GILEAD | Medical Information

Vemlidy® (tenofovir alafenamide) Lipid Abnormalities

This document is in response to your request for information regarding Vemlidy® (tenofovir alafenamide [TAF]) for the treatment of chronic HBV (CHB) and lipid abnormalities observed in clinical studies.

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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]

At Week 96, among participants treated with TAF, LDL-cholesterol and TG levels were increased and TC and HDL-cholesterol levels were decreased, with no change in TC to HDL ratio relative to baseline and remained similar at Week 120.

Clinical Data on TAF and Lipid Abnormalities

Studies 108 and 110 (Week 96 and Year 8 results vs baseline), Study 4018 (Week 96 vs baseline), and Study 4035 (Week 48 vs baseline; participants with moderate to severe renal impairment, ESRD, or hepatic impairment):

- In participants treated with TAF, lipid parameters were observed to change minimally to modestly in clinical studies at Weeks 48 and 96, with small increases in TC, LDL, TG, and small decreases in HDL noted through Week 384 (Year 8) in Studies 108 and 110.[2-6]
- TC to HDL ratio was either slightly decreased or unchanged at Weeks 48 and 96 across clinical studies and minimally increased over 8 years in Studies 108/110. Additionally, at Week 96, there was no significant difference in ASCVD risk in terms of change from baseline between participants treated with TAF or TDF in Studies 108 and 110.[2-6]
- Across clinical studies, treatment with TDF resulted in decreases in lipid parameters. Switching from TDF to TAF resulted in increases in lipid parameters to levels consistent with those seen in participants treated with TAF throughout the studies.[2-6]

Real-World Studies on TAF and Lipid Abnormalities

- Korean cohort study: In the entire cohort, patients who received TAF had lower cumulative incidence rates of ASCVD, AMI or coronary revascularization, and ischemic stroke over 5 years than those who received TDF.[7]
- Japanese retrospective study: Starting at 24 weeks after switching and continuing through 3 years of follow-up, patients who switched from TDF to TAF had significant increases in TC, LDL, HDL, and TG compared with patients who switched from ETV.[8]
- Chinese retrospective study: After 24 weeks, TC levels were significantly increased from baseline and TG levels did not change significantly in the TAF group, whereas both TC

and TG levels were significantly decreased in the TDF group. At Week 24, TC and TG levels were significantly higher in the TAF group than in the TDF group.[9]

- Chinese and Turkish studies: After switching to TAF from other antivirals, there were no significant changes in lipid profiles through up to 12 months of treatment.[10,11]
- Taiwanese study: After switching to TAF, there were significant increases in all lipid parameters in participants who switched from TDF, but not in those who switched from ETV. There were no significant changes in ASCVD risk scores in either switch group.[12]
- Chinese study (TAF vs TDF vs ETV): At Week 48, significantly lower TC levels were observed with TDF than with TAF. No significant differences were seen in lipid parameters between TAF and ETV.[13]

Product Labeling[1]

Clinical Trials Experience

Laboratory abnormalities: serum lipids

Changes from baseline in TC, HDL, LDL, TG, and TC to HDL ratio among subjects treated with TAF and TDF in Trials 108 and 110 are presented in Table 1.

Table 1. Lipid Abnormalities: Mean Change From Baseline in Lipid Parameters in Patients With CHB Infection and Compensated Liver Disease in Trials 108 and 110 (Week 96 Analysis)[1]

Lipid Panel Results	TAF (n=866)		TDF (n=432)	
	Baseline	Change From Baseline[a] to Week 96	Baseline	Change From Baseline[a] to Week 96
TC (fasted), mg/dL	188 (n=835)	-1 (n=742)	193 (n=423)	-25 (n=368)
HDL-cholesterol (fasted), mg/dL	60 (n=835)	-5 (n=740)	61 (n=423)	-12 (n=368)
LDL-cholesterol (fasted), mg/dL	116 (n=835)	+7 (n=741)	120 (n=423)	-10 (n=368)
TG (fasted), mg/dL	102 (n=836)	+13 (n=743)	102 (n=423)	-7 (n=368)
TC to HDL ratio	3 (n=835)	0 (n=740)	3 (n=423)	0 (n=368)

[a]The change from baseline is the mean of within-subject changes from baseline for subjects with both baseline and Week 96 values.

In the OL phase, lipid parameters at Week 120 in subjects who remained on TAF were similar to those at Week 96. In subjects who switched from TDF to TAF, mean change from Week 96 to Week 120 in TC was 23 mg/dL, HDL was 5 mg/dL, LDL was 16 mg/dL, TG was 30 mg/dL, and TC to HDL ratio was 0 mg/dL.

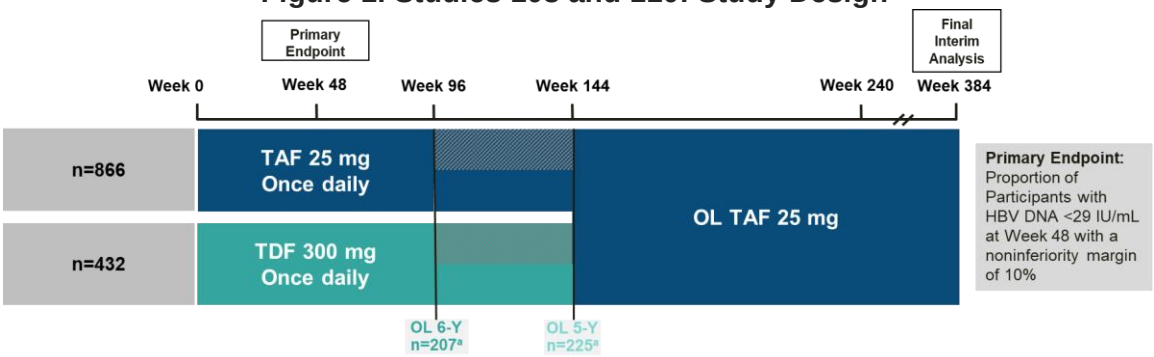
Clinical Data on TAF and Lipid Abnormalities

