GILEAD | Medical Information

Vemlidy® (tenofovir alafenamide) Use in Severe Hepatic Impairment

This document is in response to your request for information regarding the use of Vemlidy® (tenofovir alafenamide [TAF]) in patients with severe hepatic impairment.

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The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vemlidy/vemlidy_pi.

Summary

Product Labeling[1]

No dosage adjustment of TAF is required in patients with mild hepatic impairment (CP A). The safety and efficacy of TAF in patients with decompensated cirrhosis (CP B or C) have not been established; therefore, TAF is not recommended in patients with decompensated (CP B or C) hepatic impairment.

Clinical Data on TAF Use in Severe Hepatic Impairment

In Study 4035, a phase 2 study of participants with moderate to severe hepatic impairment (N=31), switching to TAF from TDF and/or another OAV resulted in virologic suppression and ALT normalization in 77% and 72% of participants, respectively, and stable renal and bone parameters through Week 96.[2,3]

In a prospective cohort study of participants with decompensated cirrhosis and ascites (N=182), 56.3% of the participants (71/126) who completed 24 weeks of TAF treatment achieved undetectable HBV DNA levels, 76.2% had ALT normalization, and 54.8% had resolution of ascites.[4]

In a multicenter, real-world study of TAF treatment in patients with CHB and decompensated cirrhosis (N=106), the proportion of patients with undetectable HBV DNA increased from 57.55% (n/N=61/106) at baseline to 95.65% at Week 48 (n/N=44/46; $P<0.001$), and the proportion with ALT normalization increased from 67.92% (n/N=72/106) to 89.13% (n/N=41/46; $P=0.004$).[5]

In a prospective cohort study of participants with decompensated cirrhosis (N=56) and poor response to prior NUC therapy or LLV, switching to TAF resulted in higher rates of CVR and improved liver function. Stable renal parameters were also maintained over 48 weeks.[6]

In a retrospective cohort study of TAF use in patients with CHB and decompensated cirrhosis (TAF-naive, n=137; switched to TAF, n=66), 59.6% were recompensated and 97.5% achieved virologic suppression at Week 96. Rates of recompensation, HBV DNA levels, and MELD scores were not significantly different between the TAF-naive and TAF-switch groups at Week 96.[7]

In a retrospective study of TAF (n=61) vs TDF (n=70) in patients with HBV-associated decompensated cirrhosis, detectable HBV DNA in the TAF group decreased from 27.9% to 13.1% by Week 48 (*P*=0.044), with 76.5% achieving virologic response (*P*<0.001), while HBeAg positivity slightly increased (27.9% to 31.1%). After PS-matching (n=38 per group), both treatments achieved virologic suppression; however, the TAF group showed improved renal safety and greater ALT normalization than the TDF group, with no significant differences between groups in APRI, FIB-4, or CP scores.[8]

PK Studies on TAF Use in Severe Hepatic Impairment

TAF total exposure was 46% lower in participants with severe hepatic impairment (CPT Class C, n=10) than in matched-control participants with normal hepatic function (n=10). The AUC levels for unbound TAF were comparable between groups. Most AEs were mild, and there were no discontinuations due to an AE.[9]

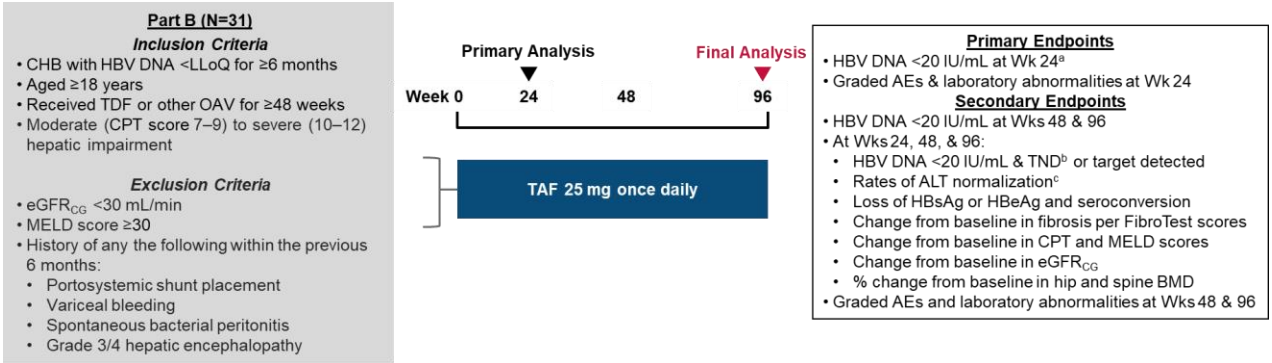
Clinical Data on TAF Use in Severe Hepatic Impairment

