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Safety and Effectiveness of Tenofovir Alafenamide in the Turkish Population: A Systematic Review

Tenofovir Alafenamidin Türk Popülasyonunda Güvenliği ve Etkinliği: Sistematik İnceleme

Fehmi Tabak[1], Suna Yapalı[2], Mustafa K. Çelen[3], Rahmet Güner[4]

[1]*İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Infectious Diseases, İstanbul, Turkey*
[2]*Acıbadem University Faculty of Medicine, Department of Gastroenterology, İstanbul, Turkey*
[3]*Dicle University Faculty of Medicine, Department of Infectious Diseases, İstanbul, Turkey*
[4]*Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara City Hospital, Clinic of Infectious Diseases, Ankara Turkey*

ABSTRACT

Hepatitis B virus infection is an important public health problem in the world and in Turkey. Nucleoside analogues and pegylated interferon-α are used as therapeutic agents in the management of chronic hepatitis B (CHB) infection. With current treatments, the disease is at a controllable point. Unfortunately, although cure studies continue, the cure treatments in the near future will not be an alternative. Tenofovir disoproxil fumarate (TDF) has been used for the treatment of CHB infection since 2008. Beside its high antiviral activity and lack of resistance, long-term use of TDF may lead to a decline in renal functions and bone mineral density. As a prodrug, tenofovir alafamide (TAF) provides considerable reduction (%90) in systemic exposure to tenofovir and has a better safety profile. TAF was used in some special cases (osteoporosis and decreased renal functions) in Turkey. In 2020, TAF was reimbursed for naive and treatment-experienced patients CHB patients. Evidence for the efficacy and safety of TAF continues to accumulate at an accelerating rate, especially following removal of reimbursement restrictions in 2020. In this review, we aim to summarize the real-world evidence obtained about TAF treatment in the last two years in Turkey.

Keywords: Chronic HBV infection, efficacy, tenofovir alafenamide

ÖZ

Hepatit B virüsü enfeksiyonu dünyada ve Türkiye'de önemli bir halk sağlığı sorunudur. Nükleosid analogları ve pegile interferon-α, kronik hepatit B (KHB) enfeksiyonunun tedavisinde terapötik ajanlar olarak kullanılır. Mevcut tedavilerle hastalık kontrol edilebilir bir noktaya geldi. Ne yazık ki kür çalışmaları devam etse de yakın gelecekte kür tedavileri alternatif olamayacaktır. Tenofovir disoproksil fumarat (TDF), 2008'den beri KHB enfeksiyonunun tedavisinde kullanılmaktadır. Yüksek antiviral aktivitesi ve direnç eksikliğinin yanı sıra TDF'nin uzun süreli kullanımı böbrek fonksiyonlarında ve kemik mineral yoğunluğunda azalmaya neden olabilir. Bir ön ilaç olarak tenofovir alafamid (TAF), tenofovire sistemik maruziyette önemli ölçüde azalma (%90) sağlar ve daha iyi bir güvenlik profiline sahiptir. Türkiye'de bazı özel durumlarda (osteoporoz ve böbrek fonksiyonlarında azalma) TAF kullanılmıştır. 2020 yılında TAF'ye, daha önce tedavi görmemiş ve tedavi deneyimi olan KHB hastaları için geri ödeme yapılmıştır. TAF'nin etkinliği ve güvenliğine ilişkin kanıtlar, özellikle 2020'de geri ödeme kısıtlamalarının kaldırılmasının ardından artan bir hızla birikmeye devam ediyor. Bu derlemede Türkiye'de son iki yılda TAF tedavisine ilişkin elde edilen gerçek dünya kanıtlarını özetlemeyi amaçladık.