Studies 108 and 110

Study design

Studies 108 and 110 were phase 3 clinical trials that evaluated the safety and efficacy of TAF compared to TDF in predominantly nucleos(t)ide-naïve participants with CHB. A total of 1298 adult participants monoinfected with CHB and with compensated liver function were randomly assigned to receive TAF 25 mg or TDF 300 mg for 144 weeks in Studies 108 (HBeAg-; n=425) and 110 (HBeAg+; n=873) followed by OL TAF to Week 384 (Year 8). A subset of participants, after completing 96 weeks of double-blind TAF or TDF, entered the OL phase of TAF treatment (Figure 1).[14-16]

Figure 1. Studies 108 and 110: Study Design[2,15]



[a]Participants who received TDF during the double-blind period and then switched to TAF.

Cardiovascular risk analysis at Week 96

Changes from baseline in fasting lipid levels were compared between patients who received TAF and those who received TDF to determine the effect of these medications on cardiovascular risk. All participants who met the American College of Cardiology criteria for a 10-year ASCVD risk assessment at baseline and who had ≥1 post-baseline result were included in this analysis (TAF, n=400; TDF, n=220). American College of Cardiology/ American Heart Association pooled cohort equations were used, and shifts in the 10-year ASCVD risk from baseline to Week 96 were evaluated with intermediate (≥7.5%) and high-risk (≥20%) cutoffs. The key endpoints were changes from baseline to Week 96 in fasting lipid levels, estimated 10-year ASCVD risk, and proportion of participants who were eligible for lipid-lowering therapy according to American Heart Association guidelines.[6]

Results

From baseline to Week 96, significant increases in LDL levels, TG levels, and TC to HDL ratio and significant decreases in HDL levels were observed with TAF treatment, whereas TDF treatment resulted in significant decreases in TC, LDL, HDL, and TG levels and a significant increase in TC to HDL ratio (Table 2). Changes in fasting TC, LDL, HDL, and TG levels were significantly different between the TAF and TDF arms at all time points assessed (starting at Week 4 for TC and TG, and at Week 24 for LDL and HDL) through Week 96. In the overall population (TAF, n=1093; TDF, n=539), a greater proportion of participants who received TAF than those who received TDF became eligible for

lipid-lowering therapy (6.4% vs 1.1%; *P*<0.0001); however, few of these eligible participants initiated therapy (4.9% vs 0%, respectively).[6]

Table 2. Studies 108 and 110: Lipid Parameters Measured From Baseline to Week 96[17]

Fasting Lipid Parameter		TAF (n=400)	TDF (n=220)
TC, median (IQR), mg/dL	Baseline	187 (168–213)	192 (171–215)
	Week 96	187 (164–210)	167 (151–192)
	Change from baseline	0[a]	-25[a]
	P-value for change from baseline	0.15	<0.0001
TG, median (IQR), mg/dL	Baseline	97 (71–126)	97 (74–118)
	Week 96	105 (74–140)	85 (67–118)
	Change from baseline	8[a]	-12[a]
	P-value for change from baseline	<0.0001	<0.0001
LDL, median (IQR), mg/dL	Baseline	114 (97–136)	120 (103–141)
	Week 96	122 (102–147)	111 (95–132)
	Change from baseline	8[a]	-9[a]
	P-value for change from baseline	<0.0001	<0.0001
HDL, median (IQR), mg/dL	Baseline	60 (48–72)	62 (50–72)
	Week 96	53 (44–63)	48 (39–57)
	Change from baseline	-7[a]	-14[a]
	P-value for change from baseline	<0.0001	<0.0001
TC to HDL ratio, median (IQR)	Baseline	3.2 (2.6–3.9)	3.2 (2.6–3.8)
	Week 96	3.5 (2.9–4.3)	3.5 (2.9–4.2)
	Change from baseline	0.3	0.3
	P-value for change from baseline	<0.0001	<0.0001

[a]*P*<0.0001 for comparison between treatment arms.

Over 96 weeks, no significant shifts in 10-year ASCVD risk categories were observed in either treatment arm, with a few participants who did not meet the intermediate- or high-risk thresholds at baseline shifting to the intermediate- or high-risk categories at Week 96.[6,17] The proportions of participants at intermediate and high risk at Week 96 who did not meet these thresholds at baseline were 5.8% and 1.7%, respectively, in the TAF arm and 6.4% and 1.1%, respectively, in the TDF arm. Median changes in 10-year risk were similar between the TAF and TDF groups at Weeks 24 and 96. At Weeks 48 and 72, increases in 10-year ASCVD risk were significantly greater in the TAF group than in the TDF group (*P*=0.0028 and *P*=0.0005, respectively). The incidences of treatment-emergent cardiovascular events were similar between the TAF (5/400; 1.3%) and TDF (5/220; 2.3%) arms.[6]

