GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Use in LDV/SOF Treatment-Experienced Patients

This document is in response to your request for information regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) for the treatment of HCV infection in adult patients previously treated with Harvoni® (ledipasvir/sofosbuvir [LDV/SOF]).

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]

The efficacy of SOF/VEL has not been established in patients who have previously failed treatment with other regimens that include an NS5A inhibitor.

SOF/VEL is indicated for the treatment of 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.

Both SOF and VEL were fully active against substitutions associated with resistance to other classes of DAAs with different mechanisms of action, such as NS5B non-nucleoside inhibitors and NS3 protease inhibitors. The efficacy of SOF/VEL has not been established in patients who have previously failed treatment with other regimens that include an NS5A inhibitor.

Clinical Data on SOF/VEL Use in LDV/SOF TE Patients

In a phase 3 study, all participants who were LDV/SOF TE (n=20) achieved SVR12 after 12 or 24 weeks of SOF/VEL + RBV.[2] The most common AEs (>10% of participants) were viral upper respiratory infection, anemia, and headache.[2,3]

In a real-world study of participants who were LDV/SOF TE, SVR12 rates were 85% (11/13) after SOF/VEL and 74% (58/78) after SOF/VEL + RBV. No safety data were presented.[4]

Clinical Data on SOF/VEL Use in LDV/SOF TE Patients

Japan Retreatment Study

Study design and demographics

Izumi et al conducted a phase 3, multicenter, open-label, randomized trial that evaluated the use of SOF/VEL in DAA-experienced participants with HCV GT 1 and 2.[2]

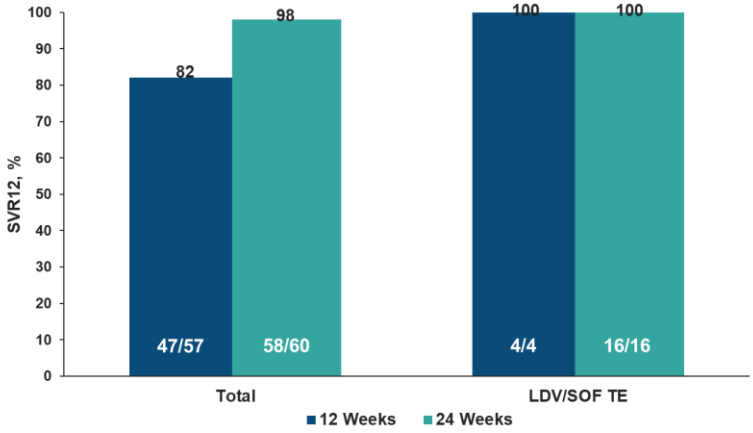
Figure 1. Study Design (Izumi et al)[2,3]

Table 1. Baseline Demographics and Disease Characteristics (Izumi et al)[2,3]

Key Demographics and Characteristics		SOF/VEL + RBV 12 Weeks (n=57)	SOF/VEL + RBV 24 Weeks (n=60)
Age, mean, years		62	63
Male, n (%)		23 (40)	27 (45)
Asian race, n (%)		57 (100)	60 (100)
Cirrhotic, n (%)		18 (32)	21 (35)
GT, 1a/1b/2a/2b, %		4/79/12/5	2/78/13/7
HCV RNA, mean (range), $\log_{10}$ IU/mL		6.3 (4.8–7.1)	6.2 (4.3–7.1)
Number of prior DAAs, n (%)	1	11 (19)	8 (13)
	2	35 (61)	41 (68)
	≥3	11 (19)	11 (18)
Prior DAAs, n (%)	Daclatasvir-based	44 (77)	41 (68)
	SOF-based	12 (21)	22 (37)
	LDV/SOF	4 (7)	16 (27)

Efficacy

Figure 2. SVR12 Rates (Izumi et al)[2,3]



Safety

Table 2. Safety Parameters (Izumi et al)[2,3]

