Real-World Experiences With a Direct-Acting Antiviral Agent for Patients With Hepatitis C Virus Infection

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ABSTRACT

Context: Traditional hepatitis C virus treatment was limited by low cure rates, side effects, and stringent monitoring requirements. Sofosbuvir, a direct-acting antiviral agent with a cure rate of 96%, was introduced in 2013. However, trials frequently excluded patients with advanced liver disease and prior treatment experience. This study aims to elucidate the real-world cure rates and sofosbuvir safety profile.

Methods: A retrospective cohort study was conducted at Kaiser Permanente Southern California involving patients with hepatitis C virus who received sofosbuvir treatment. Patients age 18 years and older were included, and pregnant patients were excluded. The primary end point was sustained virologic response at 12 weeks posttreatment. Secondary end points were safety and medication adherence. Multiple logistic regression analysis was used to compare patients with genotypes 1 and 2 infections.

Results: Of the 213 study patients, 42.3% had cirrhosis, and 38% were treatment-experienced. Most patients (69.5%) received dual therapy (sofosbuvir + ribavirin), whereas the remainder (30.5%) received triple therapy (sofosbuvir + ribavirin + interferon). The overall rate of sustained virologic response at 12 weeks posttreatment rate was 72.9% for genotype 1 infection, 64.7% in the treatment-experienced subgroup, and 66.7% in the cirrhosis subgroup. Rates of sustained virologic response at 12 weeks posttreatment for genotypes 2 and 3 were 90.8% and 55%, respectively. Most patients experienced anemia and fatigue. Women and patients with a lower baseline viral load were statistically more likely to be cured.

Conclusion: Real-world cure rates were similar to rates seen in clinical trials for genotype 2 infection and lower for genotype 1 infection. Patients with genotype 1 and 3 infection did better with triple therapy compared with dual therapy. Patients tolerated therapy well with side effects, serious adverse events, and discontinuation rates similar to clinical trials. Women and patients with lower baseline hepatitis C viral load were more likely to achieve sustained virological response at 12 weeks posttreatment.

INTRODUCTION

Nearly 3.5 million Americans have the hepatitis C virus (HCV), and about 50% are unaware of their infection status.[1] As many as 25% of patients with chronic HCV infection progress to cirrhosis within 30 years, and 6% eventually develop liver cancer; HCV is the leading cause of liver transplant and liver cancer in the US.[2] The primary goal of HCV treatment is to achieve virologic cure defined as sustained virologic response (SVR), an undetectable HCV ribonucleic acid (RNA) in the blood, at 12 weeks posttreatment (SVR12).[1] SVR12 decreases all-cause mortality and liver-related complications.[1] Before 2011, HCV treatment options were limited to interferon and ribavirin, which were associated with low SVR rates, many serious adverse effects, and stringent monitoring requirements.[1,3] In 2011, the addition of protease inhibitor direct-acting antiviral agents boceprevir and telaprevir increased SVR rates to 66% and 79%, respectively, with triple-therapy regimens.[3] However, treatment potential of these agents was limited by restricted use for patients with HCV genotype 1 infection, low SVR rates in some populations (ie, 42% in patients with cirrhosis and 29% to 64% in treatment-experienced patients), high rates of resistance, drug-drug interactions, and the required concurrent use of interferon and ribavirin.[3-6]

Newer direct-acting antiviral agents (DAA) simeprevir and sofosbuvir were introduced in 2013 with associated SVR rates as high as 85% and 96%, respectively.[7,8] However, simeprevir also is a protease inhibitor with limitations similar to those encountered with boceprevir and telaprevir use.[7] Conversely, sofosbuvir is an oral nucleotide NS5B polymerase inhibitor approved for the treatment of genotypes 1 to 6 with reported 90% SVR rates, well-tolerated side effects, and fewer drug-drug interactions.[6,8]

Sofosbuvir is effective when used with interferon and ribavirin (triple therapy) and with ribavirin alone (dual therapy). Triple therapy for 12 weeks has resulted in SVR rates as high as 90% for patients with genotypes 1, 4, 5, and 6 infection.[9] Dual therapy for 12 to 16 weeks for patients with genotype 2 infection has produced SVR rates as high as 97%.[9-11] Dual therapy for 24 weeks in genotype 3 achieved SVR rates of 85%.[11] And triple therapy for 12 weeks for treatment-experienced patients with genotypes 2 and 3 infection, including those who failed sofosbuvir dual therapy, achieved SVR rates of 83% to 100%.[12,13]