Anahtar Kelimeler: Kronik HBV enfeksiyonu, etkililik, tenofovir alafenamid

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Address for Correspondence: Fehmi Tabak MD, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Infectious Diseases, İstanbul, Turkey
E-mail: fehmitabak@yahoo.com **ORCID ID:** orcid.org/0000-0001-8632-2825 **Received:** 08.08.2023 **Accepted:** 01.09.2023

Introduction

Hepatitis B virus (HBV) infection remains a healthcare challenge affecting more than 250 million people worldwide (1). Turkey has a significant HBV burden with a prevalence of 4.57% (2,3). The main goals of HBV therapy are to prevent the development of cirrhosis, hepatic decompensation, hepatocellular carcinoma, and death from HBV-related liver disease through the suppression of viral replication (4). Nucleoside analogues (NAs) and pegylated interferon-α are used as therapeutic agents in the management of chronic hepatitis B (CHB) infection (1).

NAs suppress viral replication in the longterm and improve liver-related outcomes. Tenofovir disoproxil fumarate (TDF) has been used for the treatment of CHB infection since 2008. In addition to its high antiviral activity and lack of resistance, TDF may have a negative impact on renal and bone metabolism (1,5). As a prodrug, tenofovir tenofovir alafenamide (TAF) provides considerable reduction (90%) in systemic exposure to tenofovir and has a better safety profile (6).

TAF was first included in the reimbursement list with a restriction on its use for the treatment of CHB patients with renal and bone conditions or with other comorbidities in Turkey in 2018 (7). Evidence for the efficacy and safety of TAF continues to accumulate at an accelerating rate, especially following the removal of reimbursement restrictions in 2020. In this review, we summarize the real-world evidence obtained regarding TAF treatment in the last two years in Turkey.

Materials and Methods

Search Strategy

The search strategy consisted of searching PubMed, Scopus, Web of Science, Google Scholar, and abstracts from five major liver meetings and congresses (The National Viral Hepatitis Congress, The National Hepatology Congress, The Gastroenterology Week, and AASLD-TASL Digital Hepatology Connect and AASLD Liver Meeting) between January 1, 2020 and December 30, 2021. Because the restrictions of TAF use only in patients with renal and/or bone issues were omitted in 2020, data from 2020 and 2021 were used. Reports describing the use of TAF were included. The titles and abstracts were screened to detect the relevance of the study, and the full texts of the relevant studies were obtained and reviewed. Search strings for hepatitis, HBV, tenofovir alafenamide, TAF, Turkey, and Türkiye were used. The references of the cited articles were searched for additional articles that may have been missed. The data in this review are reported according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (8) (Figure 1).

Results

A search of medical literature yielded 11 studies from Turkey (9, 10,11,12,13,14,15,16,17,18,19,20).

Treatment-naive Cases

Three studies presented treatment effectiveness and/or safety characteristics of treatment-naive patients given TAF (9,10,11) (Table 1).

Biological and chemical response: Clinical effectiveness in treatment-naive cases was examined in only two meeting abstracts. Tabak et al. (9) presented the percentage of cases with undetectable HBV-DNA (<20 IU/mL) and normal alanine transaminase (ALT) levels (<35 IU/L for men, <25 IU/L for women) in three consecutive moments (baseline, 3rd, and 6th month). The percentage of cases with normal ALT levels rose from approximately 40% to approximately 80%. In addition, HBV-DNA became undetectable in 89.1% of cases. Türker et al. (10) reported 89.1% and 80% virologic and biochemical responses.

Safety outcomes: Three studies reported safety outcomes (9,10,11) (Table 2). Tabak et al. (9) and Türker et al. (10) reported no significant difference in renal function. Karasahin et al. (11) showed a significant increase in estimated glomerular filtration rate (eGFR) in the 3rd month and then regressed to its baseline level in the 6th month.

The lipid profile was examined in two studies (9,10). Total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein cholesterol, and triglyceride levels did not change significantly.

Treatment-experienced Cases

In treatment-experienced cases, TDF was the leading agent in their treatment history. Investigators reported that approximately 70-80% of cases switched to TAF from TDF. In Table 3, 4, baseline characteristics and efficacy and safety endpoints of TAF cases are given, respectively.

Biological and chemical response: Although investigators did not share the statistical significance, it could be observed in the numerical increase in viral suppression and ALT normalization. Virologic response increased from approximately 70% to 80% 12 months after switching to TAF.