Study 4035

Study design and demographics[2]

Study 4035 was a phase 2, open-label, 96-week study that evaluated the efficacy and safety of switching from TDF and/or other OAVs to TAF 25 mg daily in participants with CHB and moderate (CPT score 7–9) to severe (CPT score 10–12) hepatic impairment who were virally suppressed (n=31). Efficacy endpoints included assessments of viral suppression (HBV DNA <20 IU/mL; M=F; primary endpoint assessed at Week 24), biochemical response (normal ALT level), serologic response (HBeAg/HBsAg loss and seroconversion), and change in fibrosis (FibroTest). Safety endpoints included rates of AEs, laboratory abnormalities, changes in fasting lipid levels, and renal and bone parameters. Data from Part B of the study are summarized below; data from Part A (participants with moderate to severe impairment) are not summarized.

Figure 1. Study 4035: Study Design[2]



Abbreviation: LLoQ=lower limit of quantitation.
[a]Evaluated in subgroups according to age (<65 years and ≥65 years) and by male or female sex.
[b]Considered to be HBV DNA <LLoQ or complete virologic suppression.
[c]ULN aligned with AASLD criteria (male, 35 U/L; female, 25 U/L). Rates of ALT normalization (ie, participants with ALT level >ULN at baseline who later achieved levels ≤ULN) were also recorded.
Note: Primary and secondary efficacy endpoints were evaluated via an ITT (M=F) approach. Additional prespecified per protocol analyses for the primary endpoint, FDA Snapshot analyses (at Weeks 24, 48, and 96), and M=E analyses of virologic suppression and ALT normalization were also performed.

Of the 31 participants who enrolled in the study, 25 completed 96 weeks of treatment; before Week 24, 1 participant discontinued due to participant decision, and before Week 96, 2 died, 1 discontinued treatment due to an AE, and 1 each discontinued due to participant or investigator decision.

Table 1. Study 4035: Baseline Demographics and Characteristics[2,3]

Key Demographics and Characteristics		Overall (N=31)
Age, mean ± SD, years		55±10.8
Age ≥65 years, n (%)		6 (19)
Male, n (%)		21 (68)
Race, Asian/White/Black/other, n (%)		25 (81)/4 (13)/1 (3)/1 (3)
HBeAg-, n (%)		28 (90)
HBV DNA TND, n (%)		20 (65)
ALT, median (IQR), U/L		27 (18–33)
≤ULN by AASLD criteria,[a] n (%)		21 (68)
History of cirrhosis, n (%)		30 (97)
FibroTest score ≥0.75, n (%)		19 (61)
CPT	Class A/B/C, n (%)	19 (61)[b]/9 (29)/3 (10)
	Score, mean (range)	6 (5–10)
MELD score, mean ± SD		10.7±3.4
eGFR, median (IQR)	CG, mL/min	98.5 (72.5–129.8)
	CKD-EPI, mL/min/1.73 m^2	94 (83.5–102.4)
Osteoporosis (T-score <-2.5), spine/hip, n (%)		6 (9)/1 (3)
Select comorbidities, HTN/DM/CVD/hyperlipidemia, n (%)		7 (23)/7 (23)/4 (13)/4 (13)
Previous OAVs, TDF/ETV/3TC/ADV/LdT/other, n (%)		21 (68)/14 (45)/14 (45)/10 (32)/2 (6)/2 (6)[c]

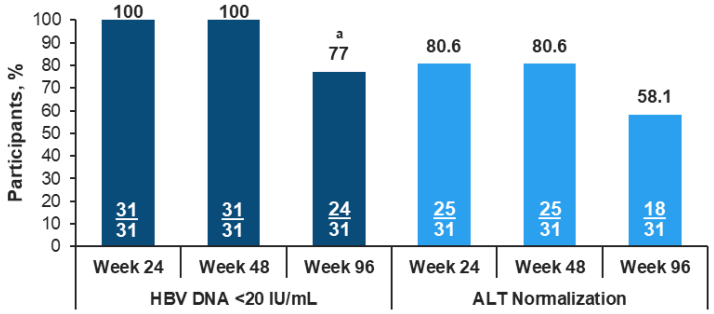
Abbreviations: 3TC=lamivudine; ADV=adefovir; CVD=cardiovascular disease; DM=diabetes mellitus; ETV=entecavir; FTC=emtricitabine; HTN=hypertension; LdT=telbivudine.
[a]Females, <25 U/L; males, <30 U/L.
[b]Each had CPT scores ≥7 at screening or according to medical history.
[c]Previous FTC/TDF and TDF + ETV.

