GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Use in HCV GT 3

This document is in response to your request for information regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) in patients with HCV genotype (GT) 3.

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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 and with decompensated cirrhosis for use in combination with RBV.

Clinical Data on SOF/VEL Use in Patients With HCV GT 3

- A retrospective integrated analysis of SOF/VEL phase 3 studies showed an SVR12 rate of 95% in patients with GT 3. SVR12 rates were similar regardless of GT and cirrhosis status, but not treatment experience, in patients with GT 3. Overall, the most common AEs were headache, fatigue, and nausea.[2]
- A meta-analysis (N=1088) reviewed the safety and efficacy of 12 weeks of SOF/VEL ± RBV in patients with GT 3 compensated cirrhosis and found that SVR12 was similar in patients treated with or without the addition of RBV in both ITT and PP analyses. The addition of RBV was associated with a 4-fold higher risk of treatment-related AEs (RR: 4.2; 95% CI: 1.29–13.68; I^2=0%).[3]
- An integrated analysis of SOF/VEL phase 2 and 3 studies in participants with GT 3 and compensated cirrhosis showed an ITT SVR12 rate of 94%.[4] The most common AEs were fatigue, headache, nausea, and insomnia.[5-8]

Real-World Data on SOF/VEL Use in Patients With HCV GT 3

In 12 real-world cohorts, including patient cohorts with compensated or decompensated cirrhosis, IDU, mental disorders, and/or homelessness or incarceration, SVR12/24 rates ranged from 78% to 100% in patients with GT 3 who were treated with SOF/VEL ± RBV. In studies reporting safety, outcomes were similar to those observed in clinical trials.[9-20]

Clinical Data on SOF/VEL Use in Patients With HCV GT 3

Integrated Post Hoc Analysis of Phase 3 Studies

Study design and demographics

A retrospective integrated analysis of the phase 3 ASTRAL-1, -2, -3,[5,21] and 5[6]; POLARIS-2 and -3[8,22]; Russian and Swedish (Chulanov et al[23]); and Indian (Sood et al[24]) studies was conducted to evaluate the efficacy and safety of 12 weeks of SOF/VEL in patients with HCV GTs 1 to 6. Patients with decompensated cirrhosis were excluded from this analysis.[2]

Table 1. Baseline Demographics and Disease Characteristics of Integrated Analysis (Shafran et al)[2]

Key Demographics and Characteristics	SOF/VEL Patients (N=1938)
Age, mean, years	52
Male, %	61
BMI, mean, kg/m^2	26.6
Race, White/Asian/Black or African American/other, %	77/13/8/2
HCV GT 1/2/3/4/5/6, %	38/16/31/10/2/3
Compensated cirrhosis, %	26
Fibrosis by FibroTest, F0-1/F2/F3/F4, %	32/25/15/28
TE, n (%)	494 (25)
Previous treatment (n=494), interferon/DAA-based/other, %	79/14/7
Comorbid HCV/HIV, %	5

Efficacy[2]

The overall SVR12 rate was 98% (1891/1938), and the GT3 SVR12 rate was 95% (583/611). SVR12 rates by GT and cirrhosis status, prior treatment history, and baseline RASs are presented in Figure 1, Figure 2, and

Figure 3. Patients with GT 3 and baseline RASs had a numerically lower SVR12 rate (92%) than patients with other GTs; thus, baseline RASs had no impact on SVR12 rates in patients with GTs 1, 2, 4, 5, and 6.

Figure 1. SVR12 Rates by GT and Cirrhosis Status (Shafran et al)[2]

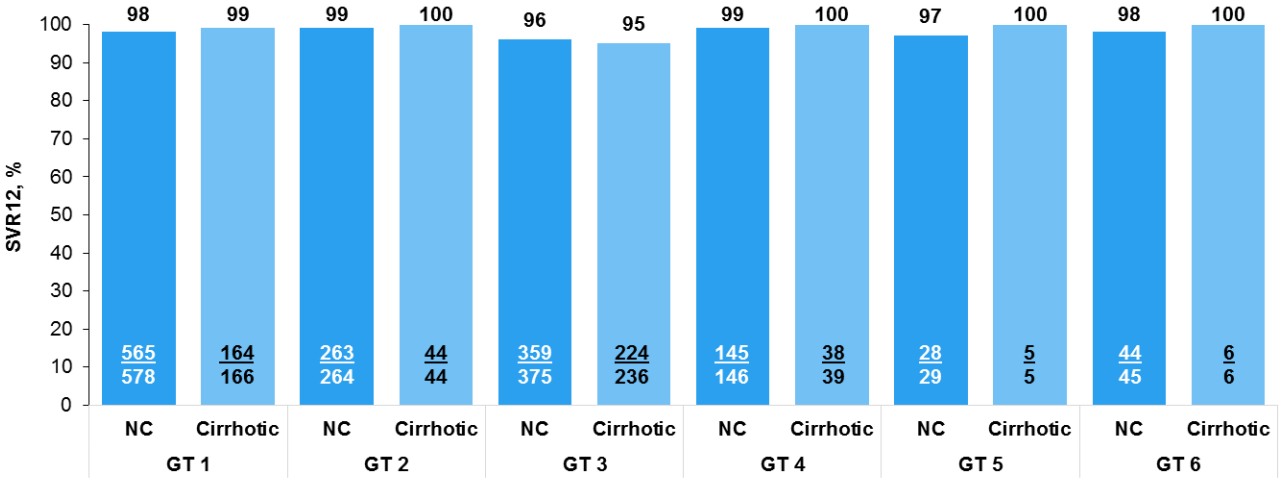


Figure 2. SVR12 Rates by GT and Treatment History (Shafran et al)[2]