Safety outcomes: Renal function remained stable in three studies (9,12,13). Kalkan et al. (15) reported a marked statistically significant improvement in renal function.

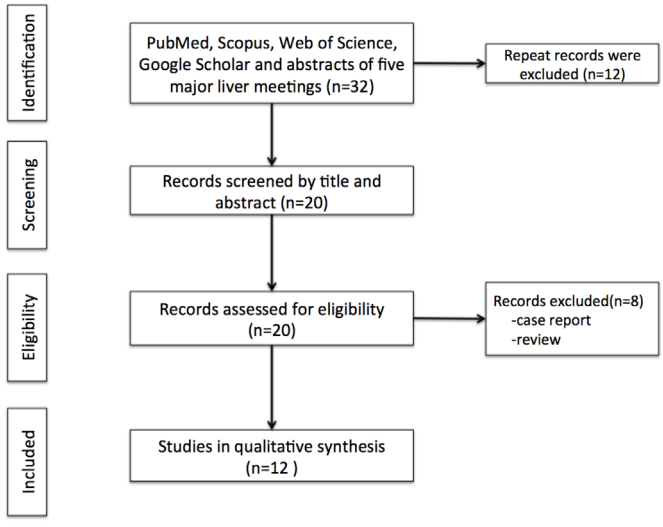

Figure 1. PRISMA flow diagram of literature review process for the studies of tenofovir alafenamide use in Turkey

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Table 1. Baseline characteristics and treatment effectiveness of the treatment-naive patients given tenofovir alafenamide

References	Baseline characteristics							Treatment effectiveness							
								HBV-DNA <20 IU/mL, %				Normal ALT (%)**			
	n	Median age (years)	Gender (male, n,%)	ALT (IU/L, median)	HBeAg-negative (n, %)	Fibrosis (median)	HAI (median)	Baseline	6th months	12th months	p	Baseline	6th months	12th months	p
Tabak et al. (9)	71	48	35 (48.5)	33	43 (84.3)	2	7		79.4	84.7		45.9	76.3	77.8	
Türker et al. (10)	202	50	122 (60.4)	40	118 (80.3)	2	7		74.7	89.1		38.2	73.2	80.0***	<0.05
Karasahin et al. (11)	105	58	68(64.8)												

*Based on Ishak's scoring, **<35 IU/L for male, <25 IU/L for female. ***p<0.05, HAI: Histologic activity index

Table 2. Safety outcomes of the treatment-naive patients given tenofovir alafenamide*

References	Parameter	Baseline	3rd months	6th months	12th months	p
Tabak et al. (9)	HDL, mg/dL, median (SD)	65 (35.0)		110 (37.1)	96 (26.9)	>0.05
	LDL, mg/dL, median (SD)	99 (39.9)		90 (29.9)	88 (24.7)	>0.05
	Cholesterol, mg/dL, median (SD)	202 (46.1)		226 (28.0)	212 (67.2)	>0.05
	Triglyceride, mg/dL, median (SD)	134.5 (88.3)		184 (56.4)	156 (48.8)	>0.05
	Creatinine, mg/dL	0.80		0.97	0.78	
	eGFR, mL/min	90.5		89.5	101	
Türker et al. (10)	HDL, mg/dL, median (SD)	53 (27.3)		52 (32.2)	56 (34.6)	>0.05
	LDL, mg/dL, median (SD)	107 (37.3)		100 (37.2)	97 (31.1)	>0.05
	Cholesterol, mg/dL, median (SD)	189 (59.1)		208 (41.7)	166 (28.2)	>0.05
	Triglyceride, mg/dL, median (SD)	103 (66.2)		142.5 (75.3)	146 (63.4)	>0.05
	Creatinine, mg/dL	0.80		0.89	0.85	
	eGFR, mL/min	99		95	94	
Karasahin et al. (11)**	eGFR, mL/min, (n=5)	67.60 (41.04)	76.40 (41.04)	67.20 (40.64)		<0.001
	Phosporus, mg/dL, (n=4)	3.68 (1.83)		3.59 (1.73)		0.115
	T-score, hip, (n=1)	-1.2		NA		
	T-score, spine, (n=1)	-2.6		NA		

