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Vemlidy® (tenofovir alafenamide) Comparison With TDF

This document is in response to your request for information regarding Vemlidy® (tenofovir alafenamide [TAF]) compared with tenofovir disoproxil fumarate (TDF) for use in patients with chronic HBV (CHB).

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Summary

Clinical Data on TAF vs TDF in Participants With CHB

Phase 3 Studies 108 and 110 compared the efficacy and safety of TAF with TDF in participants with CHB. Participants received DB TAF or TDF for 2 or 3 years, followed by OL TAF for up to 6 years.[1-3]

Week 48 Primary Endpoint:

- TAF was non-inferior to TDF in viral suppression at Week 48 in both TN and TE participants.[1,2]
- The majority of AEs were mild to moderate in severity through Week 48.[1,2]

Year 8 Final Analysis:

- Rates of viral suppression (HBV DNA <29 IU/mL) ranged from 91% to 98% across TAF8y and TDF→TAF treatment arms through Year 8. ALT normalization rates increased after switching from TDF to TAF and were comparable across treatment groups and by HBeAg status.[4]
- HBeAg loss and seroconversion rates progressively increased through Year 8 and were similar in the TAF8y and TDF→TAF arms.[4]
- In resistance testing, 2% of participants (n=29) qualified for sequence analysis. No amino acid substitutions that reduced susceptibility to TAF were detected at Year 8.[4]
- TAF was generally well tolerated, with Grade ≥3 AEs occurring in 8% of participants in the TAF8y arm, 8% in the TDF2y→TAF6y arm, and 6% in the TDF3y→TAF5y arm. Improvements in $eGFR_{CG}$ and changes in BMD and lipid profiles are provided below.[4]
- A subanalysis of bone and renal safety outcomes according to the presence or absence of risk factors for TDF-related toxicities demonstrated stable renal and bone safety findings after treatment with TAF through Year 8.[5]

Real-World Data on TAF vs TDF in Patients With CHB

Over 36 months of treatment, TN patients with CHB who received TAF (n=502) had viral suppression and ALT normalization rates similar to those of patients who received TDF

(n=2245). In general, greater lipid level decreases were observed in the TDF group than in the TAF group.[6]

Clinical Data on TAF vs TDF in Participants With CHB

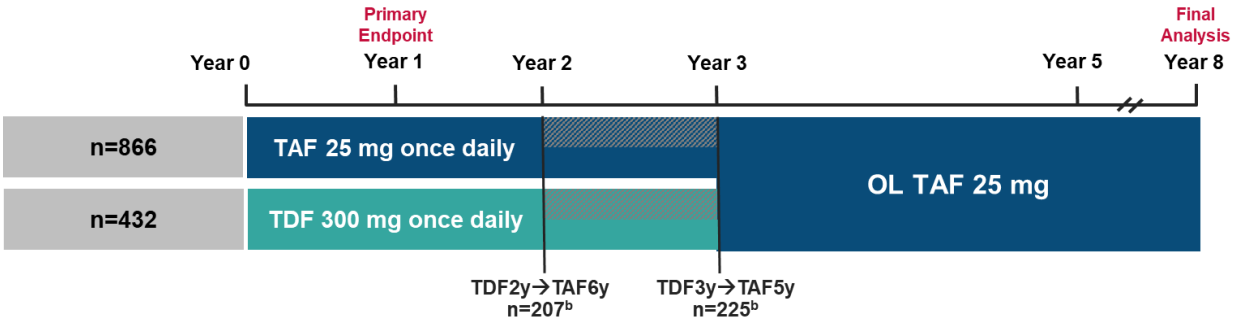
Studies 108 and 110

Study design and demographics

Studies 108 and 110 were phase 3 clinical trials that compared the efficacy and safety of TAF with TDF in predominantly nucleos(t)ide-naïve participants with CHB. A total of 1298 adult, monoinfected participants with compensated liver function were randomly assigned in a 2:1 ratio to receive either DB TAF 25 mg or TDF 300 mg, followed by OL TAF for up to 6 years. Upon completion of the blinded phase, eligible participants from both arms were enrolled into an OL phase and received one of the following: DB then OL TAF for a total of 8 years (TAF8y), DB TDF for 2 years then OL TAF for 6 years (TDF2y→TAF6y), or DB TDF for 3 years then OL TAF for 5 years (TDF3y→TAF5y; Figure 1).[4]

The primary endpoint was the proportion of participants with undetectable HBV DNA (<29 IU/mL) at Week 48. Secondary endpoints included changes in hip and spine BMD, changes in SCr levels, dipstick proteinuria, biochemical response (ALT normalization), serologic response (HBsAg seroconversion), and change in fibrosis measured by FibroTest.[1,2]

Figure 1. Studies 108 and 110: Study Design[4,7a]



[a]Shaded areas represent participants who entered the OL phase of TAF treatment at Year 2 or Year 3.
[b]Number of participants who received DB TDF and switched to TAF.

