GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Use for 8 Weeks

This document presents available data regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) in patients for an 8-week duration for the treatment of HCV. SOF/VEL is not indicated for an 8-week treatment duration.

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.

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

Summary

Product Labeling[1]

In patients ≥3 years of age with HCV GTs 1, 2, 3, 4, 5, or 6, SOF/VEL for 12 weeks is the recommended treatment duration in TN or TE patients without cirrhosis and with compensated cirrhosis (Child-Pugh A); and SOF/VEL + RBV for 12 weeks is the recommended treatment duration in TN or TE participants with decompensated cirrhosis (Child-Pugh B or C). Treatment for 8 weeks is not indicated.

Clinical Data on SOF/VEL Use for 8 Weeks

In a randomized, open-label study in participants with HCV ± HIV and without cirrhosis, treatment with 8 weeks of SOF/VEL was non-inferior to current treatment recommendations for 12 weeks in the overall PP population (SVR12, 98.8% vs 99%, respectively), and rates of treatment completion were similar between groups (99.1% vs 98.6%).[2]

Two phase 2 studies evaluated the efficacy and safety of SOF/VEL ± RBV for 8 weeks in TN participants without cirrhosis and with HCV GTs 1, 2, or 3.[3,4] SVR12 rates ranged from 75% to 100% in participants with GT 1 or 2 ± baseline NS5A RAVs.[5] The presence or absence of baseline RAVs did not correlate with SVR12 rates.[3] Safety results are summarized below.

A phase 2 study evaluated the efficacy and safety of SOF/VEL for 8 weeks in 20 adult participants with acute HCV monoinfection. Ninety percent of participants in the ITT population achieved SVR12 (95% CI: 69.9–97.2%). Six SOF/VEL-related AEs that were all mild in severity occurred.[6]

Real-World Data on SOF/VEL Use for 8 Weeks

A real-world cohort study evaluated 90 TN patients without cirrhosis and with HCV GT 3 and F2/3 fibrosis who were treated with SOF/VEL for 8 weeks. SVR12 rates were high in each study population assessed: ITT, 95.6% (95% CI: 89–98.8%); PP, 100% (95% CI: 95.7–100%).[7]

Clinical Data on SOF/VEL Use for 8 Weeks

Randomized, Open-Label, Non-Inferiority Study[2]

Study design and demographics

An open-label, randomized, non-inferiority study evaluated the efficacy and treatment completion rates of SOF/VEL for 8 vs 12 weeks in adults with chronic HCV in India (N=880). Eligible participants had chronic HCV with or without HIV, and no clinical or biochemical evidence of cirrhosis. Participants were randomly assigned (1:1) to receive 8 or 12 weeks of SOF/VEL. Exclusion criteria included cirrhosis, co-infection with HBV, prior exposure to direct-acting antivirals, hepatocellular carcinoma or other malignancies, portal vein thrombosis, and select special populations vs other comorbid conditions. The primary objective of the study was to compare SVR12 (lower limit of detection, 15 IU/mL) rates between treatment groups in the PP population (8 weeks, n=415; 12 weeks, n=401) with a non-inferiority margin of 5%; the secondary objective was treatment completion rates.

Table 1. Baseline Demographics and Disease Characteristics Overall and by Treatment Duration (ITT Population; Goel et al)[2]

Key Demographics and Characteristics	Overall (N=880)	8-Week Group (n=443)	12-Week Group (n=437)
Age,[a] years	38 (12.7)	37.6 (12.7)	38.4 (12.6)
Male, n (%)	48.3 (51.7)	48.5 (51.5)	48.1 (51.9)
HCV RNA,[a] $\log_{10}$ IU/mL	6 (1.1)	6 (1)	6 (1.1)
HCV GT (n=860), 1/3/4, n (%)	130 (15.4)/714 (82.8)/ 16 (1.7)	77 (17.6)/353 (80.8)/ 7 (1.6)	53 (12.5)/361 (85.3)/ 9 (2.1)
FIB-4[a]	1.6 (1.1)	1.5 (1)	1.7 (1.2)
APRI[a]	0.9 (0.8)	0.9 (0.8)	1 (0.8)
Liver stiffness,[a] kPa	6.6 (2.1)	6.6 (2.2)	6.6 (2)
ALT,[a] IU/mL	85 (75)	84 (74)	86 (76)

