GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Use Without Ribavirin in Decompensated Cirrhosis

This document is in response to your request for information regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) without ribavirin (RBV) in patients with HCV infection and decompensated cirrhosis.

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 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. The recommended treatment duration of SOF/VEL ± RBV is 12 weeks.

Clinical Data on SOF/VEL Use Without RBV in Decompensated Cirrhosis

In the phase 3 ASTRAL-4 study of SOF/VEL in TN and TE participants with decompensated cirrhosis and HCV GTs 1 through 6, participants were randomly assigned in a 1:1:1 ratio to receive SOF/VEL for 12 weeks, SOF/VEL + RBV for 12 weeks, or SOF/VEL for 24 weeks.[2]

- In a post hoc analysis, there were no significant differences in SVR12 rates between the treatment groups: SOF/VEL for 12 weeks, 83%; SOF/VEL for 24 weeks, 86%; SOF/VEL + RBV for 12 weeks, 94% (each, *P*>0.05; significance level set at 0.0167).[2,3]
- The most common AEs (≥10%) that occurred in the SOF/VEL for 24 weeks group were fatigue (23%), nausea (20%), headache (19%), and insomnia (10%).[2]

In an observational study (N=40), participants with HCV and ESRD on HD received SOF/VEL for 12 weeks (24 weeks if they had decompensated cirrhosis, n=3).[4]

- The overall SVR12 rate was 97.5% (39/40); the participant who did not achieve SVR12 had decompensated cirrhosis.
- Safety data were not provided according to cirrhosis status. No interruptions in treatment due to AEs occurred. There were no significant changes from baseline to the SVR12 checkpoint in hepatic or kidney function (mean ± SD eGFR: at baseline, 13.54±11.38 mL/min/1.73 m^2; at SVR12, 13.27±10.32 mL/min/1.73 m^2; *P*=0.54).

Clinical Data on SOF/VEL Use Without RBV in Decompensated Cirrhosis

ASTRAL-4: SOF/VEL ± RBV for 12 or 24 Weeks[2]

Study design and demographics

ASTRAL-4 was a phase 3, open-label study in TN and TE participants with HCV GTs 1 through 6 with decompensated cirrhosis (CPT Class B). Participants were randomly assigned in a 1:1:1 ratio to receive SOF/VEL daily for 12 weeks, SOF/VEL + RBV for 12 weeks, or SOF/VEL for 24 weeks.

Of the 267 participants enrolled, 78% were GT 1, 4% were GT 2, 15% were GT 3, 3% were GT 4, and <1% were GT 6 Most participants (95%) had a baseline MELD score ≤15, and 55% were TE. Although all participants had CPT Class B cirrhosis at screening, 27 participants had CPT Class A or C cirrhosis at treatment initiation.

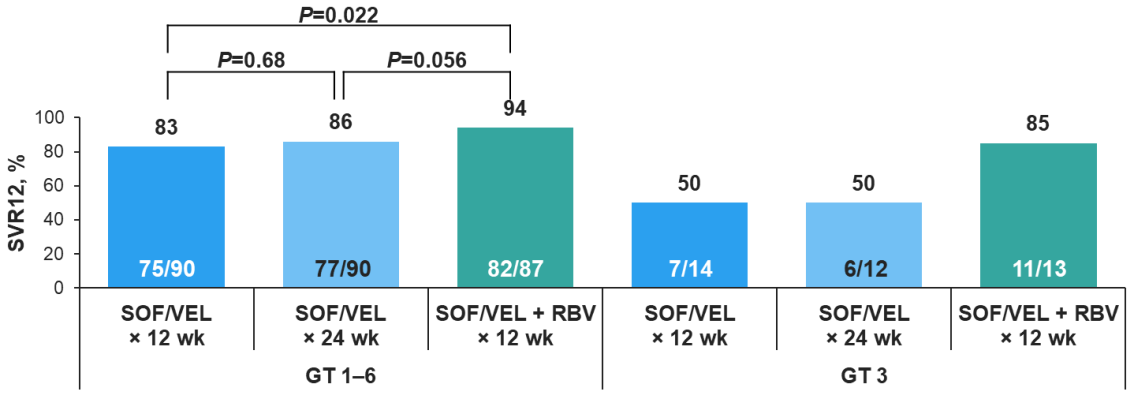
Table 1. ASTRAL-4: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		SOF/VEL		SOF/VEL + RBV × 12 Weeks (n=87)
		12 Weeks (n=90)	24 Weeks (n=90)	
Age, mean (range), years		58 (42–73)	58 (46–72)	58 (40–71)
Male, n (%)		57 (63)	63 (70)	66 (76)
Race, n (%)	White	79 (88)	81 (90)	79 (91)
	Black	6 (7)	6 (7)	5 (6)
	Asian	3 (3)	2 (2)	0
	Other	2 (2)	1 (1)	3 (3)
HCV RNA	Mean (SD), $\log_{10}$ IU/mL	6 (0.5)	5.9 (0.6)	5.8 (0.6)
	≥800,000 IU/mL, n (%)	59 (66)	45 (50)	45 (52)
HCV GT, 1a/1b/2/3/4/6, %		56/20/4/16/4/0	61/18/4/13/2/1	62/16/5/15/2/0
CPT score, ≤6/7/8/9/10, %		3/40/34/21/1	8/23/38/24/7	7/26/47/15/5
MELD score, n (%)	<10	36 (40)	26 (29)	29 (33)
	10–15	50 (56)	59 (66)	54 (62)
	≥16	4 (4)	5 (6)	4 (5)
eGFR, mean (range), mL/min		89 (15–169)	90 (43–198)	90 (50–167)