Table 1. Studies 108 and 110: Baseline Demographics and Disease Characteristics[4]

Key Demographics and Characteristics		TAF (n=866)	Combined TDF→TAF Arms (n=432)
Age, mean (SD), years		40 (11.8)	41 (12.3)
Male, n (%)		544 (63)	275 (64)
Race, n (%)	Asian	687 (79)	333 (77)
	White	167 (19)	87 (20)
BMI, mean ± SD, kg/m^2		24±4.13	24.4±3.95
HBeAg+, n (%)		569 (66)	290 (67)
ALT, median (Q1, Q3), U/L		80 (56, 123)	80 (53, 130)
Prior nucleos(t)ide treatment, n (%)		211 (24)	108 (25)
FibroTest score, n/N (%)	0–0.48 (no/mild)	601/846 (71)	297/421 (71)
	0.49–0.74 (moderate/severe)	169/846 (20)	82/421 (19)
	0.75–1 (cirrhosis)	76/846 (9)	42/421 (10)

Key Demographics and Characteristics	TAF (n=866)	Combined TDF→TAF Arms (n=432)
$eGFR_{CG}$, median (Q1, Q3), mL/min	106 (91, 125)	104.5 (90, 124)
Osteoporosis by hip BMD T-score,[a] n (%)	12 (1)	2 (<1)
Osteoporosis by spine BMD T-score,[a] n (%)	57 (7)	29 (7)
Hyperlipidemia, n (%)	76 (9)	44 (10)

[a]T-score less than -2.5.

Efficacy results through Week 48 (primary endpoint)

TAF 25 mg demonstrated non-inferiority to TDF in viral suppression at Week 48 in both TN and TE adults.[1,2]

Table 2. Studies 108 and 110: Summary of Efficacy Results at Week 48[1,2]

n/N (%) or %	Study 108 (HBeAg-; N=425)			Study 110 (HBeAg+; N=873)		
	TAF (n=285)	TDF (n=140)	*P*-Value	TAF (n=581)	TDF (n=292)	*P*-Value
HBV DNA <29 IU/mL	268/285 (94)[a]	130/140 (92.9)[a]	0.47	371/581 (63.9)[b]	195/292 (66.8)[b]	0.25
Baseline HBV DNA <7 log_{10} IU/mL	221/230 (96)	107/116 (92)	-	-	-	-
Baseline HBV DNA ≥7 log_{10} IU/mL	47/55 (85)	23/24 (96)	-	-	-	-
Baseline HBV DNA <8 log_{10} IU/mL	-	-	-	254/309 (82)	123/150 (82)	-
Baseline HBV DNA ≥8 log_{10} IU/mL	-	-	-	117/272 (43)	72/142 (51)	-
Nucleos(t)ide naïve	212/225 (94)	102/110 (93)	-	302/444 (68)	156/223 (70)	-
Nucleos(t)ide experienced	56/60 (93)	28/30 (93)	-	69/137 (50)	39/69 (57)	-
ALT normalization[c]	50	32	<0.001	45	36	0.014
HBeAg loss	-	-	-	78/565 (14)	34/285 (12)	0.47
HBeAg seroconversion	-	-	-	58/565 (10)	23/285 (8)	0.32
HBsAg loss	-	-	-	4/576 (<1)	1/288 (<1)	0.52
HBsAg seroconversion	-	-	-	3/576 (<1)	0	0.22

[a]Reasons for failure: HBV DNA ≥29 IU/mL (2% TAF, 3% TDF); missing data (<1% TAF, 1% TDF); discontinuation due to AE (1% TAF, 1% TDF); discontinuation for other reasons (2% TAF, 3% TDF).
[b]Reasons for failure: HBV DNA ≥29 IU/mL (31% TAF, 30% TDF); missing data (<1% TAF, 0 TDF); discontinuation due to AE or death (1% TAF, 1% TDF); discontinuation due to any other reason (3% TAF, 2% TDF).
[c]ULN=30 IU/L for males and 19 IU/mL for females.