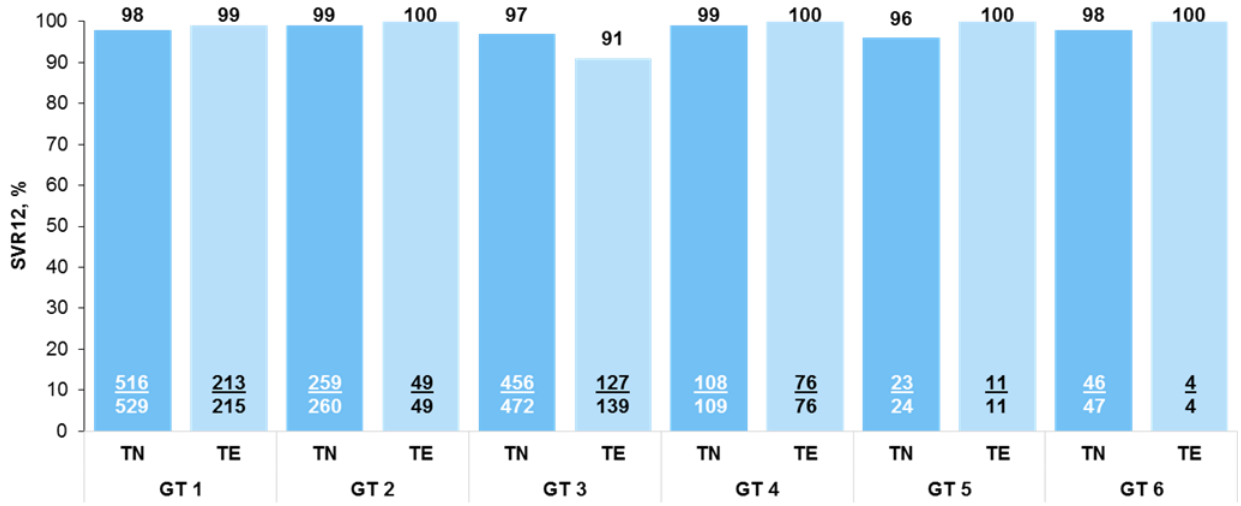
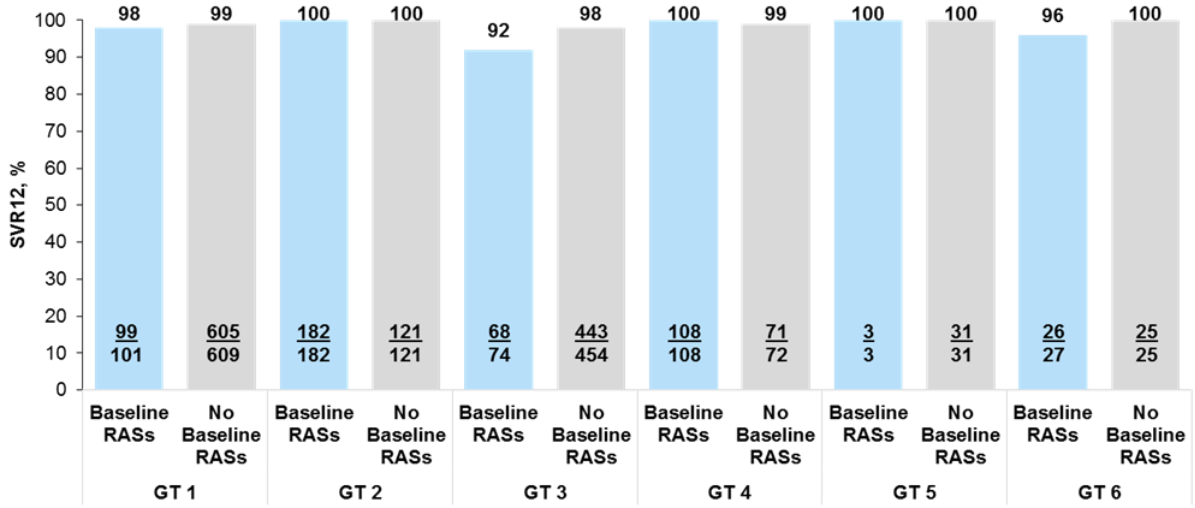


Figure 3. SVR12 Rates by GT and Baseline NS5A RASs (Shafran et al)[2]



Safety[2]

No treatment-related SAEs were reported. The most common treatment-emergent AEs included headache, fatigue, and nausea (Table 2).

Table 2. Safety Parameters (Shafran et al)[2]

Safety Parameters, n (%)		SOF/VEL Patients (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)
SAEs		40 (2)
Grade 3–4 AEs		56 (3)
Grade 3–4 laboratory abnormalities		139 (7)
Discontinuation due to AEs		7 (<1)
Deaths		4 (<1)

Meta-Analysis of SOF/VEL ± RBV in Patients With GT 3 Compensated Cirrhosis[3]

Study design

A meta-analysis was conducted to assess the efficacy and safety of 12 weeks of SOF/VEL ± RBV in patients with GT 3 compensated cirrhosis. Studies up to June 2021 were included in the analysis, which consisted of two RCTs and five cohort studies (N=1088). The primary outcome was SVR12, and the secondary outcome was any treatment-related AE that required transfusion due to anemia or a drop in Hgb ≥2 g/dL.

Efficacy and safety

In patients with GT 3 compensated cirrhosis, SVR12 was similar in patients treated with or without the addition of RBV in both the ITT (RR: 1.03; 95% CI: 0.99–1.07; I^2=0%) and PP (RR: 1.03; 95% CI: 0.99–1.07; I^2=48%) analyses. In patients with GT 3 compensated cirrhosis and baseline RAS, SOF/VEL + RBV was associated with numerically higher SVR12 rates than SOF/VEL without RBV (96% vs 87%, *P*=0.12). In TE patients with GT 3 compensated cirrhosis, the addition of RBV to SOF/VEL did not significantly increase SVR12.

Treatment-related AEs that met the definition for the secondary outcome measure occurred at an overall pooled rate of 7.2%, and treatment-related AEs in those who received SOF/VEL + RBV occurred at a rate 4 times that of patients who received SOF/VEL without RBV (RR: 4.2; 95% CI: 1.29–13.68; I^2=0%).

Integrated Efficacy Analysis

Study design and demographics[4]

An integrated retrospective analysis assessed the efficacy data from 337 patients with HCV GT 3 infection and compensated cirrhosis who were enrolled in one phase 2 and five phase 3 clinical trials, including the pivotal ASTRAL and POLARIS studies, and were treated with SOF/VEL for 12 weeks.

