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Vemlidy® (tenofovir alafenamide) Prophylaxis for Patients Undergoing Chemotherapy or Immunosuppressive Therapy

This document is in response to your request for information regarding the use of Vemlidy® (tenofovir alafenamide [TAF]) as prophylaxis for patients undergoing chemotherapy or immunosuppressive therapy to prevent HBV reactivation.

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Summary

Clinical Data on TAF as Prophylaxis to Prevent HBV Reactivation

In a prospective Japanese study, none of the participants experienced HBV reactivation or HBV reactivation-related hepatitis after 6 and 12 months of TAF, either prior to or while on antitumor or immunosuppressive therapy.[1]

In an interim analysis of a prospective study, after a mean follow-up of 10.1 months, HBV reactivation was observed in 1.9% of participants after the use of prophylactic TAF prior to chemotherapy, with no reports of clinical reactivation. Additionally, 2.9% experienced hepatitis flares, but with a decrease in HBV DNA levels. Of the participants who completed 48 weeks of TAF, 79.7% had HBV DNA levels <20 IU/mL.[2]

In an interim analysis of a prospective RCT, HBV reactivation occurred in 0% of the prophylactic TAF arm and 26.7% of the observation arm within 48 weeks in participants treated with biologic DMARDs (P=0.005).[3]

In a retrospective analysis, the virologic response rate with TAF treatment was 96.1%, with 0% HBV reactivation at Year 1 in patients diagnosed with cancer who were HBsAg+. The effects on kidney parameters were similar between TAF, ETV, and TDF.[4]

In an observational study, no patients experienced HBV reactivation or related morbidity/mortality when prophylactic TAF was used in participants undergoing chemotherapy or immunosuppressive therapy. Of the 30 patients with detectable HBV DNA at baseline, 77% later had undetectable HBV DNA.[5]

In a retrospective case series analysis, prophylactic TAF was successful in suppressing HBV reactivation in 8 out of 11 patients. The remaining 3 patients were treated for HBV reactivation, and 90.9% had undetectable HBV DNA by Week 24.[6]

Clinical Practice Guidelines on TAF as Prophylaxis to Prevent HBV Reactivation

Recommendations from several clinical practice guidelines are summarized in this document.[7-13]

Clinical Data on TAF as Prophylaxis to Prevent HBV Reactivation

NORTE Study Group: Prophylactic TAF in Preventing HBV Reactivation or HBV-Related Hepatitis[1]

Study design and demographics

A prospective multicenter study conducted in Japan evaluated the efficacy of TAF in preventing HBV reactivation among HBsAg+ and/or HBV DNA+ participants who initiated TAF prior to antitumor or immunosuppressive therapy or in preventing HBV reactivation-related hepatitis in participants with resolved HBV infection who initiated TAF while on antitumor or immunosuppressive therapy due to HBV reactivation (de novo HBV reactivation/reappearance). Investigators defined HBV reactivation as a 100-fold increase from baseline in HBV DNA among participants with detectable HBV DNA levels at baseline or an increase in HBV DNA to ≥1.3 log IU/mL among those with undetectable levels at baseline among HBsAg+ participants and defined HBV reactivation-related hepatitis as HBV reactivation and serum ALT levels >3 × ULN. A total of 106 participants received TAF for ≥6 months to prevent HBV reactivation (n=87) or de novo HBV reactivation-related hepatitis (n=19); 94 participants received TAF for 12 months to prevent HBV reactivation (n=77) or de novo HBV reactivation-related hepatitis (n=17).

Table 1. Baseline Demographics and Disease Characteristics (Suda et al)[1]

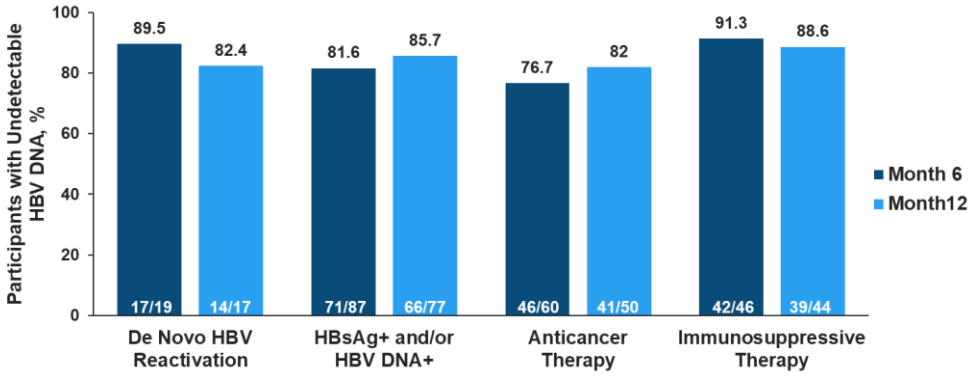
Key Demographics and Characteristics	TAF (N=106)
Age, median (range), years	70 (50–90)
Male, n	63
HBV carrier, n (%)	82 (77.4)
CHB, n (%)	5 (4.7)
De novo HBV reactivation or reappearance, n (%)	19 (18)
HBV DNA level, median (range), log IU/mL	2.42 (0–7.6)
HBsAg, median (range), IU/mL	40.7 (0–29,041)
HBeAg+ status, n (%)	4 (3.8)
Primary disease, malignancy/autoimmune disease/other,[a] n	60/34/12
Anticancer therapy/immunosuppressive therapy, n	60/46
ALT/AST level, median (range), IU/L	18 (5–299)/23 (11–299)
eGFR, median (range), mL/min/1.73 m^2	69.3 (18.6–134.9)