Safety results through Week 48[1,2]

The majority of AEs in Studies 108 and 110 were mild or moderate in severity. None of the SAEs that occurred were considered to be treatment-related, and study drug discontinuations due to AEs were 1% in both TAF and TDF arms of Studies 108 and 110.

Table 3. Studies 108 and 110: Overall Safety Through Week 48[1,2]

Safety Outcomes, n (%) or n/N (%)	Study 108 (HBeAg-)		Study 110 (HBeAg+)	
	TAF (n=285)	TDF (n=140)	TAF (n=581)	TDF (n=292)
Any AE	210 (74)	99 (71)	398 (69)	192 (66)
Grade 3/4 AE	12 (4)	6 (4)	27 (5)	11 (4)
SAE	14 (5)	9 (6)	22 (4)	12 (4)
Discontinuation due to AE	3 (1)	2 (1)	6 (1)	3 (1)

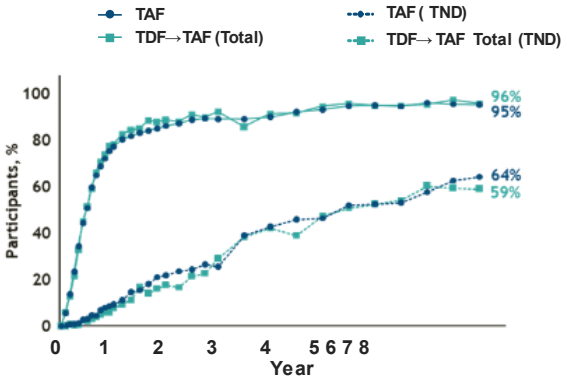
Safety Outcomes, n (%) or n/N (%)		Study 108 (HBeAg-)		Study 110 (HBeAg+)	
		TAF (n=285)	TDF (n=140)	TAF (n=581)	TDF (n=292)
Deaths		0	1 (<1)[a]	1 (<1)[b]	0
AEs in ≥5% of participants in either treatment group	Headache	40 (14)	14 (10)	42 (7)	22 (8)
	URTI	35 (12)	10 (7)	51 (9)	22 (8)
	Nasopharyngitis	30 (11)	15 (11)	56 (10)	16 (5)
	Cough	18 (6)	8 (6)	37 (6)	19 (7)
	Fatigue	16 (6)	9 (6)	33 (6)	14 (5)
	Nausea	15 (5)	9 (6)	NR	NR
	Back pain	14 (5)	7 (5)	NR	NR
	Arthralgia	11 (4)	10 (7)	NR	NR
	Diarrhea	NR	NR	27 (5)	15 (5)
	Upper abdominal pain	NR	NR	19 (3)	15 (5)
Grade 3/4 laboratory abnormalities[c]		82/282 (29)	30/140 (21)	187 (32)	96 (33)
Grade 3/4 laboratory abnormalities in ≥1% of participants in either treatment group[c]	Urine erythrocytes	17/252 (7)	9/127 (7)	42/516 (8)	26/259 (10)
	Occult blood	17 (6)	7 (5)	49 (8)	23/286 (8)
	Urine glucose	15 (5)	2 (1)	26 (5)	3/286 (1)
	Fasting LDL cholesterol >300 mg/dL	14/277 (5)	1/135 (1)	23/560 (4)	0/282
	Amylase >2 × ULN	14 (5)	3 (2)	9 (2)	7/287 (2)
	Non-fasting glucose >250 mg/dL	10 (4)	2 (1)	16/574 (3)	5/287 (2)
	ALT/AST >5 × ULN	8 (3)/8 (3)	4 (3)/4 (3)	62 (11)/20 (3)	36 (13)/19 (7)
	Creatine kinase ≥10 × ULN	7 (2)	3 (2)	18 (3)	10 (3)
	Fasting glucose >250 mg/dL	4/280 (1)	0	NR	NR
	TC >300 mg/dL	3/280 (1)	0	NR	NR
	GGT >5 × ULN	0	3 (2)	3 (1)	3 (1)
	ANC <750 cells/mcL	NR	NR	7 (1)	1/286 (<1)

Abbreviations: ANC=absolute neutrophil count; NR=not reported.
[a]A 51-year-old, male, Asian participant with cirrhosis died due to HCC at Week 56 (non-treatment-emergent).
[b]A 54-year-old, female, Asian participant died due to H1N1 influenza at Week 14 (non-treatment-emergent).
[c]Laboratory abnormality results were based on data from the following number of participants per study, unless otherwise indicated: Study 108, TAF=282 and TDF=140; Study 110, TAF=577 and TDF=288.