*Baseline characteristics of these patients were given in Table 1. **This study includes 105 patients: median age 58 years, male 68 (64.8%), osteoporosis 11 (12.6%), cirrhosis 48 (49.5%), haemodialysis 5 (4.9%), solid organ transplantation 48 (49%), steroid use 78 (74.3%). HDL: High-density lipoprotein, LDL: Low-density lipoprotein, SD: Standard deviation, eGFR: Estimated glomerular filtration rate, NA: Not available

Table 3. Baseline characteristics and treatment effectiveness of the treatment-experienced patients switched to tenofovir alafenamide

Referefences	Baseline characteristics										Treatment effectiveness							
											Normal ALT (%)**				Undetectable HBV-DNA (%)			
	n	Age (years, median)	Gender (male, n, %)	ALT (U/L, median)	HBeAg positive (n,%)	Fibrosis*	HAI*	Previous treatment (%)	Duration of previous treatment (months, median)	Reason to switch	Baseline	6 months	12 months	p	Baseline	6 months	12 months	p
Sarı et al. (12)	391	44	235 (60)	23	238 (85)	2	7	TDF: 81.6, ETV: 8.2, LAM: 6.1, TEL: 2.9, ADV: 1.1			71.6	81.5	83.9		80.7	79.4	84.7	
Tabak et al. (9)	504	54	288 (59.1)	22.5	345 (86.5)	2	7	TDF: 83.9, ETV: 6.9, LAM: 5.6, TEL: 2.8, ADV: 0.8	52	GFR 61 (12.1), proteinuria/ albuminuria 49 (9.7), transplantation 11 (2.2), steroids 6 (1.2), fractures 2 (0.4), hemodialysis 2 (0.4)	72.3	79.1	80.0		79.4	90.2	87.0	
Sürme et al. (13)	565	53	336 (59.5)					TDF 83.9, ETV: 7.6, LAM: 5.1, TEL: 2.7, ADV: 0.7	12		71.9	79.1	79.6		78.6	87.8	85.4	
Akar (14)	27	48	16 (59)	51	3 (11)	3	8				7		0		7		0	
Kalkan et al. (15)	237	38	160 (67.5)	33							43.2			48.3	97.2		98.2	1

*Based on Ishak's scoring, **<35 IU/L for male, <25 IU/L for female. ***p<0.05, ALT: Alanine transaminase, HBeAg: Hepatitis B e antigen, HBV: Hepatitis B virus, HAI: Histologic activity index, TDF: Tenofovir disoproxil fumarate, ETV: Entecavir, LAM: Lamivudine, TEL: Telbivudine, ADV: Adefovir

Table 4. Safety characteristics and treatment effectiveness of the treatment-experienced patients switched to tenofovir alafenamide*

Reference	Feature	Baseline	6th months	12th months
Sarı et al. (12)	HDL, mg/dL median (SD)	44.5 (19.1)	44.5 (18.2)	51 (15.3)
	LDL, mg/dL median (SD)	114 (54.5)	132.5 (33.2)	136 (44.1)
	Cholesterol, mg/dL, median (SD)	176 (52.7)	206 (39.1)	199 (52.7)
	Triglyceride, mg/dL, median (SD)	102 (65.4)	125.5 (77.7)	113 (50.9)
	Creatinine, mg/dL	0.86	0.86	0.88
	eGFR, mL/min	92	84.2	87.2
Tabak et al. (9)	Creatinine, mg/dL	0.83	0.86	0.85
	eGFR, mL/min	94	90	86.9
Sürme et al. (13)	Creatinine, mg/dL	0.80	0.89	0.85
	eGFR, mL/min	99.0	95	94
Karasahin et al. (11)*	eGFR, mL/min, (n=105)	99.21 (20.56)	103.41 (19.11)	
	Phosphorus, mg/dL, (n=117)	2.82 (0.44)	2.90 (0.44)	
	T-score hip, (n=78)	-1.57 (0.65)	-1.46 (0.72)	
	T-score, spine, (n=78)	-1.77 (0.83)	-1.50 (1.05)	
Akar (14)	GFR (mL/min), mean ± SD	100 (14)		102 (5)
	Phosphorus (mg/dL), mean ± SD	2.3 (0.4)		2.9 (0.6)
Kalkan et al. (15)	GFR (mL/min), mean,	102.27		**<0.001**
	Phosphorus (mg/dL), mean,	2.82		0.226
	Creatinine (mg/dL), mean	0.90		**0.011**
	T-score hip, mean	-1.74		**0.001**
	T-score, spine, mean	-1.56		0.608
	LDL (mg/dL), mean	101.3		107.9
	HDL (mg/dL), mean	58.6		60.2
	Cholesterol (mg/dL), mean	196.9		204.2
	TG (mg/dL), mean	196.3		196.4