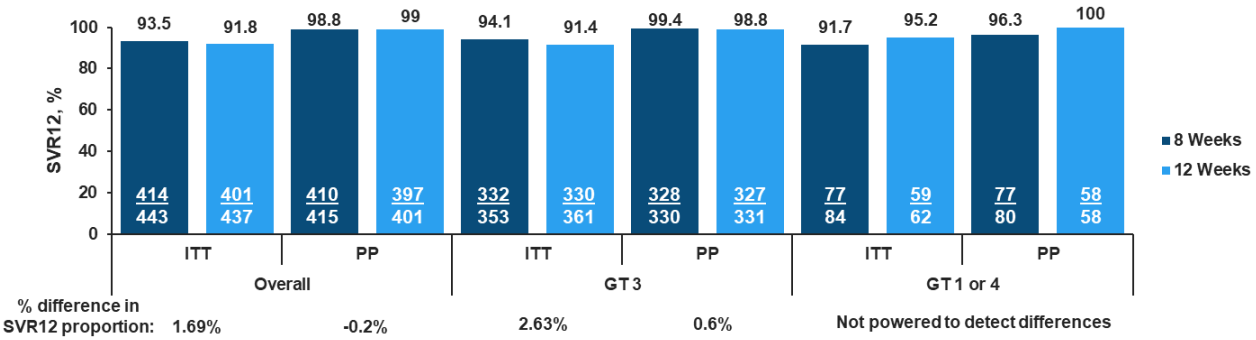
Abbreviations: APRI=AST-to-platelet ratio index; FIB-4=Fibrosis-4.
[a]The presentation of data was not specified (ie, mean [SD]).

Results

Overall, 415 participants in the 8-week group and 401 participants in the 12-week group completed treatment and were included in the PP analysis.

Treatment with 8 weeks of SOF/VEL was non-inferior to treatment for 12 weeks (PP analysis, -0.2% difference between SVR12 rates; Figure 1). In subgroup analyses, treatment with 8 weeks of SOF/VEL was also non-inferior to treatment for 12 weeks among those with HCV GT 3; however, the study was not powered to detect a difference between treatment groups in those with HCV GT 1 or 4.

Figure 1. SVR12 Rates Overall and by GT Subgroups in ITT and PP Populations (Goel et al)[2]



The rates of treatment completion in each group were not significantly different between treatment duration groups: 8 weeks, 99.1% (439/443); 12 weeks, 98.6% (431/437; *P*=not provided). Safety data were not provided.

Phase 2 Study–GT 1 or 2[2]

Study design and demographics

A randomized, multicenter, open-label, phase 2 study evaluated the efficacy and safety of SOF/VEL for 12 weeks (Part A) or SOF/VEL ± RBV for 8 weeks (Part B) in TN participants without cirrhosis. Part B included 223 participants with HCV GTs 1 or 2 who received SOF 400 mg and VEL 25 mg or VEL 100 mg ± RBV. The primary efficacy endpoint was SVR12.

Table 2. Phase 2 Study in GTs 1 or 2: Baseline Demographics and Disease Characteristics in Participants Treated With SOF/VEL 100 mg ± RBV for 8 Weeks[2]

Key Demographics and Characteristics	GT 1		GT 2	
	SOF/VEL (n=29)	SOF/VEL + RBV (n=31)	SOF/VEL (n=26)	SOF/VEL + RBV (n=26)
Age, mean (range), years	55 (21–67)	52 (18–69)	54 (24–71)	51 (28–67)
Male, n (%)	16 (55)	16 (52)	12 (46)	10 (38)
Race, White/Black/other, n (%)	24 (83)/ 5 (17)/0	24 (77)/ 5 (16)/2 (6)	24 (92)/ 2 (8)/0	25 (96)/ 0/1 (4)
HCV RNA VL, mean ± SD, log_{10} IU/mL	6.3±0.85	6.6±0.55	6.5±0.74	6.7±0.57
≥800,000 IU/mL, n (%)	21 (72)	28 (90)	21 (81)	24 (92)
IL28B GT CC, n (%)	13 (45)	9 (29)	9 (35)	7 (27)
ALT level >1.5 × upper limit of normal, n (%)	14 (48)	19 (61)	13 (50)	12 (46)
NS5A RAVs, n (%)	7 (24)	4 (13)	12 (46)	13 (50)

