GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Use in Patients With Elevated Body Weight or Body Mass Index

This document is in response to your request for information regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) for the treatment of chronic HCV infection in patients with elevated body weight or BMI.

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]

There is no information in the SOF/VEL product labeling regarding SOF/VEL and elevated body weight or BMI.

Clinical Data on the Impact of BMI on SVR in Patients Treated With SOF/VEL

In a retrospective integrated efficacy analysis of SOF/VEL–treated participants from the phase 3 ASTRAL-1, ASTRAL-2, and ASTRAL-3 studies, the SVR12 rate was 100% (70/70) in participants with obesity (BMI ≥35 kg/m^2) and 98% (945/965) in participants without obesity (BMI <35 kg/m^2).[2]

In a retrospective analysis of the effectiveness of SOF/VEL ± RBV from the EpiTer-2 study, obesity was identified as a significant negative predictor of SVR, with 94.1% of patients with a BMI >30 kg/m^2 and 97% of patients with a BMI ≤30 kg/m^2 achieving SVR (P=0.006). Obesity combined with other negative predictors of SVR (ie, nonresponse to previous therapy, cirrhosis, HCV GT 3, F4, and male sex) was associated with significantly lower SVR rates than those in patients without these factors (P<0.001).[3]

Clinical Data on the Impact of BMI on SVR in Patients Treated With SOF/VEL

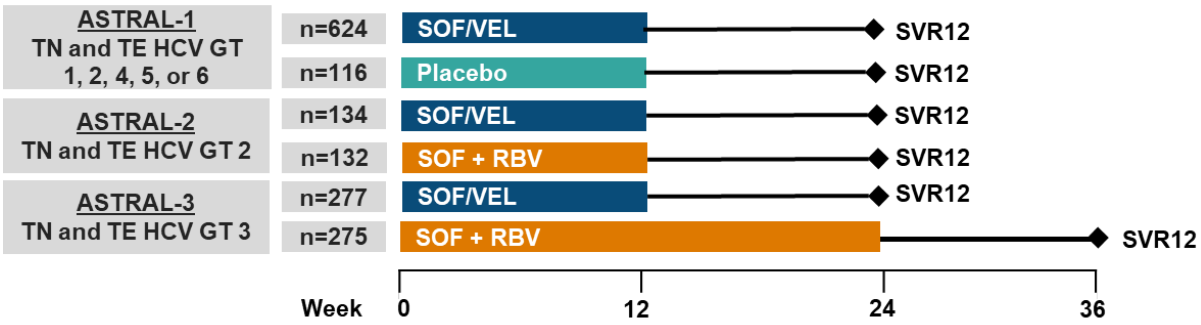
ASTRAL-1 to -3: SOF/VEL in Participants With Negative Predictors of Response[2]

Study design and demographics

ASTRAL-1, ASTRAL-2, and ASTRAL-3 were multicenter, randomized, phase 3, open-label studies that evaluated the efficacy and safety of 12 weeks of SOF/VEL in participants with chronic HCV GT 1 to 6 infection.

A retrospective integrated efficacy analysis was conducted with data from participants treated with SOF/VEL in the ASTRAL-1 to -3 studies to compare outcomes between participants with and those without negative predictors of SVR12. SVR rates were evaluated on the basis of the following factors: cirrhosis (presence vs absence), platelet count, albumin level, FibroScan result, baseline HCV RNA level, prior treatment status (TN vs TE), NS5A RAS (presence vs absence), race (Black vs non-Black), age (<65 years vs ≥65 years), obesity (BMI <35 kg/m^2 vs ≥35 kg/m^2), and abnormal blood glucose control (HbA1c <6.5% vs ≥6.5%). In addition, SVR12 was analyzed based on combinations of these factors.

