GILEAD | Medical Information

Vemlidy® (tenofovir alafenamide) Use in Patients With HBV and HCV

This document is in response to your request for information regarding Vemlidy® (tenofovir alafenamide [TAF]) for the treatment of HBV in patients with HCV.

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, Inc.

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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

Clinical Data on TAF Use in HBV and HCV

In a prospective, multicenter study of SOF/VEL treatment and prophylaxis with TAF in Chinese participants, the overall SVR12 rate was 97.6%, and rates were high across HCV GTs and in those with or without cirrhosis.[1]

In a prospective, multicenter study of SOF/VEL in TN Chinese participants with HCV GTs 1 to 6 and HBV who received prophylactic TAF, the overall, SVR12 rate was 98.3%.[2]

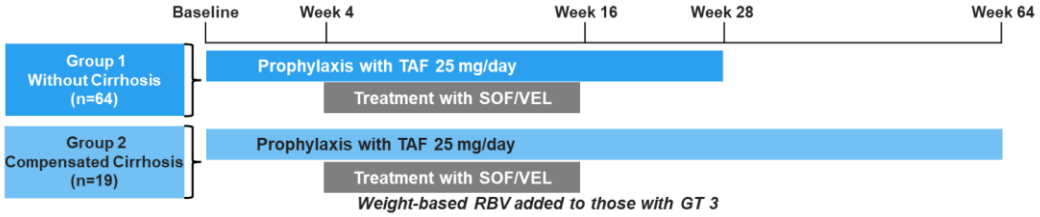
Clinical Data on TAF Use in HBV and HCV

Prospective, Multicenter Study in China[1]

Study design

A multicenter, prospective, single-arm study evaluated the efficacy and safety of SOF/VEL treatment with TAF prophylaxis in 83 participants with HCV GTs 1 to 6 and HBV. All received TAF prophylaxis and 12 weeks of SOF/VEL; participants were grouped by the presence or absence of compensated cirrhosis (Figure 1). Distribution of HCV GTs in the overall study population was as follows: GT 1, 26.5%; GT 2, 14.5%; GT 3, 21.7%; GT 6, 21.7%; not available, 15.6%.

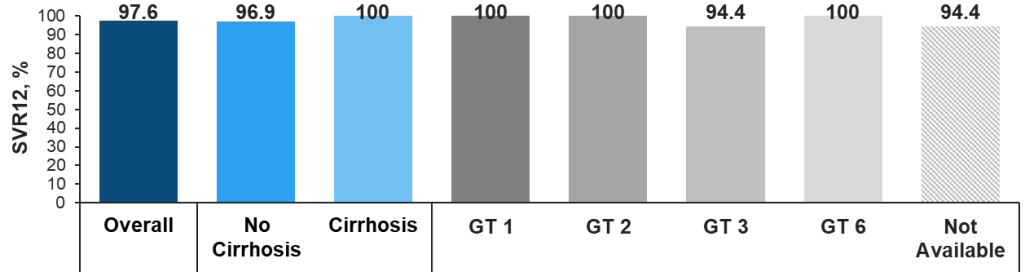
Figure 1. Prospective, Multicenter Study: Study Design[2]



Results

The overall SVR12 rate was 97.6%, and high SVR12 rates were observed for both groups and across GTs, including an SVR12 rate of 100% among those with cirrhosis (Figure 2). Overall, levels of HCV RNA and HBV DNA decreased from baseline to Week 28 (*P*-values not provided). One participant with GT 3 in Group 1 had HBV reactivation; their HBV DNA level was 2.15 $\log_{10}$ IU/mL at end of treatment with SOF/VEL but was <LLoQ at the SVR12 timepoint.

Figure 2. SVR12 Rates Overall, by Cirrhosis Status, and by HCV GTs (Lin et al)[1]



In Group 1, significant changes in laboratory parameters were observed from baseline to Week 28: ALT, 41.4 vs 17 IU/mL, respectively (*P*<0.001); AST, 38 vs 22 IU/mL (*P*<0.001); total bilirubin, 14.3 vs 13.6 mcmol/L (*P*=0.006); albumin, 42.4 vs 45.1 g/L (*P*<0.001). In Group 2, significant changes were observed from baseline to Week 64: ALT, 59 vs 22 IU/mL (*P*<0.001); AST, 60 vs 26 IU/mL (*P*<0.001); albumin, 41.3 vs 42.5 g/L (*P*=0.002); platelets, 114 vs 127.2 $\times 10^9$/L (*P*<0.001).

