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Vemlidy® (tenofovir alafenamide) Switching from Entecavir

This document presents real-world data regarding the efficacy and safety of switching from entecavir (ETV) to Vemlidy® (tenofovir alafenamide [TAF]) for the treatment of CHB.

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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]

The TAF prescribing information does not contain any clinical data regarding switching from ETV to TAF for the treatment of CHB.

Switching from ETV to TAF in Real-World Studies

- Nine studies that evaluated switching from ETV to TAF found stable or improved HBV DNA suppression, rates of ALT normalization, and serology after patients switched to TAF.[2-10]
- Results of changes in renal function varied among the studies, with some studies showing non-significant decreases in renal function[8-10] and other studies showing stable or improved renal function after patients switched to TAF.[2,5-7] One study reported a discontinuation of TAF due to an AE.[5]

Product Labeling[1]

The TAF prescribing information does not contain any clinical data regarding switching from ETV to TAF for the treatment of CHB.

Indications and Usage

TAF is an HBV nucleoside analog reverse transcriptase inhibitor and is indicated for the treatment of chronic HBV infection in adults and pediatric patients 12 years of age and older with compensated liver disease.

Switching from ETV to TAF in Real-World Studies

Switching from ETV to TAF in NUC-Naïve Participants (Nguyen et al)[2]

Study design and demographics

A prospective, multicenter (US, South Korea, Japan, and Taiwan), real-world study evaluated virologic, biochemical, and renal outcomes after participants infected with CHB were switched from ETV to TAF. Participants were treatment-naïve prior to therapy initiation with ETV, received ETV for ≥12 months, and then switched to TAF. Of the 425 participants included in this study, 90.8% were Asian, 60% were male, and 14.8% had cirrhosis. The mean age of participants was 60.7 years, and the mean duration of ETV therapy prior to switch was 6.16 years. The rate of complete viral suppression (HBV DNA <20 IU/mL) was the primary outcome of this study; ALT normalization (≤40 U/L or ≤35 U/L for men and ≤25 U/L for women), complete response rate (HBV DNA <20 IU/mL and ALT normalization), and eGFR/CKD stage were also assessed.

Results

The rate of complete viral suppression was 91.9% at baseline (time of switch) and increased to 95.57% at Week 48 (P=0.03) and 97.21% at Week 96 (P=0.02). Over 96 weeks after the switch, there was a significant decrease (P<0.001) in mean HBV DNA; however, no changes in ALT (Table 1) or CKD stage were recorded.

Table 1. Virologic, Biochemical, and Complete Response Rates from Time of Switch (Baseline) to Week 96 (Nguyen et al)[2]

	Baseline	Week 24	Week 48	Week 72	Week 96
Complete viral suppression, n/N (%)	386/420 (91.9)	385/404 (95.3)	367/384 (95.57)[a]	288/297 (96.97)[a]	174/197 (97.21)[a]
ALT ≤40 U/L, n/N (%)	385/424 (90.8)	371/406 (91.38)	349/390 (89.49)	275/301 (91.36)	164/180 (91.11)
ALT <35 U/L (men) or <25 U/L (women), n/N (%)	347/424 (81.84)	331/406 (81.53)	315/390 (80.77)	246/301 (81.73)	154/180 (85.56)
Complete response, n/N (%)	324/420 (77.14)	306/395 (77.47)	299/381 (78.84)	237/296 (80.07)	139/170 (81.76)

[a]P<0.05 vs baseline (time of switch).

From baseline to Week 96, 11% of CKD Stage 1 participants (26/235) progressed to Stage 2, and 8% of Stage 2 participants (12/151) progressed to Stages 3 through 5. Conversely, 18% of CKD Stage 2 participants (27/151) improved to Stage 1, and 19% of Stages 3 through 5 participants (7/37) improved to Stage 2.

A multivariable analysis found older age (P<0.001) and CKD Stages 2 and 3 through 5 (both P<0.001) to be significantly associated with lower eGFR on follow-up.