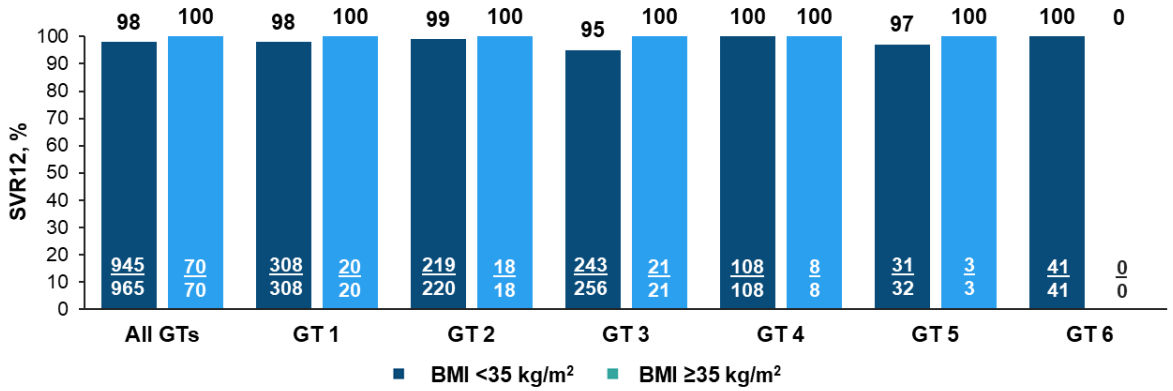
Figure 1. ASTRAL-1 to -3: Study Designs[2]



Results

The SVR12 rate was 100% (70/70) in participants with obesity (BMI ≥35 kg/m^2) and 98% (945/965) in participants without obesity (BMI <35 kg/m^2). SVR12 rates by GT are shown in Figure 2.

Figure 2. ASTRAL-1 to -3: SVR12 in Participants With BMI <35 vs ≥35 kg/m² by HCV GT[2]



EpiTer-2: Efficacy Analysis of SOF/VEL ± RVB in Patients With Negative Predictors of Response[3]

Study design and demographics

A retrospective analysis of the effectiveness of SOF/VEL ± RBV in patients with HCV infection was conducted with data from 2267 patients in the EpiTer-2 database, which was a multicenter real-world study that evaluated the efficacy of direct-acting antivirals in patients with HCV infection between 2015 and 2022. The analysis included an assessment of achievable effectiveness in the most difficult-to-cure group, as well as an evaluation of the patient group with combined factors that reduced treatment efficacy. A total of 92.3% of patients received SOF/VEL for 12 weeks and 0.7% received it for 24 weeks, whereas 5% received SOF/VEL + RBV for 12 weeks and 2.1% received it for 24 weeks. HCV RNA levels were measured at baseline, at the end of treatment, and at ≥12 weeks after the end of treatment.

Table 1. EpiTer-2: Baseline Demographics and Disease Characteristics[3]

Key Demographics and Characteristics		SOF/VEL ± RBV (n=2267)
Age, median (IQR), years		50 (40–62)
Male, n (%)		1306 (57.6)
BMI, median (IQR), kg/m²		26.1 (23.2–29)
HCV GT, 1/1a/1b/2/3/4, n (%)		46 (2)/128 (5.7)/1236 (54.6)/16 (0.7)/ 681 (30.1)/158 (7)
F0/F1/F2/F3/F4/unknown, n (%)		39 (1.7)/760 (33.5)/430 (19)/314 (13.9)/ 660 (29.1)/64 (2.8)
Child-Pugh score of B or C, n (%)		111 (4.9)
MELD score >15		58 (2.6)
Liver disease history	Decompensation	101 (4.5)
	HCC	34 (1.5)
	Liver transplantation	7 (0.3)
ALT, median (IQR), IU/L		67.8 (41–115)
Coinfection, HIV/HBV, n (%)		301 (13.3)/380 (16.8)
HCV RNA, median (IQR), IU/L		1.2^6 (0.3^6–3.1^6)

