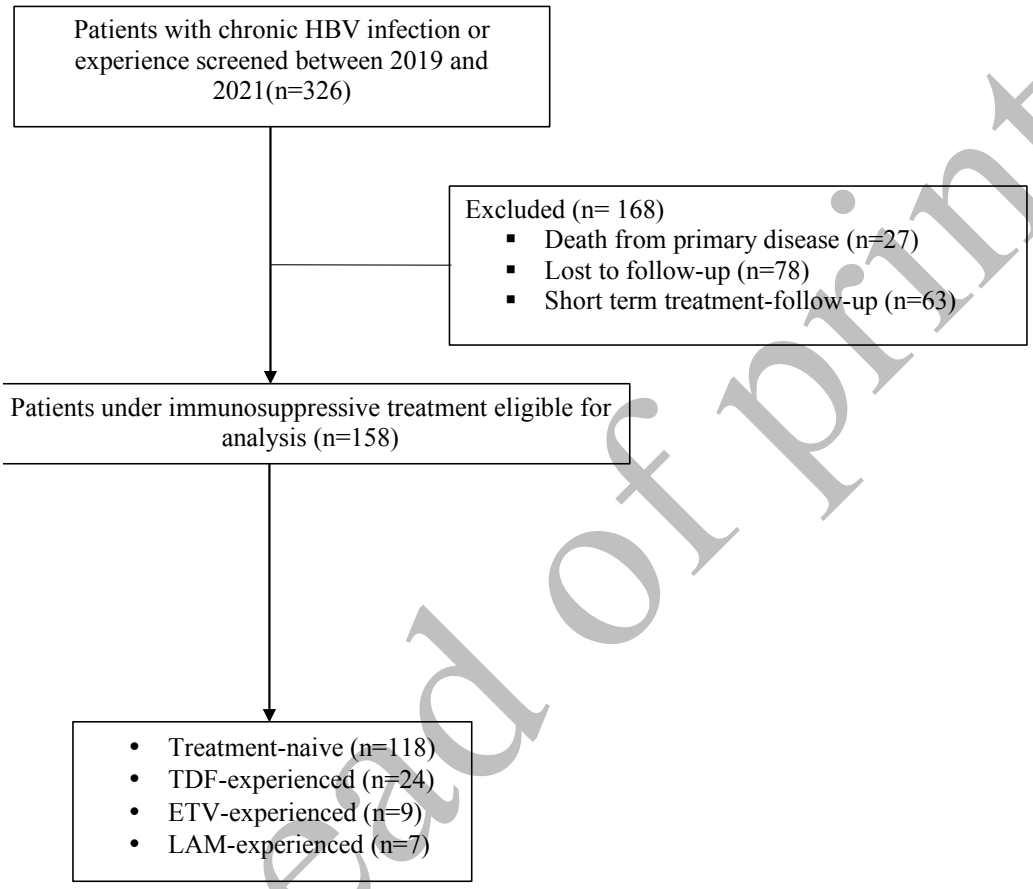
LDL (mg/dL)	122.67±38.16	124.49±36.84	105±20.66	136±0	139±4.24	0.329	0.998	0.496	0.795
eGFR (mL/min)	82.68±23.68	83.97±23.13	83.89±23.39	78.59±30.48	100.7±12	0.571	0.314	0.361	0.138
Blood phosphate (mg/dL)	3.34±0.77	3.51±0.71	3.02±0.63	3.31±0.97	3.08±0.71	0.436	0.405	0.947	0.636

Mean ± SD are given.

eGFR: Estimated glomerular filtration rate; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SD: Standard deviation.

Ahead of print

Figure 1. Study flow chart



ETV: Entecavir, HBV: Hepatitis B virus, LAM: Lamivudine, TDF: Tenofovir disoproxil fumarate

Ahead of print