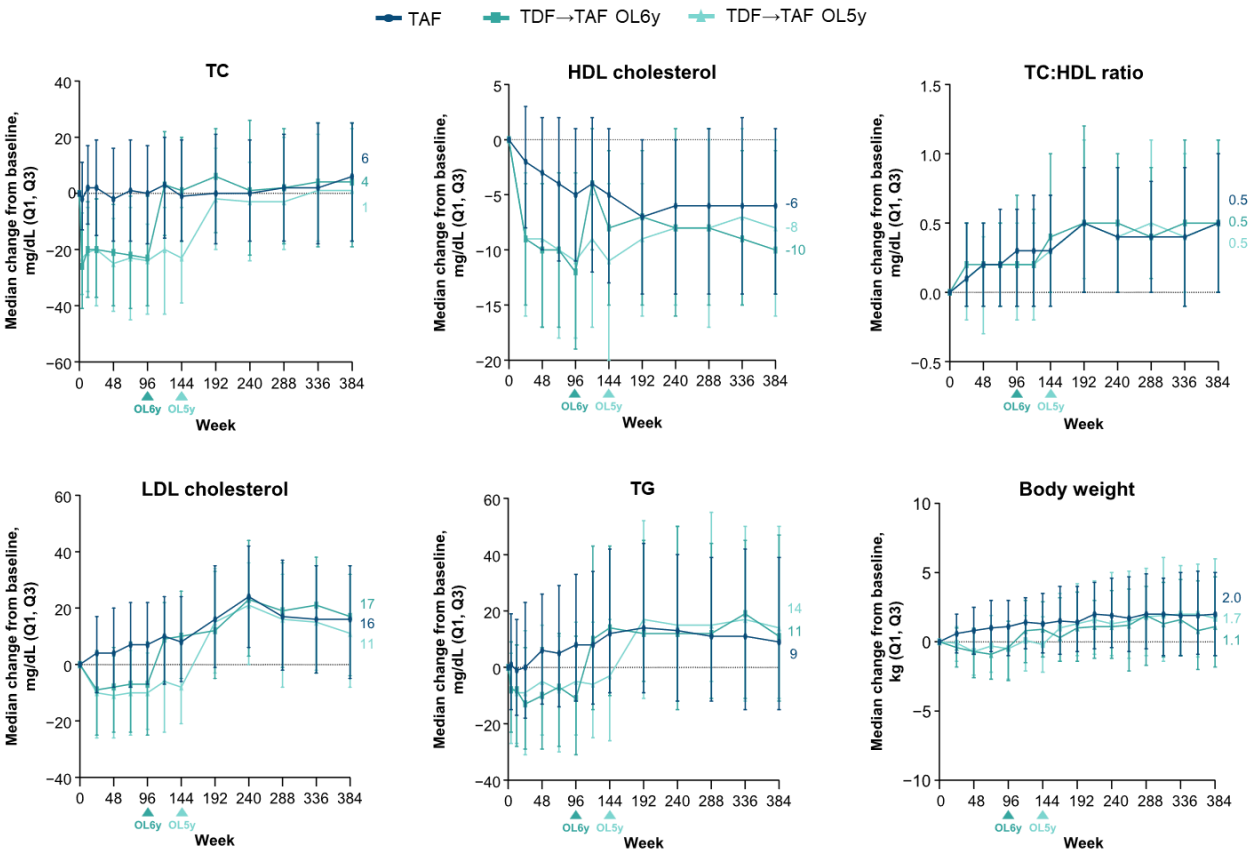
Year 8 final interim analysis lipid results[2]

In the TAF treatment arm, median TC, LDL, and TG levels increased by a small degree, and median HDL decreased by a small degree. In the TDF→OL TAF 6- and 5-year treatment arms, modest decreases in TC, LDL, HDL, and TG levels were observed during the double-blind phase of TDF treatment (due to the lipid-lowering effect of TDF), and increases in these parameters were observed once participants were switched to TAF. The TC to HDL ratio increased slightly (≤0.5 fold) in each of the treatment arms (Figure 2).

During the OL phase, Grade 3 abnormalities in fasting LDL levels were noted in 6% of participants (45/760) in the TAF treatment arm and 8% (30/373) in the combined TDF→OL TAF treatment arms. Grade 3 abnormalities in fasting cholesterol levels were noted in 1% of participants (11/767) in the TAF treatment arm and 3% (11/373) in the combined TDF→OL

TAF treatment arms. Grade 3 or 4 abnormalities in fasting TGs were noted in 1% of participants (5/767) in the TAF treatment arm and 2% (7/373) in the combined TDF→OL TAF treatment arms.

Figure 2. Studies 108 and 110: Changes in Fasting Lipid Panel and Body Weight Over 8 Years[2]

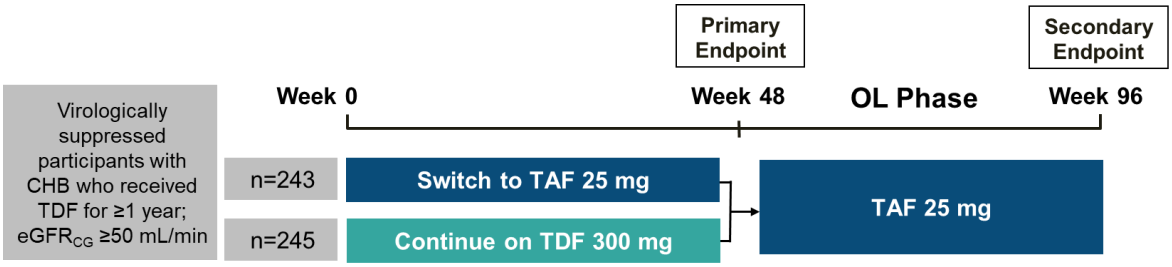


Study 4018

Study design

Study 4018, a double-blind, randomized, 96-week, phase 3 study, evaluated the safety and efficacy of switching from TDF to TAF (n=243) compared with continuing TDF (n=245) in virologically suppressed participants with CHB who had been treated with TDF for ≥48 weeks prior to screening and had an $eGFR_{CG}$ ≥50 mL/min at screening. The primary endpoint was the number of participants with HBV DNA ≥20 IU/mL (noninferiority to TDF) at Week 48. After Week 48, participants were able to enter an OL phase and received TAF.[18]

