GILEAD | Medical Information

Vemlidy® (tenofovir alafenamide) Kidney Transplant

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) infection in kidney transplant recipients.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

This document includes content from or references to clinical practice guidelines, and the inclusion of these guidelines should not be interpreted as a treatment recommendation or an endorsement of the guidelines by Gilead Sciences.

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

Product Labeling[1]

There is no information in the TAF US Prescribing Information regarding the use of TAF in kidney transplant recipients.

Dosage and Administration

Dosage in patients with renal impairment

No dosage adjustment of TAF is required in patients with estimated CrCl ≥15 mL/min or in patients with end-stage renal disease (estimated CrCl <15 mL/min) who are receiving chronic HD. On days of HD, administer TAF after completion of HD treatment. TAF is not recommended in patients with ESRD who are not receiving chronic hemodialysis.

Clinical Data on TAF Use for CHB in Kidney Transplant Recipients

Turkish Study – Kidney Transplant and HD[2]

Study design and demographics

A prospective, multicenter study assessed the efficacy and safety of TAF in treatment-naive and treatment-experienced participants with HBV who either were recipients of a kidney transplant (n=61) or received HD (n=16) between January 2019 and June 2021 from 17 tertiary centers in Turkey. Baseline characteristics are presented in Table 1. Immunosuppressive treatment for kidney transplant recipients was tacrolimus based (82%), cyclosporin based (23%), or everolimus based (15%).

Table 1. Baseline Demographics and Disease Characteristics (Adanir et al)[2]

Key Demographics and Characteristics	Renal Transplant Recipients (n=61)	Participants on HD (n=16)
Age, mean ± SD, years	47±11	54±15
Male, n (%)	43 (71)	10 (63)
Received TAF as first-line therapy, n	19	12
Detectable HBV DNA at initiation of TAF, n	13	12
Basal HBV DNA, median (IQR), IU/mL	962 (41–12,611)	5400 (35–5600)
AST/ALT level, median (IQR), U/L	20 (15–30)/18 (12–32)	17.5 (14–49)/15.5 (10–80)
SCr level, mean ± SD, mg/dL	2.2±1.6	6.9±2.6
Phosphorus level, mean ± SD, mg/dL	3.3±1.2	5.6±1.9
Duration of TAF, mean ± SD, months	11.8±7	10.4±4.7

Preliminary results

Overall, the virological and biochemical responses at 12 months in 25 treatment-naive participants were 92% and 96%, respectively. No HBV reactivation occurred in any participant who switched to TAF.

TAF was well tolerated, and no serious adverse events were reported. No significant changes in ALT, SCr, or phosphorus levels were observed.

Retrospective Cohort Study[3]

Study design and demographics

A retrospective cohort study was conducted to assess the efficacy, tolerability, and clinical outcomes of HBsAg+ kidney transplant recipients who were treated with TAF using case records of patients in Hong Kong and Taiwan between 2019 and 2022 (N=39). Patients were excluded if they had detectable HCV RNA, tested positive for anti-HCV, or had documented significant alcohol consumption. HBV DNA levels and bone and renal parameters were assessed at regular intervals during the study period. Patients were given standard prophylactic immunosuppression therapy consisting of a triple regimen of prednisolone, calcineurin inhibitors (either cyclosporine A or tacrolimus), and mycophenolate mofetil.

Table 2. Baseline Demographics and Disease Characteristics (Yap et al)[3]

Key Demographics and Characteristics	Treatment Naive (n=4)	Treatment Experienced[a] (n=35)
Age, mean ± SD, years	51.7±10.5	57.5±9.6
Male, n	1	25
HBV DNA at TAF initiation, mean ± SD, IU/mL	$9.6 \times 10^6 \pm 1.7 \times 10^7$	$2.9 \times 10^7 \pm 1.7 \times 10^8$
HBeAg+ status at TAF initiation, n	2	5
ALT level at TAF initiation, mean ± SD, U/L	54.5±59	24±13.9
SCr level at TAF initiation, mean ± SD, mcmol/L	120±21.8	152±83.5
eGFR at TAF initiation, mean ± SD, mL/min/1.73 m^2	43.6±11.9	48.2±20.9
Duration of TAF, mean ± SD, months	26.4±11.3	43.7±19

[a]Prior antiviral treatments after kidney transplant and before TAF initiation were as follows: TDF, n=15; entecavir, n=12; lamivudine, n=11; telbivudine, n=4; adefovir, n=2.
Note: There were no statistically significant differences between groups at baseline, except in HBV DNA levels at initiation of TAF (*P*=0.008).

