GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Use for 8 Weeks

This document is in response to your request for information regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) in patients for an 8-week duration in 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]

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

Two phase 2 studies evaluated the efficacy and safety of SOF/VEL ± RBV for 8 weeks in TN, NC participants with HCV GTs 1, 2, or 3.[2,3]

- SVR12 rates ranged from 75% to 100% in participants with GT 1 or 2 ± baseline NS5A RAVs.[4]
- The presence or absence of baseline RAVs did not correlate with SVR12 rates.[2]
- 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.[5]

- 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.

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

A real-world cohort study evaluated 90 TN, NC patients with HCV GT 3 and F2/3 fibrosis who were treated with SOF/VEL for 8 weeks.[6]

- SVR12 rates were high in each study population assessed: ITT, 95.6% (95% CI: 89–98.8%); PP, 100% (95% CI: 95.7–100%).

Clinical Data on SOF/VEL Use for 8 Weeks

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, NC participants. Part B included 223 participants with HCV GTs 1 or 2 who received SOF 400 mg and VEL 25 mg or 100 mg ± RBV. The primary efficacy endpoint was SVR12.

Table 1. Baseline Demographics and Disease Characteristics in Participants With GTs 1 or 2 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 level, 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 8-week treatment groups

SVR12 was achieved in 81 to 90% of participants (Figure 1). All virologic failures were due to posttreatment relapse (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 2).

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

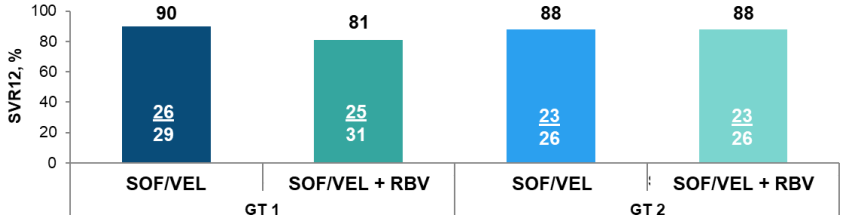
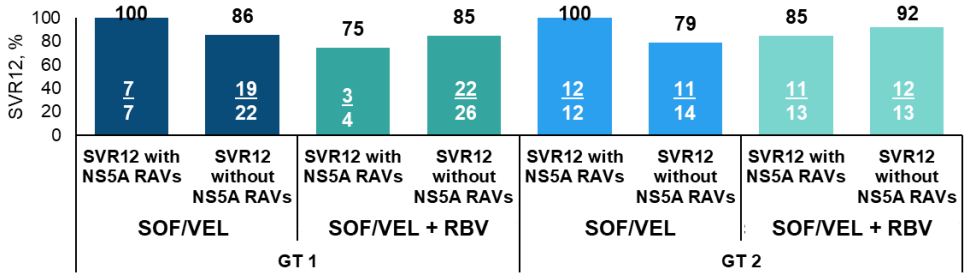


Figure 2. SVR12 Rates by GT and Baseline NS5A RAVs in the SOF/VEL 100 mg ± RBV 8-Week Treatment Group[2]



Safety (Part B): SOF/VEL 100 mg 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), 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

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 NC. The primary outcomes evaluated were the rates of SVR12 and the proportion of participants who permanently discontinued the study drug due to AEs.[3]

Table 2. Baseline Demographics and Disease Characteristics of Participants With GT 3 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 level, 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 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 levels as early as on-treatment Week 6. None experienced on-treatment virologic failure or viral 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%), 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[5]

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 level <50,000 IU/mL at baseline, and 10% had an HCV RNA level <10 IU/mL. The mean (IQR) ALT level at baseline was 249 (165–463) U/L.

Efficacy 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 levels <10 IU/mL at their last follow-up.

Seventeen participants (85%) had normal ALT levels at follow-up Weeks 4 and 12, and 16 participants (80%) had normal ALT levels at follow-up Week 8.

Safety results

Of the 28 reported AEs, 6 were considered possibly or probably related to SOF/VEL treatment and were considered mild in severity: 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[6]

Study design and demographics

Treatment outcomes were analyzed for 90 TN, NC patients 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 end of treatment results. Of the patients who did not have end of treatment 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 the end of treatment 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. 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. http://www.ncbi.nlm.nih.gov/pubmed/26551051
3. 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.
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 Results]. Last Updated: 16 November. 2018.
5. 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.
6. 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
GT=genotype
NC=non-cirrhotic
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 post-treatment
TN=treatment-naïve
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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