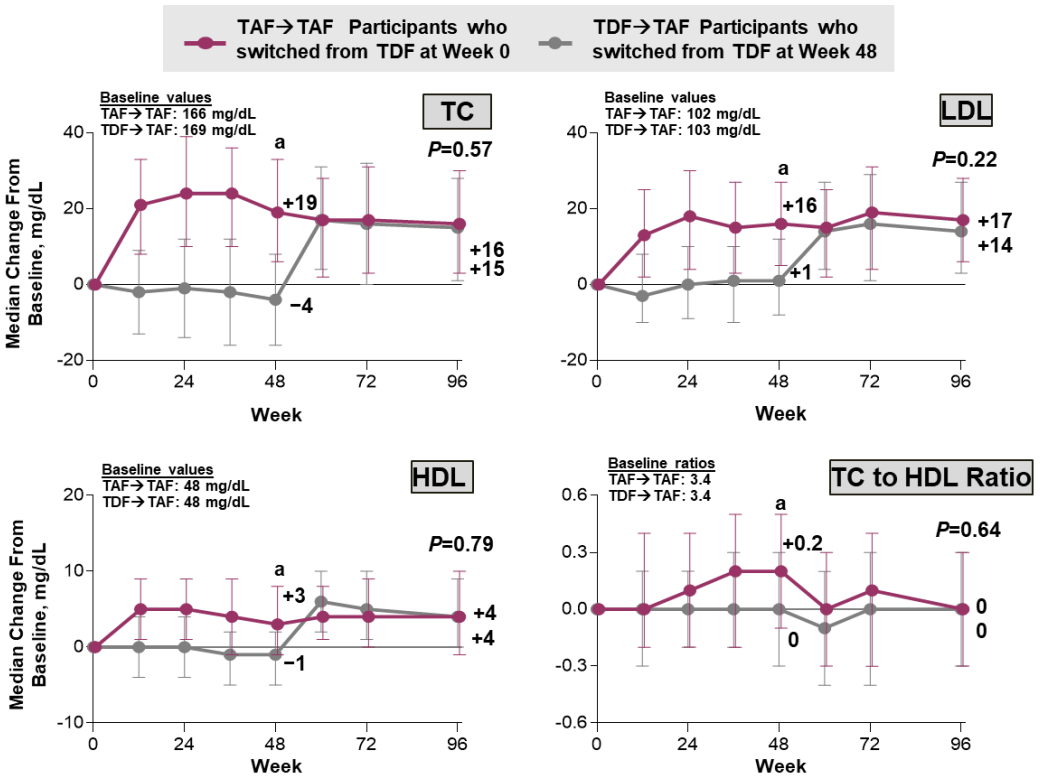
Figure 3. Study 4018: Study Design[3,18]



Week 96 lipid results[3]

Lipid parameters (TC, LDL, and HDL) increased modestly in both arms from baseline to Week 96; however, the TC to HDL ratio was unchanged in both arms at Week 96 relative to baseline (Figure 4). The proportion of participants who began lipid-lowering treatments was not different between arms. TG levels were not reported.

Figure 4. Study 4108: Changes in Fasting Lipid Panel Over 96 Weeks[3]



[a]Each *P*-value was <0.001 for the median changes in fasting lipids at Week 48.

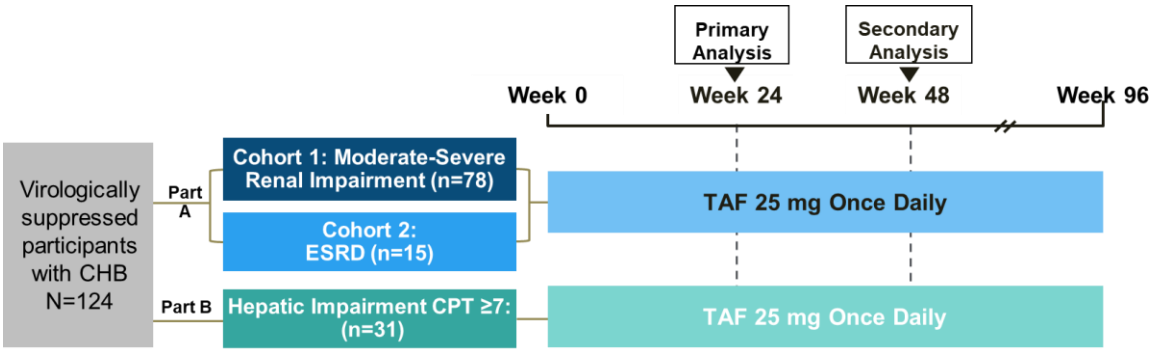
Study 4035

Study design[4,5,19,20]

Study 4035 was a phase 2, OL switch study that evaluated the efficacy and safety of switching from TDF and/or other oral antivirals to TAF in participants with CHB who are virologically suppressed and who have (1) moderate to severe renal impairment (n=78), (2) ESRD maintained on chronic hemodialysis (n=15), or (3) moderate to severe hepatic impairment (n=31). The primary endpoints were the safety and tolerability of TAF and the

proportion of participants who achieved virologic response (HBV DNA <20 IU/mL) at Week 24 (primary analysis). Analyses of the effect of each treatment on fasting lipid panels were conducted for all participants (at Week 48) and by prior CHB treatment (TDF or other oral antivirals).

Figure 5. Study 4035: Study Design[4,5,19,20]