[a]Other diseases or conditions included asthma, carpal tunnel syndrome, sudden deafness, facial nerve paralysis, hypopituitarism, irradiation pneumonitis, post renal transplantation, and pruritus.

Results

After both 6 and 12 months of TAF prophylaxis, none of the participants experienced HBV reactivation or HBV reactivation-related hepatitis. No participants discontinued TAF due to TAF-related AEs or HBV reactivation. Overall, most participants had undetectable HBV DNA levels at both at 6 and 12 months (83% and 85.1%, respectively). Rates of undetectable HBV DNA by subgroup 6 and 12 months after initiation of TAF are shown in Figure 1. Most participants who received anticancer therapy regimens (including regimens containing rituximab [8/8; 100%], an immune checkpoint inhibitor [7/8; 87.5%], or tyrosine kinase inhibitors [4/4; 100%]) or immunosuppressive therapy regimens (including regimens containing high-dose steroid, defined as ≥20 mg prednisolone for ≥4 weeks [22/24; 91.7%], or TNF inhibitors [3/3; 100%]) had undetectable HBV DNA 6 months after the initiation of TAF. Similar results were obtained at Month 12.

Figure 1. Undetectable HBV Rates by Subgroup at Month 6 and Month 12 (Suda et al)[1]



Prophylactic TAF in HBsAg+ Participants Undergoing Chemotherapy[2]

Study design and demographics

A prospective single-arm study (NCT04619082) is being conducted in Taiwan to evaluate the efficacy and safety of prophylactic TAF in HBsAg+ participants with cancer undergoing chemotherapy. Participants receive TAF 25 mg/day for 48 weeks, with the initial dose administered within 7 days before the start of chemotherapy. Baseline and follow-up assessments at Weeks 4, 12, 24, 36, and 48 include complete blood counts, total bilirubin, SCr, phosphate, and HBV DNA levels. The primary endpoint is the rate of HBV reactivation during prophylactic TAF treatment, defined as a 2-log increase in HBV DNA from baseline or a 3-log increase in participants who initially had undetectable HBV DNA levels. Clinical reactivation is defined as an ALT level increase of ≥3 × baseline level and >100 IU/L.

Table 2. Baseline Demographics and Disease Characteristics (Chen et al)[2]

Key Demographics and Characteristics	TAF (N=102)
Age, mean ± SD, years	56.49±9.88
Male, n (%)	50 (49)
HBV DNA, mean ± SD, log IU/mL	3.48±1.77
Undetectable HBV DNA, n (%)	6 (5.9)
HBeAg+ status, n (%)	7 (6.9)
Liver stiffness, mean ± SD, kPa	7.58±5.96

Key Demographics and Characteristics		TAF (N=102)
Cancer type, n (%)	Breast	34 (33.3)
	Colorectal	22 (21.6)
	Lymphoma	5 (4.9)
	Others	41 (40.2)
Chemotherapy or immunosuppressive therapy received, n (%)	Cisplatin-containing	27 (26.5)
	Rituximab-containing	5 (4.9)

Interim results

Participants were screened for the interim analysis from June 2021 to December 2023, and 102 participants were enrolled. The median follow-up period was 10.1 months.

After prophylactic TAF was administered, HBV reactivation was observed in 1.9% of participants (2/102), with no cases of clinical reactivation. Additionally, 2.9% (3/102) experienced hepatitis flares (ALT level >5 × ULN), while HBV DNA levels decreased. A total of 74 participants completed 48 weeks of TAF, and 79.7% of participants (59/74) had HBV DNA levels <20 IU/mL (Figure 2). Liver stiffness decreased numerically from baseline to Week 48 (7.58 kPa to 7.02 kPa; *P*=0.847). AKI (SCr level >1.5 × baseline level) occurred in 2.9% of participants (3/102) who were treated with cisplatin-containing regimens. The median eGFR decreased from baseline to Week 48 (*P*=0.014; Table 3) but remained within the normal range at all measured time points. Serum phosphate levels were stable throughout 48 weeks (*P*=0.071; Table 3).