Table 3. Integrated Efficacy Analysis: Baseline Demographics and Disease Characteristics (Roberts et al)[4]

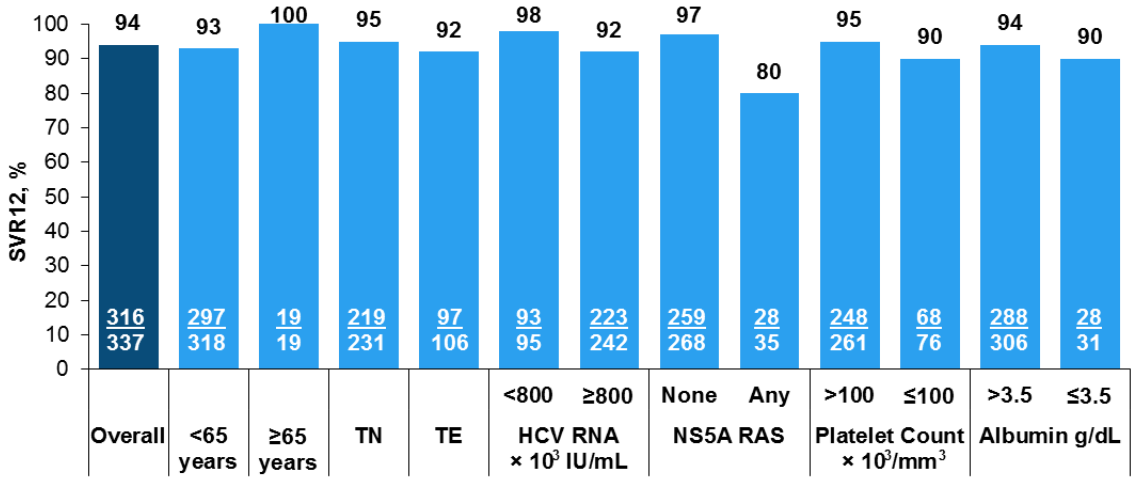
Key Demographics and Characteristics	Total (N=337)
Age, mean (range), years	53 (21–76)
Male, n (%)	247 (73)
White, n (%)	266 (79)
Comorbid HCV/HIV, n (%)	19 (6)
TE, n (%)	106 (31)
NS5A RASs, n (%)	35 (12)
A30K ± L31M, n (%)	25 (8)
Y93H, n (%)	10 (3)
FibroScan score, median (Q1, Q3), kPa	18 (14, 26)
Platelet level, median (Q1, Q3), × 10^3/mm^3	142 (102, 184)
Platelet level ≤100 × 10^3/mm^3, n (%)	76 (23)
Albumin level ≤3.5 g/dL, n (%)	31 (9)

Abbreviation: Q=quartile.

Efficacy[4]

SVR12 rates overall and by various subgroups are presented in Figure 4.

Figure 4. Integrated Efficacy Analysis: SVR12 Rates by Subgroup (ITT; Roberts et al)[4]



Of the 21 patients who did not achieve SVR12, 16 (5%) had virologic failure (14 experienced relapse, and 2 had drug levels consistent with nonadherence). Of the remaining 5 patients (2%) who did not achieve SVR12, 3 were LTFU, and 2 discontinued treatment early due to an AE. Safety was not reported in this pooled retrospective analysis.

Safety

The safety profile of SOF/VEL was assessed in three of the phase 3 trials included in the integrated analysis described above.[4]

In the ASTRAL-3 study (N=277), which evaluated SOF/VEL in TN and TE patients with GT 3, the most common AEs (>10%) included headache (32%), fatigue (26%), nausea (17%), and insomnia (11%). SAEs were reported in 2% of GT 3 patients who received SOF/VEL. There were no discontinuations due to AEs.[2]

In the ASTRAL-5 study (N=106), which evaluated SOF/VEL in TN and TE patients co-infected with HIV, the most common AEs (>5 patients) included fatigue (25%), headache (13%), upper respiratory tract infection (8%), arthralgia (8%), diarrhea (8%), insomnia (7%), and nausea (7%). Two patients experienced SAEs, and 2 patients discontinued treatment due to an AE.[3]

In the POLARIS-3 study (N=109), which evaluated SOF/VEL in GT 3 DAA-naive cirrhotic patients, the most common AEs (>5%) included headache (29%), fatigue (28%), nausea (9%), upper abdominal pain (6%), back pain (6%), and myalgia (6%). Overall, 3% of patients experienced SAEs, and 1 patient discontinued treatment due to an AE.[7,8]

Real-World Data on SOF/VEL Use in Patients With HCV GT 3

SOF/VEL vs SOF/DCV and the Effect of Age[9]

The efficacies of SOF/VEL and SOF/DCV in patients with HCV GT3 were compared using data from the National Health System (n=14,475) for SOF/VEL-treated patients in England and data from HepFreePak (n=2214) for SOF/DCV-treated patients in Pakistan. The overall

SVR12 rate with SOF/VEL was 90.5% (without cirrhosis, 91.6% [11,116/12,135]; with cirrhosis, 85.18% [1920/2254]), compared with 87.1% with SOF/DCV (without cirrhosis, 87.8% [1575/1793]; with cirrhosis, 85.3% [359/421]). In patients aged <40 years, the SVR12 rates in SOF/VEL- and SOF/DCV-treated patients were 91.33% and 89.49%, respectively. In patients aged >60 years, the SVR12 rate remained high in SOF/VEL-treated patients (89.35%) and declined in SOF/DVC-treated patients (82.78%). In patients aged ≥70 years, the SVR12 rate in SOF/VEL-treated patients dropped to 86.92%; data were not available for SOF/DCV-treated patients in this age group.

Multinational Cohort Study[10]

Study design and demographics

In an integrated analysis, data were collected from 12 clinical practice sites across Canada, France, Germany, Greece, Italy, Spain, and the US in the largest available heterogeneous patient population to assess the real-world effectiveness of SOF/VEL for 12 weeks. Patients with HCV GTs 1 through 6 and no cirrhosis or compensated cirrhosis who were TE or TN were included in the analysis (N=5552). Effectiveness was assessed in the overall population and in an effectiveness population (n=5196), which excluded patients who did not achieve SVR12/24 for non-virologic (n=332) or unknown reasons (n=24).

