GILEAD | Medical Information

Vemlidy® (tenofovir alafenamide) Persistent Viremia

This document is in response to your request for information regarding the use of Vemlidy® (tenofovir alafenamide [TAF]) for the treatment of chronic hepatitis B (CHB) in patients with persistent viremia.

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Gilead Studies on TAF Use in Persistent Viremia

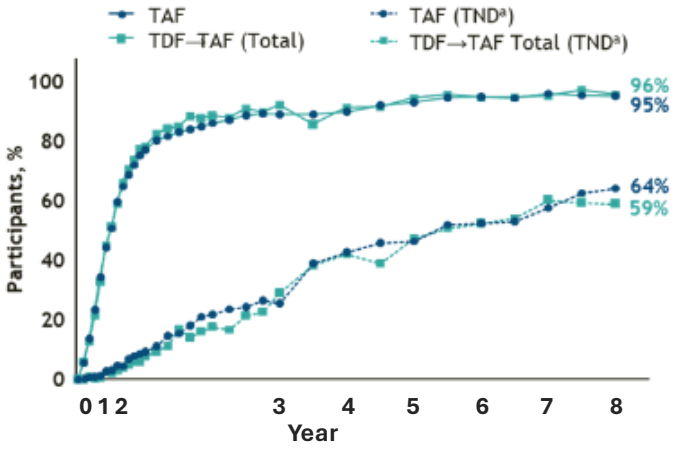
Studies 108 and 110

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 CHB and compensated liver function were randomly assigned in a 2:1 ratio to receive either double-blind TAF 25 mg or TDF 300 mg. Upon completion of the blinded phase, eligible participants from both arms were enrolled into an OL phase and received TAF. Over the course of the study, participants received one of the following treatments: double-blind then OL TAF for a total of 8 years (TAF8y), double-blind TDF for 2 years then OL TAF for 6 years (TDF2y→TAF6y), or double-blind TDF for 3 years then OL TAF for 5 years (TDF3y→TAF5y).[1]

Viral suppression through Year 8 (final analysis)

In both studies, rates of viral suppression during the double-blind phase were maintained through Year 8 across all treatment arms (Figure 1).[1]

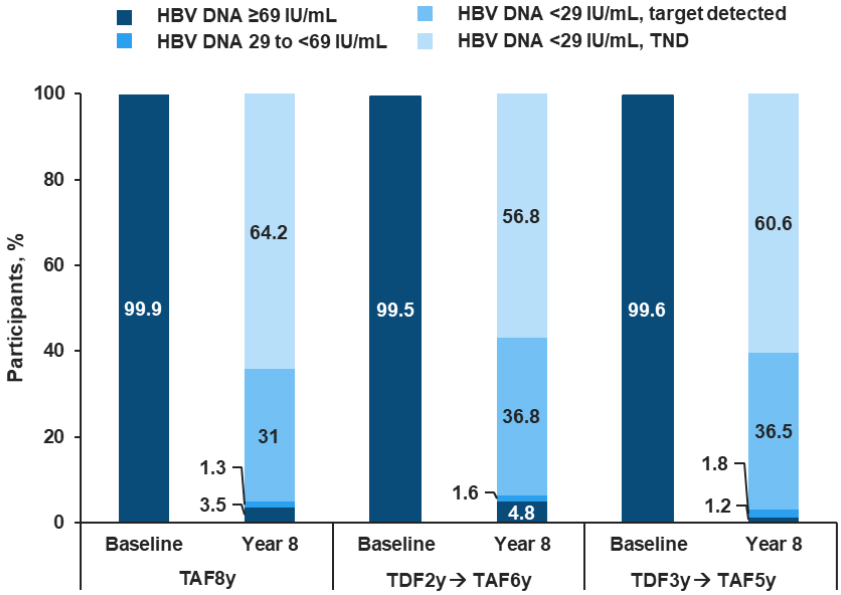
Figure 1. Studies 108 and 110: HBV DNA <29 IU/mL Through Year 8 (M=E Analysis)[1,2]



[a]Proportion of participants with undetectable HBV DNA.

Levels of HBV DNA by treatment group at baseline and Year 8 are presented in Figure 2.

Figure 2. Studies 108 and 110: HBV DNA Levels by Treatment Group at Year 8[1,2]



At Year 8, of the 42 participants who did not achieve HBV DNA <29 IU/mL, most had viral blip or virologic breakthrough, while 4 participants had persistent viremia. In a multivariate analysis, significant predictors for HBV DNA ≥29 IU/mL at Week 384 were age <50 years (compared with those ≥50 years; OR: 4.78; 95% CI: 1.45–15.71; *P*=0.01), HBV GT A (compared with those without HBV GT A; OR: 3.24; 95% CI: 1.13–9.26; *P*=0.028); and HBV GT D (compared with those without HBV GT D; OR: 4.03; 95% CI: 2.06–7.91; *P*<0.001).[3]

Resistance results at Year 8

A total of 2% of participants (n=29) met the criteria (HBV DNA ≥69 IU/mL) 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%).[1] At Year 8, the proportion of participants with persistent viremia had declined from 9/36 participants (25%)

at Year 6.[2] No amino acid substitutions that reduced susceptibility to TAF were detected at Year 8.[1]

Safety results through Year 8[1]

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

Table 1. Studies 108 and 110: Safety Results Through Year 8 (OL Safety Analysis Set)[1]