Efficacy[2]

At Week 24 (primary endpoint) and Week 48, using M=F data, 100% of participants were virologically suppressed; this rate decreased to 77% at Week 96 (Figure 2). Of the 7 participants who did not achieve virological suppression at Week 96, 6 participants did not have virological data; only 1 participant had virologic failure at Week 96 (HBV DNA, 23 IU/mL). Because the participant's HBV DNA did not meet the assay limit for sequencing (≥69 IU/mL), no resistance testing was performed. In an M=E analysis, 96% of participants (24/25) were virologically suppressed at Week 96 (Table 2). Virologic suppression rates at Week 24 were identical between subgroups according to age and sex (<65 years/≥65 years and male/female).

Normal ALT levels (AASLD criteria) were observed in 58.1% of participants at Week 96 (Figure 2). Of the 10 participants with ALT levels >ULN at baseline, several had normalized levels by Week 96: 6 (60%) at Week 24; 6 (60%) at Week 48, and 5 (50%) at Week 96.

Figure 2. Study 4035: Virologic Suppression and ALT Normalization (M=F)[2]



[a]At Week 96, 1 participant (3%) had HBV DNA 23 IU/mL, and 6 (19%) had no virological data.

None of the 3 participants who were HBeAg+ at baseline had HBeAg loss during the study, and 2 participants (7%) experienced HBsAg loss without seroconversion. Of the 15 participants who had FibroTest data available at baseline and at Week 96, 11 (73%) had no change in cirrhosis category, and 4 (27%) had improvements in cirrhosis category.

At Week 96, of the 19 participants who were CPT Class A at baseline, 14 remained in Class A, and 1 worsened to Class B (missing data, n=4). Of the 9 participants who were CPT Class B at baseline, 2 improved to Class A, and 5 remained in Class B (missing data, n=2). All 3 of the participants who were CPT Class C at baseline had improvements at Week 96: 1 to Class A and 2 to Class B.

Table 2. Study 4035: Additional Efficacy Endpoints[2,3]

Endpoints		Overall (N=31)		
		Week 24	Week 48	Week 96
HBV DNA <20 IU/mL	Per protocol	29/29 (100)	Not evaluated	Not evaluated
	M=E	31/31 (100)	31/31 (100)	24/25 (96)
HBV DNA TND		24/31 (77.4)	23/31 (74.2)	24/31 (77.4)
Change in qHBsAg, log_{10} IU/mL		-0.05±0.13	-0.1±0.14	-0.2±0.17
Change in FibroTest score		-0.05±0.11	-0.03±0.1	-0.02±0.12
Change in CPT score		-0.1±1.1	-0.2±1.1	-0.5±1.2
Change in MELD score		-0.6±1.9	0.1±2.4	-1±1.6

Abbreviation: qHBsAg=quantitative hepatitis B surface antigen.
Note: Data are presented as n/N (%) or mean ± SD.

Safety

AEs that occurred in ≥10% of participants included upper respiratory tract infection, cough, pyrexia, diarrhea, decreased BMD, ascites, constipation, oropharyngeal pain, and arthralgia. One participant required an interruption of treatment for 4 days due to gastrointestinal hemorrhage, subdural hematoma, and subarachnoid hemorrhage.[2]

Table 3. Study 4035: Safety Summary at Week 96[2,3]