Switching from ETV to TAF in Participants with Low-Level Viremia (Li et al)[3]

Study design and demographics

A real-world, prospective study conducted in China evaluated the efficacy and safety of switching from ETV to TAF vs continuing ETV monotherapy in 211 adult participants with persistent/intermittent low-level viremia (HBV DNA: >20 to <2000 IU/mL). To reduce selection bias and the potential for confounding variables, propensity score matching was used, which generated 75 participants in each group. The primary safety endpoint was the first occurrence of any AE or therapy discontinuation. The primary efficacy endpoint was CVR (HBV DNA <20 IU/mL) at Week 24.

Table 2. Baseline Demographics and Disease Characteristics for the PSM Cohort (Li et al)[3]

	Overall (N=150)	TAF (n=75)	ETV (n=75)
Age, mean (SD), years	47.6 (11.6)	46.5 (12.4)	48.7 (10.7)
Male, n (%)	121 (80.7)	59 (78.7)	62 (82.7)
BMI, mean (SD), kg/m^2	23.8 (4)	24 (3.7)	23.5 (4.4)
HBV DNA, mean (SD), $\log_{10}$ IU/mL	2.3 (0.5)	2.3 (0.6)	2.3 (0.5)
HBV GT			
B, n (%)	18 (12)	10 (13.3)	8 (10.7)
C, n (%)	111 (74)	54 (72)	57 (76)
D, n (%)	3 (2)	2 (2.7)	1 (1.3)
Unknown, n (%)	18 (12)	9 (12)	9 (12)
Diabetes, n (%)	24 (16)	12 (16)	12 (16)
Cirrhosis, n (%)	52 (34.7)	29 (38.7)	23 (30.7)
FIB-4 index, median (range)	1.81 (1.06, 3.02)	1.58 (0.92, 2.95)	1.84 (1.23, 3.02)
HBeAg+, n (%)	102 (68)	50 (66.7)	52 (69.3)
ALT, mean (SD), U/L	33.1 (17)	33.7 (18.2)	32.5 (15.8)
AST, mean (SD), U/L	33.8 (18.6)	34 (19.7)	33.7 (17.5)
Platelets, mean (SD), ×10^9/L	156.2 (66.8)	160.5 (65.1)	152 (68.5)
Total bilirubin, mean (SD), µmol/L	13.8 (6.3)	14 (6.8)	13.6 (5.8)
SCr, mean (SD), µmol/L	78.1 (15.8)	79.1 (17.3)	77.2 (14.3)
eGFR, mean (SD), mL/min/1.73 m^2	98.1 (16.3)	96.9 (16.8)	99.3 (15.8)
Duration of previous ETV treatment, median (range), months	25 (20, 32)	26 (21, 32)	24 (18.5, 33)

Efficacy results

In the PSM cohort, 54.7% and 62.7% of participants in the TAF group achieved complete virological response compared with 6.7% and 9.3% of participants in the ETV group at Weeks 12 and 24, respectively (*P*<0.001 for both; Table 3). The mean decrease in HBV DNA level was also significantly greater in the TAF group compared to the ETV group through Week 24 (Table 3). In post hoc subgroup analyses, switching to TAF vs continuing ETV had a statistically significant impact on achieving CVR at Week 24 in the PSM cohort (odds ratio: 16.4; 95% CI: 6.6–40; *P*<0.001). The odds of achieving CVR at Week 24 in the PSM cohort were greater in the TAF group than in the ETV group regardless of sex, age, family history of chronic HBV, HBV DNA level at baseline, HBeAg status at baseline, and cirrhosis.

The rate of HBeAg loss and seroconversion was higher in the TAF group than in the ETV group in the PSM cohort; however, the difference was not statistically significant. Neither group achieved HBsAg loss, although the rate of HBsAg loss in the TAF group was numerically higher but not significantly greater than that in the ETV group.

A significantly greater proportion of participants in the TAF group than in the ETV group achieved ALT normalization according to the AASLD criteria (≤35 U/L [males]; ≤25 U/L [females]) at Week 24.