Safety Parameters, n (%)		SOF/VEL + RBV 12 Weeks (n=57)	SOF/VEL + RBV 24 Weeks (n=60)
AEs		46 (81)	45 (75)
AEs in >10% of participants	Viral upper respiratory infection	20 (35)	13 (22)
	Anemia	14 (25)	13 (22)
	Headache	11 (19)	2 (3)
Grade 3–4 AE		0	4 (7)
Grade 3–4 laboratory abnormality		6 (11)	16 (27)
Serious AEs		0	4 (7)
Treatment related		0	0
Treatment discontinuation due to AE		1 (2)[a]	2 (3)[b]
Death		0	0

[a]Rash (n=1, Day 8).
[b]Hepatic angiosarcoma (n=1, Day 97), depression (n=1; Day 62).

Observational Cohort of HCV GT 1a in VA Registry[4]

Study design and demographics

Participants with HCV GT 1a within the VA Hepatitis C Clinical Registry who failed ≥8 weeks of LDV/SOF before June 30, 2017, were evaluated following retreatment to assess the impact of RASs on SVR (HCV RNA less than the lower limit of quantification at ≥10 weeks following treatment completion). The following proportions of RASs were observed: NS5A, 78%; NS3, 49%; and NS5B, 6%.

Table 3. Baseline Demographics and Retreatment Regimens of GT 1a VA Cohort (Backus et al)[4]

Key Demographics and Retreatment Regimens		LDV/SOF Failures (N=439)
Age, mean, years		63
Male, %		98
African American, %		44
FIB-4 >3.25, %		35
History of decompensation, %		19
Most common retreatment regimens, n (%)	EBR/GZR + SOF + RBV	100 (23)
	SOF/VEL + RBV	81 (18)
	SOF/VEL/VOX	58 (13)
Retreatment duration, <12/12/16/24 weeks, %		8/49/14/27

Abbreviations: EBR=elbasvir; FIB-4=Fibrosis-4 index; GZR=grazoprevir; VOX=voxilaprevir.

Results

Table 4. SVR Rates by Retreatment Regimen (Backus et al)[4]

SVRs by Retreatment Regimen, % (n/N)	Resistance Testing		
	SVR With Any Resistance Testing	SVR Without Resistance to Retreatment RASs	SVR With Resistance to Retreatment RASs
Overall	86 (372/432)	86 (197/228)	86 (175/204)
SOF/VEL	85 (11/13)	91 (10/11)	50 (1/2)
SOF/VEL + RBV	74 (58/78)	69 (29/42)	81 (29/36)

No safety data were presented.

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Izumi N, Takehara T, Chayama K, et al. Sofosbuvir-velpatasvir plus ribavirin in Japanese patients with genotype 1 or 2 hepatitis C who failed direct-acting antivirals. *Hepatol Int.* 2018;12(4):356-367. https://www.ncbi.nlm.nih.gov/pubmed/30030720
3. Izumi N, Takehara T, Chayama K, et al. Efficacy and Safety of Sofosbuvir/Velpatasvir Plus Ribavirin for 12 or 24 Weeks in Genotype 1 or 2 HCV-infected Japanese Patients with Prior Treatment Failure to DAA-Based Regimens [Presentation]. Paper presented at: American Association for the Study of Liver Diseases (AASLD); 11-15 November, 2017; Boston, MA.
4. Backus LI, Belperio PS, Shahoumian T, Loomis T, Winters MA, Holodniy M. Real-World Impact of Resistance-Associated Substitutions on Re-Treatment after Ledipasvir/Sofosbuvir Virologic Failure in Hepatitis C Patients (VA) [Poster]. Paper presented at: AASLD; 09-13 November, 2018; San Francisco, CA.

Abbreviations

AE=adverse event
DAA=direct-acting antiviral
GT=genotype
LDV=ledipasvir
RAS=resistance-associated substitution
RBV=ribavirin
SOF=sofosbuvir
SVR=sustained virologic response
SVR12=SVR 12 weeks post-treatment
TE=treatment-experienced
VA=Veterans Affairs
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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