Clinical trial SVR rates for patients with cirrhosis are 80% for genotypes

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1, 4, 5, and 6; 78% for genotype 2; and 62% to 92% for genotype 3.[9-11] However, a major limitation of these clinical trials was the low representation of patients with cirrhosis in the treatment cohort.[9-11] The VALENCE study reported an overall 93% SVR rate for patients with genotype 2 infection.[11] Patients with cirrhosis constituted only 15% of the study population, and subgroup analysis in this group revealed SVR rates of 78% to 100%.[11]

When these patients were treated, the American Association for the Study of Liver Disease and the Infectious Diseases Society of America HCV clinical practice guidelines recommended prioritizing treatment for patients with advanced fibrosis, cirrhosis, liver transplant, and extrahepatic complications—populations excluded and/or underrepresented in clinical trials.[1] Other authors also focused on the disconnect between clinical trials and real-world practice.[14] The generalizability of clinical trials necessitates external validation because trial populations do not reflect target populations.[14] Because of the lack of real-world data on DAA agents, observational studies are needed to determine the effectiveness of these agents in practice. The objective of this retrospective cohort study was to evaluate the real-world SVR rates, adverse effects, and medication adherence associated with sofosbuvir-based dual and triple therapy.

METHODS

Study Population

Kaiser Permanente Southern California (KPSC) is a large integrated health care delivery system with a membership exceeding 4 million patients. Care is delivered to members at 14 hospitals and more than 200 outpatient clinics. All interactions with the health care system are captured in an electronic medical record system, and the data are available for research purposes. Emergency care delivered at outside facilities is captured in a claims system that is also available for research. At the time of this study, 15,525 KPSC patients had HCV infection—70.8% genotype 1, 16.3% genotype 2, and 10.6% genotype 3. KPSC members were eligible for the study if they were at least age 18 years and treated with sofosbuvir for chronic HCV; the only exclusion criterion was pregnancy. Treatment-experienced patients were those who had failed previous HCV treatment. Treatment-naïve patients had never received HCV treatment or were unable to complete previous treatments because of intolerance. Patients were also classified on the basis of the presence or absence of cirrhosis.

Study Design

A retrospective cohort study of patients who received sofosbuvir and ribavirin with or without interferon was conducted between October 2014 and January 2015. Patient demographics, baseline laboratory data, prior treatments, and comorbidities were collected from KPSC electronic medical records. Additional information collected via chart review included start and end of therapy using antiviral agents, duration of treatment, Emergency Department (ED) visits and hospital admissions, side effects, and serious adverse events. Cirrhosis status was determined via chart review and based on International Classification of Diseases, Ninth Edition (ICD-9) codes (codes 571.2, 571.5, 571.6, 577.8, and 070.70), signs of end-stage liver disease on ultrasound, liver biopsy data, or documentation by gastroenterologists. The primary end point was the SVR12 rate at 12 weeks or later after completion of therapy. Secondary end points were adverse events and medication adherence. This study was approved by the KPSC institution review board.

Safety Analysis

Side effects from the hepatitis C regimen documented in patients' charts were recorded and included fatigue, nausea, headache, rash, insomnia, irritability, arthralgia, and pruritis. Drug-induced anemia was defined as at least a 2-g/dL decrease in hemoglobin level from baseline in the absence of other sources for blood loss. Serious adverse events were defined as side effects necessitating care at the ED or hospital admission.

Medication Adherence

Medication adherence was determined using the medication possession ratio (MPR), which is the total DAA days of supply divided by the sum of the days between the first and last prescription filled and the day supply that was dispensed at the last fill.[15] A calculated MPR of 80% and higher was used to define patients as adherent.[16]

Statistical Analysis

For the primary end point evaluating SVR12, analysis was restricted to patients who successfully completed therapy and returned for follow-up HCV RNA testing. The rationale for using this criteria to determine SVR12 was that inclusion of patients who were lost to follow-up or who never repeated their laboratory testing could artificially lower calculated rates of SVR12. All patients who received at least 1 dose of study medication were included in the safety analysis. A multiple logistic regression analysis was conducted to compare patients with genotypes 1 and 2 infection using genotype, age, sex, cirrhosis-status, treatment history, baseline viral load, and MPR as variables. Statistical Analysis Software version 9.3 (SAS institute Inc, Cary, NC) was used for the analysis.

