GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Retreatment of HCV Infection After Previous SOF/VEL Use

This document is in response to your request for information regarding efficacy and safety data of the use of Epclusa® (SOF/VEL) for the retreatment of HCV infection in patients previously treated with SOF/VEL.

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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/epclusa/epclusa_pi.

Summary

Product Labeling[1]

SOF/VEL is indicated for the treatment of adults and pediatric patients ≥3 years of age with chronic HCV GT 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis, or with decompensated cirrhosis for use in combination with RBV.

Clinical Data on Retreatment of HCV Infection After Previous SOF/VEL Use

A single-arm, multicenter, retreatment study evaluated the efficacy and safety of SOF/VEL + RBV for 24 weeks in participants previously treated for HCV infection with SOF/VEL ± RBV (n=41) or SOF/VEL/VOX (n=28).[2]

- SVR12 was achieved in 91% of participants (63/69) retreated with 24 weeks of SOF/VEL + RBV.
- Overall, SOF/VEL + RBV was safe and well tolerated, with 1 treatment discontinuation due to an AE; no deaths were reported.

A retrospective analysis was conducted in patients who received retreatment of HCV infection with SOF-based regimens (n=36), including SOF/VEL ± RBV for 12 or 24 weeks. Five patients who had previously received SOF/VEL and were retreated with SOF/VEL were included in this study (GT 3, n=3; GT 1, n=1; and unspecified GT, n=1).[3]

- The SVR12 rate was 100% for patients who completed treatment.
- There were 5 deaths before retreatment and 2 deaths after retreatment.

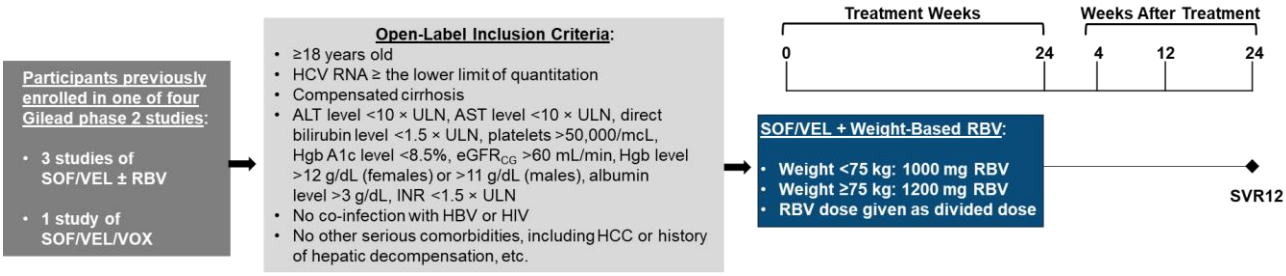
Clinical Data on Retreatment of HCV Infection After Previous SOF/VEL Use

SOF/VEL + RBV Use After Prior SOF/VEL ± RBV or SOF/VEL/VOX Treatment Failures[2]

Study design and demographics

A single-arm, multicenter, retreatment study evaluated the efficacy and safety of 24 weeks of SOF/VEL + RBV (weight-based RBV dose) treatment for HCV infection in 69 participants previously treated for HCV infection in prior Gilead-sponsored phase 2 studies.

Figure 1. Study Design (Gane et al)[2]



Abbreviation: $eGFR_{CG}$=eGFR calculated by the Cockcroft-Gault method.

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

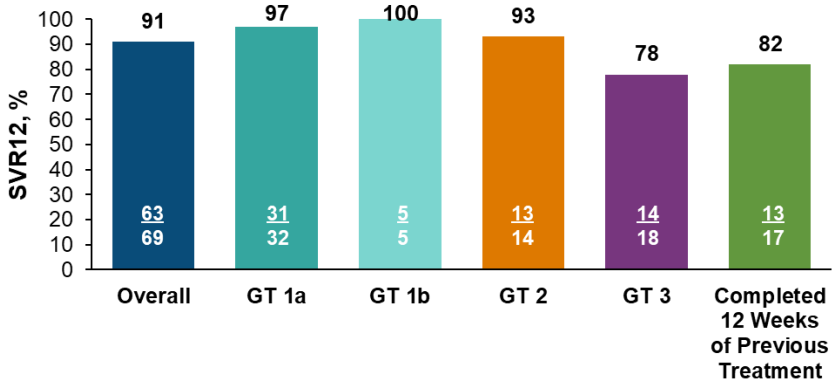
Key Demographics and Characteristics		SOF/VEL + RBV (N=69)
Age, mean (range), years		57 (31–74)
Male, n (%)		53 (77)
Race, White/Black/Pacific Islander/Asian, %		88/4/4/3
BMI, mean (range), kg/m^2		28 (19–44)
HCV GT, 1a/1b/2/3, %		46/7/20/26
HCV RNA, mean (range), log_{10} IU/mL		6.4 (4.4–7.4)
Cirrhosis, n (%)		18 (26)[a]
ALT level >1.5 × ULN, n (%)		34 (49)
IL28B, *CC*/*CT*/*TT*, %		33/67/20
Previous HCV treatment, n (%)	SOF/VEL/VOX	28 (41)
	SOF/VEL	27 (39)
	SOF/VEL + RBV	14 (20)
Previous VEL dose, 25 mg/100 mg, n (%)		28 (41)/41 (69)
Length of prior HCV treatment, n (%)	4–6 weeks	25 (36)
	8 weeks	27 (39)
	12 weeks	17 (25)
Response to previous HCV treatment, n (%)	Relapse or breakthrough	68 (99)
	No response	1 (1)
Time to HCV retreatment, median (range), days		356 (101–600)