Efficacy (Part B): SOF/VEL 100 mg ± RBV 8-week treatment groups

SVR12 was achieved in 81 to 90% of participants (Figure 2). All virologic failures were due to posttreatment relapses (GT 1: SOF/VEL, n=3; SOF/VEL + RBV, n=5; GT 2: SOF/VEL, n=3; SOF/VEL + RBV, n=3). The presence or absence of baseline RAVs did not correlate with SVR12 rates in participants who received SOF/VEL ± RBV for 8 weeks (Figure 3).

Figure 2. Phase 2 Study in GTs 1 or 2: SVR12 Rates by GT in the SOF/VEL 100 mg ± RBV 8-Week Treatment Group[2]

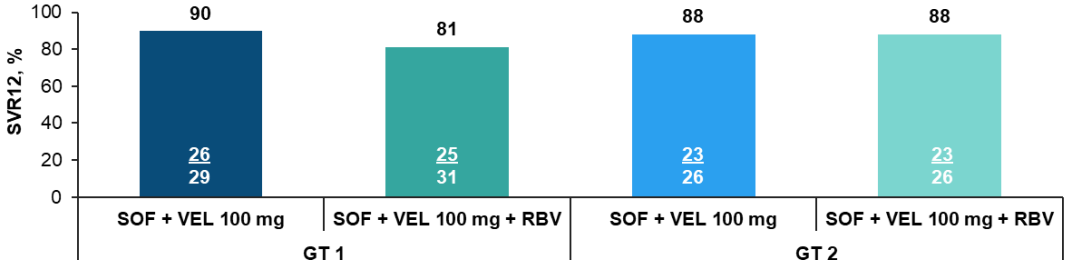
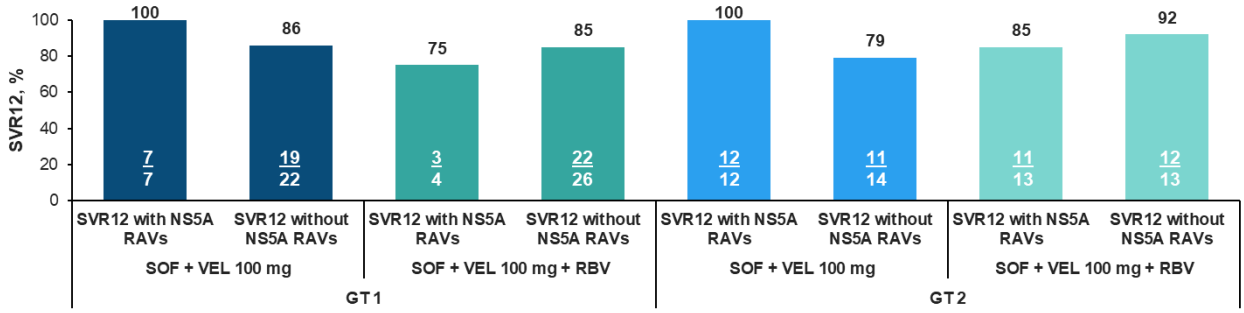


Figure 3. Phase 2 Study in GTs 1 or 2: SVR12 Rates by GT and Baseline NS5A RAVs in the SOF/VEL 100 mg ± RBV 8-Week Treatment Group[2]



Safety (Part B): SOF/VEL 100 mg ± RBV 8-week treatment groups

There were no deaths, treatment-related SAEs, or discontinuations due to AEs in participants who were treated with SOF/VEL + RBV. The AEs reported among those who received SOF/VEL or SOF/VEL + RBV included headache (n=9 vs n=10, respectively), nausea (n=7 vs n=8), constipation (n=3 vs n=1), fatigue (n=2 vs n=21), diarrhea (n=2 vs n=6), insomnia (n=1 vs n=5), nasopharyngitis (n=0 vs n=3), and rash (n=0 vs n=3).