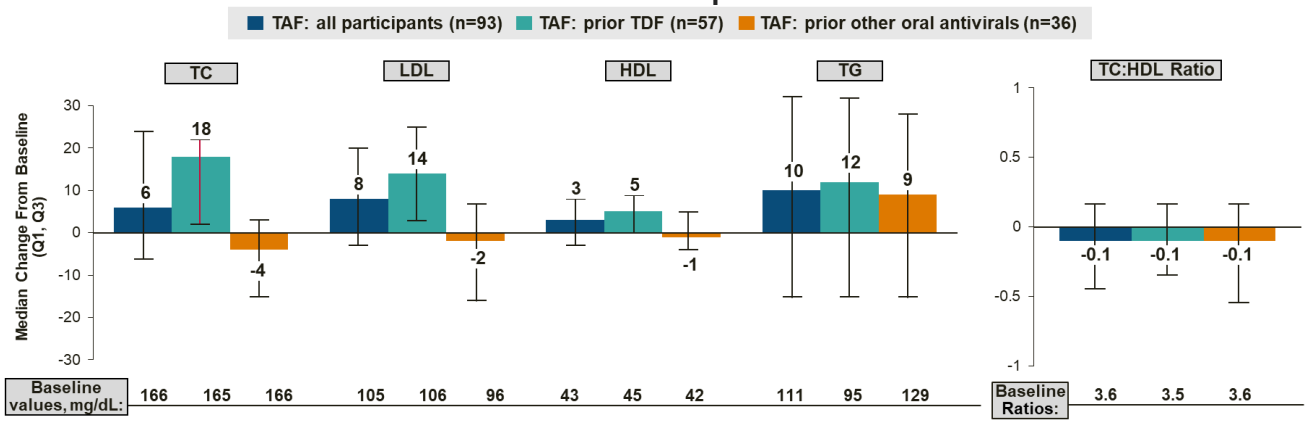


Note: The study included participants who were virologically suppressed with HBV DNA levels <20 IU/mL at screening and HBV DNA levels less than the lower limit of quantitation for ≥24 weeks and had received TDF and/or other oral antivirals for ≥48 weeks. Moderate-severe renal impairment was defined by a CrCl of 15 to <60 mL/min, and ESRD was defined by a CrCl <15 mL/min. Participants in the hepatic impairment cohort had CPT scores of 7 to ≤12 at screening (or had a history of a CPT score of ≥7 and any CPT score ≤12 at screening) and CrCl ≥30 mL/min.

Renal impairment subanalysis: Week 48 lipid results[4,5]

At Week 48, participants who had previously used TDF had the greatest increases in TC, LDL, HDL, and TG levels; participants who previously used other oral antivirals had decreases in TC, LDL, and HDL levels. There was a slight decrease in the TC to HDL ratio that was similar across all groups (Figure 6).

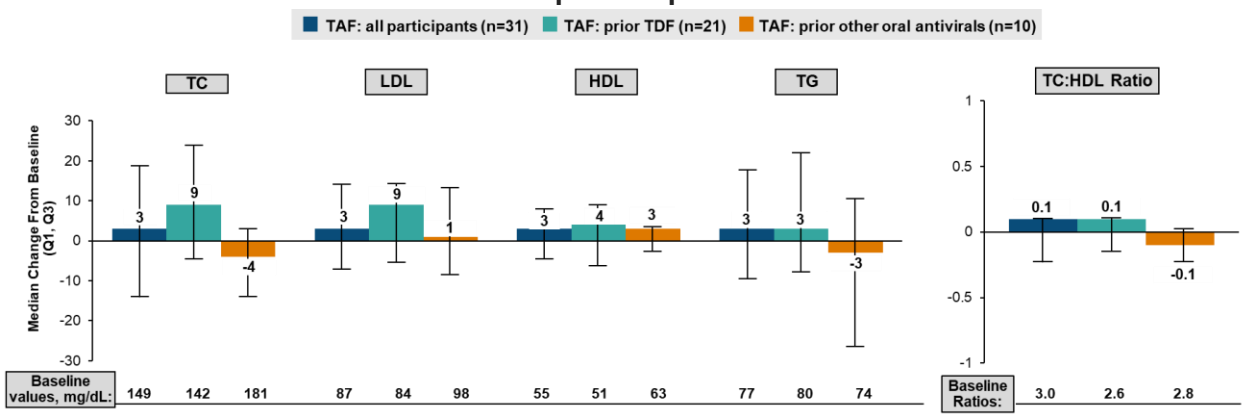
Figure 6. Study 4035: Changes in Fasting Lipid Panel at Week 48 in Participants With Moderate to Severe Renal Impairment and ESRD[4]



Hepatic impairment subanalysis: Week 48 lipid results[5]

At Week 48, participants who had previously received TDF had the greatest increases in TC, LDL, HDL, and TG levels; participants who previously used other oral antivirals had decreases in TC and TG levels and increases in LDL and HDL levels. There were only slight changes in the TC to HDL ratio, and they were similar across all groups (Figure 7).

Figure 7. Study 4035: Changes in Fasting Lipid Panel at Week 48 in Participants With Hepatic Impairment[5]



Real-World Studies on TAF and Lipid Abnormalities

Korean Retrospective Study[7]

A population-based cohort study evaluated the long-term risk of ASCVD in patients with CHB who received TAF (n=16,120) or TDF (n=28,594).

After 5 years of treatment and compared to those who received TDF, before PS matching, patients who received TAF had a lower cumulative incidence rate of ASCVD (4.6/1000 PY vs 6.88/1000 PY; SHR, 0.64; 95% CI, 0.54–0.75; *P*<0.001), AMI or coronary revascularization (1.42/1000 PY vs 1.86/1000 PY; SHR, 0.73; 95% CI, 0.54–0.98; *P*=0.04), and ischemic stroke (0.56/1000 PY vs 1.08/1000 PY; SHR, 0.49; 95% CI, 0.31–0.77; *P*=0.002).

In a similar comparison within the PS-matched cohort (N=15,159; TAF:TDF, 1:1), patients who received TAF still had a lower cumulative incidence rate of ASCVD (4.67/1000 PY vs 6.67/1000 PY; SHR, 0.70; 95% CI, 0.58–0.85; *P*<0.001),ischemic stroke (0.59/1000 PY vs 1.06/1000 PY; SHR, 0.57; 95% CI, 0.34–0.95; *P*=0.03), and a comparable incidence rate for AMI or coronary revascularization (1.41/1000 PY vs 1.74/1000 PY; SHR, 0.81; 95% CI, 0.57–1.16; *P*=0.26) than those who received TDF.

Select factors which were associated with ASCVD development are shown in Table 3.