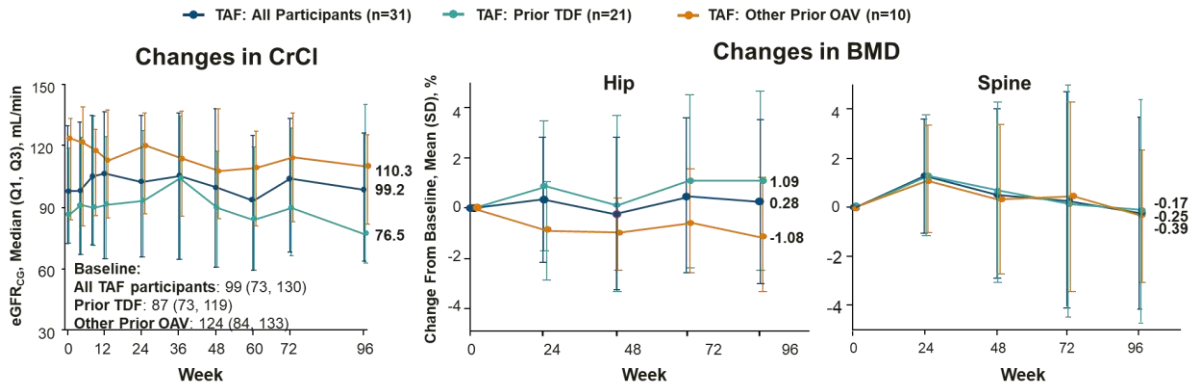
Key AEs and Laboratory Abnormalities, n (%)	Overall (N=31)
Participants with any AE	24 (77.4)
Participants with a study drug-related AE	4 (12.9)
Participants with an SAE[a]	10 (32)
Participants with a Grade 3–4 AE[a]	8 (25.8)
Discontinuation of study drug due to an AE	1 (3)[b]
Death[c]	2 (6.5)
Participants with laboratory abnormalities, Grade 3/4	13 (42)/4 (13)

Key AEs and Laboratory Abnormalities, n (%)		Overall (N=31)
Grade 3–4 laboratory abnormalities reported in ≥2 participants	Lymphocytes decreased	7 (23)
	Platelets decreased	4 (13)
	Bilirubin increased	4 (13)
	Hgb decreased	3 (10)
	Urine glucose	3 (10)
	Fasting serum glucose	2 (6)

[a]No Grade 3 or 4 AEs or SAEs were considered related to study treatment by the study investigators.
[b]Blood Cr increased (Grade 2, considered related to study treatment by the study investigators) in a 73-year-old male with CKD Stage 2 at baseline, which increased to Stage 3 and led to study drug discontinuation at Week 60.
[c]Neither death was related to treatment: respiratory failure (n=1, Day 612); aspiration pneumonia (n=1, Day 651).

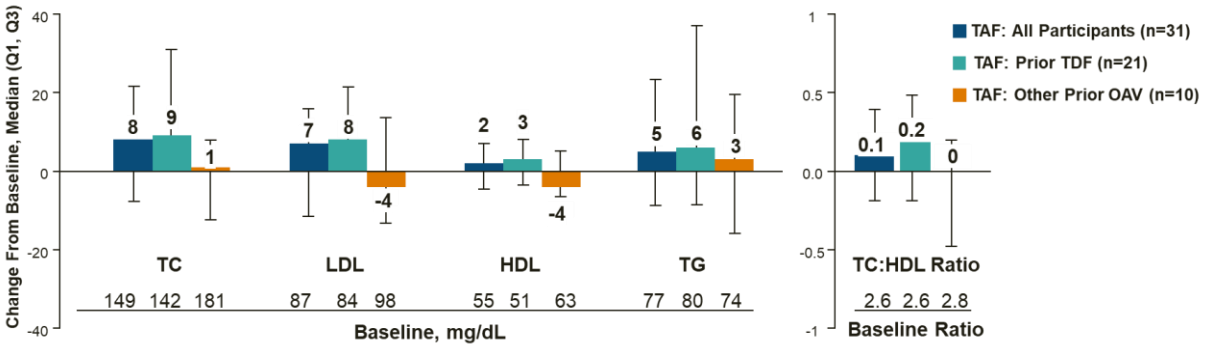
Following the switch to TAF, bone and renal parameters were stable through Week 96 (Figure 3). Overall, median (IQR) eGFR values decreased from baseline to Week 96; overall $eGFR_{CKD\text{-}EPI}$ changes were similar to those observed for $eGFR_{CG}$. Most participants had stable or improved CKD stages at Week 96; however, 2 participants had a worsened CKD stage (baseline to Week 96, Stage 1 to Stage 2 [n=1]; Stage 2 to Stage 4 [n=2]). In addition, after treatment was switched to TAF, proximal tubular markers (retinol-binding protein:Cr and β2M:Cr) initially decreased from baseline by approximately 20% but remained stable thereafter. Small decreases in markers of bone turnover (C-type collagen sequence [bone resorption] and procollagen type 1 N-terminal propeptide [bone formation]) were also noted.[2,3]

Figure 3. Study 4035: Changes in Renal and Bone Parameters From Baseline to Week 96 Overall and by Prior Use of TDF or Other OAVs[2,10]



Overall, small increases in TC, LDL, and HDL levels were seen in participants after they switched to TAF but were not considered clinically important (Figure 4).[2]

Figure 4. Study 4035: Fasting Lipid Changes From Baseline to Week 96 Overall and by Prior Use of TDF or Other OAVs[2,10]



TAF in Participants With Decompensated Cirrhosis and Ascites[4]

Study design and demographics

A prospective cohort study was conducted to evaluate the efficacy and safety of TAF 25 mg daily for 24 weeks in participants with CHB and decompensated cirrhosis with ascites (N=182). Most participants (70.9%) were male, and the mean age was 53.2 years.