Generally, numerical decreases in LSM, APRI, and FIB-4 from baseline to Week 28 were observed in Group 1 (*P*=not significant). In Group 2, significant decreases in liver fibrosis assessments were observed from baseline to Week 64: 19.4 vs 16.7 kPa, respectively (*P*=0.003); APRI, 1.6 vs 0.6 (*P*=0.007); FIB-4, 4.3 vs 1.3 (*P*=0.004). No drug-related adverse events were reported.

Prospective, Multicenter Study in TN Chinese Participants[2]

Study design and demographics

A multicenter, prospective, single-arm, open-label study (NCT04997564) evaluated the safety and efficacy of SOF/VEL in TN Chinese participants with HBV who received prophylactic TAF and HCV GTs 1 to 6. Participants received TAF from Day 0 to Week 28 and SOF/VEL from Week 4 to Week 16. Of the 60 participants, 47 did not have cirrhosis, and 13 had compensated cirrhosis. The primary endpoint was SVR12 for HCV, which was assessed at Week 28.

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

Key Demographics and Characteristics		No Cirrhosis (n=47)	Compensated Cirrhosis (n=13)	Total (N=60)
Age, mean (range), years		49 (32–76)	56 (36–73)	51 (32–76)
Female, n (%)		19 (43.1)	3 (25)	22 (39.3)
LSM, mean (range), kPa		6.9 (5.6–9.8)	20.5 (16.4–37.1)	9.3 (6.5–13.2)
HBV DNA	Mean (range), log_{10} IU/mL	2.7 (2.1–3.2)	2.9 (2.1–3.7)	2.7 (2.1–3.4)
	≥LLoQ, n (%)	25 (50)	5 (35.7)	30 (46.9)
HBsAg mean (range), log_{10} IU/mL		2.1 (0.8–3.1)	1.6 (0.3–2.5)	2 (0.8–3)
HBsAb+, n (%)		3 (6)	0	3 (4.7)
HBeAg+, n (%)		1 (2)	1 (7.1)	2 (3.1)
HCV RNA	Mean (SD), log_{10} IU/mL	5.8 (1.1)	5.8 (0.9)	5.8 (1.2)
	≥5 log_{10} IU/mL, n (%)	36 (76.6)	11 (84.6)	47 (78.3)
HCV GT, n (%)	GT 1	12 (25.5)	5 (38.5)	17 (28.3)
	GT 2	9 (19.1)	2 (15.4)	11 (18.3)
	GT 3a	6 (12.8)	1 (7.7)	7 (11.7)
	GT 3b	8 (17)	2 (15.4)	10 (16.7)
	GT 6	13 (27.7)	2 (15.4)	15 (25)

Abbreviations: HBsAb=hepatitis B surface antibody; HBeAg=hepatitis B envelope antigen.

Results

Overall, SVR12 was achieved by 98.3% of participants (59/60; Table 2); the 1 participant who did not achieve SVR12 did not have cirrhosis and had HCV GT 1b. The SVR12 rate was 100% for HCV GTs 2, 3a, 3b, and 6; the SVR12 rate for GT 1 was 94.11%.

Table 2. SVR Rates at Study Weeks 4, 16, and 28 (Chen et al)[2]

	No Cirrhosis (n=47)			Compensated Cirrhosis (n=13)			Total (N=60)		
	Week 4	Week 16	Week 28 (SVR12)	Week 4	Week 16	Week 28 (SVR12)	Week 4	Week 16	Week 28 (SVR12)
SVR, %	4.3	97.9	97.9	7.7	100	100	5	98.3	98.3

Of the 28 participants who were HBV DNA+ at baseline, 2 participants remained HBV DNA+ at Week 28, and no participants experienced HBV reactivation. There was no significant difference in LSM between baseline and Week 16 in participants without cirrhosis (*P*=0.69) or with compensated cirrhosis (*P*=0.246).