Efficacy results through Year 8 (final analysis)

In both studies, rates of viral suppression were high during the DB phase and continued through Year 8 across all treatment arms (Figure 2).[4]

Figure 2. Studies 108 and 110: HBV DNA <29 IU/mL Through Year 8 (M=E Analysis)[4,7]



Abbreviation: TND=target not detected.

Through Year 8, the rates of HBeAg loss and seroconversion progressively increased and were similar among treatment arms (Figure 3). HBsAg loss with or without seroconversion occurred at low rates (2–3%), and 0.9% of participants (12/1298) overall discontinued due to achieving HBsAg seroconversion.[4]

Figure 3. Studies 108 and 110: HBeAg Loss and Seroconversion Through Year 8 (M=E Analysis)[4,7]

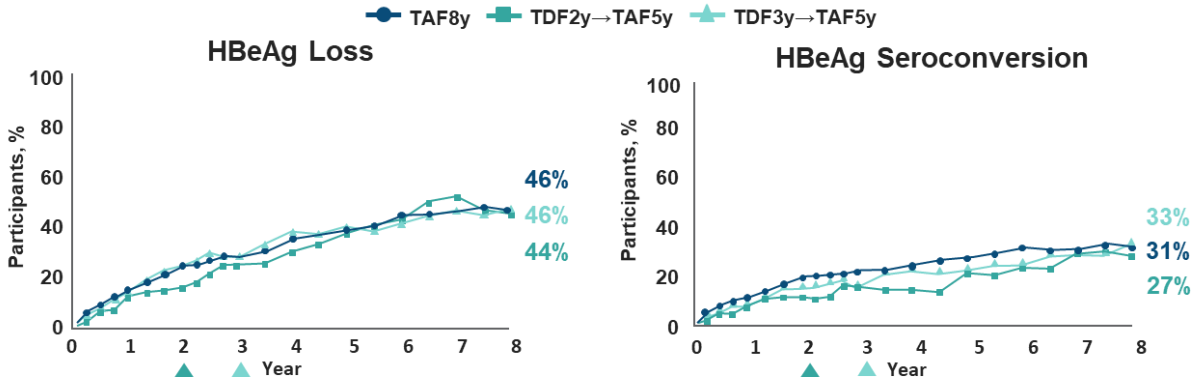


Table 4. Studies 108 and 110: HBsAg Loss and Seroconversion at Year 8 (M=E Analysis)[4,7]

	TAF8y		TDF2y→TAF6y		TDF3y→TAF5y	
	HBeAg-	HBeAg+	HBeAg-	HBeAg+	HBeAg-	HBeAg+
HBsAg loss, n/N (%)	8/199 (4)	9/384 (2)	0/41	4/76 (5)	1/58 (2)	3/109 (3)
HBsAg seroconversion, n/N (%)	6/199 (3)	6/384 (2)	0/41	4/76 (5)	0/58	3/109 (3)
HBsAg mean change (SD), log_{10} IU/mL	-0.62 (0.924)	-0.89 (1.211)	-0.5 (0.526)	-1.09 (1.424)	-0.61 (0.758)	-1.09 (1.268)

High rates of ALT normalization were observed in the TAF8y arm, regardless of HBeAg status. ALT normalization rates increased after switching to TAF in participants randomly assigned to TDF in the DB period before switching to OL TAF at Year 2 or 3.[4]

At Year 8, approximately 30% of all participants with baseline cirrhosis (ie, FibroTest score ≥0.75) continued to show evidence of cirrhosis, but most participants had improved to a lower FibroTest category.[4]

Resistance results at Year 8[4]

A total of 2% of participants (n=29) met the criteria for a sequence analysis of HBV pol/RT to scan for potential resistance mutations: viral blip, n=17 (59%); virologic breakthrough, n=9 (31%); and persistent viremia, n=3 (10%). No amino acid substitutions that reduced susceptibility to TAF were detected at Year 8.

Safety results through Year 8[4]

The OL safety analysis included data from any participant who received ≥1 dose of OL TAF (Table 5).