Table 3. Statistically Significant Efficacy Endpoints in the PSM Cohort at Weeks 12 and 24 (Li et al)[3]

	Complete Virological Response, n (%)	HBV DNA Decrease, Mean (SD), log_{10} IU/mL	ALT Normalization (AASLD Criteria), n/N (%)
Week 12			
TAF	41 (54.7)	1.84 (0.66)	10/25 (40)
ETV	5 (6.7)	0.91 (0.59)	5/27 (18.5)
P-value	<0.001	0.023	0.088
Week 24			
TAF	47 (62.7)	1.99 (0.68)	12/25 (48)
ETV	7 (9.3)	0.76 (0.66)	4/27 (14.8)
P-value	<0.001	0.002	0.022

Safety results

Both TAF and ETV were well tolerated, with most AEs being mild to moderate in severity. In the PSM cohort, 47% of participants in the TAF group and 44% of participants in the ETV group reported AEs. Upper respiratory tract infection (TAF and ETV, n=4 [5.3%] each) and nasopharyngitis (TAF, n=4 [5.3%]; ETV, n=5 [6.7%]) were the most frequently reported AEs. One participant in each group reported an SAE (TAF, bladder stone; ETV, herpes zoster); however, neither was considered related to treatment.

Three participants who received TAF and had a history of dyslipidemia and/or elevated LDL cholesterol level at baseline experienced a Grade 3 elevation in LDL cholesterol level. One participant who received TAF and had a history of diabetes and/or elevated glucose level at baseline experienced a Grade 3 elevation in fasting glucose level. No participant in the ETV group experienced a Grade 3 elevation in LDL cholesterol or fasting glucose level.

Switching from an NUC to TAF (Ogawa et al)[4]

Study design and demographics

A prospective, multinational (Japan, Korea, Taiwan, and the US), real-world trial is ongoing to examine virologic, biochemical, and renal outcomes of participants infected with CHB who were switched from an NUC to TAF. All participants received treatment with an NUC for ≥12 months prior to switch. The primary outcomes were complete viral suppression (HBV DNA <20 IU/mL) and biochemical response (ALT 35 U/L for men and 25 U/L for women). Changes in ALT, HBV DNA, and eGFR from therapy switch to end of follow-up were also recorded.

Table 4. Baseline Demographics and Disease Characteristics Among Participants who Switched from ETV to TAF (Ogawa et al)[4]

	ETV→TAF (n=199)
Age, mean, years	58.3±10.9
Male, n (%)	116 (58.3)
BMI, mean, kg/m^2	23.8±4
Race/ethnicity	
Non-Asian, n (%)	1 (0.5)
Asian, n (%)	198 (99.5)
Concomitant disease	
Diabetes, n (%)	31 (15.6)
Hypertension, n (%)	41 (20.6)
Hyperlipidemia, n (%)	17 (8.5)
Cirrhosis, n (%)	27 (13.6)
FIB-4 index, mean	1.9±1.4
HBeAg+, n (%)	31 (15.7)
Undetectable HBV DNA, n (%)	186 (93.5)
ALT, mean, U/L	25±16
AST, mean, U/L	27±11
Platelets, mean, 10^9/L	202±58
Albumin, mean, g/dL	4.4±0.5
Total bilirubin, mean, mg/dL	1±1.1
SCr, mean, mg/dL	0.8±0.2
eGFR, mean, mL/min	89±16
Lumbar T-score, mean	-1.1±1.5
Lumbar Z-score, mean	0.01±1.3

Results

In participants who received ETV prior to switch, complete viral suppression increased from 93.5% (186/199) at time of switch to 97.4% (189/194) at Month 6 and 96.8% (122/126) at Month 12. No change was observed in biochemical response between the time of switch and Month 12 (75.4% vs 74.4%). From baseline to Month 18, HBV DNA decreased significantly, and eGFR increased significantly (Table 5).