Phase 2 Study–GT 3

Study design and demographics[3]

Cohort 4 of a six-cohort, phase 2, multicenter, open-label study evaluated the efficacy, safety, and tolerability of 8 weeks of SOF/VEL 100 mg ± RBV in participants with chronic HCV GT 3 who were TN and did not have cirrhosis. The primary outcomes evaluated were the rates of SVR12 and the proportion of participants who permanently discontinued the study drug due to AEs.

Table 3. Phase 2 Study in GT 3: Baseline Demographics and Disease Characteristics of Participants Treated With SOF/VEL 100 mg ± RBV for 8 Weeks[4]

Key Demographics and Characteristics	SOF/VEL (n=27)	SOF/VEL + RBV (n=26)
Age, mean ± SD, years	50±10.2	47±10.3
Male, n (%)	17 (63)	11 (42.3)
Race/ethnicity, White/Asian/Native Hawaiian or other Pacific Islander/American Indian or Alaska Native/other, n	20/1/3/0/3	19/0/6/1/0
HCV RNA VL, mean ± SD, $\log_{10}$ IU/mL	6±0.71	6.2±0.92
≥800,000 IU/mL, n (%)	16 (59.3)	19 (73.1)
IL28B GT CC, n	15	14

Efficacy: SOF/VEL 100 mg ± RBV 8-week treatment groups[4]

All participants (n=26) who received SOF/VEL + RBV for 8 weeks achieved SVR12, and 96.3% of participants (26/27) who received SOF/VEL for 8 weeks achieved SVR12. All participants had undetectable HCV RNA VLs as early as on-treatment Week 6. None experienced on-treatment virologic failure or virologic relapse.

Safety[4]

There were no SAEs, discontinuations due to AEs, or deaths in either treatment group. The AEs reported in ≥10% of participants treated with 8 weeks of SOF/VEL 100 mg vs SOF/VEL 100 mg ± RBV were insomnia (22% vs 8%, respectively), diarrhea (15% vs 4%), fatigue (15% vs 27%), nausea (15% vs 12%), headache (11% vs 15%), lethargy (11% vs 12%) upper respiratory tract infection (11% vs 15%), rash (7% vs 15%), back pain (0 vs 12%), and pruritus (0 vs 12%).

HepNet Acute HCV-V Study[6]

Study design and demographics

An open-label, single-arm, multicenter, phase 2 pilot study evaluated the efficacy and safety of 8 weeks of SOF/VEL in 20 adult participants with acute HCV monoinfection. The primary endpoint was SVR12 and was considered met if the lower bound of the 95% CI was >83%.

The majority (95%) of participants were men, the mean ± SD age was 37.4±9.3 years, and 65% of participants were receiving emtricitabine/tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis. The study included participants with GTs 1 to 4; most participants (60%) had GT 1a. All participants had HCV RNA >1000 IU/mL at screening. At baseline, the median (IQR) HCV RNA was 104,307 (7842–1,726,734) IU/mL, 40% of participants had an HCV RNA VL <50,000 IU/mL, and 10% had an HCV RNA VL <10 IU/mL. The mean (IQR) ALT level at baseline was 249 (165–463) U/L.

Efficacy and safety results

Among the ITT population (n=20; all participants who received ≥1 dose of SOF/VEL), 90% of participants (n=18; 95% CI: 69.9–97.2%) achieved SVR12, which did not meet the primary endpoint. The 2 participants who did not achieve SVR12 were lost to follow-up; both had HCV RNA VL <10 IU/mL at their last follow-up.

Eight-five percent of participants (n=17) had normal ALT levels at follow-up Weeks 4 and 12, and 16 participants (80%) had normal ALT levels at follow-up Week 8.

Of the 28 reported AEs, 6 were mild in severity and were considered possibly or probably related to SOF/VEL treatment: skin irritations, n=2 (3 events in 2 participants); sleeping disorders, n=1; flatulence, n=1; headache, n=1.