Table 5. Studies 108 and 110: Safety Results Through Year 8 (OL Safety Analysis Set)[4]

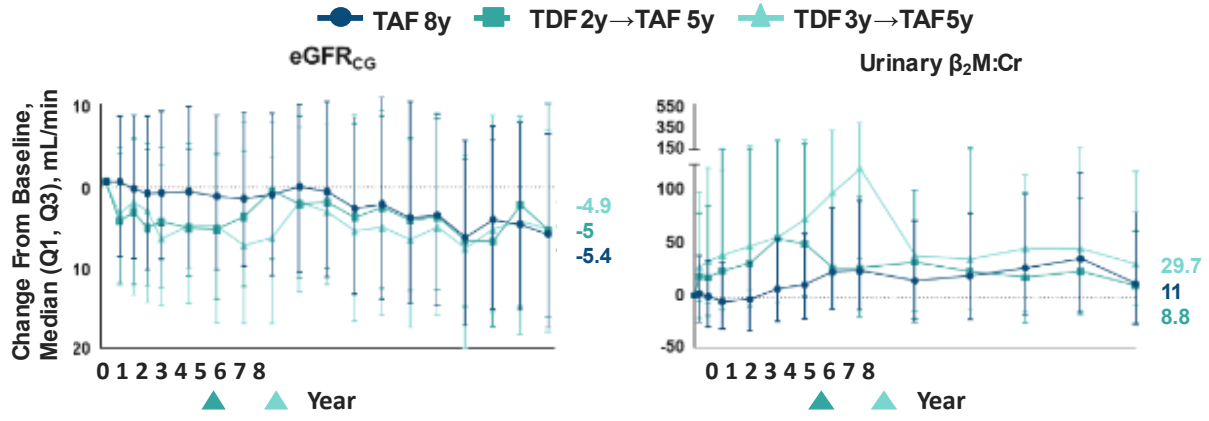
Safety Outcomes, n or n/N (%)		TAF8y (n=775)	Combined TDF→TAF Arms (n=382)
Any AE		525 (68)	271 (71)
Any study drug-related AEs		43 (6)	18 (5)
Grade ≥3 AEs		60 (8)	27 (7)
Study drug-related Grade ≥3 AEs		2 (<1)[a]	0
SAEs		97 (13)	49 (13)
Study drug-related SAEs		4 (1)[b]	0
AEs that led to discontinuation		9 (1)[c]	3 (<1)[d]
Deaths[e]		3/866 (<1)	3/432 (<1)
HCC[f]		7 (<1)	3 (<1)
AEs occurring in ≥5% of participants	Headache	59 (8)	30 (8)
	URTI	55 (7)	27 (7)
	Nasopharyngitis	52 (7)	23 (6)
	Arthralgia	41 (5)	23 (6)
	Hypertension	37 (5)	26 (7)
	Back pain	34 (4)	23 (6)
	Cough	28 (4)	27 (7)

[a]Cerebrovascular accident, renal neoplasm (each, n=1).
[b]ALT increase, cerebrovascular accident, osteonecrosis, renal neoplasm (each, n=1).
[c]Cardiopulmonary failure, cerebrovascular accident, GGT increased, HCC, myelodysplastic syndrome, osteonecrosis, osteoporosis, pancreatic carcinoma, proteinuria (each, n=1).
[d]Ascites, pemphigoid, tuberculosis (each, n=1). All occurred in the TDF3y→TAF5y arm.
[e]TAF: HCC, H1N1 influenza, pancreatic cancer (each, n=1). TDF: cardiopulmonary arrest, HCC, bilateral pneumonia (each, n=1).
[f]Over the course of the entire study, 21 participants developed HCC.

Renal safety through Year 8

From baseline to Year 8, the median $eGFR_{CG}$ decreased in all treatment arms (Figure 4). Participants in the TDF→TAF arms demonstrated improvements in $eGFR_{CG}$ and urinary β_2:Cr after switching to TAF (Figure 4).