Table 5. Rates of HBV DNA, ALT Level, and eGFR over 18 Months (Ogawa et al)[4]

	Baseline	6 Mo	12 Mo	15–18 Mo	*P*-Value
HBV DNA, mean, IU/mL	0.5±0.9	0.3±0.7	0.4±0.7	0.4±0.6	0.02
ALT, mean, U/L	25±16	26±18	27±19	27±25	0.8
eGFR, mean, mL/min	89±16	89±16	89±16	90±14	0.01
eGFR >90 mL/min, n (%)	105 (52.8)	103 (53.1)	74 (55.6)	30 (52.6)	0.95
eGFR 60–90 mL/min, n (%)	85 (42.7)	80 (41.2)	55 (41.4)	25 (43.9)	
eGFR <60 mL/min, n (%)	9 (4.5)	11 (5.7)	4 (3)	2 (3.5)	

A multivariable analysis found baseline HBV DNA (*P*<0.001)/HBeAg+ status (*P*=0.03), baseline ALT level (*P*<0.001), and age (*P*<0.001) to have a significant association with changes in HBV DNA, ALT level, and eGFR, respectively.

Seven SAEs were reported; however, none was considered related to TAF, and none resulted in treatment discontinuation.

Switching from ETV to TAF vs Continuing on ETV in NUC-Naïve Participants (Hagiwara et al)[5]

Study design and demographics

A prospective, single-center, comparative study was performed in Japan to address the clinical efficacy and safety of switching from ETV to TAF (n=24) compared with continuing therapy with ETV (n=24) in NUC-naïve participants infected with genotype C CHB (HBsAg+ and HBV DNA+ [<2.1 log copies/mL] for ≥6 months before treatment with long-term ETV [≥2 years]). There were no significant differences in baseline characteristics. There were 3 participants (15%) in each group who were HBeAg+. Participants were required to have an HBsAg level ≥800 IU/mL or an HBsAg level between 80 and 800 IU/mL with an HBsAg level fluctuation of less than or equal to -0.1 log IU/mL/year prior to screening. The primary endpoint was the change from baseline in serum HBsAg level at Week 48.

Efficacy results

No significant differences were observed in changes in serum HBsAg or ALT levels from baseline to Week 24 or Week 48 between the TAF and ETV groups.

Overall, there were no significant changes in HBsAg levels within or between groups at Weeks 24 and 48. However, in participants with low baseline HBsAg (<800 IU/mL) who switched to TAF, there was a significantly greater decrease in HBsAg compared to those with high baseline HBsAg (>800 IU/mL). In participants with low baseline HBsAg, there was also a numerically greater improvement in the TAF group than in the ETV group (-0.132 and -0.043, respectively; *P*=0.135). The presence or absence of HBeAg did not affect the level of HBsAg in this study.

Safety results

No significant differences were observed in changes in eGFR or serum phosphorus levels between the TAF and ETV treatment groups. Furthermore, markers of glomerular and tubular function were similar between the groups.

Bone mineral density in the lumbar vertebrae and femur were measured at Week 48, and no significant difference was observed between the treatment groups.

Switching from ETV to TAF (Uchida et al)[6]

Study design and demographics

A prospective study in Japan compared the safety and efficacy of TAF for 48 weeks with that of ETV in participants infected with CHB (N=159) before and after they switched from ETV to TAF. Previous ETV therapy had been for a median of 6.4 years but was evaluated from 48 weeks before switching to TAF. Participants were divided into two cohorts. Cohort 1 consisted of 92 participants (48 men, 44 women) who switched to TAF monotherapy between March and May 2018. Participants with HCV or HIV co-infection, those receiving immunosuppressive agents, and those with underlying decompensated cirrhosis and/or end-stage HCC were excluded from Cohort 1 but included in Cohort 2 (n=127 [61 men, 66 women], including 60 participants who were also included in Cohort 1). Efficacy was determined by the change in serum HBsAg levels during the 48-week treatment period.