Figure 2. HBV DNA <20 IU/mL Rates After Prophylactic TAF (Chen et al)[2]

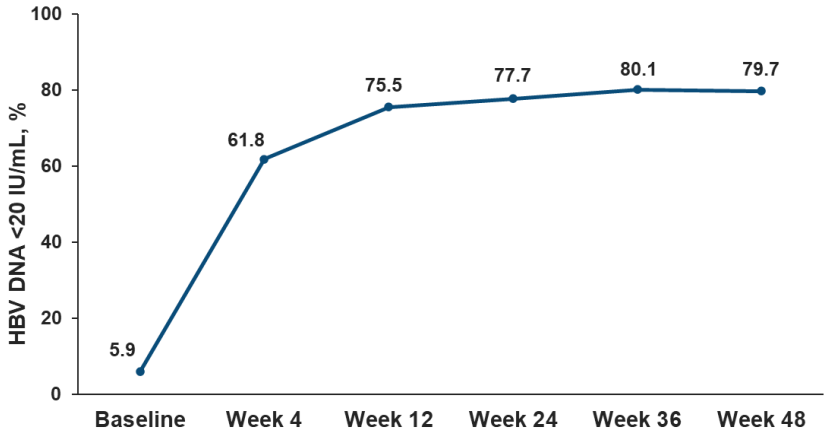


Table 3. Median eGFR and Serum Phosphate Levels After Prophylactic TAF (Chen et al)[2]

	Baseline	Week 4	Week 12	Week 24	Week 36	Week 48	*P*-Value
eGFR, median, mL/min/1.73 m^2	104.7	106.82	104.72	99.14	97.47	96.22	0.014
Phosphate levels, mg/dL	3.61	-	3.63	3.65	3.5	3.5	0.071

AEs were reported in 42.2% of participants (43/102), and 18.6% (19/102) reported serious AEs. The most common AEs were nausea (n/N=31/102; 30.4%) and vomiting (n/N=18/102; 17.6%). No participant discontinued TAF due to AEs, and there were no deaths related to TAF.

RCT of Prophylactic TAF in HBsAg+ Participants Undergoing Biologic DMARD Therapy[3]

Study design and demographics

A prospective RCT (NCT05001672) is being conducted to evaluate the rate of HBV reactivation with or without prophylactic TAF in HBsAg+ participants with inflammatory arthritis treated with biologic DMARDs (N=60). Participants treated with biologic DMARDs are randomized in a 1:1 ratio to either the prophylactic TAF arm or the observation arm. The TAF arm receives TAF 25 mg/day for 144 weeks, whereas the observation arm is monitored for 48 weeks, then receives TAF after 48 weeks. In the observation arm, however, TAF is initiated if participants meet the 2018 AASLD criteria for HBV reactivation or the Taiwan National Health Insurance criteria for CHB treatment before Week 48. The primary endpoint is the HBV reactivation rate over 1 year with and without prophylactic TAF.

Table 4. Baseline Demographics and Disease Characteristics (Huang et al)[3]

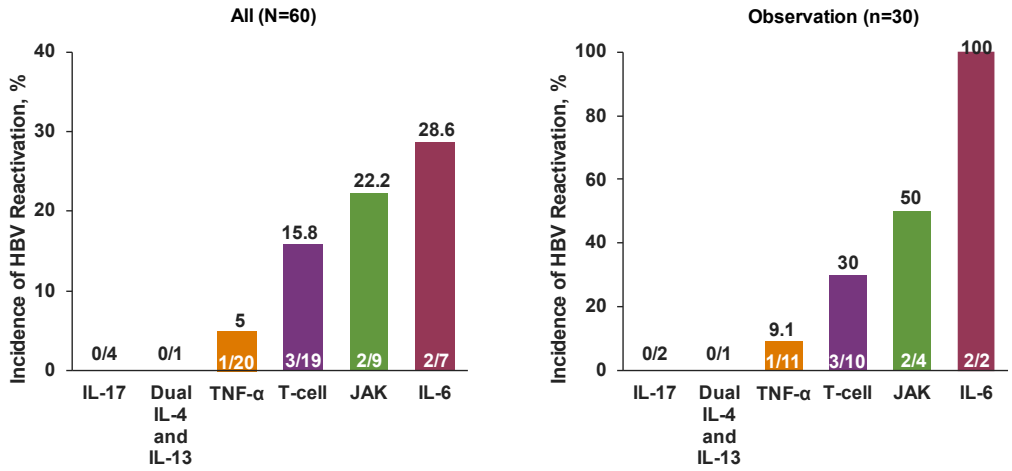
Key Demographics and Characteristics		TAF (n=30)	Observation (n=30)
Age, median (range), years		65 (51–70)	63 (53–71)
Female, n (%)		22 (73.3)	25 (83.3)
HBV DNA level, median (range), IU/mL		124 (26–363)	817 (168–14,300)
HBV DNA level ≥2000 IU/mL, n (%)		6 (20)	12 (40)
HBsAg, median (range), IU/mL		394.59 (40.245–1016.95)	156.167 (20.75–735.018)
HBeAg+ status, n (%)		0	0
ALT level, median (range), U/mL		20 (14–24)	19 (14–30)
Total bilirubin level, median (range), mg/dL		0.5 (0.41–0.74)	0.46 (0.4–0.58)
Biologic DMARD type,[a] n (%)	TNF-α	9 (30)	11 (36.7)
	T-cell	9 (30)	10 (33.3)
	JAK	5 (16.7)	4 (13.3)
	IL-6	5 (16.7)	2 (6.7)
	IL-17	2 (6.7)	2 (6.7)
	Dual IL-4 and IL-13	0	1 (3.3)