Most participants did not experience significant adverse effects. No further safety data were reported.

Clinical Guidelines on TAF Use in HBV and HCV

AASLD Guidelines

Please refer to the AASLD clinical guideline for full recommendations regarding the management of these patients, which may be found at https://www.aasld.org/practice-guidelines. The AASLD guidelines contain recommendations for HBsAg+ patients who are not already on HBV-suppressive therapy; these recommendations are provided in Table 3.

Table 3. AASLD Recommendations for the Management of Patients With HBV and HCV Who Are Treated With DAAs[3,4]

Meets AASLD Criteria for HBV Treatment	Initiate HBV therapy at the same time as HCV DAA therapy or before
Does Not Meet AASLD Criteria for HBV Treatment	Initiate prophylactic antiviral therapy and continue until 12 weeks after completion of DAA therapy **OR** Monitor HBV DNA levels every 4–8 weeks during treatment and for 3 months after HCV DAA therapy. Start HBV treatment if there is a rise in HBV DNA >10-fold above baseline or to >1000 IU/mL in those with previously undetectable or unquantifiable HBV DNA levels

EASL Guidelines

Please refer to the EASL clinical guidelines for full recommendations regarding the management of these patients, which may be found at https://easl.eu/publications/clinical-practice-guidelines. The EASL guidelines include recommendations, which are provided in Table 4.

Table 4. EASL Recommendations for the Management of Patients With HBV and HCV Who Are Treated With DAAs[5]

Recommendation	Level of Evidence and Grade of Recommendation
Treatment of HCV with DAAs may cause reactivation of HBV. Patients who fulfill the standard criteria for HBV treatment should receive NA treatment.	Evidence level II Grade of recommendation: 1
HBsAg+ patients who undergo DAA therapy should be considered for concomitant NA prophylaxis until Week 12 post DAA and be monitored closely.	Evidence level II–2 Grade of recommendation: 2
HBsAg- and anti-HBc+ patients who undergo DAA treatment should be monitored and tested for HBV reactivation in case of ALT elevation.	Evidence level II Grade of recommendation: 1

Abbreviations: HBc=hepatitis B core; NA=nucleos(t)ide analog.

References

1. Lin N, Han Y, Chen H, et al. Evaluating the safety and efficacy of SOF/VEL treatment and prophylactic use of TAF in patients with chronic HBV/HCV coinfection: A multicenter study [Poster]. Paper presented at: AASLD The Liver Meeting; November 15-19, 2024; San Diego, CA.
2. Chen H, Kang Q, Pan J, Zeng Z, Yu Y, Xu X. The efficacy and safety of 12 week SOF/VEL regimen combined with prophylactic use of TAF for treatment naive genotype1 6 HCV/HBV co infection adult patients with or without compensated cirrhosis in China: a multi center prospective, single arm, open label trial. [Poster 1896-A]. Paper presented at: AASLD - The Liver Meeting; November 10-14, 2023; Boston, MA.
3. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology.* 2018;67(4):1560-1599.
4. AASLD-IDSA HCV Guidance Panel. Hepatitis C Guidance 2018 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. *Clin Infect Dis.* 2018;67:1477-1492. https://www.ncbi.nlm.nih.gov/pubmed/30215672

5. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the Management of Hepatitis B Virus Infection. *J Hepatol.* 2017;67(2):370-398. http://www.ncbi.nlm.nih.gov/pubmed/28427875

Abbreviations

AASLD=American association for the Study of Liver Diseases
APRI=AST to platelet ratio index
DAA=direct-acting antiviral
EASL=European Association for the Study of the Liver
FIB-4=Fibrosis-4
GT=genotype
HBsAg=hepatitis B surface antigen
LLoQ=lower limit of quantification
LSM=liver stiffness measurement
SOF=sofosbuvir
SVR=sustained virologic response
SVR12=sustained virologic response 12 weeks after end of treatment
TAF=tenofovir alafenamide
TN=treatment-naïve
VEL=velpatasvir

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
🖱 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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