Efficacy and safety

Of the 126 participants who had completed the 24-week treatment at the time of the analysis, 56.3% (n=71) achieved undetectable HBV DNA levels, and 76.2% (n=96) achieved ALT normalization at Week 24. From baseline to Week 24 of TAF treatment, statistically significant changes in the incidence of ascites, laboratory values, and liver severity scores were observed (Table 4). There was no significant difference from baseline to Week 24 in eGFR or in levels of WBCs, platelets, Hgb, triglycerides, blood urea nitrogen, or Cr.

Table 4. Clinical Parameters With Significant Changes From Baseline to Week 24 (Deng et al)[4]

Clinical Parameters		Baseline (N=182)	Week 24 (n=126)	*P*-Value
Ascites, n (%)	None	0	69 (54.8)	<0.001
	Grade 1 (mild)	126 (69.2)	40 (31.7)	
	Grade 2 (moderate)	48 (26.4)	12 (9.5)	
	Grade 3 (severe)	8 (4.4)	5 (4)	
Laboratory values (n=109)	RBC, mean ± SD, mmol/L, 10^{12}/L	4.18±0.7	4.46±1.29	0.018
	ALT, median (Q1, Q3), U/L	30.3 (19, 51.6)	24.8 (18.5, 33.7)	0.009
	AST, median (Q1, Q3), U/L	37.6 (25.8, 56.4)	29.8 (22.4, 36.5)	<0.001
	TB, median (Q1, Q3), mcmol/L	23.9 (16.5, 34.8)	18.9 (14.1, 25.8)	<0.001
	INR, median (Q1, Q3)	1.31 (1.2, 1.51)	1.21 (1.13, 1.33)	0.001
	Albumin, mean ± SD, g/L	36.8±7.74	40.6±6.69	<0.001
	TC,[a] mean ± SD, mmol/L	3.64±0.97	4.1±1.18	0.004
	HDL, mean ± SD, mmol/L	1.02±0.43	1.19±0.37	0.009
CP score, median (Q1, Q3)		7 (6, 9)	6 (5, 7)	<0.001
MELD score, median (Q1, Q3)		11.38 (9.18, 13.81)	9.43 (8.26, 12.29)	<0.001
APRI score, median (Q1, Q3)		1.35 (0.8, 2.91)	1.13 (0.69, 1.84)	0.002
FIB-4 score, median (Q1, Q3)		5.22 (2.83, 8.47)	4.13 (2.18, 6.97)	0.003

[a]At baseline, n=133; at Week 24, n=67.

Through 24 weeks of treatment, 6 participants developed gastroesophageal variceal bleeding, 5 developed hepatic encephalopathy, and 3 developed HCC. One death was reported.

Real-World Study: TAF Use in Decompensated Cirrhosis[5]

Study design

A multicenter, real-world study conducted in China assessed the effectiveness and safety of TAF treatment for CHB in patients with decompensated cirrhosis (N=106). The primary endpoint was the proportion of patients with undetectable HBV DNA (<20 IU/mL) after 48 weeks of treatment. Secondary endpoints included ALT normalization at 48 weeks. At baseline, most patients (n=72) were male, and the mean ± SD age was 53.5±9.26 years.

Efficacy and safety

From baseline to Week 48, the proportion of patients with undetectable HBV DNA improved significantly, from 57.55% (n/N=61/106) to 95.65% (n/N=44/46; *P*<0.001). The proportion of patients with normal ALT, defined as <40 U/L in both sexes, also increased significantly from 67.92% (n/N=72/106) at baseline to 89.13% (n/N=41/46) at Week 48 (*P*=0.004). After 48 weeks of TAF treatment, the proportion of patients with a CPT Class of B or C decreased significantly from 60.38% (n/N=64/106) at baseline to 30.43% (n/N=14/46) at Week 48 (*P*=0.004). Overall, 3 cases of HCC were reported. There were no cases of liver transplantation or drug-related AEs or SAEs, including deaths.