*Baseline characteristics of these patients were given in Table 3. HDL: High-density lipoprotein, LDL: Low-density lipoprotein, eGFR: Estimated glomerular filtration rate, SD: Standard deviation, TG: Triglyceride

Sarı et al. (12) reported a numerical increase in LDL and total cholesterol levels compared with the basal level with no statistical significance.

Cases with Special Health Conditions

Data in this category were reported in six studies (9,16,17,18,19,20) (Table 5).

Biological and chemical response: Three studies (9,16,17) reported TAF prophylaxis in immunosuppressed patients, and no reactivation at 12th month was reported (Table 5).

Similarly, the effectiveness data revealed a high virologic response in patients undergoing chronic hemodialysis and renal transplant.

Safety outcomes: Studies by Gokcan et al. (18) and Yapalı et al. (19) reported no change in lipid profile or renal function.

Discussion

Clinical practice guidelines have proposed the preference of TAF or entecavir (ETV) over TDF in elderly patients and those with a current bone mineral density (BMD) and renal condition (21,22). Recent evidence showed its superiority to ETV in terms of both virological and biochemical responses (23). TAF has been widely used in both treatment-naive and experienced patients, most likely because of its better safety and efficiency profiles.

In treatment-naive patients, the virologic response (having lower HBV-DNA levels, <29 IU/mL) was reported as 94% in hepatitis B e antigen (HBeAg)-negative (24) and 93% in HBeAg-positive cases (25) in phase III studies at the 48th week. In the cohort of Türker et al. (10), the virologic response rate (defined as having lower HBV-DNA levels <20 IU/mL) was reported as 89.1% at the same time point. The proportion of HBeAg-negative cases was 80.3% in this cohort. In these phase III studies, the ALT normalization rate (<30 for men, 19 for women) was reported as 50% in HBeAg-negative and 45% in HBeAg-positive cases. Normalization rate cases having normal ALT levels at the end of the study were reported to be approximately 78-80% (9,10). The observed ALT normalization rate might be considered as a sign of additional benefit of TAF treatment according to the results of studies indicating decreased rates of hepatocellular carcinoma, encephalopathy, and ascites in cases with normal ALT levels (26).

A pooled analysis of phase III studies reported signs of worsening of the lipid profile with TAF, with respect to the observed scores in TDF treatments (6% vs. 1% for LDL >190 mg/dL, 1% vs

Table 5. Characteristics of patients in special groups given tenofovir alafenamide