Efficacy

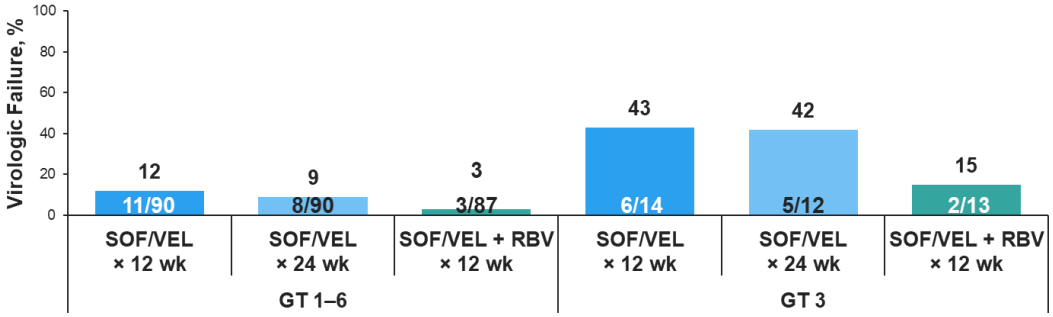
SVR12 rates for each of the three treatment groups are shown in Figure 1. In a post hoc analysis, there were no significant differences in SVR12 rates among the three treatment groups. (Figure 1). A total of 22 participants experienced virologic failure (Figure 2), and 20 of those participants experienced relapse. Two participants with GT 3 experienced virologic breakthrough.

Figure 1. ASTRAL-4: SVR12 Rates Overall and in Participants With GT 3[2,3]



Note: *P*-values were calculated for a post hoc analysis; however, the study was not adequately powered to determine differences between treatment groups.

Figure 2. ASTRAL-4: Virologic Failure Rates Overall and in Participants With GT 3[2]



Safety

Overall safety outcomes by treatment group are in Table 2. Decreases in Hgb, lymphocytes, and platelets were observed in all three treatment groups.

Table 2. ASTRAL-4: Safety Outcomes[2]

Safety Outcomes, n (%)		SOF/VEL		SOF/VEL + RBV × 12 Weeks (n=87)
		12 Weeks (n=90)	24 Weeks (n=90)	
Serious AEs		17 (19)	16 (18)	14 (16)
Discontinuations due to AEs		1 (1)	4 (4)	4 (5)
Deaths[a]		3 (3)	3 (3)	3 (3)
Common AEs (>10% of participants in any group)	Fatigue	23 (26)	21 (23)	34 (39)
	Headache	23 (26)	17 (19)	18 (21)
	Nausea	22 (24)	18 (20)	22 (25)
	Pruritus	10 (11)	4 (4)	4 (5)
	Insomnia	9 (10)	9 (10)	12 (14)
	Diarrhea	6 (7)	7 (8)	18 (21)
	Anemia	4 (4)	3 (3)	27 (31)
	Dyspnea	4 (4)	2 (2)	9 (10)
	Muscle spasm	3 (3)	4 (4)	10 (11)
	Cough	2 (2)	0	9 (10)
Reduced Hgb level	<10 g/dL	7 (8)	8 (9)	20 (23)
	<8.5 g/dL	1 (1)	1 (1)	6 (7)