Figure 4. Studies 108 and 110: Renal Parameter Changes Through Year 8 (M=E Analysis)[4]

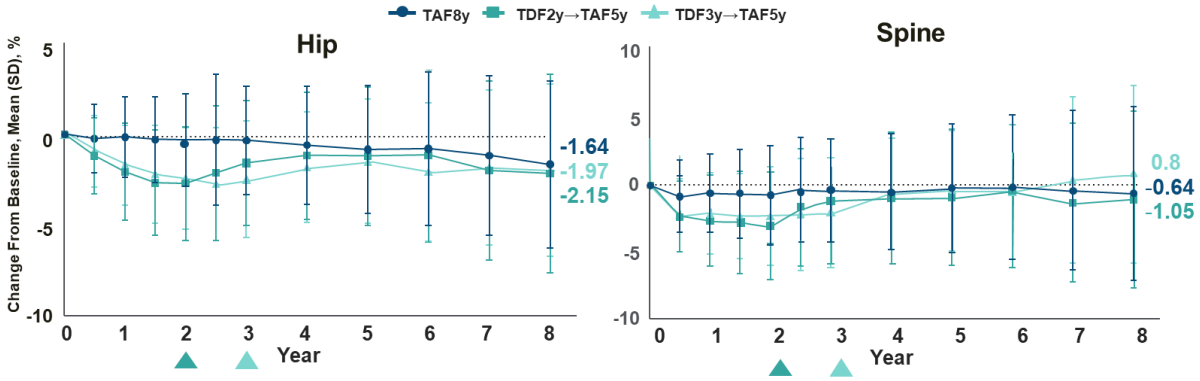


Bone safety through Year 8

At Year 8, changes in BMD from baseline in the TAF8y arm were minimal, with mean percentage decreases from baseline of <2% in hip and spine BMD (Figure 5). Among

participants in the TDF→TAF arms, early decreases in hip and spine BMD that occurred during TDF treatment improved over time after participants switched to TAF at Year 2 or 3.

Figure 5. Studies 108 and 110: Mean Changes in BMD from Baseline to Year 8 (M=E Analysis)[4]



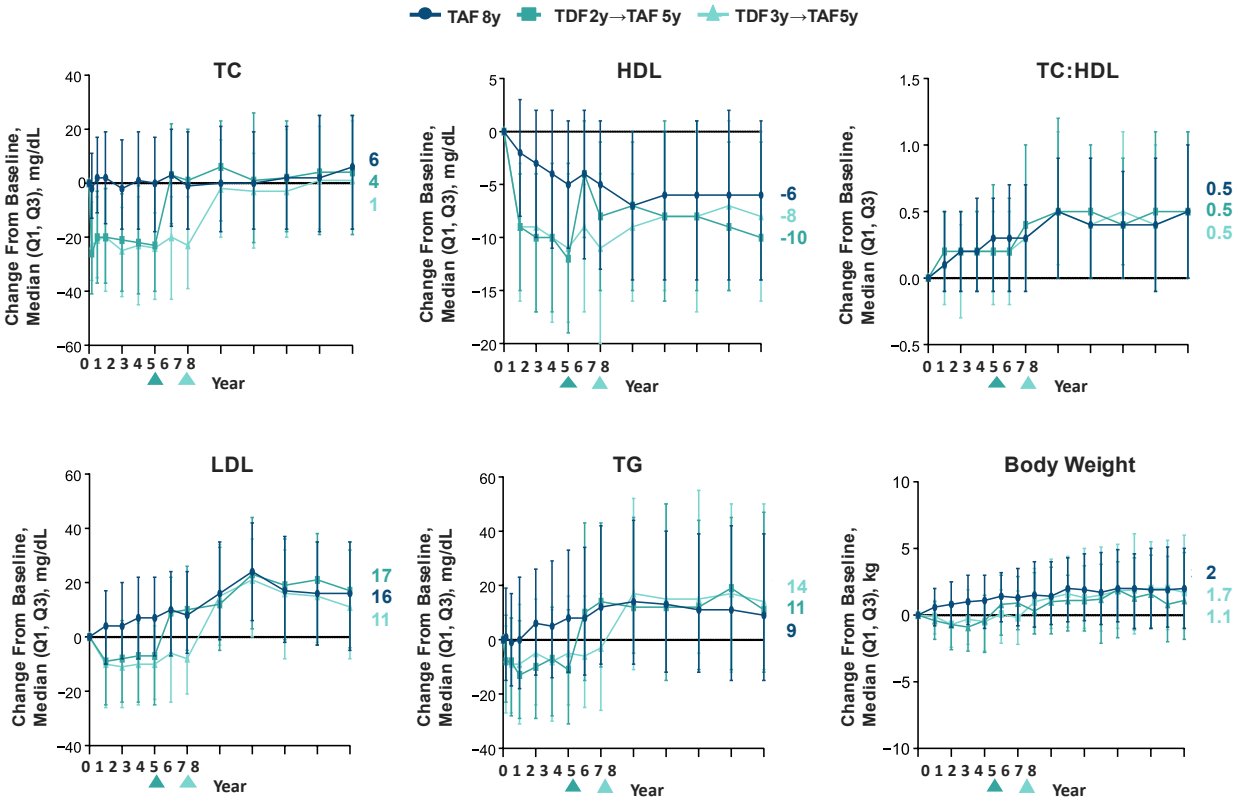
In the TAF8y arm at Year 8, the median percentage decrease in bone biomarkers from baseline was 2.7% for CTX resorption and 9.03% for P1NP formation. Compared with the TAF8y arm, larger decreases in hip and spine BMD and larger increases in CTX P1NP were seen in the TDF→TAF arms during the DB phase; switching to TAF resulted in increased BMD and smaller increases in CTX and P1NP.