[a]The listed biologic DMARD types are targeted inhibitors.

Interim results

The incidence of HBV reactivation was 0% (n/N=0/30) in the prophylactic TAF arm and 26.7% (n/N=8/30) in the observation arm within 48 weeks (*P*=0.005). The median (range) time to HBV reactivation in the observation arm was 31.5 (11.4–48.5) weeks. The incidence of HBV reactivation was higher in participants treated with IL-6, JAK, and T-cell inhibitors than in participants treated with other biologic DMARDs (Figure 3). As a result of the reactivation cases in the observation arm, there will be no further enrollment in this study.

Figure 3. Incidence of HBV Reactivation by Biologic DMARD Type[a] (Huang et al)[3]



[a]Biologic DMARD types are targeted inhibitors.

Retrospective Taiwanese Study in HBsAg+ Patients Undergoing Chemotherapy[4]

Study design and demographics

A retrospective analysis was conducted in Taiwan that compared the efficacy and renal safety of ETV, TDF, and TAF during chemotherapy in patients diagnosed with cancer who were HBsAg+ (N=970). Achievement of undetectable HBV DNA was considered a virologic response. SCr levels were monitored over 1 year while patients received chemotherapy.

Table 5. Baseline Disease Characteristics (Lee et al)[4]

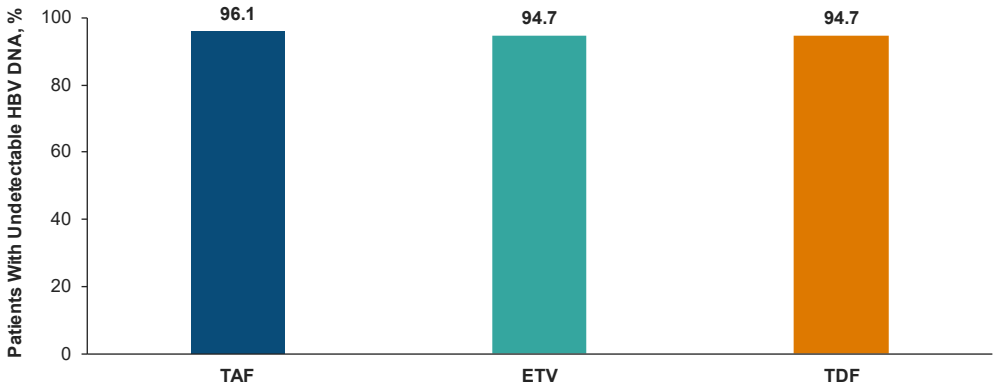
Key Characteristics	TAF (n=188)	ETV (n=582)	TDF (n=200)
NUC duration, mean ± SD, months	10±4	17±13	13±9
Ongoing NUC therapy, n (%)	122 (65)	162 (28)	7 (4)
Follow-up period, mean ± SD, months	12±3	23±16	25±16
HBV DNA, mean ± SD, log IU/mL	2.9±1.9	3±1.7	2.8±1.6
Undetectable HBV DNA, n (%)	53 (31)	134 (24)	49 (26)
HBeAg+, n (%)	11 (5.9)	32 (5.5)	5 (2.5)
eGFR, mean ± SD, mL/min	85±23	81±23	87±19
Chronic kidney disease stage, 1/2/3/4/5, %	59/31.9/8/1.1/0	49.8/37.5/10.8/1.2/0.7	59.5/37.5/3/0/0

Abbreviation: NUC=nucleos(t)ide analogue.

Efficacy

The virologic response rates at Year 1 were similar among patients who received TAF, ETV, or TDF (Figure 4), and HBV reactivation was infrequent (TAF, 0; ETV, 2 [0.5%]; TDF, 1 [0.7%]). The majority of patients who switched from TDF to TAF during chemotherapy maintained virologic response after they switched.