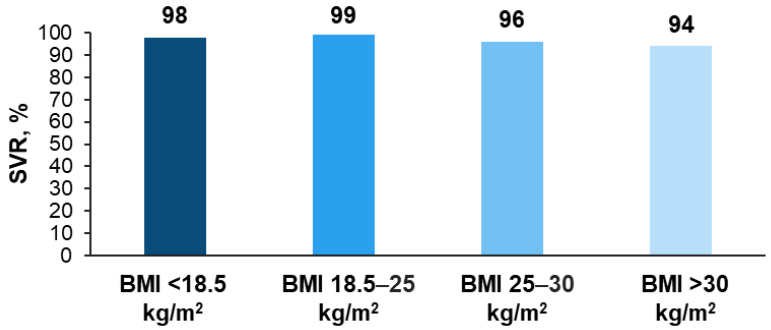
Key Demographics and Characteristics		SOF/VEL ± RBV (n=2267)
Previous treatment, n (%)	Interferon-based	114 (51.4)
	Interferon-free	108 (48.6)
Nonresponders, n (%)	Overall	222 (9.8)
	Null response	45 (20.3)
	Relapse	128 (57.7)
	Unknown type of nonresponse	28 (12.6)
	Discontinuation due to safety	21 (9.5)

Abbreviations: HCC=hepatocellular carcinoma; MELD=Model of End-Stage Liver Disease.

Results

In the per-protocol analysis, 93.1% of patients overall (2040/2192) achieved undetectable HCV RNA at the end of treatment, and 96.4% of patients (2078/2155) achieved SVR. Obesity, defined as BMI >30 kg/m^2 was identified as a significant negative predictor of SVR, with 94.1% of patients (396/421) with a BMI >30 kg/m^2 and 97% of patients (1682/1734) with a BMI ≤30 kg/m^2 achieving SVR (*P*=0.006). SVR rates by BMI subgroup are presented in Figure 3.

Figure 3. EpiTer-2: SVR Rates by BMI Subgroup[4]



Obesity, in combination with other negative predictors of SVR (ie, nonresponse to previous therapy, cirrhosis, HCV GT 3, F4, and male sex), was associated with significantly lower SVR rates compared with patients without negative predictors of SVR (Table 2).

Table 2. EpiTer-2: SVR Rates in Patients With Multiple Negative Predictors of SVR[3]

Parameter	SVR, n/N (%)	*P*-Value	OR (95% CI)
BMI >30 kg/m^2 + GT 3 + F4	51/60 (85)	<0.001	0.09 (0.04–0.23)
BMI ≤30 kg/m^2 + non-GT 3 + non-F4	843/857 (98.4)		
BMI >30 kg/m^2 + GT 3 + F4 + male	34/43 (79.1)	<0.001	0.05 (0.02–0.16)
BMI ≤30 kg/m^2 + non-GT 3 + non-F4 + female	367/372 (98.7)		
BMI >30 kg/m^2 +GT 3 + F4 + male + nonresponder	8/12 (66.7)	<0.001	0.02 (0–0.11)
BMI ≤30 kg/m^2 + non-GT 3 + non-F4 + female + TN	338/342 (98.8)		

Abbreviation: OR=odds ratio.

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Agarwal K, Patel K, Samuel D, et al. Sofosbuvir/Velpatasvir for 12 Weeks Results in High SVR12 Rates in Patients With Negative Predictors of Response to Treatment: an Integrated Analysis of Efficacy fom the ASTRAL-1, ASTRAL-2, and ASTRAL-3 Studies [Poster SAT-195]. Paper

presented at: European Association for the Study of the Liver (EASL); 13-17 April, 2016; Barcelona, Spain.
3. Flisiak R, Zarebska-Michaluk D, Berak H, et al. Treatment of the most difficult-to-cure hepatitis C virus-infected population with sofosbuvir / velpatasvir. *Pol Arch Intern Med.* 2024;134(2). https://www.ncbi.nlm.nih.gov/pubmed/38164647
4. Flisiak R, Zarebska-Michaluk D, Berak H, et al. Treatment of the most difficult-to-cure hepatitis C virus-infected population with sofosbuvir / velpatasvir [Supplementary material]. *Pol Arch Intern Med.* 2024;134(2).

Abbreviations

F=fibrosis
GT=genotype
RAS=resistance-associated substitution
RBV=ribavirin
SOF=sofosbuvir
SVR=sustained virologic response
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

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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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