Efficacy after switching from ETV to TAF in Cohort 1

Significant decreases in serum HBsAg levels were observed during the 48 weeks of treatment with ETV and at Week 48 after switching to TAF (P<0.001 for both).

The declines in HBsAg were not significantly different between the TAF and ETV groups. The degree of reduction, however, was significantly higher with TAF than with ETV among participants without underlying cirrhosis (0.068 log IU/mL/48 weeks vs 0.037 log IU/mL/48 weeks; P=0.03), in participants with genotype B HBV (0.086 log IU/mL/48 weeks vs 0.012 log IU/mL/48 weeks; P=0.014), and in participants with undetectable hepatitis B core-related antigen (0.070 log IU/mL/48 weeks vs 0.028 log IU/mL/48 weeks; P=0.038). HBsAg loss was not observed in any participant during the 48 weeks of treatment with TAF, and viral breakthrough was not experienced by any participant after they switched to TAF.

When changes in HBsAg levels were examined (Table 6), TAF was found to exhibit superior antiviral effects compared with ETV (improvement with TAF: n=33; vs ETV: n=16; P=0.022).

Table 6. HBsAg Changes with ETV and TAF Therapy (Uchida et al)[6a]

	HBsAg Increased with ETV (n=24)	HBsAg Remained Unchanged with ETV (n=40)	HBsAg Decreased with ETV (n=27)
HBsAg increased with TAF, n	3	9	5
HBsAg remained unchanged with TAF, n	8	18	11
HBsAg decreased with TAF, n	13	13	11

[a]"Increased" or "decreased" was defined as an increase or decrease in the serum HBsAg level by ≥0.08 log IU/mL.

Medication adherence and satisfaction level after switching to TAF per questionnaire in Cohort 2

A questionnaire was given between 2 and 6 months after TAF initiation to participants in Cohort 2; 77 participants (61%) stated that they were satisfied with their treatment after they switched to TAF. Furthermore, switching from ETV to TAF was associated with an increase in patient-reported adherence.

Safety after switching from ETV to TAF in Cohort 1

Switching to TAF caused transient increases in serum AST and ALT levels. The median ALT level increased from 16 U/L to 17 U/L at Week 8 (*P*=0.002), persisted at 17 U/L through Week 24 (*P*=0.038), and decreased to baseline levels by the end of Week 48 (*P*=0.055 vs Week 8). Changes in AST levels were similar but were not statistically significant. No significant decrease in eGFR or serum phosphorus level was observed after participants were switched to TAF.

One participant discontinued TAF after 4 weeks of therapy due to diarrhea; this participant was excluded from subsequent analyses. After stopping TAF and restarting therapy with ETV, the participant no longer experienced diarrhea.

Switching from Long-Term Treatment with ETV to TAF (Chen et al)[7]

Study design

A real-world study in China evaluated virologic and safety outcomes in a cohort of 69 participants with CHB who switched to treatment with TAF after receiving ETV for ≥96 weeks. HBV DNA, HBsAg, ALT, liver stiffness, eGFR, and controlled attenuation parameter were measured from 24 weeks prior to TAF switch to the time of switch (ETV phase), and through 24 weeks after switching to TAF (TAF phase).

Results

The proportion of participants with undetectable HBV DNA levels (<20 IU/mL) increased significantly after switching to TAF, from 57.9% to 60.3% of participants during the ETV phase, up to 91.4% during the TAF phase (*P*<0.05). HBsAg levels decreased significantly more during the TAF phase than during the ETV phase in the overall population (-0.1 log IU/mL vs -0.037 log IU/mL, respectively; *P*=0.0338) and among participants with low-level viremia (-0.103 log IU/mL vs -0.042 log IU/mL, respectively; *P*=0.0238). The proportion of participants with low-level viremia who achieved undetectable HBV DNA levels was also greater during TAF treatment: 25% (4/16) after 24 weeks of treatment with ETV and 83.3% (10/12) after 24 weeks of treatment with TAF. There were no significant changes in the rates of ALT normalization (ALT <50 U/L), measurements of liver stiffness, controlled attenuation parameter, or eGFR during treatment.