Table 4. Baseline Demographics and Disease Characteristics of the Overall and Effectiveness Populations (Mangia et al)[10]

Key Demographics and Characteristics	Overall Population (N=5552)	Effectiveness Population (n=5196)
Age, mean (SE), years	56 (2.6)	56 (2.8)
Male, n (%)	3225 (58.1)	2902 (55.9)
Caucasian or White, n (%)	3683 (66.3)	3523 (67.8)
TN, n (%)	4815 (86.7)	4521 (87)
TE (DAA naive), n (%)	698 (12.6)	642 (12.4)
Compensated cirrhosis, n (%)	1147 (21)	1078 (21)
HCV GT, 1/2/3/4/5–6/mixed or unknown, %	31/30/33/5/1/1	31/30/32/5/1/1
Comorbid HCV/HIV, n (%)	204 (3.7)	186 (3.6)
Former or ongoing IDU, n (%)	743 (13.4)	689 (13.3)

Effectiveness

SVR12/24 rates were 98.9% (5141/5196) in the effectiveness population and 92.6% (5141/5552) in the overall population. In patients with F4 (compensated) cirrhosis in the effectiveness population, the SVR12/24 rate was 97.9% (1055/1078). SVR12/24 rates were 98% (1649/1677) in the overall GT 3 subgroup and 97% (314/324) among patients in the GT 3 subgroup with compensated cirrhosis.

Per logistic regression analysis in a pooled subset of patients in the effectiveness population, compensated cirrhosis was associated with an increased risk of not achieving SVR12/24 due to virological reasons (odds ratio, 2.53; 95% CI: 1.38–4.55; *P*=0.002). Safety results during treatment were not presented in this study.

British Columbia Hepatitis Testers Cohort: Patients With and Without Cirrhosis[11]

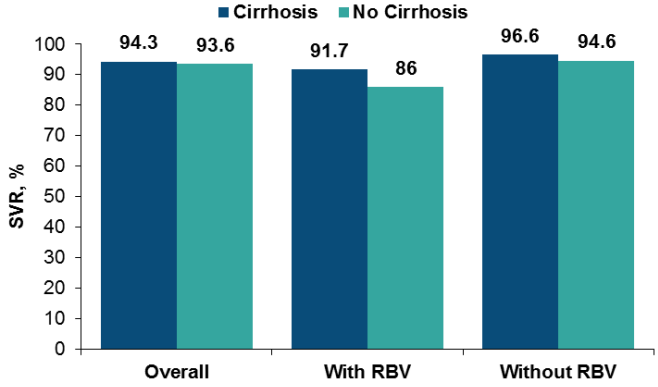
Study design and demographics

The effectiveness of SOF/VEL ± RBV was assessed among patients in the British Columbia Hepatitis Testers Cohort who initiated treatment prior to December 31, 2018 (N=2821). The study included patients with GTs 1 through 6. Among patients with GT 3 (n=1072), the median age was 55 years, 62% were male, 90% were White, 87% were treated with SOF/VEL, 13% were TE, 5% had cirrhosis (3% were decompensated), and 11% were co-infected with HIV. SVR was defined as negative HCV RNA ≥10 weeks after the end of treatment.

Effectiveness

The overall SVR rate in GT 3 patients with cirrhosis was 94.6% (2670/2821); in patients without cirrhosis, it was 93.7% (1004/1072). SVR rates in patients with GT 3 with and without cirrhosis and by SOF/VEL ± RBV use are presented in Figure 5. Per logistic regression analysis, a history of injecting drugs and treatment with RBV were factors associated with not achieving SVR in GT 3 patients. Safety outcomes were not reported.

Figure 5. SVR Rates of the GT 3 Population Treated With SOF/VEL ± RBV (Wilton et al)[11]



British Columbia Hepatitis Testers Cohort: GTs 1, 2, and 3[12]

Study design and demographics

The British Columbia Hepatitis Testers Cohort was used to evaluate the effectiveness of SOF/VEL ± RBV in patients with GTs 1 to 3. The cohort included 1801 patients with HCV infection. Patients who had received ≥1 prescription for SOF/VEL ± RBV through June 2018 were included. Patients were required to have ≥12 weeks of follow-up to assess treatment completion and ≥12 weeks of follow-up for SVR assessment. To allow for variations in clinical practice, SVR was defined as undetectable HCV RNA at ≥10 weeks after the end of treatment, instead of 12 weeks after the end of treatment.

Table 5. Baseline Demographics and Disease Characteristics (Janjua et al)[12]

Key Demographics and Characteristics	SOF/VEL ± RBV (N=1801)
Age, median, years	58
Male, n (%)	1148 (64)

Key Demographics and Characteristics	SOF/VEL ± RBV (N=1801)
TE, n (%)	236 (13)
GT 1/2/3, %	35/19/40
Cirrhosis, n (%)	90 (5)
Diabetes, n (%)	125 (7)
Comorbid HIV, n (%)	172 (10)
Recent IDU, n (%)	322 (18)
Past IDU, n (%)	309 (17)

Efficacy

SVR rates were 93% (584/628), 96% (338/351), and 92% (670/725) in the GT 1, 2, and 3 subgroups, respectively. A multivariate analysis identified IDU as associated with an overall lower SVR rate; 46% of injection drug users who did not achieve SVR were LTFU. Use of RBV in combination with SOF/VEL was associated with a lower rate of SVR. Safety was not reported.

Incarcerated and Community Cohort–Singapore[13]

Study design and demographics

A retrospective, observational study evaluated the safety and efficacy of SOF/VEL ± RBV for 12 weeks in a cohort of community and incarcerated patients with HCV who were treated in a Singapore hospital between January 2018 and December 2019. The primary endpoint was SVR12 in GT 3 patients.

