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Epclusa® (sofosbuvir/velpatasvir) SVR4 and SVR24

This document is in response to your request for information regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) and SVR4 and SVR24 data from phase 3 studies.

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.

Product Labeling[1]

There is no information in the SOF/VEL product labeling regarding SVR4 and SVR24. SVR12, defined as HCV RNA less than the lower level of quantification at 12 weeks after the cessation of treatment, was the primary endpoint in all the clinical trials.

Clinical Data on SOF/VEL Use and SVR4 or SVR24

ASTRAL Studies

Five phase 3 registrational studies evaluated the efficacy and safety of SOF/VEL. ASTRAL-1, -2, and -3 evaluated the efficacy and safety of SOF/VEL in 1035 participants with HCV GT 1 through 6, including treatment-experienced participants (28%) and those with compensated cirrhosis (21%).[2-4]

ASTRAL-4 evaluated SOF/VEL ± RBV in 267 participants with decompensated cirrhosis (classified as Child-Pugh-Turcotte Class B). ASTRAL-5 evaluated 12 weeks of SOF/VEL treatment in 106 treatment-naive or treatment-experienced participants with HCV GT 1 through 4 who also had HIV.[2-4]

POLARIS Studies

Three phase 3 registrational studies evaluated the efficacy and safety of SOF/VEL/VOX compared with SOF/VEL. POLARIS-2 and POLARIS-3 evaluated 12 weeks of SOF/VEL treatment in 549 participants with GT 1 through 6 ± cirrhosis who were DAA-naive. POLARIS-4 evaluated 12 weeks of SOF/VEL treatment in 151 participants with GT 1 through 4 ± cirrhosis who were DAA treatment-experienced with a regimen that did not contain an NS5A inhibitor.[5,6]

Pooled ASTRAL and POLARIS Data

Table 1. ASTRAL and POLARIS: SOF/VEL Use and SVR4, SVR12, and SVR24[3,7-11]

Study	ClinicalTrials.gov Identifier	SVR4, % (95% CI)	SVR12, % (95% CI)	SVR24, % (95% CI)
ASTRAL-1	NCT02201940	99.2 (98.1–99.7)	99 (97.9–99.6)	99 (97.9–99.6)
ASTRAL-2	NCT02220998	99.3 (95.9–100)	99.3 (95.9–100)	99.3 (95.9–100)
ASTRAL-3	NCT02201953	96.8 (93.9–98.5)	95.3 (92.1–97.5)	95.3 (92.1–97.5)
ASTRAL-4	NCT02201901	-	-	-
12 weeks	-	92.2 (84.6–96.8)	83.3 (74–90.4)	83.3 (74–90.4)
12 weeks + RBV	-	95.4 (88.6–98.7)	94.3 (87.1–98.1)	94.3 (87.1–98.1)
24 weeks	-	90 (81.9–95.3)	87.8 (79.2–93.7)	87.8 (79.2–93.7)
ASTRAL-5	NCT02480712	95.3 (89.3–98.5)	95.3 (89.3–98.5)	95.3 (89.3–98.5)
POLARIS-2	NCT02607800	98.9 (97.4–99.6)	98.2 (96.4–99.2)	98 (96.2–99.1)
POLARIS-3	NCT02639338	97.2 (92.2–99.4)	96.3 (90.9–99)	96.3 (90.9–99)
POLARIS-4	NCT02639247	91.4 (85.7–95.3)	90.1 (84.1–94.3)	90.1 (84.1–94.3)

Integrated safety analysis

A retrospective integrated analysis of the ASTRAL-1, -2, -3, and 5, POLARIS-2 and -3, Russian and Swedish (Chulanov et al[12]), and Indian (Sood et al[13]) studies was conducted to evaluate the efficacy and safety of 12 weeks of SOF/VEL for HCV treatment. Patients with decompensated cirrhosis were excluded from this analysis.[14] A summary of safety data is provided in Table 2.

Table 2. ASTRAL-1, -2, -3, and -5 and POLARIS-2 and -3: Integrated Safety Summary[14]

Safety Parameters, n (%)		SOF/VEL (N=1938)
AEs		1352 (70)
Treatment-emergent AEs occurring in ≥5% of patients	Headache	464 (24)
	Fatigue	376 (19)
	Nausea	199 (10)
	Nasopharyngitis	149 (8)
	Insomnia	122 (6)
	Diarrhea	120 (6)
	Asthenia	99 (5)
Serious AEs		40 (2)
Grade 3–4 AEs		56 (3)
Grade 3–4 laboratory abnormalities		139 (7)
Discontinued due to AEs		7 (<1)
Deaths		4 (<1)

Abbreviation: AE=adverse event.

Guidelines on Assessing SVR

Per AASLD guidelines, “Undetectable or unquantifiable HCV RNA 12 weeks or longer after treatment completion is defined as an SVR, which is consistent with cure of hepatitis C infection.”[15]

In their Guidance for Industry, the US Department of Health and Human Services FDA Center for Drug Evaluation and Research states that antiviral treatment efficacy refers to SVR assessed 12 weeks following cessation of treatment.[16]

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Abbreviations

AASLD=American Association for the Study of Liver Diseases
DAA=direct-acting antiviral
GT=genotype
RBV=ribavirin
SOF=sofosbuvir
SVR=sustained virologic response
SVR4/24=sustained virologic response 4/24 weeks after end of treatment
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:

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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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