Switching to TAF in Participants With Decompensated Cirrhosis and Poor Response to Prior NUC Treatment or LLV[6]

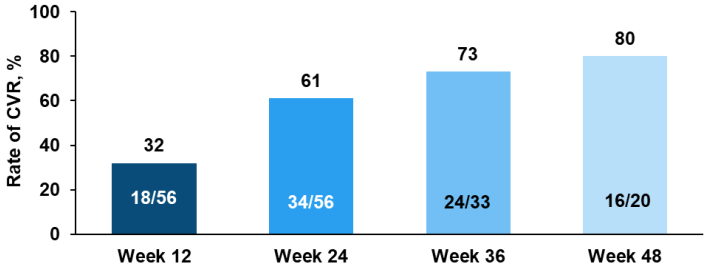
Study design

A prospective cohort study was conducted to evaluate the safety and efficacy of switching participants with decompensated cirrhosis (N=56) to TAF due to poor response to prior NUC therapy (HBV DNA ≥2000 IU/mL; n=30) or LLV (HBV DNA <2000 IU/mL; n=26) for ≥6 months. After switchover to TAF, virologic/biochemical responses were evaluated at 12-week intervals for 48 weeks.

Efficacy and safety

The overall CVR rate after participants switched to TAF improved and was significantly higher at Week 48 than at Week 12 (80% vs 32.14%; *P*<0.05; Figure 5). In the subgroup analysis, participants in the LLV group achieved a higher rate of CVR than did participants in the poor response group at Week 12 (61.54% vs 6.67%, respectively); there was no statistical difference in the rate of CVR between groups from Week 24 through Week 48.

Figure 5. Overall CVR (Zeng et al)[6]



Significant mean reductions of -0.44 log_{10} IU/mL in HBsAg level and -3.38 log_{10} IU/mL in HBV DNA level were observed at Week 48 compared with baseline (*P*<0.05).

The mean CPT score improved significantly from baseline to Week 48 (5.45 vs 8.66; *P*<0.05; Table 5). A significant improvement from baseline to Week 48 in the proportion of participants with CPT Class A was also observed (21.43% vs 85%; *P*<0.05).

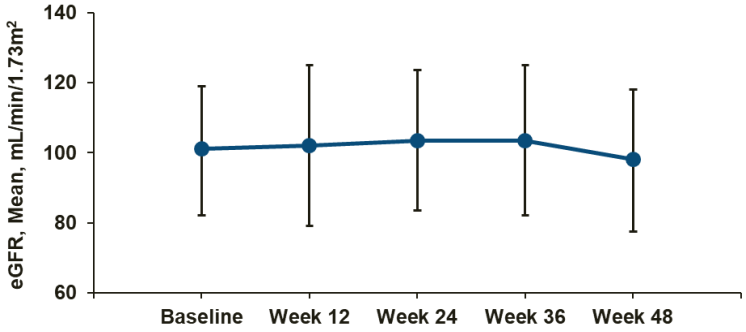
Table 5. CPT Scores From Baseline Through Week 48 (Zeng et al)[6]

	Baseline	Week 12	Week 24	Week 36	Week 48
CPT score	8.66	7.09	6.46	6.6	5.45[a]

[a]The CPT score at Week 48 was significantly different from the score at baseline (*P*<0.05).

No significant changes in SCr or phosphorus levels or eGFR were observed during the treatment period (Figure 6). A decrease in the median level of urinary β2M from 1.14 mg/L at baseline to 0.98 mg/L at Week 24 was observed; however, this change was not statistically significant.

Figure 6. Changes in $eGFR_{CKD-EPI}$ From Baseline Through Week 48 (Zeng et al)[6]



Note: Changes in mean $eGFR_{CKD-EPI}$ from baseline through Week 48 were not statistically significant.

Retrospective Study: TAF in Decompensated Cirrhosis[7]

A retrospective cohort study evaluated the efficacy and safety of TAF in patients with CHB and decompensated cirrhosis. Patients from four hospitals in China who received ≥96 weeks of treatment between January 2019 and February 2024 were eligible. A total of 203 patients had data through Week 96; 137 were TAF naive, and 66 had switched to TAF treatment. The primary endpoint was the rate of recompensation at Week 96, according to Baveno VII criteria. Secondary endpoints included changes in virological, serological, and biochemical parameters throughout treatment. Outcomes were compared between TAF-naive patients and those who switched to TAF.

At baseline, liver function tests (ALT, TB, and INR) and CP, MELD, and FIB-4 scores were significantly higher in the TAF-naive group than in the TAF-switch group (Table 6). At

Week 96, 59.6% of patients (121/203) were recompensated, and 97.5% (198/203) achieved virologic suppression. CP scores were similar at baseline, but starting at Week 24 and continuing through Week 96, were significantly lower among those who achieved recompensation than among those who did not; MELD scores decreased in a similar manner and were not significantly different between these groups during the study. Rates of recompensation, HBV DNA levels, and MELD scores were not significantly different between the TAF-naive and TAF-switch groups at Week 96.