Table 6. Baseline Demographics and Characteristics (Wong et al)[13]

Key Demographics and Characteristics	SOF/VEL ± RBV	
	Incarcerated (n=662)	Community (n=117)
Age, median (IQR),[a] years	51 (43–58)	55 (51–60)
Male, n (%)	607 (91.7)	102 (87.2)
GT 3, n (%)	451 (68.1)	79 (67.5)
TE, n (%)	27 (4.1)	7 (6)
Fibrosis stages, F1/F2/F3/F4[a]/not available, %	33.3/11.2/12.7/25.8/17.1	24.7/11.1/12/42.7/9.4
HCC, n (%)	10 (1.5)	4 (3.4)
Comorbid HCV/HIV, n (%)	5 (0.8)	2 (1.7)
Comorbid HCV/HBV, n (%)	9 (1.4)	1 (0.9)

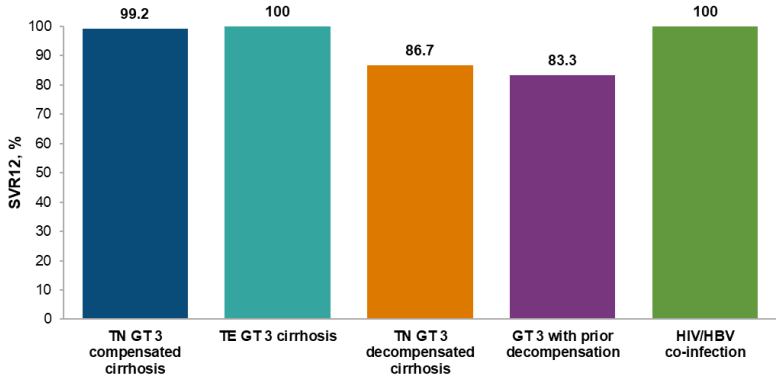
[a]*P*≤0.005 for comparison between groups.

Efficacy and safety

A total of 530 patients with GT 3 were included in the ITT analysis (all treated patients with SVR12 who were included in final data analysis, including patients who were LTFU or discontinued treatment early), and 527 patients with GT 3 were included in the PP analysis (all patients in the ITT population who completed treatment and had available SVR12 data). The overall SVR12 rates in the ITT and PP cohorts were 98.3% and 99.5%, respectively. For patients with and without GT 3, the PP SVR12 rates were 99.2% and 100%, respectively. A total of 4 patients with GT 3 (2 patients with decompensated cirrhosis and 2 patients without cirrhosis) had virological failures. Figure 6 summarizes SVR12 rates by

subgroup. For the subgroup analyses, SVR12 results were similar to those in the PP analyses.

Figure 6. SVR12 Rates by Subgroup (ITT Analysis; Wong et al)[13]



Among patients with GT 3, no deaths occurred during treatment. One patient who still achieved SVR12 discontinued treatment early (at 8 weeks) due to SOF/VEL-induced myositis, which resolved after treatment discontinuation.

Multinational Cohort Study[14]

Study design and demographics

The effectiveness and safety of SOF/VEL were evaluated in patients with GT 3 HCV and compensated cirrhosis across 17 real-world cohorts from 9 countries (Australia, Canada, France, Germany, Israel, Italy, Spain, the UK, and the US). This study included patients who were initiated on SOF/VEL (n=496) and SOF/VEL + RBV (n=236) by their treating physician in clinical practice.

Table 7. Baseline Demographics of PP Population (Fagiuoli et al)[14]

Key Demographics	SOF/VEL (n=496)	SOF/VEL + RBV (n=236)
Age, mean, years	55	53
Male, n (%)	334 (72)	147 (75)
White, n (%)	268 (67)	127 (76)
TE, n (%)	53 (11)	49 (21)

Effectiveness

The SVR12 rate was 93% in the SOF/VEL group and 97% in the SOF/VEL + RBV group (*P*=0.08). Among patients who received SOF/VEL, 27 (5%) experienced virologic failure, and 2 of these failures occurred while the patients were receiving treatment. Of the patients who received SOF/VEL + RBV, 8 (3%) experienced virologic failure.

Safety

Safety was assessed in the mITT population (n=940). Between treatment initiation and the SVR12 time point, 9 deaths were reported, and none was treatment related. At or after the SVR12 time point, 4 patients were diagnosed with HCC; of these, 1 achieved SVR12. One patient decompensated at Week 8 but achieved SVR12.

Greek Cohort[15]

Study design and demographics

The effectiveness of SOF/VEL ± RBV in patients with GT 3 HCV who received treatment between 2014 and February 2018 at 20 centers in Greece was evaluated. Patients with fibrosis, decompensated cirrhosis, history of liver transplantation, or severe extrahepatic manifestations were included.

Table 8. Baseline Demographics and Disease Characteristics of Patients With GT 3 (Manolakopoulos et al)[15]

Key Demographics and Characteristics		SOF/VEL ± RBV (n=503)
Age, mean, years		47
Male, %		81
TE, %		23
Diabetes, %		4
Cirrhosis, %		33
Decompensated, %		6
HCV RNA level, mean, IU/mL		4.3×10^6
DAA treatment type, %	SOF/VEL	52
	SOF/VEL + RBV	48

Efficacy and safety

SVR12 status was available for 173 patients who had 3 months of posttreatment follow-up. Of these patients, 94% achieved SVR12. Of the 11 patients who failed treatment, 6 had cirrhosis, and 4 were TE. Safety outcomes were not reported.

Kaiser Permanente Northern California Study[16]

Study design and demographics

A study evaluated the efficacy of SOF/VEL ± RBV for 12 weeks in patients with HCV GT 2 or 3, including those with cirrhosis.

Table 9. Baseline Demographics and Disease Characteristics (Lai et al)[16]

Key Demographics and Characteristics	SOF/VEL		SOF/VEL + RBV	
	GT 2 (n=198)	GT 3 (n=159)	GT 2 (n=16)	GT 3 (n=120)
Age, median, years	62	58	60	59
Male, %	64	59	75	61
TE, %	10	12	69	40
Cirrhotic, %	15	8	63	70
Comorbid HIV, %	1.5	3	–	–

Efficacy and safety

The SVR12 rates were 99% and 94% among patients with GT 2 who were treated with SOF/VEL and SOF/VEL + RBV, respectively, and 99% and 95% among patients with GT 3.

Virologic relapse accounted for all patients who did not achieve SVR12. Safety data from this cohort have not been published.