Figure 4. Virologic Response Rate at Year 1 (Lee et al)[4]

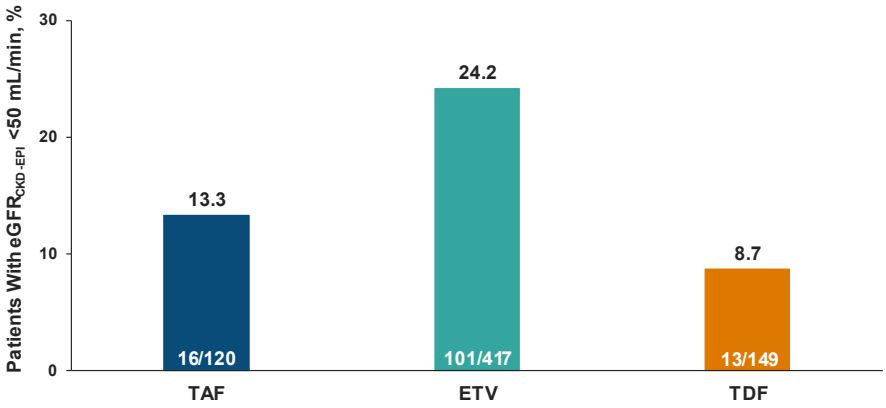


Note: For comparisons between all groups, *P*=0.877.

Renal safety

There was a significant difference among treatment groups in the proportion of patients who had an $eGFR_{CKD\text{-}EPI}$ <50 mL/min at Year 1 (*P*<0.001; Figure 5). Patients who switched from TDF to TAF during chemotherapy maintained stable eGFR levels.

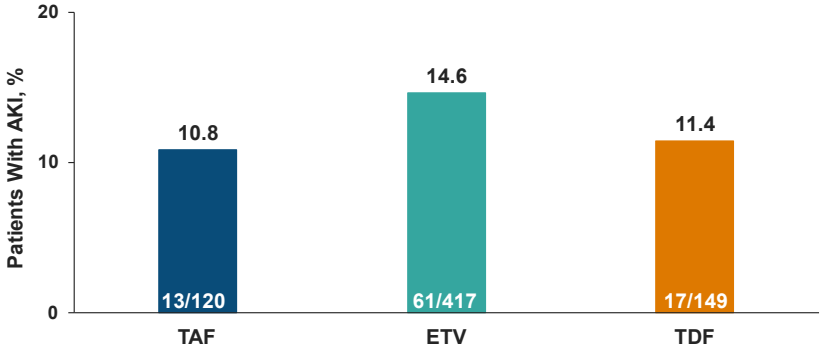
Figure 5. Patients With $eGFR_{CKD\text{-}EPI}$ <50 mL/min at Year 1 (Lee et al)[4]



Note: For comparisons between all groups, *P*<0.001.

The occurrence of AKI was not significantly different among treatment groups (*P*=0.42; Figure 6).

Figure 6. Patients With AKI at Year 1 (Lee et al)[4]



Note: For comparisons between all groups, *P*=0.42.

A multivariate analysis found that the use of a cisplatin-containing regimen and baseline albumin, SCr, and total bilirubin levels were independent predictors of AKI during chemotherapy (Table 6). Antiviral therapy was not significantly associated with the occurrence of AKI in this analysis.

Table 6. Predictors of AKI Using a Multivariate Analysis (Lee et al)[4]

Variable	Hazard Ratio	95% CI	*P*-Value
Cisplatin-containing regimen	1.437	1.072–1.925	0.015
SCr level, mg/dL	1.384	1.164–1.646	<0.001
Albumin level, g/dL	0.544	0.426–0.696	<0.001
Total bilirubin level, mg/dL	1.449	1.002–2.096	0.049

Observational Study of TAF as Prophylaxis Against HBV Reactivation[5]

Study design and demographics

A multicenter, observational study evaluated the efficacy and safety of TAF as prophylaxis against HBV reactivation (defined as HBsAg+ and/or the presence or elevation of HBV DNA) in patients who were receiving chemotherapy or immunosuppressive therapy. At the initiation of chemotherapy or immunosuppressive therapy, patients received TAF for prophylaxis at a dose of 25 mg/day.

Of the 326 patients with HBV infection and benign or malignant diseases who received TAF as prophylactic treatment, those with ≥6 months of follow-up (n=158) were included in the analysis; among these patients, the mean (SD) follow-up period was 17.1 (7.8) months.

Table 7. Baseline Demographics and Disease Characteristics (Gunduz et al)[5]

Key Demographics and Characteristics		TAF (n=156)
Age, mean ± SD, years		59.55±12.2
Male, n		83
Detectable HBV DNA, n		30
HBeAg+ status, %		5
Primary disease, %	Solid tumors	33.5
	Rheumatic diseases	32.9
	Myeloproliferative diseases	32.2
Chemotherapy or immunosuppressive therapy received, %	Cytotoxic chemotherapy	48
	B cell-depleting therapy	17
	Anti-TNF therapy	13
	Other treatments	12
	Glucocorticoid therapy	8
TN/TE, n		118/40[a]

[a]Poster value corrected based on author communication.