Results

Treatment-naive and treatment-experienced patients achieved undetectable levels of HBV DNA after a mean ± SD of 6±5.2 months and 13.8±9.6 months, respectively (*P*=0.106). One treatment-experienced patient (2.6%) had virologic breakthrough (HBV DNA assay >500 IU/mL after they achieved virologic suppression) at Month 21. Two treatment-experienced patients who were HBeAg+ before TAF initiation experienced HBeAg seroconversion.

ALT normalization occurred in a mean ± SD of 4.5±2.1 months in the treatment-naive group; mean ALT levels in the treatment-experienced group stayed within normal limits for the duration of the study. Overall, there were no statistically significant changes in eGFR from baseline to Month 24, and in serum phosphate levels and BMD (ie, hip, spine, and forearm T-score) from baseline to Month 36. Five patients (12.8%) developed hypophosphatemia at a mean ± SD of 17.4±10.5 months. Osteopenia was reported in 3 patients at Months 18, 20, and 24, and new-onset osteoporosis was reported in 1 patient at Month 24.

One patient in the treatment-experienced group died secondary to septic shock. Renal allograft failure was reported in 4 patients: 1 treatment-naive patient after 3 months and 3 treatment-experienced patients after a mean ± SD of 12.5±9 months. Liver cirrhosis was reported in 1 patient (2.6%) in the treatment-experienced group after they received 25 months of TAF.

Prospective Cohort Study in Taiwan[4]

Study design and demographics

Safety, virologic efficacy, and adherence to therapy are being evaluated in a prospective cohort study in kidney transplant recipients in Taiwan who switch to TAF from another NA (NCT05410496). Eligible participants could have switched to TAF due to concerns with achieving virological or biochemical response, treatment compliance, or safety with the NA used for treatment. Participants who had an eGFR <15 mL/min/1.73 m^2, were coinfected with HIV or HCV, had an active malignancy, were pregnant or breastfeeding, or had a known allergy to TAF-containing regimens were excluded. Thirty participants who were followed for ≥24 weeks were included in this preliminary analysis.

Table 3. Baseline Demographics and Disease Characteristics (ITT; Lee et al)[4]

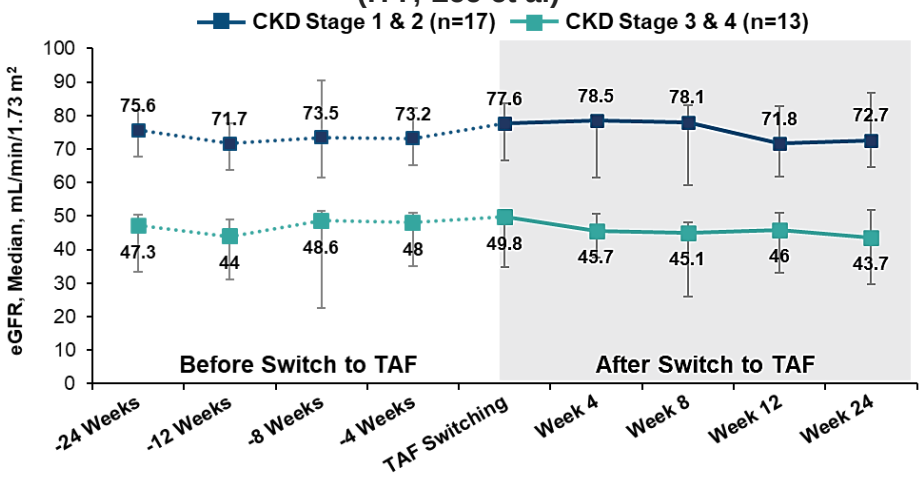
Key Demographics and Characteristics	TAF (N=30)
Age, median (IQR), years	58.5 (53–64.8)
Male, n (%)	18 (60)
HBV DNA undetected, n (%)	24 (80.8)
HBV qHBsAg, median (IQR), IU/mL	146.2 (19.3–471.4)
HBeAg+, n (%)	9 (30)
ALT level, median (IQR), U/L	18 (13.8–30.5)
SCr level, median (IQR), mg/dL	1.17 (0.95–1.5)
eGFR, median (IQR), mL/min/1.73 m^2	60.7 (50.3–79.7)
CKD stage, 1–2/3–4, n (%)	17 (56.7)/13 (43.3)
Prior NA, ETV/LAM/TDF, n (%)	27 (90)/2 (6.7)/1 (3.3)

Preliminary results

Safety and adherence

Two adverse events led to withdrawal of TAF treatment: skin allergy (TAF related) and edema (unrelated to TAF). Changes in the following renal laboratory parameters were not significantly different between study timepoints: eGFR (24 weeks before and after switching to TAF) and urine fractional excretion of phosphate and urine β2 microglobulin:Cr ratio (at time of switching to TAF to 24 weeks after switching).