GECCO Study[17]

Study design and demographics

GECCO is an ongoing, prospective, multicenter German study evaluating the safety and efficacy of SOF/VEL (n=239) and SOF/VEL + RBV (n=54) in participants with GT 3.

Table 10. GECCO: Baseline Demographics and Disease Characteristics[17]

Key Demographics and Characteristics		SOF/VEL ± RBV (N=293)
Age, median, years		48
Male, n (%)		205 (70)
Cirrhotic, compensated/decompensated, %		88/12
TE, n (%)		64 (22)
Comorbid HIV, n (%)		28 (9)
Laboratory values	Hgb, mean, g/dL	14.4
	Platelets, mean, cells/nL	197
	ALT, mean, ×-fold upper limit of normal	1.7
	Bilirubin, mean, mg/dL	0.5
	Albumin, mean, g/dL	41.7
	INR, mean	1.03

Effectiveness and safety

The SVR12 rate was 99.5% (213/214) in the PP population of participants with GT 3 and 98.2% (55/56) among those with compensated cirrhosis. One participant did not achieve SVR12 and experienced virologic relapse.

There were 2 deaths in the mITT population: 1 cardiac arrest at Week 4 of treatment and 1 fatal gastrointestinal bleed at Week 8 of treatment. Both deaths were reported as unrelated to treatment by the treating physician. There were no discontinuations due to AEs.

Italian HCV GT 3 Cohort[18]

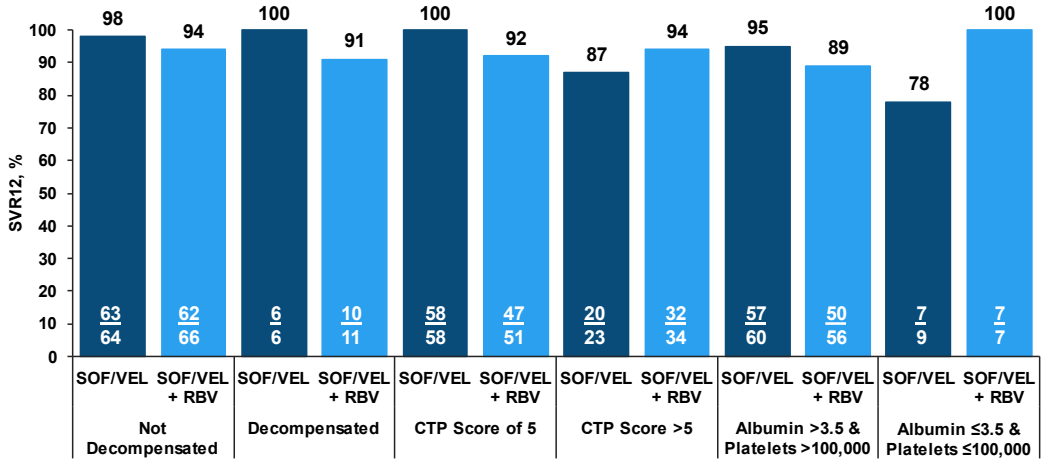
Study design and demographics

Treatment outcomes of 276 patients with GT 3 HCV infection and compensated or decompensated cirrhosis who were prescribed SOF/VEL ± RBV in 33 centers in Italy were assessed. More patients received 12 weeks of SOF/VEL treatment without RBV (59%) than with RBV (41%), and the mean age was 54 and 53 years in the groups that received SOF/VEL without and with RBV, respectively.

Efficacy

SVR12 rates by treatment group, cirrhosis status, CTP score, and laboratory values are presented in Figure 7.

Figure 7. SVR12 Rates in Patients With GT 3 (Pasulo et al)[18]



Note: Among those with a CTP score of 5, SVR rates were significantly higher for those treated without RBV than for those treated with RBV (*P*=0.045). All other differences were not statistically significant.

Xinjiang, China Study[19]

Study design and demographics

The effectiveness of 12 to 24 weeks of SOF/VEL ± RBV in patients with HCV GT 3 was evaluated in a real-world setting in Xinjiang, China. Patients who received treatment between June 2018 and November 2023 were included in the analysis (N=258). Patients with a history of DAA treatment failure and those with decompensated cirrhosis received either SOF/VEL monotherapy for 24 weeks or SOF/VEL + RBV for 12 weeks; all other patients received SOF/VEL for 12 weeks. The primary endpoint was SVR12.

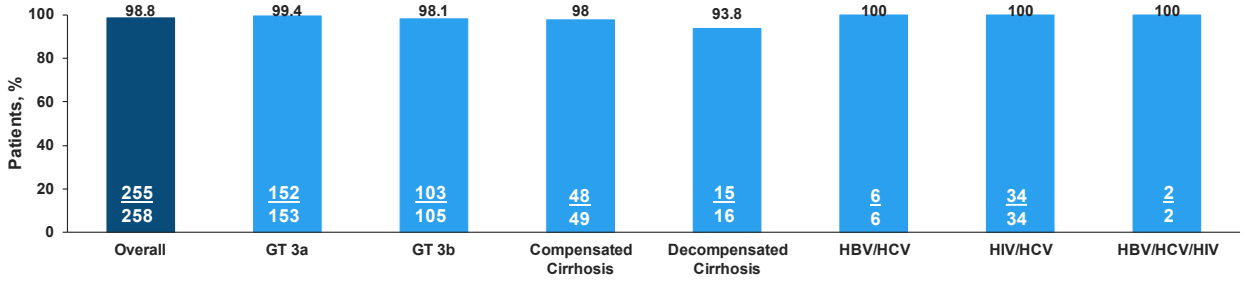
Table 11. Baseline Demographics and Disease Characteristics (Wubuliaishan et al)[19]

Key Demographics and Characteristics		SOF/VEL ± RBV (N=258)
Age, mean ± SD, years		44.02±10.5
Male, n (%)		176 (68.22)
GT subtype, n (%)	GT 3a	153 (59.3)
	GT 3b	105 (40.7)
Cirrhosis, n (%)		65 (25.2)
Compensated, n (%)		49 (18.99)
Decompensated, n (%)		16 (6.2)
TN, n (%)		252 (97.67)
Comorbid HBV/HCV, n (%)		6 (2.32)
Comorbid HIV/HCV, n (%)		34 (13.18)
Comorbid HBV/HCV/HIV, n (%)		2 (0.78)

Results

The overall SVR12 rate and SVR12 rates by HCV GT subtype, cirrhosis status, and comorbid conditions are presented in Figure 8. Three patients experienced virologic relapse due to reported poor adherence to treatment.