Results

During the follow-up period, no patients experienced HBV reactivation or HBV-related morbidity or mortality, and 77% of the 30 patients with detectable HBV DNA at baseline later had undetectable HBV DNA. No interruptions to chemotherapy or immunosuppressive therapy were reported.

TAF as prophylaxis against HBV reactivation was well tolerated, and no serious AEs were reported. Renal function did not change significantly from baseline to the Month 24 end of follow-up period. Although ALT and serum phosphate levels changed significantly from baseline at one or more time points during follow-up in TN patients, changes were not statistically significant at 24 months. Similar findings occurred with fasting glucose in both TN and TE patients. In terms of lipid profile, only TG levels were significantly elevated from baseline at 6 and 24 months in TN patients (Table 8).

Table 8. Laboratory Results (Gunduz et al)[5]

	Baseline	6 Months	12 Months	18 Months	24 Months
TN (n=118)					
ALT, mean ± SD, IU/L	34.38±67.32	24.48±21.7[a]	27.01±36.85	–	30.07±30.22
Blood PO_4, mean ± SD, mg/dL	3.52±0.81	3.4±0.71	3.29±0.61[a]	3.36±0.59	3.34±0.64
GFR, mean ± SD, mL/min	83.23±26.46	84.23±23.66	82.86±26.09	84.05±27.77	91.53±27.28
TC, mean ± SD, mg/dL	200.48±55.05	199.48±49.99	222.27±50.05	236.75±99.99	252.25±91.99
TG, mean ± SD, mg/dL	147.46±90.11	179.3±111.7[a]	165.17±106.72	168.9±95.53	168.7±77.73[a]
HDL, mean ± SD, mg/dL	46.15±14.54	45.57±11.49	53.05±16.29	54.57±20.94	60.13±21.66
LDL, mean ± SD, mg/dL	125.79±43.82	119.53±35.26	146.63±39.81	149.33±90.73	140.5±91.32
FBG, mean ± SD, mg/dL	110.73±37.06	117.57±37.68	122.87±61.55[a]	112.41±38.09	102.95±22.54
TE (n=24)[b]					
ALT, mean ± SD, IU/L	24.23±12.24	28.81±28.65	57.33±85.63	–	61±57.04
Blood PO_4, mean ± SD, mg/dL	3.34±0.77	3.51±0.71	3.02±0.63	3.31±0.97	3.08±0.71
GFR, mean ± SD, mL/min	82.68±23.68	83.97±23.13	83.89±23.39	78.59±30.48	100.7±12
TC, mean ± SD, mg/dL	203±48.85	199.5±50.2	183.33±29.74	208±0	216.5±12.02
TG, mean ± SD, mg/dL	141.44±75.16	142.64±39.55	116.33±30.24	156±0	141.5±20.51
HDL, mean ± SD, mg/dL	47.63±17.9	46.5±10.33	63.33±22.05	69±0	62.5±9.19
LDL, mean ± SD, mg/dL	122.67±38.16	124.49±36.84	105±20.66	136±0	139±4.24
FBG, mean ± SD, mg/dL	93.81±13.07	122.89±41.79[a]	105±37.09	107.5±46.48	91.67±17.36

Abbreviations: FBG=fasting blood glucose; PO_4=phosphate; TC=total cholesterol.
[a]Comparison to baseline value(s) was statistically significant.
[b]Results based only on 24 patients who switched from TDF to TAF.

Retrospective Japanese Case Series Analysis[6]

Study design and demographics

A retrospective case series analysis was conducted in Japan (N=77) from January 2010 to June 2020 to evaluate the safety and efficacy of TAF (n=11) compared to ETV (n=66) as prophylaxis against or treatment for HBV reactivation during chemotherapy or immunosuppressive therapy.

Table 9. Baseline Demographics and Disease Characteristics (Inada et al)[6]

Key Demographics and Characteristics	TAF (n=11)	ETV (n=66)
Age, median (range), years	69 (52–81)	68 (39–87)
Male, n	7	34
HBV carrier/previous infection, n	7/4	50/16
ALT, median (range), U/mL	17 (11–1489)	18.5 (7–1363)
HBeAg status, +/-/missing, n	2/8/1	9/44/13
HBsAg, median (range), IU/mL	398.66 (90,005–113,000)	280 (0–24,114.97)