[a]Six of the 37 participants with GT 1 and 12/18 participants with GT 3 had cirrhosis. No participants with GT 2 had cirrhosis.

Efficacy

SVR12 rates are presented in Figure 2.

Figure 2. SVR12 Rates (Gane et al)[2]



Four participants did not achieve SVR12 as a result of virologic relapse, 2 participants had virologic failure during treatment, and 1 participant experienced HCV reinfection at posttreatment Week 24.

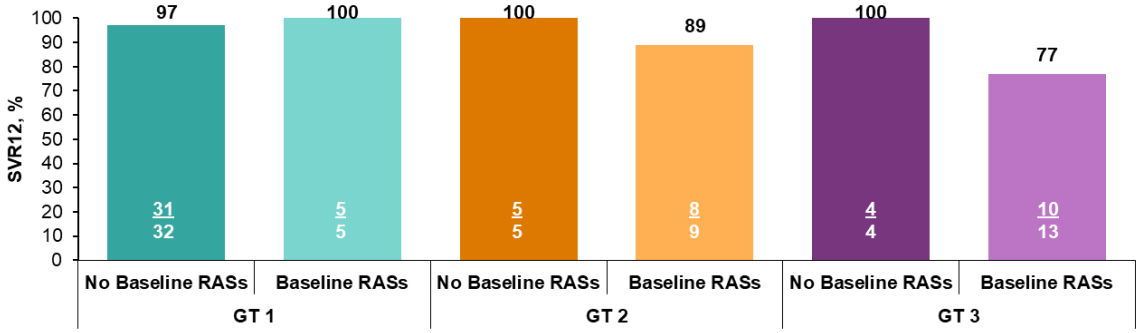
Table 2. Responses During and After SOF/VEL + RBV: Overall and by GT (Gane et al)[2]

Endpoints, n or n/N (%)		Overall (N=69)	GT 1 (n=37)	GT 2 (n=14)	GT 3 (n=18)
SVR12 by cirrhosis status	No cirrhosis	49/51 (96)	31/31 (100)	13/14 (93)	5/6 (83)
	Cirrhosis	14/18 (78)	5/6 (83)	0	9/12 (75)
Virologic failure	During treatment	2 (3)	1 (3)	0	1 (6)
	Posttreatment relapse	3 (5)	0	1 (7)	2 (12)

Resistance analysis

SVR12 by baseline GT and RASs is presented in Figure 3.

Figure 3. SVR12 Rates by GT and Presence of RASs at Baseline (Gane et al)[2]



Safety

Overall, 61 patients (88%) experienced an AE. Two patients reported a serious AE, including nephrolithiasis (Day 59 in a 31-year-old female with GT 1a) and HCC (posttreatment Day 31 in a 54-year-old male with GT 3 and cirrhosis). The most common AEs included fatigue (n=22), nausea (n=15), headache (n=12), insomnia (n=11), pruritus (n=10), rash (n=9), irritability (n=9), and upper respiratory tract infection (n=9).
One participant discontinued SOF/VEL and RBV due to AEs. Three participants

discontinued RBV due to AEs (worsening cough, vomiting, and depressed mood), and each participant achieved SVR12. No deaths were reported.

Retrospective Study on Retreatment in DAA-Experienced Patients[3]

Study design and demographics

A retrospective analysis conducted in consecutive patients who were referred for care at a clinic in New Delhi, India, between May 2015 and January 2020. Included in the analysis were patients who had received DAA-based treatment for chronic HCV and failed to achieve SVR12 or had a relapse after achieving SVR12. Patients co-infected with HBV or HIV were not included. Patients were retreated with SOF-based regimens for 12 or 24 weeks; retreatment regimen choice was not informed by RAS analysis. A subgroup of randomly selected patients in whom DAAs failed underwent next-generation sequencing of the HCV genome. The majority of participants (63.9%) were male, and the mean age was 45.7 years.