Table 6. Demographics and Disease Characteristics at Baseline and Week 96 (Deng et al)[7]

Key Demographics and Characteristics	At Baseline		At Treatment Week 96	
	TAF-Naive (n=66)	TAF-Switch (n=137)	TAF-Naive (n=66)	TAF-Switch (n=137)
Age, years	51.4±10.1	53±10.1	–	–
Male, n (%)	47 (71.2)	92 (67.2)	–	–
HBV DNA, log_{10} IU/mL	4.59±2.31	1.19±0.89[a]	1.11±0.67	1.19±0.89
ALT, IU/L	48.7 (29.8, 91.3)	23.6 (17, 34.9)[a]	22.6 (17.7, 30.2)	21.8 (15.1, 28.8)
TB, mcmol/L	31.1 (21, 48.9)	21.6 (15.3, 30.8)[a]	17.7 (12, 26.3)	19.6 (15, 26)
Platelets, 10^9/L	87.5 (60, 112.8)	78 (108, 148)	86 (63.5, 149.8)	78 (52.5, 117)
INR	1.41 (1.23, 1.6)	1.28 (1.19, 1.44)[a]	1.11 (1.04, 1.24)	1.21 (1.13, 1.38)[a]
Cr, mcmol/L	71.5±31.9	74.5±22.5	65.1±12.3	68.5±17.9
CP scores	8.59±1.94	7.1±1.55[a]	5.31±0.48	6.06±1.27[a]
MELD scores	13.7±4.6	11.4±3.3[a]	8.61±2.14	10.12±2.83
FIB-4 scores	5.9 (3.7, 10.1)	4.7 (2.6, 7.4)[a]	2.68 (1.29, 5.1)	4.37 (2.39, 6.12)

[a]*P*<0.05 for comparison between the TAF-naive and TAF-switch groups.
Note: The study did not specify how the data were presented (ie, mean ± SD or median [Q1, Q3]).

Retrospective Study: TAF in HBV-Associated Decompensated Cirrhosis[8]

Study design and demographics

A retrospective study evaluated the effectiveness and safety of TAF vs TDF over 48 weeks in patients with HBV-associated decompensated cirrhosis. Overall, 61 patients treated with TAF and 70 treated with TDF and who had follow-up data through Week 48 were included. PS-matching was conducted to mitigate baseline demographic imbalances, and 38 patients were included in each group. Key baseline demographics and characteristics in the overall cohort and after PS-matching are included in Table 7.

Table 7. Baseline Demographics and Disease Characteristics (Chen et al)[8]

Key Demographics and Characteristics	Before PS-Matching		After PS-Matching	
	TAF (n=61)	TDF (n=70)	TAF (n=38)	TDF (n=38)
Age, mean ± SD, years	52.31±9.48	55.21±11.44	53.05±8.85	52.39±11.18
Male, n (%)	47 (77)	55 (78.6)	29 (80.6)	27 (75)
Detectable HBV DNA, n (%)	17 (27.9)	40 (57.14)	14 (36.8)	20 (52.6)
HBeAg+, n (%)	17 (27.9)	19 (27.14)	11 (28.9)	11 (28.9)
ALT, mean ± SD, U/L	32.08±20.67	52.76±57.87	36.66±22.33	30.32±17.75
Normal ALT, n (%)	48 (78.69)	46 (71)	27 (71.1)	32 (84.2)
eGFR, mean ± SD, mL/min/1.73 m^2	94.63±25.21	106.15±18.4	101.88±18.82	103.58±20.97
SCr, mean ± SD, mcmol/L	82.08±34.96	67.94±16.3	71.8±20.98	71±19.42

Results

Overall TAF group

In the TAF group from baseline to Week 48, the proportion of patients with detectable HBV DNA decreased from 27.9% to 13.1% (*P*=0.044), with 76.5% achieving virologic response (P<0.001). Over the same period, the percentage of patients with HBeAg+ status slightly increased, from 27.9% to 31.1% (*P*=0.887). From baseline to Week 48, mean ALT decreased non-significantly (from 26 U/L to 25 U/L; *P*=0.332), with 85.25% of patients achieving ALT normalization. SCr and eGFR remained stable, with an eGFR decline ≥25% occurring in 5.7% of patients. Non-significant reductions were observed in APRI (*P*=0.096), FIB-4 (*P*=0.334), and CP scores (*P*=0.959) from baseline to Week 48. No additional safety data were reported.