Key Demographics and Characteristics		TAF (n=11)	ETV (n=66)
Treatment duration, median (range), days		216 (128–567)	1120 (126–3278)
Original disease, n	Malignant lymphoma	3	16
	Other cancer	5	29
	Other (rheumatoid arthritis, etc)	3	21
Purpose of treatment: prevention/reactivation/de novo hepatitis, n		8/3/2	50/16/4
ALT, median (range), U/mL		17 (11–1489)	18.5 (7–1363)
eGFR, median (range), mL/min/1.73 m^2		70.9 (35.3–99.3)	72.9 (4.1–129.5)

Efficacy

Treatment with TAF was successful in suppressing HBV reactivation in the 8 patients receiving prophylaxis (Table 10). The remaining 3 patients were treated for HBV reactivation (2 of these patients had de novo hepatitis with ALT flare). In these patients, treatment with TAF resulted in a significant decrease in serum HBV DNA from Week 0 to Week 24 (mean ± SD, 3.34±2.98 and 0.29±0.96 log IU/mL, respectively; *P*=0.005). The decrease in HBV DNA was similar between the ETV and TAF groups (mean ± SD, -2.83±1.45 vs -3.04±2.47, respectively; *P*=0.857), and by Week 24, a similar proportion of TAF- and ETV-treated patients achieved undetectable HBV DNA (ETV, 78.8%; TAF, 90.9%; *P*=0.681).

Table 10. Background and Clinical Course of Patients Who Received TAF for HBV Reactivation Prophylaxis While on Chemotherapy or Immunosuppressive Therapy (Inada et al)[6]

Pt #	Disease	Chemotherapy or Immunosuppressive Therapy	HBV Status at Baseline	Purpose of TAF Treatment	Outcome
1	Malignant lymphoma	R-CHOP	Previous infection	Reactivation with ALT flare	No recurrence Chemotherapy free TAF treatment in progress
2	Malignant lymphoma	R-CHOP	Previous infection	Reactivation with ALT flare	No recurrence Ongoing chemotherapy TAF treatment in progress with a small amount of prednisolone
3	Microscopic polyangiitis	Prednisolone, methotrexate, tacrolimus	Previous infection	Reactivation with ALT flare	No recurrence
4	Malignant lymphoma	R-CHOP	Previous infection	Prophylaxis	No reactivation after temporary HBV DNA elevation due to TAF discontinuation Chemotherapy free TAF treatment in progress after 2 months of cessation
5	Chronic lymphocytic leukemia	R-CHOP	Carrier	Prophylaxis	No reactivation Chemotherapy free TAF treatment in progress

Pt #	Disease	Chemotherapy or Immunosuppressive Therapy	HBV Status at Baseline	Purpose of TAF Treatment	Outcome
6	Chronic lymphocytic leukemia	Rituximab, pirarubicin, cyclophosphamide, vincristine, prednisolone	Carrier	Prophylaxis	No reactivation Ongoing chemotherapy TAF treatment in progress
7	Cholangio-cellular carcinoma	Gemcitabine, cisplatin	Carrier	Prophylaxis	No reactivation Ongoing chemotherapy TAF treatment in progress
8	Lung cancer	Tegafur/uracil	Carrier	Prophylaxis	No reactivation Ongoing chemotherapy TAF treatment in progress
9	Breast cancer	Adriamycin, cyclophosphamide	Carrier	Prophylaxis	No reactivation Ongoing chemotherapy TAF treatment in progress
10	Rheumatoid arthritis	Methotrexate, prednisolone	Carrier	Prophylaxis	No reactivation Ongoing chemotherapy TAF treatment in progress
11	Sudden sensorineural hearing loss	Prednisolone	Carrier	Prophylaxis	No reactivation Chemotherapy free TAF treatment in progress

Abbreviations: Pt=patient; R-CHOP=rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone.

Renal safety

There was no significant decrease in eGFR in patients who had received TAF (mean ± SD, 72.2±19 and 68.6±18.2 mL/min/1.73 m^2 at Week 0 and Week 24, respectively, *P*=0.185). Additionally, there was no significant difference in the decrease in eGFR between the ETV and TAF groups (mean ± SD, -0.62±11.22 vs -3.67±13.19; *P*=0.291).

Clinical Practice Guidelines on TAF as Prophylaxis to Prevent HBV Reactivation

Table 11. Summary of Clinical Guidelines: AASLD, AGA, EASL, BMT, ASCO, NCCN, and ECIL-9[7-14]

	Prophylactic Antiviral Therapy	Duration of Prophylaxis After Completion of an Immunosuppressive Regimen	Recommended Agents
AASLD[7]	• Recommended for HBsAg+, HBcAb+ patients before immunosuppressive or cytotoxic therapy • HBsAg-, HBcAb+ patients: monitor for ALT, HBV DNA, and HBsAg with the intent of on-demand therapy, except for patients who are receiving anti-CD20 antibody therapy or undergoing SCT, for whom anti-HBV prophylaxis is recommended	≥6 months (or 12 months for patients receiving anti-CD20 therapies)	ETV, TDF, or TAF