Safety Outcomes, n (%)		SOF/VEL		SOF/VEL + RBV
		12 Weeks (n=90)	24 Weeks (n=90)	× 12 Weeks (n=87)
Reduced lymphocyte count	350 to <500/mm^3	10 (11)	8 (9)	12 (14)
	<350/mm^3	3 (3)	6 (7)	12 (14)
Reduced platelet count	25,000 to <50,000/mm^3	15 (17)	18 (20)	10 (11)
	<25,000/mm^3	1 (1)	0	0

[a]Two participants died <30 days after they discontinued study treatment, and 7 participants died >30 days after the end of treatment; all deaths were deemed unrelated to study treatment. Most of the deaths were due to complications of end-stage liver disease (ie, liver failure, sepsis, or multiorgan failure).

Real-World, Observational Study in Participants With ESRD on HD[4]

Study design and demographics

A single-center, real-world, observational study in India evaluated the efficacy and safety of SOF/VEL in 40 TN participants with HCV and ESRD who planned to start maintenance HD. No genotyping was performed. The study included 3 participants with decompensated cirrhosis who received SOF/VEL for 24 weeks. All other participants (non-cirrhotic or with compensated cirrhosis) were treated for 12 weeks.

Table 3. Overall Baseline Demographics and Disease Characteristics (Behera et al)[4]

Key Demographics and Characteristics	Overall (N=40)
Age, mean ± SD, years	49.87±12.13
Male, n (%)	32 (80)
Chronic HCV, n (%)	31 (77)
HCV RNA, mean ± SD, × 10^6 IU/mL	2.61±7.83
Liver stiffness, mean ± SD, kPa	8.77±3.68
F0–F1/F2/F3/F4, n (%)	17 (43)/11 (27)/7 (17)/5 (13)
Cirrhosis, compensated/decompensated, n (%)	6 (15)/3 (8)
eGFR, mean ± SD, mL/min/1.73 m^2	13.54±11.38

Abbreviation: F=fibrosis

Efficacy and safety

The SVR12 rate was 97.5% (39/40); 1 participant with decompensated cirrhosis did not achieve SVR12. Three participants underwent kidney transplantation; of these, 1 died 28 days post transplant, and 2 did not have HCV recurrence through 2 years post transplant.

Safety data were not provided according to cirrhosis status. Overall, the most common AEs were lightheadedness (15%; n=6), nausea (12.5%; n=5), fatigue (10%; n=4) and headache (10%; n=4). No changes in hepatic or kidney function occurred during SOF/VEL treatment or during follow-up. The mean ± SD eGFR did not significantly change over the course of the study: baseline, 13.54±11.38 mL/min/1.73 m^2; at SVR12, 13.27±10.32 mL/min/1.73 m^2 (P=0.54). The mean ± SD Hgb did not significantly change from pretreatment to SVR12 (8.85±1.79 g/dL vs 8.65±1.45 g/dL, respectively; P>0.05). No interruptions in treatment due to AEs occurred.

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Curry MP, O'Leary JG, Bzowej N, et al. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. *N Engl J Med.* 2015;373(27):2618-2628.
3. Curry MP, O'Leary JG, Bzowej N, et al. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis [Supplementary Appendix]. *N Engl J Med.* 2015;373(27):2618-2628.
4. Behera MK, Majji P, Behera S, et al. The Fixed Dose Combination of Sofosbuvir and Velpatasvir is Safe and Effective in Patients of Chronic Hepatitis C With End-stage Renal Disease. *J Clin Exp Hepatol.* 2024;14(4):101367.

Abbreviations

AE=adverse event
CPT=Child-Pugh-Turcotte
ESRD=end-stage renal disease
GT=genotype
HD=hemodialysis
MELD=model for end-stage liver disease
RBV=ribavirin
SOF=sofosbuvir
SVR12=sustained virologic response 12 weeks after end of treatment
TE=treatment-experienced
TN=treatment-naive
VEL=velpatasvir

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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