Figure 8. SVR12 Rates Overall and by Subgroups (Wubuliaishan et al)[19]



No patients discontinued SOF/VEL ± RBV due to AEs. No other safety data were reported.

Chinese Cohort[20]

Study design and demographics

The effectiveness of SOF/VEL ± RBV for 12 weeks was evaluated in a real-world cohort of 154 Chinese patients with HCV GT 3. Patients without decompensated cirrhosis or HIV who received this treatment at two hospitals in China between June 2018 and May 2020 were included in this analysis.

Table 12. Baseline Demographics and Disease Characteristics (Yue et al)[20]

Key Demographics and Characteristics		Overall (N=154)	GT 3a (n=52)	GT 3b (n=102)
Age, mean (SD), years		46.13 (9.63)	43.87 (9.2)	47.28 (9.68)
Male, n (%)		101 (65.6)	36 (69.2)	65 (63.7)
Treatment history, n (%)	TN	150 (97.4)	52 (100)	98 (96.1)
	TE (DAA naive)	4 (2.6)	0	4 (3.9)
	Cirrhosis, yes/no	59 (38.3)/95 (61.7)	13 (25)/39 (75)	46 (45.1)/56 (54.9)
Treatment, n (%)	SOF/VEL	69 (44.8)	30 (57.7)	39 (38.2)
	SOF/VEL + RBV	85 (55.2)	22 (42.3)	63 (61.8)

Effectiveness

Overall, 93.2% of patients with cirrhosis achieved SVR12, including 100% of patients with GT 3a and 91.3% of patients with GT 3b (Figure 9); 93.2% of patients with cirrhosis who were treated with SOF/VEL + RBV achieved SVR12 (Figure 10).

Figure 9. SVR12 Rates in Patients Overall and According to Cirrhosis Status and GT 3 Subtype (Effectiveness Population; Yue et al)[20]

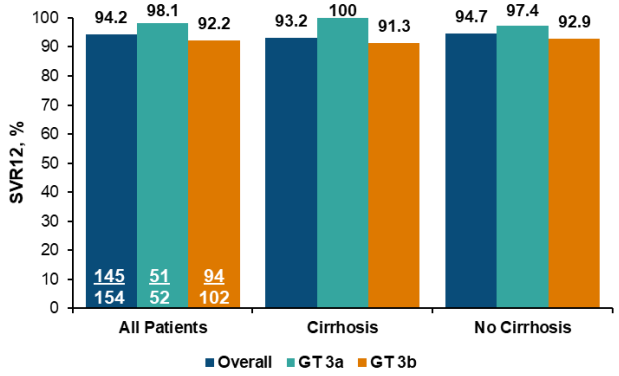
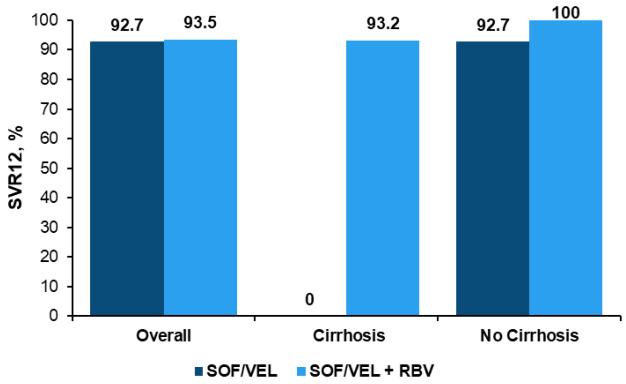


Figure 10. SVR12 Rates in Patients According to Cirrhosis Status and Treatment Regimen (Effectiveness Population; Yue et al)[20]



Safety

No severe AEs or clinically relevant laboratory abnormalities occurred. Anemia (5.8%) and fatigue (5.2%) were the most frequently occurring AEs. Other AEs included headache and poor appetite (4.5% each); abdominal discomfort (3.2%); myalgia and rash (1.9% each); and insomnia, nausea, and photosensitivity (1.3% each).

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Shafran S, Feld J, Jacobson I, et al. Sofosbuvir/Velpatasvir, a Pangenotypic Single-Tablet Regimen: Integrated Analysis of Phase 3 Clinical Trials in Genotypes 1-6 [Poster Number 23]. Paper presented at: International Viral Hepatitis Elimination Meeting (IVHEM); 07-08 December, 2018; Amsterdam, the Netherlands.
3. Loo JH, Xu WX, Tay WX, et al. Is routine Ribavirin mandatory for Genotype 3 Hepatitis C compensated cirrhosis patients receiving Sofosbuvir/Velpatasvir? A meta-analysis. Paper presented at: European Association for the Study of the Liver (EASL); 22-26 June 2022, 2022; London.
4. Roberts SK, Buti M, Foster GR, et al. Sofosbuvir/Velpatasvir for Patients With Chronic Genotype 3 HCV Infection With Compensated Cirrhosis: an Integrated Analysis of Phase 2 and Phase 3 Clinical Trials [Poster 628]. Paper presented at: AASLD: The Liver Meeting® 2018; 09-13 November, 2018; San Francisco, CA.
5. Foster GR, Afdhal N, Roberts SK, et al. Sofosbuvir and Velpatasvir for HCV Genotype 2 and 3 Infection. *The New England Journal of Medicine.* 2015;373(27):2608-2617.
6. Wyles D, Brau N, Kottilil S, et al. Sofosbuvir and Velpatasvir for the Treatment of Hepatitis C Virus in Patients Coinfected with Human Immunodeficiency Virus Type 1: An Open-Label, Phase 3 Study. *Clin Infect Dis.* 2017;65(1):6-12.
7. Foster GR, Thompson A, Ruane PJ, et al. A Randomized, Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir for 8 Weeks and Sofosbuvir/Velpatasvir for 12 Weeks for Patients with Genotype 3 HCV Infection and Cirrhosis: The POLARIS-3 Study [Presentation]. Paper presented at: American Association for the Study of Liver Diseases (AASLD); 11-15 November, 2016; Boston, MA.
8. Jacobson IM, Lawitz E, Gane EJ, et al. Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials. *Gastroenterology.* 2017;153(1):113-122.
9. Hamid SS, Qureshi HI, Chaudhry AR, et al. THU-232 Treatment of genotype 3 chronic hepatitis C infection: age reduces the efficacy of treatment with sofosbuvir and daclatasvir but the reduction