Table 3. Korean Retrospective Study: Multivariable Analyses of Select Factors Associated with ASCVD Development in Patients Treated with TAF or TDF[7]

Variable		aHR	95% CI	*P*-Value
TAF vs TDF		0.73	0.62–0.87	<0.001
Male vs female		1.59	1.34–1.89	<0.001
Age, years	18–39	1	Reference	–
	40–49	2.28	1.78–2.93	<0.001
	50–59	3.17	2.47–4.06	<0.001
	60–69	4.57	3.45–6.05	<0.001
	≥70	9.12	6.19–13.44	<0.001

Variable		aHR	95% CI	*P*-Value
Smoking	Never	1	Reference	–
	Previously	1.15	0.9–1.49	0.27
	Currently	1.36	1.07–1.74	0.01
	Unknown	Not estimable	–	0.96
Comorbidities	Hypertension	1.31	1.1–1.56	0.002
	Diabetes mellitus	1.08	0.9–1.3	0.42
	Dyslipidemia	0.95	0.81–1.1	0.47
	CKD	1.36	0.67–2.75	0.39
AST	<40 U/L	1	Reference	–
	≥40 U/L	1.36	1.05–1.78	0.02
	N/A	1.11	0.17–7.06	0.92

Abbreviations: aHR=adjusted hazard ratio; CKD=chronic kidney disease.

Japanese Retrospective Study[8]

A multicenter, retrospective cohort study in Japan evaluated the long-term effects on lipids of switching from ETV or TDF to TAF monotherapy treatment in 324 patients with CHB. Eligible patients had been treated with ETV (n=193) or TDF (n=131) for ≥2 years and had ≥144 weeks of follow-up during TAF treatment. Changes in fasting lipid parameters were a primary endpoint of the study.

At 3 years after switching, compared with patients who switched from ETV to TAF, those who switched from TDF had significant increases in TC (ETV→TAF, +7 mg/dL; TDF→TAF, +24 mg/dL; *P*<0.001), LDL (ETV→TAF, +5 mg/dL; TDF→TAF, +15 mg/dL; *P*<0.01), HDL (ETV→TAF, -2 mg/dL; TDF→TAF, +6 mg/dL; *P*<0.001), and TG (ETV→TAF, +7 mg/dL; TDF→TAF, +15 mg/dL; *P*<0.01). These differences in fasting lipid levels were significant starting at 24 weeks after switching and were maintained during the study follow-up. In contrast, the TC to HDL ratio remained stable throughout the follow-up period in both treatment groups.

Chinese Retrospective Study[9]

A retrospective study evaluated the lipid effect of 24 weeks of treatment with TAF or TDF in 298 patients with CHB (TAF, n=143; TDF, n=155).

After 24 weeks, patients in the TAF group had significantly increased TC levels compared to baseline (4.48 mmol/L vs 4.22 mmol/L vs; *P*=0.009) and TG levels remained stable compared to baseline (0.98 mmol/L vs 1.01 mmol/L; *P*=0.71), whereas patients in the TDF group had significant decreases in both TC and TG (*P*<0.001) compared to baseline. At Week 24, TC and TG levels were significantly higher (*P*<0.001) in the TAF group than in the TDF group; the difference in levels between the two groups was not significant at baseline.

In a PS-matched cohort (N=160; TAF:TDF, 1:1), the proportion of patients with TC ≥5.2 mmol/L significantly decreased in the TDF group from baseline to Week 24 (*P*=0.008), and was also significantly lower in the TDF group than in the TAF group at Week 24 (*P*=0.022). There were no significant changes observed in the proportion of patients with TG ≥1.7 mmol/L from Week 0 to Week 24 in both the TAF and TDF groups.

In multivariate analyses, TAF treatment vs TDF (OR, 3.646; 95% CI: 2.011–6.642; *P*<0.001) and baseline ALT level (OR, 1.002; 95% CI: 1–1.003; *P*=0.014) were independent factors associated with a >10% increase in TC levels at 24 weeks. Similar results were found in univariate analyses.

Chinese Real-World Study[10]

A real-world study evaluated the lipid changes associated with TAF in patients with CHB and diabetes (N=53). The majority of patients were male (90.6%), the median age was 50.1 years, and the median HbA1c was 6.9%. Forty patients included in this study had switched from another nucleoside analogue to TAF. Lipid parameters were tested at Weeks 12 and 24.

Lipid measurements at baseline and Weeks 12 and 24 are presented in Table 4. Switching to TAF did not have a significant effect on lipid profiles.

Table 4. Chinese Real-World Study: Lipid Measurements Through Week 24[10]

		Treatment Naïve (n=13)	Switch (n=40)
TC, median ± SD, mmol/L	Baseline	5.23±1.46	4.38±0.96
	Week 12	4.56±1.11	4.59±0.92
	Week 24	5.22±1.44	4.57±0.84
	P-value	0.427	0.569
TG, median ± SD, mmol/L	Baseline	1.51±0.81	1.45±0.61
	Week 12	1.25±0.39	1.56±0.87
	Week 24	1.36±0.54	1.66±1.04
	P-value	0.606	0.622
LDL, median ± SD, mmol/L	Baseline	3.51±1.27	2.76±0.96
	Week 12	3.19±0.92	2.91±0.98
	Week 24	3.75±1.45	2.98±1.04
	P-value	0.587	0.663
HDL, median ± SD, mmol/L	Baseline	1.11±0.15	1.02±0.27
	Week 12	1.09±0.17	1.05±0.26
	Week 24	1±0.2	1.01±0.22
	P-value	0.349	0.791
TC to HDL ratio, median ± SD	Baseline	4.72±1.2	4.49±1.11
	Week 12	4.23±1.07	4.51±1.11
	Week 24	5.47±2.08	4.64±0.91
	P-value	0.185	0.859

Kidney injuries occurred in 29 patients, and 11 of those were considered to be related to TAF. After patients switched from TDF to TAF, LDL and eGFR increased, and urine β2-microglobulin decreased.