Lipid changes through Year 8

In the TAF8y treatment arm, median TC, LDL, and TG levels increased, and median HDL levels decreased at Year 8. In the TDF→TAF treatment arms, modest decreases in TC, LDL, HDL, and TG levels were observed during the DB phase of TDF treatment, and increases in these parameters similar to levels seen in the TAF8y group were observed once participants were switched to TAF. The median change in TC:HDL from baseline to Year 8 was 0.5 in all treatment arms (Figure 6).

During the OL phase, Grade ≥3 abnormalities in fasting LDL levels were noted in 6% of participants (45/760) in the TAF8y treatment arm, 9% (15/173) in the TDF2y→TAF6y arm, and 8% (15/200) in the TDF3y→TAF5y arm. Grade ≥3 abnormalities in fasting cholesterol levels were noted in 1% (11/767) of participants in the TAF8y treatment arm, 1% (2/173) in the TDF2y→TAF6y arm, and 5% (9/200) in the TDF3y→TAF5y arm.

Figure 6. Studies 108 and 110: Median Changes in Fasting Lipid Panel and Body Weight Through Year 8[4]



Renal and bone safety subanalysis according to risk factors[5]

Study design and demographics

A pooled subanalysis of Studies 108 and 110 evaluated the long-term renal and bone safety of TAF in participants with ≥1 risk factor for TDF-associated renal and bone toxicities (eg, age >60 years, T-score less than -2.5 on DXA of hip and/or spine, $eGFR_{CG}$ <60 mL/min, UA:Cr >30 mg/g, and serum phosphorus level <2.5 mg/dL). Hip and spine DXA scans, serum bone biomarkers, $eGFR_{CG}$, and biomarkers of renal tubular function through Year 8 of treatment were compared between those with and those without risk factors. A total of 1059 participants did not have risk factors, and 239 (18%) had ≥1 risk factor in the TAF8y and TDF→TAF arms (Table 6).

Table 6. Subanalysis of Studies 108 and 110: Baseline Demographics and Disease Characteristics Among Participants With ≥1 Risk Factor for Renal and Bone Toxicities[5]

Key Demographics and Characteristics	Participants With ≥1 Risk Factor	
	TAF8y (n=151)	TDF→TAF (n=88)
Male, n (%)	91 (60)	53 (60)
Race, Asian/White/Native Hawaiian or Pacific Islander/ Black or African American, %	81/17/1/1	80/20/0/0
HBeAg-, n (%)	73 (48)	40 (46)
FibroTest score ≥0.75, n/N (%)	26/145 (18)	14/87 (16)

Key Demographics and Characteristics		Participants With ≥1 Risk Factor	
		TAF8y (n=151)	TDF→TAF (n=88)
Risk factors for TDF-associated renal and bone toxicities, n or n (%)	Number of risk factors, 1/2/≥3	133/17/1	75/12/1
	Osteoporosis by hip/spine	60 (40)	30 (34)
	UA:Cr >30 mg/g	44 (29)	28 (32)
	Age >60 years	42 (28)	28 (32)
	Serum phosphorus level <2.5 mg/dL	19 (13)	12 (14)
	$eGFR_{CG}$ <60 mL/min	5 (3)	4 (5)

Results

Among those in the TAF8y arm who had ≥1 TDF risk factor (median changes: -8.3, -5.8, and -10.6 mL/min in the TAF8y, TDF2y→TAF6y, and TDF3y→TAF5y arms, respectively) or no risk factors (-4.6, -5, and -3.1 mL/min in the TAF8y, TDF2y→TAF6y, and TDF3y→TAF5y arms), small decreases from baseline in $eGFR_{CG}$ were observed and were consistent with age-related decreases. Improvements in $eGFR_{CG}$ were noted after participants switched from TDF to TAF in both those with and those without risk factors; a greater recovery in eGFR was noted among those in the TDF2y→TAF6y arm than among those in the TDF3y→TAF5y arm. β_2:Cr and RBP:Cr remained stable, and tubular protein levels recovered among participants who switched from TDF to TAF and had ≥1 risk factor.