Figure 1. eGFR Before and After Switching to TAF According to CKD Stage (ITT; Lee et al)[4]



Median (IQR) bone mineral density (trabecular bone) scores were not significantly different between baseline and Week 24 (1.3 [1.3–1.4] vs 1.4 [1.3–1.4], respectively). Significantly more participants achieved a full score on the Morisky 8-item questionnaire (a measure of adherence) at Week 24 after they switched than with previous NA treatment: 96.4% vs 71.4%, respectively (*P*=0.013; per-protocol analysis [n=28]).

Efficacy

Compared with baseline, at Week 24, more participants had undetectable HBV DNA (76.7% vs 96.7%, respectively; *P*=0.014) and ALT normalization (73.3% vs 86.7%, respectively; *P*=0.045). Similar qHBsAg values were observed at baseline and Week 24 (146.2 vs 137.7 IU/mL, respectively).

Clinical Practice Guidelines

American Association for the Study of Liver Diseases[5]

The American Association for the Study of Liver Diseases 2018 Hepatitis B Guidance provides recommendations for nonliver solid organ transplant recipients. All patients should be evaluated for HBV infection and tested for HBsAg, HBcAb, and HBsAb prior to receiving a nonliver solid organ transplant. Any patient who does not have HBsAb should receive the HBV vaccination prior to transplant. Nonliver organ transplant recipients who are HBsAg positive should receive antiviral therapy prior to or at the time of surgery and continue therapy indefinitely to prevent or treat reactivation of HBV. TAF, TDF, and ETV are the

preferred antiviral drugs due to the low rates of resistance associated with their long-term use. Recipients who are HBsAg negative or HBcAb positive should either be monitored for reactivation without prophylactic therapy or receive prophylactic antiviral therapy for the first 6 to 12 months following the transplant. If these patients receive a graft from an HBcAb-positive donor, monitoring is required; however, prophylactic therapy is not. All patients not receiving antiviral therapy should have ALT and HBV DNA levels monitored every 3 months for the first year after transplantation and after receipt of any T-cell–depleting therapies.

References

1. Enclosed. Gilead Sciences Inc, VEMLIDY® (tenofovir alafenamide) tablets, for oral use. U.S. Prescribing Information. Foster City, CA.
2. Adanir H, Etik DO, Yildirim AE, et al. Efficacy and Safety of Tenofovir Alafenamide in Hepatitis B Virus-Infected Patients with Chronic Hemodialysis and Renal Transplantation: A Preliminary Result [Poster]. Paper presented at: American Association for the Study of Liver Diseases (AASLD) The Liver Meeting Virtual; 12-15 November, 2021.
3. Yap DYH, Wu CK, Tang C, et al. A long term bone and renal safety of TAF treatment on renal transplant recipients. *Biomed J.* 2025:100833.
4. Lee TY TH, Chen CH,, Sheng-Shun Yang, Ming-Ju Wu, et al. Tenofovir alafenamide switching therapy in kidney transplant recipients with chronic HBV infection – tentative analysis of a prospective study [Poster]. Paper presented at: Asian Pacific Association for the Study of the Liver (APASL); 15-19 February, 2023.
5. Terrault NA, Lok AS, McMahon BJ, et al. Update on Prevention, Diagnosis, and Treatment and of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance. *Hepatology.* 2018;67:1560-1599.

Abbreviations

CHB=chronic hepatitis B virus
CKD=chronic kidney disease
ETV=entecavir
HBc=hepatitis B virus core
HBcAb=antibody to hepatitis B core antigen
HBeAg+=hepatitis B envelope antigen positive
HBsAb=antibody to hepatitis B surface antigen
HBsAg=hepatitis B surface antigen
HD=hemodialysis
LAM=lamivudine
NA=nucleos(t)ide analogue
qHBsAg=quantitative measurement of hepatitis B surface antigen
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

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
https://www.gilead.com/utility/contact/report-an-adverse-event

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

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