is less marked with sofosbuvir and velpatasvir. [Poster Presentation #THU-232]. *Journal of Hepatology.* 2025;82(S1):S70–S858.
10. Mangia A, Milligan S, Khalili M, et al. Global Real-World Evidence of Sofosbuvir/Velpatasvir as Simple, Effective HCV Treatment: Analysis of 5552 Patients from 12 Cohorts. *Liver Int.* 2020.
11. Wilton J, Wong S, Yu A, et al. Real-World Effectiveness of Sofosbuvir/Velpatasvir for Treatment of Chronic Hepatitis C in British Columbia, Canada: A Population-Based Cohort Study. *Open Forum Infect Dis.* 2020;7(3):ofaa055.
12. Janjua NZ, Wong S, Yu A, et al. Effectiveness of Sofosbuvir / Velpatasvir in Treating Hepatitis C Virus Infection in Real-World Setting [Poster 608]. Paper presented at: AASLD; 09-13 November, 2018; San Francisco, CA.
13. Wong YJ, Thurairajah PH, Kumar R, et al. Efficacy and safety of sofosbuvir/velpatasvir in a real-world chronic hepatitis C genotype 3 cohort. *J Gastroenterol Hepatol.* 2020.
14. Fagiuoli S, Agarwal K, Mangia A, et al. Effectiveness of Sofosbuvir/Velpatasvir for 12 Weeks in HCV Genotype 3 Patients with Compensated Cirrhosis in Clinical Practice Cohorts from Around the World [Abstract]. Paper presented at: American Association for the Study of Liver Disease (AASLD); 09-13 November, 2018; San Francisco, CA.
15. Manolakopoulos S, Sevastianos V, Triantafyllou K, et al. Sofosbuvir/Velpatasvir (SOF/VEL) ± Ribavirin (RBV) in the Treatment of Genotype 3 (GT3) Chronic Hepatitis C (CHC) Patients. Heraclis: A Hellenic Multicenter Real-Life Cohort Clinical Study [Poster 636]. Paper presented at: AASLD; 09-13 November, 2018; San Francisco, CA.
16. Lai JB, Witt MA, Ready J, Witt DJ. Real-World Effectiveness of Sofosbuvir/Velpatasvir (SOF/VEL)-Based Therapy for Hepatitis C Virus Genotype 2 and 3: Analysis in a Large North American Integrated Health Care System [Poster 1530]. Paper presented at: The Liver Meeting® 2017 - The 68th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD); 20-24 October, 2017; Washington, D. C.
17. von Felden J, Vermehren J, Ingiliz P, et al. High efficacy of sofosbuvir/velpatasvir and impact of baseline resistance-associated substitutions in hepatitis C genotype 3 infection. *Aliment Pharmacol Ther.* 2018.
18. Pasulo L. Treatment of Genotype 3 Cirrhotic Patients with 12 Weeks Sofosbuvir/Velpatasvir With or Without Ribavirin: Real Life Experience from Italy [Poster 592]. Paper presented at: AASLD; 09-13 November, 2018; San Francisco, CA.
19. Wubuliaishan M, Sun W, Yu H, et al. Sofosbuvir/Velpatasvir Effectiveness in Treating Chronic Hepatitis C Genotype 3: A Real-World Study in Xinjiang, China.[poster #1450]. Paper presented at: AASLD: The Liver Meetings; November 15-19, 2024; San Diego, California.
20. Yue W, Liu L, Xiao A, et al. Effectiveness and safety of 12 weeks of sofosbuvir/velpatasvir with or without ribavirin in genotype 3 hepatitis C virus-infected patients: a realworld study of China [Poster]. Paper presented at: American Association for the Study of Liver Diseases (AASLD) The Liver Meeting Virtual; 12-15 November, 2021.
21. Feld JJ, Jacobson IM, Hezode C, et al. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. *N Engl J Med.* 2015;373(27):2599-2607.
22. Bourliere M, Gordon SC, Flamm SL, et al. Sofosbuvir, Velpatasvir, and Voxilaprevir for Previously Treated HCV Infection. *N Engl J Med.* 2017;376(22):2134-2146.
23. Chulanov V, Weiland O, Zhdanov K, et al. Sofosbuvir/Velpatasvir Is Safe and Effective in a Phase 3 Study of Genotype 1–3 HCV-infected Russian and Swedish Patients [Presentation]. Paper presented at: 27th Annual Conference of the Asian Pacific Association for The Study of the Liver (APASL); 14-18 March, 2018; New Delhi, India.
24. Sood A, Duseja A, Kabrawala M, et al. The Sofosbuvir/Velpatasvir Single Tablet Regimen Administered for 12 Weeks with Minimal Monitoring in India [Presentation] Paper presented at: Asian Pacific Association for The Study of the Liver (APASL); 14-18 March, 2018; New Delhi, India.

Abbreviations

AE=adverse event
CTP=Child-Turcotte-Pugh
DAA=direct-acting antiviral
DCV=daclatasvir
GT=genotype
HCC=hepatocellular carcinoma
IDU=intravenous drug use
LTFU=lost to follow-up
mITT=modified intent to treat
NC=non-cirrhotic
PP=per protocol
RAS=resistance-associated substitution
RBV=ribavirin
RR=relative risk
SAE=serious adverse event
SOF=sofosbuvir
SVR=sustained virologic response
SVR12/24=SVR 12/24 weeks after end of treatment
TE=treatment-experienced
TN=treatment-naïve
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.

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