Retrospective Comparison of Sequential ETV→TAF vs Continuous ETV Treatment (Itokawa et al)[8]

Study design and demographics

A retrospective, multicenter study in Japan compared the efficacy and safety of switching from treatment with ETV to TAF (sequential therapy) with those of continuous treatment with ETV. Included patients had been receiving ETV as monotherapy for ≥1 year prior to Day 0 (the date that patients in the sequential group switched therapy), had HDV DNA levels <1.3 log IU/mL for >6 months, and had received TAF treatment (sequential therapy group) or ETV treatment (continuous ETV group) for >1 year after Day 0. Propensity score matching was performed to adjust for differences in baseline demographic and clinical characteristics. The primary endpoint was the change in HBsAg level from Day 0 to Week 48.

A total of 342 patients were enrolled (sequential therapy, n=113; continuous ETV, 229) and, after propensity score matching, 71 patients from each group were included in the analyses. Baseline characteristics were similar between groups in the PSM cohort (Table 7). From Week -48 to Day 0 (during treatment with ETV monotherapy), median changes in HBsAg levels were -0.09 log IU/mL (range, -0.44, 0.41) in the sequential therapy group and -0.06 log IU/mL (range, -0.41, 1.07) in the continuous ETV group.

Table 7. Baseline Demographics and Disease Characteristics for the PSM Cohort (Itokawa et al)[8]

	Sequential ETV→TAF (n=71)	Continuous ETV (n=71)
Age, median, (range), years	61 (36, 86)	58 (34, 78)
Male, %	45	42
HBV DNA, median (range), log IU/mL	ND (ND, <1.3+)	ND (ND, <1.3+)
HBsAg, median (range), log IU/mL	2.86 (-0.85, 4.45)	2.72 (-0.77, 4.29)
HBcrAg, median (range), log IU/mL	3.1 (<2.9, 6.7)	3.4 (<2.9, >7)
Cirrhosis, %	13	16
HBeAg+, %	6	7
HBV GT, A/B/C/missing, %	0/10/46/15	0/11/45/15
Platelets, median (range), $\times 10^3/mm^3$	17.4 (5.5, 45.8)	18.5 (3.1, 44.6)
ALT, median (range), IU/L	20 (10, 87)	19 (7, 118)
eGFR, median (range), mL/min/1.73 m^2	72 (37, 124.5)	76 (38, 117)
Duration of previous ETV treatment, median (range), months	52 (14, 175)	57 (12, 188)

Abbreviation: ND=not detected.

Efficacy results

Levels of HBsAg and HBcrAg decreased significantly, and ALT levels decreased nonsignificantly, from Day 0 to Week 48 in both treatment groups; however, decreases in all three parameters were similar between groups (Table 8). Rates of ALT normalization at Week 48 were also similar between groups. In subgroup analyses of changes in HBsAg according to baseline factors, changes in HBsAg from Day 0 to Week 48 were similar between treatment groups (Table 9).

Table 8. Efficacy Results in the Overall PSM Cohort (Itokawa et al)[8]

	Sequential ETV→TAF (n=71)	Continuous ETV (n=71)	*P*-Value[a]
ALT normalization (<30 IU/L) at Week 48, n (%)	62 (87.3)	59 (83.1)	0.637
Changes from Day 0 to Week 48			
HBsAg, median (range), log IU/mL	-0.02[b]	-0.03[b]	0.22
ALT, median (range), IU/L	-1	0	0.304
HBcrAg, median (range), log IU/mL	-0.1[b]	-0.1[b]	0.807

[a]*P*-value for the comparison between groups.
[b]*P*<0.05, for the within-group change from Day 0 to Week 48.