References	Special group	Indication	n	Age (mean, years)	Male (n, %)	Baseline characteristics	Effectiveness outcome	Safety outcome
Tabak et al. (9)	Immunosuppressed	Prophylaxis	58	57	24 (41.4%),	HBeAg (-) 90.3%, HBsAg (-) 64.3%, median ALT: 20 U/L.	Normal ALT: baseline 74.5%, 6th months 73.5%, 12th months 72%	Cr (mg/dL): baseline 0.97, 6th months 0.85, 12th months 0.77. eGFR (mL/min): baseline 58, 6th months 96, 12th months 92.5
Yörük et al. (16)	Immunosuppressed	Prophylaxis	145	58	67 (46.2%)	HBeAg (-) 92.9%, HBsAg (-) 55.3%,	No reactivation on 12th months Normal ALT: baseline 69%, 6th months 78%, 12th months 72.7%	Cr (mg/dL): baseline 0.97, 6th months 0.89, 12th months 0.77. eGFR (mL/min): baseline 90.5, 6th months 96, 12th months 92.7
Gündüz et al (17)	Immunosuppressed	Prophylaxis	171	60.7	84 (49%)	HBsAg (-) 38%	No reactivation during follow up of 6 months (mean)	The renal function tests and lipid profiles did not significantly change. No serious adverse events were reported at the follow-up.
Gokcan et al. (18)	HBV Cirrhosis	Treatment	34	64	50%	Median ALT: 29 IU/L, median HBV-DNA 6,200 IU/L, 11.8% TAF-naive, 19.7% decompensated	ALT normalized in all cases between 3-12 months. No reactivation. No HBV-related death	TAF was well-tolerated
	Post-transplant HBV	Treatment	76	57	80	Median ALT: 22 IU/L. Tacrolimus use, 90%, everolimus 47%. TAF-naive 22.4%	The virologic and biochemical response was observed in all patients	Renal function tests and lipid profiles remained stable during the treatment. No serious adverse effects were reported.
Yapalı et al. (19)	HBV Cirrhosis	Treatment	72	64	54	Median ALT: 29 IU/L, median HBV-DNA 6,200 IU/L, decompensated cirrhosis 21%, treatment naive 21%, most common indications for TAF: Renal dysfunction, osteoporosis	On 4 months (median) follow up, ALT normalized (>40 IU/L) 90%. No reactivation, no HBV-related death.	Lipid profile and renal functions did not change.
	Post-transplant HBV	Treatment	125	57	78	Median ALT: 23 IU/L, median HBV-DNA 6,200 IU/L, tacrolimus use 78%, everolimus use 38%	On 6 months (median) follow up, no HBV reactivation	Lipid profile and renal functions did not change.
Adanır et al. (20)	HBV Cirrhosis	Treatment	16	54.6	63	Treatment-naive (n=25), TAF-naive (n=12)	Follow up 10.4 months (mean). Among treatment-naive patients, viral and biochemical responses at 12 months: 92% and 96%.	No reactivation
	Post-transplant HBV	Treatment	61	11	31	Tacrolimus use 82%, cyclosporine 23%, everolimus 15%	Follow-up 7 months (mean). In all patients, viral and biochemical responses were obtained on 3 to 12 months.	

HBV: Hepatitis B virus, HBeAg: Hepatitis B e antigen, HBsAg: Hepatitis B surface antigen, ALT: Alanine transaminase, TAF: Tenofovir alafamide, Cr: Creatinine eGFR: Estimated glomerular filtration rate

0% for total cholesterol more than 300 mg/dL) (27). This difference could be a result of high plasma tenofovir levels in TDF-treated patients. In contrast to the relative lowering effect of TDF, Jeong et al. (28) reported no difference in lipid profiles between TAF-treated and non-HBV-infected controls. In addition, in the cohort of Tabak et al. (9), no significant change was reported in total cholesterol and its subfractions over 48 weeks. It could be inferred that these findings support the opinion that changes in lipid levels after TAF switching represents "returning to normal"(6).

While Tabak et al. (9) reported a numerical decrease in serum creatinine level at the 48th week; phase III studies reported serum creatinine level increase as 0.01 mg/dL (0.00 to 0.02) at the same time-point (24,25). In addition, in contrast to findings in phase III studies (-1.8 and-5.4 mL/min median change in GFR, respectively), Tabak et al. (9) reported a numerical increase in GFR at the 48th week compared with baseline (101 vs 90.5). Additionally, Karasahin et al. (11) reported that an emerging numerical increase in GFR (76.40 mL/min) at the 24th week regressed to baseline level at the 48th week (67.60 mL/min vs 67.60 mL/min).