Real-World Data on SOF/VEL Use for 8 Weeks

Scottish Hepatitis C Database[7]

Study design and demographics

Treatment outcomes were analyzed for 90 TN patients without cirrhosis and with HCV GT 3 and F2/3 fibrosis (patients with F0/1 and significant extrahepatic manifestations were eligible) who were treated with 8 weeks of SOF/VEL. Eighty-two patients (91.1%) received concomitant OAT, including 49 patients (54.4%) who received OAT from Glasgow City Alcohol and Drug Services. Of these 49 patients, 8 (16.3%) had self-reported IV drug use, and 14 (28.6%) had self-reported non-IV drug use. SVR12 rates were assessed in the ITT (all patients who began SOF/VEL) and PP (patients who completed 8 weeks of treatment, excluding those without SVR12 data and those who experienced reinfection) study populations.

The majority of patients (80%) were male; 3.3% and 1.1% also had HIV and HBV, respectively; and 6.6% had a VL >6.77 log IU/mL. The mean ± SD HCV VL was 5.7±0.9 log IU/mL. The mean ± SD liver stiffness measurement was 8.5±1.5 kPa; and 2.2%, 66.7%, and 31.1% of patients had fibrosis stage of F0/1, F2, and F3, respectively.

Results

Eighty-six patients (95.6%; 95% CI: 89–98.8%) in the ITT population and 84 patients (100%; 95% CI: 95.7–100%) in the PP population achieved SVR12.

Eighty-two patients (91.1%) had EoT results. Of the patients who did not have EoT results, 4 discontinued SOF/VEL early (2 of whom achieved SVR12), 1 died due to a drug overdose after the completion of SOF/VEL but before the SVR12 assessment, and 1 had an undetectable HCV VL at EoT but was deemed to have had a reinfection, since they did not achieve SVR12 (VL, 184 IU/mL). No safety data were reported.

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Goel A, Rungta S, Kumar V, et al. Eight versus twelve weeks of sofosbuvir/velpatasvir for treatment-naïve, non-cirrhotic chronic hepatitis C: An interim analysis of a multicentric, open label, randomized, non-inferiority (RESOLVE) trial [Oral presentation]. Paper presented at: The Liver Meeting; 7-11 November, 2025; Washingtong, DC.
3. Everson GT, Towner WJ, Davis MN, et al. Sofosbuvir With Velpatasvir in Treatment-Naive Noncirrhotic Patients With Genotype 1 to 6 Hepatitis C Virus Infection: A Randomized Trial. *Ann Intern Med.* 2015;163(11):818-826.
4. ClinicalTrials.gov. Efficacy and Safety of Sofosbuvir Containing Regimens for the Treatment of Chronic HCV Infection in Participants With Chronic Genotype 1, 2, 3, or 6 HCV Infection. ClinicalTrials.gov Identifier: NCT01826981 [Study Details]. Last Updated: 16 November. 2018.
5. ClinicalTrials.gov. Efficacy and Safety of Sofosbuvir Containing Regimens for the Treatment of Chronic HCV Infection in Participants With Chronic Genotype 1, 2, 3, or 6 HCV Infection. ClinicalTrials.gov Identifier: NCT01826981 [Study Results]. Last Updated: 16 November. 2018.
6. Maasoumy B, Ingiliz P, Spinner CD, et al. Sofosbuvir plus velpatasvir for 8 weeks in patients with acute hepatitis C: The HepNet acute HCV-V study. *JHEP Rep.* 2023;5(3):1-6.

7. Boyle A, Marra F, Peters E, et al. Eight weeks of sofosbuvir/velpatasvir for genotype 3 hepatitis C in previously untreated patients with significant (F2/3) fibrosis. *J Viral Hepat.* 2020;27(4):371-375.

Abbreviations

AE=adverse event
EoT=end of treatment
GT=genotype
IL28B=interleukin 28B
OAT=opioid agonist therapy
PP=per protocol
RAV=resistance-associated variant
RBV=ribavirin
SAE=serious adverse event
SOF=sofosbuvir
SVR12=sustained virologic response 12 weeks after end of treatment
TN=treatment-naive
TE=treatment-experienced
VEL=velpatasvir
VL=viral load

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Epclusa US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_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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