	Prophylactic Antiviral Therapy	Duration of Prophylaxis After Completion of an Immunosuppressive Regimen	Recommended Agents
AGA[10]	• Antiviral prophylaxis is strongly recommended prior to immunosuppressive therapy in patients with a high (>10%) risk of reactivation • Antiviral prophylaxis is conditionally recommended in patients with a moderate risk of HBV resistance. Active monitoring may be pursued instead if the patient prefers to avoid long-term antiviral use and their associated costs.	≥6 months (≥12 months in patients receiving B cell-depleting therapies)	Antiviral agents with a high barrier to resistance
EASL[11]	• HBsAg+ patients at high (>10%) or moderate risk (1–10%) • HBsAg-, HBcAb+ at high or moderate risk of HBV reactivation and detectable HBV DNA • HBsAg-, HBcAb+ patients with undetectable HBV DNA at high risk of reactivation	≥6–12 months (≥18 months in high-risk populations, eg, patients receiving B cell-depleting therapies) Treatment discontinuation should follow established criteria for withdrawal, particularly in patients with detectable HBV DNA prior to starting antiviral therapy	ETV, TDF, or TAF
BMT[8]	• HCT recipients who are HBsAg+, HBcAb+ and have detectable HBV DNA • HCT candidates who are HBsAg+ and/or have detectable HBV DNA: start prophylaxis 3 to 6 months before HCT (if HCT is not urgent) • HCT candidates who are HBsAg-, HBcAb+ with detectable HBV DNA	6 months for autologous or allogeneic HCT; longer for patients with GVHD	LAM
ASCO[12]	• Recommended for HBsAg+, HBcAb+ patients before immunosuppressive or cytotoxic therapy • HBsAg-, HBcAb+ patients with high risk of reactivation • HBsAg-, HBcAb+ patients: monitor for ALT, HBV DNA, and HBsAg with the intent of on-demand therapy, except for patients who are receiving anti-CD20 antibody therapy or undergoing SCT, for whom anti-HBV prophylaxis is recommended	≥6 months after stopping therapy (≥12 months in patients who are receiving anti-CD20 monoclonal antibodies)	ETV, TDF, or TAF

	Prophylactic Antiviral Therapy	Duration of Prophylaxis After Completion of an Immunosuppressive Regimen	Recommended Agents
NCCN[13]	• Considered in HBsAg+, HBcAb+ patients with high risk of reactivation and planned allogeneic HCT or B-cell–depleting therapy • HBsAg+, HBcAb+ patients with planned HCT and active HBV infection: antiviral therapy should be given for 3–6 months prior to conditioning • HBsAg+, HBcAb+ patients with planned HCT without active HBV infection: antiviral prophylaxis should be considered and started shortly before transplantation	≥6–12 months after stopping therapy	ETV, tenofovir
ECIL-9[9]	Antivirals should be given on Day 1 of treatment in: • HBsAg+ patients undergoing treatment with anti-CD 20, 38 or 19 antibodies; CAR-T therapy; chemotherapy; anti-TNF; corticosteroids; TKIs; ICIs; methotrexate or allogenic HCT • HBsAg-, HBcAb+ patients undergoing treatment with anti-CD 20, 38 or 19 antibodies; immunotherapy; CAR-T therapy; or allogenic HCT	Treatment with antivirals should be continued until complete remission of underlying disease is confirmed	ETV, TDF, or TAF

Abbreviations: AGA=American Gastroenterological Association; ASCO=American Society of Clinical Oncology; BMT=*Bone Marrow Transplant*; CAR-T=chimeric antigen receptor T-cell therapy; CD=cluster-of-differentiation; EASL=European Association for the Study of the Liver; ECIL-9=Ninth European Conference on Infections in Leukaemia; GVHD=graft-versus-host disease; HBcAb=hepatitis B core antibody; HCT=hematopoietic cell transplantation; ICI=immune checkpoint inhibitor; LAM=lamivudine; NCCN=National Comprehensive Cancer Network; SCT=stem cell transplantation; TKI=tyrosine kinase inhibitor.

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Abbreviations

AASLD=American Association for the Study of Liver Diseases
AE=adverse event
AKI=acute kidney injury
CHB=chronic hepatitis B
CKD-EPI=Chronic Kidney Disease Epidemiology Collaboration equation
DMARD=disease-modifying antirheumatic drug
ETV=entecavir
HBeAg=hepatitis B envelope antigen
HBsAg=hepatitis B surface antigen
IL=interleukin
JAK=Janus kinase
RCT=randomized controlled trial
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TE=treatment-experienced
TG=triglycerides
TN=treatment-naïve
TNF=tumor necrosis factor
ULN=upper limit of normal

Product Label

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