RESULTS

During our study period, 231 patients with HCV received treatment and their charts were reviewed. Among patients, 65.3% were men, 61.0% were white, 42.3% had cirrhosis, and 38.0% were treatment experienced. Eight patients discontinued therapy early: 6 patients could not tolerate HCV therapy side effects: and 2 patients received a liver transplant. Ten patients were lost to follow-up; 3 patients lost health insurance, 4 patients died within 12 weeks of completing therapy, and 3 patients failed to complete follow-up HCV RNA testing. Causes of death were esophageal cancer, myocardial infarction, necrotizing fasciitis, and liver allograft rejection. All of these deaths were unrelated to HCV therapy. Eighteen patients were excluded, leaving 213 patients for the primary analysis. The highest number of patients had genotype 2 infection, followed by genotypes 1 and 3 (3 patients had genotype 4 and 1 patient had genotype 6). Interferon therapy was contraindicated for about one-quarter of patients with genotype 1 infection, so they received dual therapy for 24 weeks. The remaining patients with genotype 1 infection received the recommended triple therapy for 12 weeks. Nearly all patients with genotype 2 infection received dual therapy for 12 weeks. About one-third of patients with genotype 3 infection received dual therapy for 24 weeks, and the remaining received triple therapy for 12 weeks (Tables 1 and 2, Figure 1).

Overall, 81.7% of patients who were treated achieved SVR12. The highest success rate was seen in patients with genotype 2 infection, and the lowest rates were achieved for those with genotype 3 infection. Patients who did not have cirrhosis achieved higher SVR rates than patients with cirrhosis with genotypes 1 and 2 infection. Similarly, treatment-naïve patients achieved higher SVR rates than treatment-experienced patients with genotypes 1 and 2 infection. Patients with genotype 1 infection who completed triple therapy achieved higher SVR rates (76.9%) than those who completed dual therapy (61.1%) (Table 2).

The treatment-experienced patients with genotype 3 infection had higher SVR rates than treatment-naïve patients. Patients with cirrhosis and genotype 3 infection also had higher SVR rates than patients without cirrhosis. Six of the 15 patients with cirrhosis and genotype 3 infection received triple therapy for 12 weeks, resulting in 5 (83.3%) patients achieving SVR12. The remaining 9 cirrhosis and genotype 3 infection patients received dual therapy for 24 weeks, resulting in 4 (44.4%) patients achieving SVR12 (Table 2).

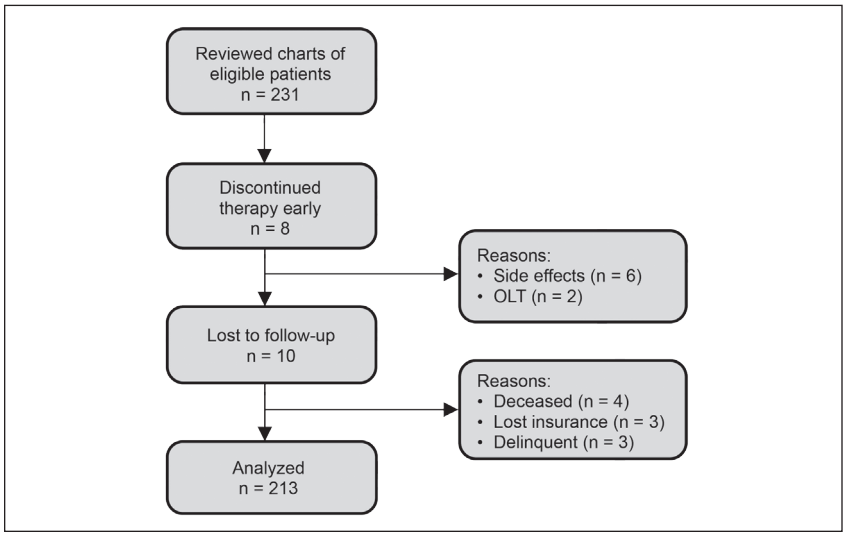

Figure 1. Consort flow diagram of patients.

OLT = orthotopic liver transplantation.

Patients with liver transplant, liver cancer, and those with HIV co-infection had lower SVR12 rates of 60%, 78.9%, and 70%, respectively (Table 2).

Most patients (95.7%) reported at least one side effect. The most frequent side effects (> 20%) were drug-induced anemia, fatigue, nausea, arthralgia, and headache. Patients who received triple therapy experienced the most side effects. Patients

Table 1. Characteristics of 213 patients at hepatitis C virus treatment initiation with sofosbuvir and ribavirin (with or without interferon)