Regardless of the presence or absence of risk factors, mean percent changes from baseline in hip and spine BMD were small in those in the TAF8y arm. Serum levels of markers of bone turnover were stable among those with ≥1 risk factor. Recovery in hip and spine BMD measurements occurred after participants switched from TDF to TAF in both those with and those without risk factors; serum markers of bone turnover decreased after switching and eventually stabilized in participants with as well those without risk factors.

Among those with ≥1 TDF risk factor, 68% and 74% of participants in the TAF8y and TDF→TAF arms experienced any AEs. No participants in either group experienced a study drug-related Grade 3 or 4 AE or study drug-related SAE.

Real-World Data on TAF vs TDF in Patients With CHB

TAF vs TDF in TN Patients With CHB[6]

Study design

A real-world study was conducted to evaluate the safety and efficacy of TAF (n=502) compared with TDF (n=2245) in TN patients with CHB. Outcomes included rates of virological response and ALT normalization, incidence of HCC, and changes in renal function and lipid profiles through 36 months. PS-matching was conducted for 495 pairs.

Results

The rates of virological response (HBV DNA <15 IU/mL) were not significantly different for the TAF group vs the TDF group: 47.8% vs 42.4%, respectively, at Month 6; 70.3% vs 67.9% at Month 12; 81.2% vs 84.3% at Month 24; and 83.3% vs 86.1% at Month 36 (P>0.05 for all in the PS-matched cohorts). The rates of ALT normalization, based on local laboratory criteria (<40 U/L), were also similar between the TAF and TDF groups: 77.5% vs 73%, respectively, at Month 6; 79.7% vs 78.2% at Month 12; 90.6% vs 85.8% at Month 24; and 86.2% vs 85.7% at Month 36 (P>0.05 for all). Based on AASLD 2018 criteria (males,

<35 U/L; females, <25 U/L), the TAF group had significantly higher rates of ALT normalization than the TDF group at Months 6 and 18 and numerically higher rates at Month 12. No statistically significant differences between the TAF and TDF group were seen in the PS-matched cohort.

The risk of developing HCC was not statistically different between the TAF and TDF groups in the overall study cohort (*P*=0.3) or in the PS-matched cohort (*P*=0.6). Among patients with eGFR ≥30 mL/min/1.73^2 at baseline, the differences between treatment groups in the median increases in SCr levels from baseline to Months 6 and 12 were smaller in the TAF group than in the TDF group (each, *P*<0.05) and were statistically nonsignificant at Months 24 and 36. The TDF group demonstrated significant decreases from baseline to Months 12, 24, and 36 in TC, TG, and HDL levels, compared with the TAF group (each, *P*<0.001); differences between groups in changes in median LDL levels were statistically nonsignificant (each, *P*>0.05).

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Abbreviations

β_2:Cr=β-2 microglobulin to Cr ratio
AASLD=American Association for the Study of Liver Diseases
AE=adverse event
BMD=bone mineral density
CHB=chronic hepatitis B
CTX=C-terminal telopeptide of type 1 collagen
DB=double-blind
DXA=dual x-ray absorptiometry
$eGFR_{CG}$=eGFR rate per Cockcroft-Gault equation
GGT=γ-glutamyl transferase
HBeAg=hepatitis B envelope antigen
HBsAg=hepatitis B surface antigen
HCC=hepatocellular carcinoma
M=E=missing=excluded
OL=open-label
P1NP=N-terminal propeptide of type 1 procollagen
pol/RT=polymerase-reverse transcriptase
PS=propensity score
Q=quartile
RBP:Cr=retinol-binding protein to Cr ratio
SAE=serious adverse event
TAF=tenofovir alafenamide
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TE=treatment-experienced
TG=triglycerides
TN=treatment-naive
UA:Cr=urine albumin to Cr ratio
ULN=upper limit of normal
URTI=upper respiratory tract infection

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Vemlidy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vemlidy/vemlidy_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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