Turkish Real-World Study[11]

Study design and demographics

A multicenter, real-world study in Turkey evaluated efficacy outcomes and changes in renal and lipid measurements for up to 12 months after switching to TAF in treatment-experienced patients with CHB (N=509). The majority of patients were male (59.3%), the median age was 53 years, the median ALT was 23 U/L, 86.1% were HBeAg-, and 24% had an HBV DNA >20 IU/mL. The majority of patients switched from TDF (83.9%); others switched from ETV (6.8%), lamivudine (5.5%), telbivudine (3%), or adefovir (0.8%). Most patients (90.6%) had been receiving treatment with other antivirals for >12 months prior to the switch to TAF. At baseline, the median histological activity index score was 7 and the median fibrosis score was 2.

Results

Of the 509 patients who initiated the study, data were available for 283 at Month 6, and 203 at Month 12. The reasons for switching to TAF are shown in Table 5.

Table 5. Turkish Real-World Study: Reason for Switch to TAF Treatment[11]

Switch Indication	n (%)	Switch Indication	n (%)
Osteoporosis	206 (40.5)	Proteinuria/albuminuria	49 (9.6)
Blood phosphate level	108 (21.2)	Transplantation	11 (2.2)
Physicians' decision	65 (12.8)	Steroid	6 (1.2)
GFR	62 (12.2)	Fracture history	2 (0.4)
Medicine affecting bone mineral density	59 (11.6)	Dialysis	2 (0.4)

Virologic suppression (HBV DNA <20 IU/mL) and ALT normalization (per American Association for the Study of Liver Diseases criteria) improved significantly from baseline to Month 12 (P<0.05). Lipid levels and renal function parameters did not change significantly (P>0.05) for up to 12 months after switching to TAF. Lipid measurements at baseline through Month 12 are presented in Table 6.

Table 6. Turkish Real-World Study: Lipid Measurements Up to 12 Months After Switching to TAF[11]

	Month 0	Month 3	Month 6	Month 12	*P*-Value
HDL, median ± SD, mg/dL	45±18.3	49±14.2	47±18	51±12.8	>0.05
LDL, median ± SD, mg/dL	116±43.3	125±37.9	129±43	132±45.3	>0.05
TC, median ± SD, mg/dL	184.5±45.1	200±46.8	203±54.2	205±55.5	>0.05
TG, median ± SD, mg/dL	102±59.5	129±66.5	113.5±81.4	97±75.1	>0.05

TAF was well tolerated; the most common adverse events were headache (8%), nausea (3%), fatigue (3%), and rash (1%).

Taiwanese Observational Study[12]

Study design and demographics

A prospective, multicenter, observational study in Taiwan evaluated changes in body weight (primary endpoint) for up to 48 weeks after switching to TAF treatment in 177 participants with CHB who had previously been treated with TDF (n=99) or ETV (n=78). Secondary endpoints included changes from baseline in lipid profiles (assessed 24 and 48 weeks after switching) and ASCVD score (assessed at 48 weeks). At baseline, the TDF switch group had significantly lower levels of TG (P=0.009), TC (P<0.001), LDL (P=0.001), and HDL than the ETV switch group (P=0.005).

Results

During 48 weeks of TAF treatment, there were significant increases in all lipid parameters in the TDF switch group, whereas lipid profiles did not change significantly from baseline to Week 48 in the ETV switch group (Table 7). In addition, significant (P≤0.032) increases in body weight were seen from baseline in the TDF switch group through Week 48, whereas body weight did not change significantly from baseline in the ETV switch group.

Table 7. Taiwanese Observational Study: Lipid Parameter Results[12]

		TDF Switch (n=93)	ETV Switch (n=63)
TC, mean ± SD, mg/dL	Baseline	165.3±33.3	194.3±35.3
	Week 24	188.8±37.2[a]	193.2±34.4
	Week 48	191.2±41[a]	194.5±34.5
TG, mean ± SD, mg/dL	Baseline	88.7±50.4	107.9±58.4
	Week 24	98.2±59.5[b]	105.9±60.6
	Week 48	103.2±68.6[c]	98±40
LDL, mean ± SD, mg/dL	Baseline	107.1±28	123.7±28.9
	Week 24	123.7±33.7[a]	122.8±29
	Week 48	124.8±35.3[a]	127.1±27.4
HDL, mean ± SD, mg/dL	Baseline	48±12.3	52.5±13.9
	Week 24	53.5±13.7[a]	52.9±14.7
	Week 48	53.5±13.7[a]	52.5±15.1

[a]*P*<0.001 for change from baseline. [b]*P*=0.018 for change from baseline. [c]*P*=0.002 for change from baseline.

Mean (± SD) ASCVD risk scores in both treatment groups showed no significant changes between baseline and Week 48 (TDF switch: 7.2±9.8 at baseline and 7.8±9.7 at Week 48; *P*=0.064; ETV switch: 10.1±12.8 at baseline and 10.6±14.3 at Week 48; *P*=0.309).