In total, 36 patients underwent retreatment and had complete follow-up data (Table 3). Five patients were previously treated and retreated with SOF/VEL (GT 3, n=3; GT 1, n=1; unspecified GT, n=1).

Table 3. Previous DAA Regimens and Retreatment Regimens by GT (Elhence et al)[3]

GT	n	Previous DAA Regimens	Retreatment Regimens	n per Retreatment Regimen
GT 1	8	LDV/SOF × 24 wk; SOF + DCV × 12 wk; SOF + RBV × 12 wk	SOF/VEL × 12 wk	3
		SOF/VEL × 12 wk	**SOF/VEL × 24 wk**	**1**
		SOF + RBV × 24 wk; LDV/SOF × 12 wk	SOF/VEL + RBV × 24 wk	2
		SOF + RBV × 24 wk; LDV/SOF × 24 wk	LDV/SOF + RBV × 24 wk	2
GT 2	1	SOF + DCV × 12 wk	SOF/VEL + RBV × 24 wk	1
GT 3	23	SOF + DCV × 12 wk (n=10); SOF + DCV + RBV × 12 wk (n=2); **SOF/VEL × 12 wk (n=2)**	**SOF/VEL + RBV × 24 wk**	14
		SOF/VEL × 12 wk	**SOF/VEL + RBV × 12 wk**	**1**
		SOF + DCV × 12 wk (n=4); SOF + DCV + RBV × 12 wk (n=1); SOF + DCV + RBV × 24 wk (n=1); PEG IFN + SOF +RBV × 12 wk (n=1)	SOF/VEL × 12 wk	7
		SOF + RBV × 24 wk	SOF + DCV + RBV × 24 wk	1
Unspecified GT	4	LDV/SOF × 12 wk; SOF + DCV × 12 wk	SOF/VEL × 12 wk	2
		SOF/VEL × 12 wk; SOF + DCV × 24 wk	**SOF/VEL + RBV × 24 wk**	2

Abbreviations: DCV=daclatasvir; LDV=ledipasvir; PEG IFN=pegylated interferon.
Note: Bolded cells indicate patients who were TE with SOF/VEL and received retreatment with SOF/VEL. Within the previous DAA regimen column, each of the listed regimens corresponds to 1 patient, unless otherwise specified.

Results

Of the 36 patients who underwent retreatment, 26 patients completed their retreatment course and achieved SVR12, and 5 were lost to follow-up. The SVR12 rates according to GT were as follows: GT 1, 100% (7/7); GT 2, 100% (1/1); GT 3, 75% (15/20; patients who completed retreatment, 100% [15/15]); unspecified GT, 100% (3/3).

Six patients (16.7%) who were retreated developed HCC, including 4 patients with GT 3, 1 with GT 1, and 1 with unspecified GT. Two patients developed HCC after achieving SVR12, and 2 patients who were SOF/VEL TE and retreated with SOF/VEL developed HCC. All 6 patients had cirrhosis, including 5 with decompensated cirrhosis. Five patients died before retreatment was completed (GT 3, n=3: HCC, n=2; acute-on-chronic liver failure, n=1; GT 1, n=1: renal failure; and unspecified GT, n=1: HCC), and an additional 2 patients died from HCC after completing retreatment.

Seventeen patients underwent assessment for RAS, and no observed substitutions affected SVR12 rates. No patients in this subgroup were previously treated with SOF/VEL and retreated with SOF/VEL.

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Gane EJ, Shiffman ML, Etzkorn K, et al. Sofosbuvir-Velpatasvir With Ribavirin for 24 Weeks in HCV Patients Previously Treated With a Direct-Acting Antiviral Regimen. *Hepatology.* 2017. http://www.ncbi.nlm.nih.gov/pubmed/28498551
3. Elhence A, Singh A, Anand A, et al. Real-world re-treatment outcomes of direct-acting antiviral therapy failure in patients with chronic hepatitis C. *J Med Virol.* 2021;93(8):4982-4991.

Abbreviations

AE=adverse event
DAA=direct-acting antiviral
GT=genotype
HCC=hepatocellular carcinoma
RAS=resistance-associated substitution
RBV=ribavirin
SOF=sofosbuvir
SVR12=sustained virologic response 12 weeks after end of treatment
TE=treatment experienced
ULN=upper limit of normal
VEL=velpatasvir
VOX=voxilaprevir

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
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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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