TAF vs TDF after PS-matching

Both groups achieved virologic suppression by Week 48, with reduced rates of detectable HBV DNA, while HBeAg+ status remained unchanged (Table 8). Mean SCr increased non-significantly from baseline to Week 48 in both groups; eGFR remained stable with TAF but declined with TDF, with an eGFR decline ≥25% observed in 5.2% vs 10.5% (*P*=0.39) of patients, respectively. From baseline to Week 48, mean ALT levels improved with TAF, with higher rates of ALT normalization observed over time, whereas minimal changes were observed with TDF. Non-significant between-group differences were observed in APRI (decrease with TAF [*P*=0.365] vs increase with TDF [*P*=0.763]) and FIB-4 (slight decrease with TAF [*P*=0.527] vs slight increase with TDF [*P*=0.729]) scores. CP scores remained stable in both groups.

Table 8. Change From Baseline to Week 48 in Laboratory Parameters in the PS-Matched TAF and TDF Groups (Chen et al)[8]

Laboratory Parameters	After PS-Matching					
	TAF (n=38)			TDF (n=38)		
	Baseline	Week 48	*P*-Value	Baseline	Week 48	*P*-Value
Detectable HBV DNA, n (%)	14 (36.8)	8 (21.1)	0.129	20 (52.6)	4 (10.5)	<0.001
HBeAg+, n (%)	11 (28.9)	11 (28.9)	-	11 (28.9)	11 (28.9)	-
ALT, mean ± SD, U/L	36.66 ± 22.33	31.0 ± 18.38	0.261	30.32 ± 17.75	29.42 ± 12.47	0.8
Normal ALT, n (%)	27 (71.1)	31 (81.6)	0.28	32 (84.2)	31 (81.6)	0.761
eGFR, mean ± SD, mL/min/1.73 m^2	101.88 ± 18.82	101.86 ± 22.24	0.928	103.58 ± 20.97	99.05 ± 20.33	0.343
SCr, mean ± SD, mcmol/L	71.8 ± 20.98	72.56 ± 28.77	0.921	71 ± 19.42	71.92 ± 18.09	0.831

PK Studies on TAF Use in Severe Hepatic Impairment

Multicenter, Open-Label, Single-Dose PK Study[9]

Study design

The PK of TAF was evaluated in a multicenter, open-label, parallel-design, single-dose study of TAF 25 mg in participants with severe hepatic impairment (CPT Class C, n=10) and was compared with data from matched-control participants with normal hepatic function (n=10).

PK and safety

TAF total exposures were 46% lower in participants with severe hepatic impairment than in matched-control participants. However, the free fraction of TAF increased (~2-fold) compared with that of matched controls; participants with severe hepatic impairment had lower albumin levels than normal matched controls. Additionally, the free AUC of TAF (unbound TAF) was comparable between participants with severe hepatic impairment (42.8 h·ng/mL) and matched controls (46.5 h·ng/mL).

TAF 25 mg was generally well tolerated, and no participants discontinued due to AEs. Additionally, the majority of AEs were mild (Grade 1). One participant in the severe hepatic impairment group had a Grade 3 AE/SAE of hepatic failure; this was reported post treatment on follow-up Day 27 and was considered unrelated to the study drug by the investigator.

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Abbreviations

β2M=β2-microglobulin
AASLD=American Association for the Study of Liver Disease
AE=adverse event
APRI=AST-to-platelet ratio index
AUC=area under the concentration-time curve
BMD=bone mineral density
CG=Cockcroft-Gault formula
CHB=chronic hepatitis B
CKD=chronic kidney disease
CKD-EPI=Chronic Kidney Disease Epidemiology Collaboration equation
CP=Child-Pugh
CPT=Child-Pugh-Turcotte
CVR=complete virologic response
FIB-4=Fibrosis-4 score
HBeAg=hepatitis B envelope antigen
HBsAg=hepatitis B surface antigen
HCC=hepatocellular carcinoma
LLV=low-level viremia
M=E=missing=excluded
M=F=missing=failure
MELD=Model for End-Stage Liver Disease
NUC=nucleos(t)ide analog
OAV=oral antiviral
PK=pharmacokinetic(s)
PS=propensity score
Q=quartile
SAE=serious adverse event
TAF=tenofovir alafenamide
TB=total bilirubin
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TND=target not detected
ULN=upper limit of normal

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.

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