Chinese Real-World, Retrospective Study[13]

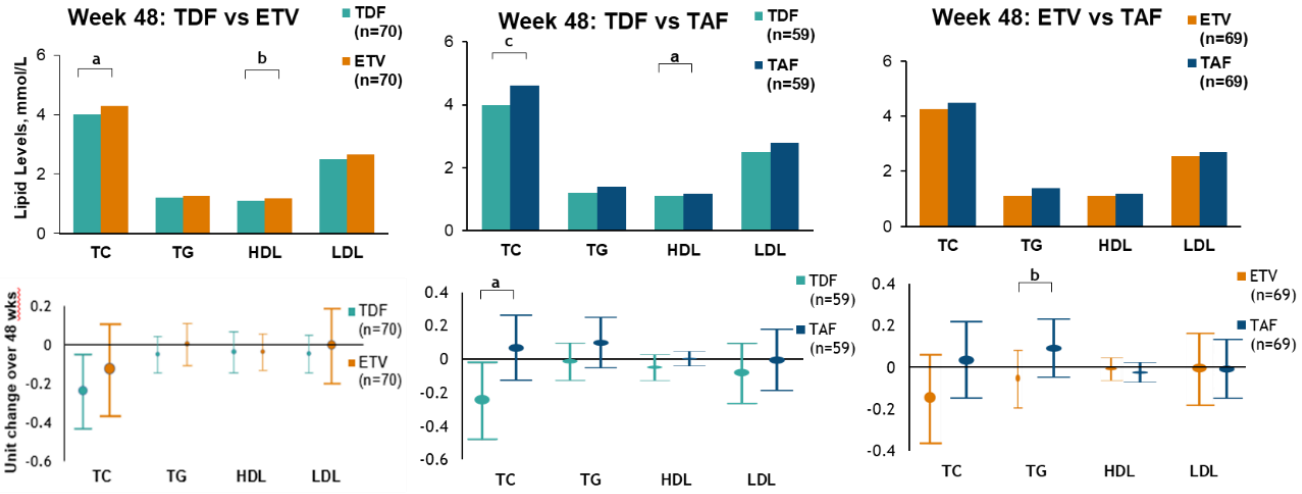
Study design

A retrospective, single-center cohort study assessed the lipid profiles of 233 treatment-naïve patients with CHB after receiving ETV, TDF, or TAF for ≥48 weeks (July 2019–March 2022) at Beijing Ditan Hospital. Propensity score matching was used to assess effects on the patients' lipid profiles, and a logistic regression model was used to estimate PSs according to baseline characteristics including age, sex, liver function tests, lipid profiles, blood cell count, creatinine, and log HBV DNA level. Analyses were run on matching cohorts for TDF:ETV (70:70), TDF:TAF (59:59), and ETV:TAF (69:69).

Results

At 48 weeks, there were no significant lipid changes from baseline in the TAF and ETV groups; however, there was a significant decrease from baseline in TC in the TDF group (baseline, 4.3 mmol/L; Week 48, 3.97 mmol/L; *P*=0.029). In terms of between-group comparisons, significantly lower TC levels were observed in the TDF group than in the ETV and TAF groups at Week 48. Patients in the TDF group also exhibited a significantly lower HDL level than patients in the TAF and ETV groups (*P*<0.05 for both). There were, however, no significant differences in lipid parameters between the ETV and TAF groups at Week 48 (Figure 8).

Figure 8. Chinese Real-World, Retrospective Study: Lipid Levels at Week 48[13]



[a]*P*<0.01. [b]*P*<0.05. [c]*P*<0.001

Network Meta-Analysis[21]

A network meta-analysis of 10 cohort studies (N=4194), including six studies with TAF, examined the effect of nucleos(t)ide analogues (TAF, TDF, or ETV) on lipid levels in patients with CHB. In general, although small decreases in TC, TG, and LDL levels and increases in HDL levels were observed with TAF and ETV compared with no antiviral treatment (inactive CHB patients), these changes were not statistically significant, and TAF and ETV were considered to have a neutral effect on lipid levels. Of the three drugs, TDF had the strongest effect on decreasing lipid levels (Table 8).

Table 8. Network Meta-Analysis: Mean Differences in Lipid Levels[21]

		Mean Difference (95% CI), mg/dL
TC	TAF vs inactive CHB patients[a]	-2.69 (-14.42 to 9.04)
	ETV vs inactive CHB patients[b]	-4.24 (-17.12 to 8.64)
	TDF vs inactive CHB patients[b]	-17.27 (-30.03 to -4.47)
	ETV vs TAF[a]	-1.56 (-6.89 to 3.78)
	TDF vs TAF[a]	-14.58 (19.7 to -9.46)
TG	TAF vs inactive CHB patients[a]	-1.69 (-13.73 to 10.34)
	ETV vs inactive CHB patients[b]	-5.97 (-36.88 to 24.93)
	TDF vs inactive CHB patients[b]	-17.47 (-47.96 to 13.02)
	ETV vs TAF[a]	1.51 (-5.62 to 8.64)
	TDF vs TAF[a]	-9.98 (-14.97 to -5)
LDL	TAF vs inactive CHB patients[a]	-1.69 (-13.73 to 10.34)
	ETV vs inactive CHB patients[b]	-2.14 (-15.22 to 10.93)
	TDF vs inactive CHB patients[b]	-7.95 (-20.95 to 5.06)
	ETV vs TAF[a]	-0.45 (-5.56 to 4.66)
	TDF vs TAF[a]	-6.25 (-11.19 to -1.32)
HDL	TAF vs inactive CHB patients[a]	1.2 (-4.67 to 7.07)
	ETV vs inactive CHB patients[b]	0.09 (-6.42 to 6.6)
	TDF vs inactive CHB patients[b]	-4.27 (-11.02 to 2.49)
	ETV vs TAF[a]	-1.11 (-3.91 to 1.7)
	TDF vs TAF[a]	-5.47 (-8.8 to -2.13)

[a]Nature of evidence was a combination of direct and indirect comparisons.
[b]Nature of evidence was indirect comparisons only.

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Abbreviations

AMI=acute myocardial infarct
ASCVD=atherosclerotic cardiovascular disease
CG=Cockcroft-Gault
CHB=chronic hepatitis B
CPT=Child-Pugh-Turcotte
ESRD=end-stage renal disease
ETV=entecavir
HBeAg=hepatitis B envelope antigen
OL=open-label
OR=odds ratio
PS=propensity score
PY=patient years
Q=quartile
SHR=subdistribution hazard ratio
TAF=tenofovir alafenamide
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TG=triglycerides

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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