Safety Outcomes, n (%)		TAF8y (n=775)	TDF2y→TAF6y (n=180)	TDF3y→TAF5y (n=202)
Any AE		525 (68)	133 (74)	138 (68)
Any study drug-related AE		43 (6)	14 (8)	4 (2)
Grade ≥3 AE		60 (8)	15 (8)	12 (6)
Study drug-related Grade ≥3 AE		2 (<1)[a]	0	0
SAE		97 (13)	24 (13)	25 (12)
Study drug-related SAE		4 (1)[b]	0	0
AE that led to discontinuation		9 (1)[c]	0	3 (1)[d]
Death[e]		3 (<1)	1 (<1)	0
HCC[f]		7 (<1)	3 (2)	0
AEs occurring in ≥5% of participants	Headache	59 (8)	13 (7)	17 (8)
	URTI	55 (7)	16 (9)	11 (5)
	Nasopharyngitis	52 (7)	11 (6)	12 (6)
	Arthralgia	41 (5)	12 (7)	11 (5)
	Hypertension	37 (5)	15 (8)	11 (5)
	Back pain	34 (4)	14 (8)	9 (5)
	Cough	28 (4)	18 (10)	9 (5)

Abbreviation: URTI=upper respiratory tract infection.
[a]Cerebrovascular accident, renal neoplasm (each, n=1).
[b]ALT increase, cerebrovascular accident, osteonecrosis, renal neoplasm (each, n=1).
[c]Cardiopulmonary failure, cerebrovascular accident, γ-glutamyl transferase increased, HCC, myelodysplastic syndrome, osteonecrosis, osteoporosis, pancreatic carcinoma, proteinuria (each, n=1).
[d]Ascites, pemphigoid, tuberculosis (each, n=1).
[e]TAF: HCC, H1N1, 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.

Study 4018 – Switch From TDF to TAF[4]

Study 4018 was a double-blind, randomized, phase 3 study to evaluate the safety and efficacy of switching from TDF to TAF (n=243) vs continuing TDF (n=245) in virologically suppressed participants with CHB who had been treated with TDF for ≥48 weeks prior to screening and had $eGFR_{CG}$ ≥50 mL/min at screening. The primary endpoint was the number of participants with HBV DNA ≥20 IU/mL (non-inferiority to TDF) at Week 48. After Week 48, all participants were eligible for OL TAF. The safety and efficacy of TAF at Week 96 was a secondary endpoint.

Week 96 resistance analysis

In the 2 participants who qualified for viral sequencing (TAF→TAF [virologic blip, Week 96]: <1% [1/243]; TDF→TAF [virologic breakthrough Weeks 60 & 72]: <1% [1/245]), no viral resistance was seen through 96 weeks.

Safety

Safety results through Week 96 are presented in Table 2.

Table 2. Study 4018: Safety Through Week 96[4]

Participants, n or n/N (%)		TAF→TAF (n=235)	TDF→TAF (n=237)
AEs	AEs	81 (34)	84 (25)
	Grade 3–4 AEs	8 (3)	7 (3)
	SAEs	8 (3)[a]	5 (2)[b]
	Study drug-related SAEs	0	0
	AEs that led to discontinuation	1 (<1)	0
	HCC	2 (<1)	1 (<1)
Laboratory abnormalities, ≥2%	Grade 3–4	12/235 (5)	28/235 (12)
	Increased total cholesterol	0	5 (2)[c]
	Increased LDL cholesterol	5 (2)[c]	13 (6)[c]
	Urine glucose	5 (2)[c]	4 (2)[c]
	Urine erythrocytes	0	4/165 (2)[c]

[a]TAF→TAF group serious AEs: HCC (n=2), anaphylactic reaction, back pain, necrotizing fasciitis, pancreatic mass, prostatitis, and squamous cell lung cancer (also led to discontinuation; each, n=1).
[b]TDF→TAF group serious AEs: acute myocardial infarction, atrial fibrillation, cardiac arrest, necrotizing pneumonia, and testicular neoplasm (each, n=1).
[c]All abnormalities were Grade 3.

References

1. Buti M, Lim YS, Chan HLY, et al. Eight-year efficacy and safety of tenofovir alafenamide for treatment of chronic hepatitis B virus infection: Final results from two randomised phase 3 trials. *Aliment Pharmacol Ther.* 2024;60(11-12):1573-1586.
2. Buti M, Lim YS, Chan HLY, et al. Eight-year efficacy and safety of tenofovir alafenamide for treatment of chronic hepatitis B virus infection: Final results from two randomised phase 3 trials [Supplemental material]. *Aliment Pharmacol Ther.* 2024;60(11-12):1573-1586. https://www.ncbi.nlm.nih.gov/pubmed/39327857
3. Gane EJ, Buti M, Fung SK, et al. Factors Associated With a Lack of Viral Suppression in Chronic HBV (CHB) Patients After 8 Years of Treatment With Tenofovir Alafenamide (TAF) or Tenofovir Disoproxil Fumarate (TDF) Followed by TAF Treatment [Poster 1418-C]. Paper presented at: American Association for the Study of Liver Diseases (AASLD) - The Liver Meeting; November 10-14, 2023; Boston, MA.
4. Lampertico P, Buti M, Ramji A, et al. A Phase 3 Study Comparing Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide With Continued TDF Treatment in Virologically Suppressed Patients With Chronic Hepatitis B: Final Week 96 Efficacy and Safety Results [Presentation]. Paper presented at: The Digital International Liver Congress; 27-29 August, 2020.

Abbreviations

AE=adverse event
CHB=chronic hepatitis B
$eGFR_{CG}$=estimated glomerular filtration rate per Cockcroft-Gault equation
GT=genotype
HCC=hepatocellular carcinoma
OL=open label
OR=odds ratio
SAE=serious adverse event
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TND=target not detected

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
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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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