Table 9. Median Changes (log IU/mL) in HBsAg From Day 0 to Week 48 in Subgroups According to Baseline Factors (Itokawa et al)[8]

	Sequential ETV→TAF (n=71)	Continuous ETV (n=71)	*P*-Value[a]
HBsAg subgroups			
HBsAg <3 IU/mL	-0.02	-0.03[b]	0.437
HBsAg ≥3 IU/mL	-0.02	-0.03[b]	0.562
HBeAg status subgroups			
HBeAg+	-0.01	-0.02	0.83
HBeAg-	-0.02[b]	-0.05[b]	0.15
HBV GT subgroups			
GT B	-0.06	-0.02	0.597
GT C	0	-0.03[b]	0.065

[a]*P*-value for the comparison between treatment groups.
[b]*P*<0.05, for the within-group change from Day 0 to Week 48.

Safety results

The median eGFR level decreased significantly from Day 0 to Week 48 in the sequential therapy group (-1 mL/min/17.3 m^2; *P*=0.036), whereas the change in eGFR was not significant in the continuous ETV group (-0.5 mL/min/17.3 m^2; *P*=0.282); however, the difference in the eGFR change between treatment groups was not statistically significant.

Retrospective Analysis of Switching from ETV, TDF, or NUC Combination Therapy to TAF (Ogawa et al)

Study design and demographics

A retrospective, multicenter cohort study in Japan was performed to evaluate virological/biochemical and renal safety outcomes in patients with CHB who switched to TAF after ≥2 years of treatment with ETV, TDF, or NUC combination therapy. The primary endpoint was the proportion of patients with CVR <10 IU/mL at Week 144 after switching to TAF. Key secondary endpoints included changes in ALT levels, HBsAg levels, and eGFR.[9]

Week 144 results are presented below.[9] Analyses at Weeks 48 and 96 have also been previously published.[11,12] A total of 478 patients were included in the Week 144 analysis population, respectively, including 174 patients in the prior ETV cohort.[9] Among the patients in the ETV cohort, the median duration of NUC treatment prior to switching was 5 years (IQR, 4.2–7.4), the median age was 61 years, 63.8% were male, 7.5% had cirrhosis, and 10.3% were HBeAg+.[9]

Efficacy results

Table 10 provides a summary of CVR rates and HBeAg loss rates at Week 144 in the prior ETV cohort. The rate of ALT normalization (per AASLD criteria) in the prior ETV cohort increased slightly, from 83.3% at baseline to 89.1% at Week 144 (*P*=0.12). Among patients with ALT elevations at baseline in the prior ETV cohort (n=29), the ALT normalization rate was 55.2% at Week 144. Although progressive decreases in HBsAg levels were observed across the 3 years of follow-up, only a small number of patients in the overall population (8% [7/391]) achieved HBsAg loss by Week 144.[9]

Table 10. Efficacy Results at Week 144 in the Prior ETV Cohort (Ogawa et al)[9]

	Week 144 (N=174)	*P*-Value
Achieved CVR,[a] %	98.9	<0.001
Patients with low-level viremia[b] at baseline who achieved CVR,[a] n/N (%)	37/39 (94.9)	–
HBeAg loss, n/N (%)	5/18 (27.8)	–

[a]HBV DNA <10 IU/mL at Week 144.
[b]HBV DNA 20–2000 IU/mL.

Safety results[9]

Median eGFR in the prior ETV cohort decreased by 2.9 mL/min/1.73 m^2 from baseline at Week 144, and the incidence of hypophosphatemia increased from 2.3% at baseline to 5.7% at Week 144. One case of hypophosphatemic osteomalacia at the time of switchover occurred in a 67-year-old woman in the prior NUC combination therapy cohort who had switched to TAF from ETV/TDF therapy. The switch to TAF resulted in a transient improvement in eGFR during the first year of treatment, viral suppression, and improved alkaline phosphatase and phosphate levels.