In treatment-experienced patients, according to the reported results from the cohort of Sarı et al. (12), the ALT normalization rate was 83.9% at the 48th week and comparable to that reported (79%) by Lampertico et al. (29) at the same time point. Lampertico et al. (29) and Kalkan et al. (15) reported similar ALT normalization rates at 24th week (48.3%) and 48th week (50%) respectively. ALT normalization rates at the 48th week after switching to TAF were reported from the data of two non-interventional studies as 70.2% (30) and 83% (31).

Changes in renal function have been reported in these cohorts. Karasahin et al. (11), Akar (14) and Kalkan et al. (15) reported an increase in GFR (2-7 mL/min) at different time points. Additionally, Kalkan et al. (15) reported a reduction in creatinine levels (0.05 mg/dL). These findings were similar to those of Lampertico et al. (29) and Byun et al. (32), who reported increases in GFR of +0.94 and +7.3 mL/min, respectively. Interestingly, Lee et al. (33) reported a reduction in GFR (-0.6% at the 24th week, -5.2% at the 72nd week). The majority of data from clinical trials and real-life studies suggest that TAF would be an advantageous choice for treating people with the potential of having or getting renal conditions.

BMD was evaluated as another safety issue by Karasahin et al. (11) and Kalkan et al. (15). Both authors reported improvement in hip and spine T-scores over treatment, and their findings reached statistical significance, except for spine T-scores in the cohort of Kalkan et al. (15). TAF use may be safer in patients with bone disease, especially considering that chronic hepatitis patients are elderly and will get older over a long treatment period.

In the cohort of Sarı et al. (12), a numerical increase in total and subfractions was observed between before and after treatment, but the changes were reported as insignificant. However, Kalkan et al. (15) reported that the observed increase in LDL and total cholesterol reached statistical significance.

As a serious event, HBV reactivation can be prevented by prophylaxis (34). However, the risk of reactivation is overlooked because patients are followed by different clinical departments (35,36). The efficacy of TAF prophylaxis was compared with that of ETV by Inada et al. (37). They found no difference in the HBV-DNA decreasing rate. In addition, they reported no difference in eGFR as a renal safety indicator. Yörük et al. (16) and Gündüz et al. (17) reported no reactivation among immunosuppressed individuals administered TAF for prophylaxis at 12 and 6 months, respectively.

Three studies reported the results of TAF use in post-transplant patients (18,19,20). Gokcan et al. (18) and Adanır et al. (20) reported virologic and biochemical responses in all liver transplant patients within one year. Yapalı et al. (19) described no HBV reactivation at 6 months' follow-up as a response.

Three studies have reported the results of TAF use in cirrhotic patients (18,19,20). Gokcan et al. (18) reported ALT normalization in all cases between 3 -12 months with no reactivation and no HBV-related death. Yapalı et al. (19) reported ALT normalization in 90% of patients in a median follow-up period of 4 months with no reactivation and no HBV-related death, while Adanır et al. (20) described viral and biochemical responses in all patients at 3 to 12 months.

Conclusion

As a prodrug, TAF provides effective viral suppression and ALT normalization. Beyond its antiviral effectiveness, ALT normalization could result in decreased risk of delayed complications, including development of hepatocellular carcinoma, encephalopathy, and esophageal varices. Safety outcomes on bone metabolism and renal functions are encouraging for TAF use in naive cases for chronic use considering the advanced/advancing age of the patients. Real-life efficiency and safety data on its prophylactic or therapeutic use in special groups, including immunosuppressed individuals, post-transplant patients, and cirrhotic patients, support its use.

Ethics

Peer-review: Internally peer reviewed.

Authorship Contributions

Concept: F.T., S.Y., M.K.Ç., R.G., Design: F.T., S.Y., M.K.Ç., R.G., Data Collection or Processing: F.T., S.Y., M.K.Ç., R.G., Analysis or Interpretation: F.T., S.Y., M.K.Ç., R.G., Literature Search: F.T., S.Y., M.K.Ç., R.G., Writing: F.T., S.Y., M.K.Ç., R.G.

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