Among patients who switched from a regimen that included TDF, total cholesterol, LDL, HDL, and triglyceride levels increased from baseline to Week 144. Among patients who had switched from non-TDF-containing regimens, cholesterol levels generally remained stable. In both the prior TDF and non-TDF groups, however, there were no significant changes from baseline in total cholesterol to HDL ratio (*P*=0.11 and 0.75, respectively). Six patients, including 1 patient who switched from ETV monotherapy, initiated antihyperlidemic agents during the follow-up period for treatment of increased LDL levels.

Retrospective Analysis of Switching from ETV to TAF in Patients with Low-Level Viremia[10]

Study design and demographics

A multicenter, retrospective, observational study in Japan evaluated changes in HBV DNA levels after switching to TAF among patients with CHB who had low-level viremia during ETV treatment. Included patients had been receiving ETV continuously for >2 years prior to switching to TAF treatment and had ≥1 detectable HBV DNA level within the year prior to switching.

A total of 23 patients were included in the analysis. At baseline, the median age was 62 years (IQR, 48–70), 13 patients (57%) were male, the median ALT level was 20 IU/L (IQR, 18–29); the median HBsAg level was 811 IU/mL (IQR, 245–3976), and, in the 14 patients with detectable HBV DNA levels, the median level was <1 log IU/mL (IQR, <1 to 1.2). Patients had received ETV for a median of 4.1 years (IQR, 3.4–5.9) prior to switching to TAF.

Efficacy results

Efficacy results for the year before switching to TAF (during ETV treatment) and in the first and second years after switching to TAF are summarized in Table 11. In analyses that compared clinical characteristics between patients who did and did not achieve persistent CVR, patients with persistent CVR were significantly more likely to have undetectable HBV DNA at the time of switching (*P*=0.02) and had significantly lower HBV DNA levels during

the second year of TAF treatment (*P*=0.002). HBsAg levels decreased progressively after switching, from 2.87 log IU/mL at Month 0 to 2.68 log IU/mL at Month 24 (*P*=0.02 vs Month 0). In analyses that examined the percent decrease in HBsAg according to subgroups by clinical characteristics at the time of switching, patients with FIB-4 index scores ≥1.3 (vs <1.3), ALT levels ≤20 IU/L (vs >20 IU/L), and HBsAg levels <811 log IU/mL (vs ≥811 log IU/mL) tended to experience greater decreases in HBsAg, but the differences were not statistically significant.

Table 11. Efficacy Results (Sato et al)[10]

	Year Before Switching	Year 1 After Switching	Year 2 After Switching
Proportion of HBV DNA values that were detectable, %	68.8	34.1a	21.3a
Persistent CVR, n/N (%)	0/23 (0)	11/23 (47.8)	14/21 (66.7)
Change in HBsAg level[b] within time period, %	-4.5	-4.8	-7.9
ALT normalization,[c] %	80.9	81.5	80.1

[a]*P*<0.001 for the comparison with the value before switching.
[b]Calculated as the percent change from the beginning of each time period.
[c]According to AASLD criteria (males, ≤35 U/L; females, ≤25 U/L). Rates calculated according to Japan Society of Hepatology criteria (≤30 U/L) were similar.

Safety results

One patient died due to acute myocardial infarction 11 months after switching to TAF; the death was considered by the physician to be unrelated to TAF treatment.

Changes in eGFR were not significant during the study period, although a numerically greater decrease in eGFR was observed after switching to TAF than during treatment with ETV (ETV, -0.41%: TAF Year 1, -2.96%; TAF Year 2, -1.12%). No other AEs were observed.

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Abbreviations

AASLD=American Association for the Study of Liver Diseases
AE=adverse event
CHB=chronic hepatitis B
CKD=chronic kidney disease
CVR=complete virological response
EC_{50}=50% effective concentration
ETV=entecavir
FIB-4=Fibrosis Index Based on 4 Factors
GT=genotype
HBcrAg=hepatitis B core-related antigen
HBeAg=hepatitis B e antigen
HBsAg=hepatitis B surface antigen
NUC=nucleot(s)ide analogue
PSM=propensity score matched
SAE=serious adverse event
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate

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

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