Characteristic	Overall[a] (N = 213)	Genotype 1 (n = 70)	Genotype 2 (n = 119)	Genotype 3 (n = 20)
Number of patients (%)[b]	213 (100.0)	70 (32.9)	119 (55.9)	20 (9.4)
Mean age (SD)	58.1 (9.25)	57.5 (8.94)	58.9 (9.89)	54.7 (6.07)
Median age (range)	58 (25-83)	57 (28-81)	60 (25-83)	55 (34-63)
Male sex, n (%)	139 (65.3)	49 (70.0)	70 (58.8)	16 (80.0)
Mean body mass index (SD)	28.7 (5.42)	28.3 (5.49)	28.3 (5.13)	31.4 (6.04)
Median body mass index (range)	28.2 (18.7-48.6)	27.4 (18.7-42.4)	27.8 (19.5-48.6)	33.4 (19.1-41.0)
Race, n (%)				
White	130 (61.0)	39 (55.7)	78 (65.5)	13 (65)
Black	17 (8.0)	13 (18.6)	3 (2.5)	1 (5)
Hispanic	49 (23.0)	12 (17.1)	31 (26.1)	5 (25)
Asian	12 (5.6)	3 (4.3)	5 (4.2)	1 (5)
Other	5 (2.3)	3 (4.3)	2 (1.7)	—
Treatment agents, n (%)				
Sofosbuvir + ribavirin	148 (69.5)	18 (25.7)	117 (98.3)	13 (65.0)
Sofosbuvir + ribavirin + interferon	65 (30.5)	52 (74.3)	2 (1.7)	7 (35.0)
Other characteristics, n (%)				
Cirrhosis	90 (42.3)	42 (60.0)	30 (25.2)	15 (75.0)
HIV co-infection	10 (4.7)	6 (8.6)	4 (3.4)	—
Liver transplant	19 (8.9)	15 (21.4)	3 (2.5)	1 (5.0)
Treatment experienced	81 (38.0)	34 (48.6)	31 (26.1)	13 (65.0)
Hepatitis C virus RNA > 800,000	120 (56.3)	41 (58.6)	66 (55.5)	10 (50.0)

[a] Includes patients with genotypes 4 and 6.

[b] Three patients had genotype 4 infection and one patient had genotype 6 infection.

+ = and; — = no data available; HIV = human immunodeficiency virus; RNA = ribonucleic acid; SD = standard deviation.

Table 2. Rates of sustained virologic response in 213 patients 12 weeks post-hepatitis C virus treatment with sofosbuvir and ribavirin (with or without interferon)

	Overall, n/N (%)	Genotype 1, n/N (%)	Genotype 2, n/N (%)	Genotype 3, n/N (%)
All patients	174/213 (81.7)	51/70 (72.9)	108/119 (90.8)	11/20 (55.0)
Sofosbuvir + ribavirin	122/148 (82.4)	11/18 (61.1)	106/117 (90.6)	5/13 (38.5)
12 weeks	97/107 (90.7)	—	97/107 (90.7)	—
16 weeks	7/8 (87.5)	—	7/8 (87.5)	—
24 weeks	18/33 (54.5)	11/18 (61.1)	2/2 (100.0)	5/13 (38.5)
Sofosbuvir + ribavirin + interferon	52/65 (80.0)	40/52 (76.9)	2/2 (100%)	6/7 (85.7)
12 weeks	49/61 (80.3)	37/48 (77.1)	2/2 (100%)	6/7 (85.7)
16 weeks	0/1 (0.0)	0/1 (0.0)	—	—
24 weeks	3/3 (100.0)	3/3 (100.0)	—	—
Cirrhosis status				
No cirrhosis	109/123 (88.6)	23/28 (82.1)	83/89 (93.3)	2/5 (40.0)
Cirrhosis	65/90 (72.2)	28/42 (66.7)	25/30 (83.3)	9/15 (60.0)
Treatment history				
Naïve	114/132 (86.4)	29/36 (80.6)	81/88 (92.0)	3/7 (42.9)
Experienced	60/81 (74.1)	22/34 (64.7)	27/31 (87.1)	8/13 (61.5)
Cirrhosis + experienced	35/50 (70.0)	14/23 (60.9)	11/14 (78.6)	8/11 (72.7)
HIV co-infection	6/10 (60.0)	2/6 (33.3%)	4/4 (100.0%)	—
Liver transplant	15/19 (78.9)	12/15 (80.0%)	3/3 (100.0%)	0/1(0.0%)
Liver cancer	7/10 (70.0)	3/5 (60.0%)	2/2 (100.0%)	2/3 (66.7%)

+ = and; — = no data available; HIV = human immunodeficiency virus.

Table 3. Side effects experienced by 231 patients during hepatitis C virus treatment with sofosbuvir and ribavirin (with or without interferon)[a]

Side effect	Overall, N = 231	Sofosbuvir + ribavirin, n = 158	Sofosbuvir + ribavirin + interferon, n = 73
Any side effect	221 (95.7)	150 (94.9)	71 (97.3)
Anemia	170 (73.6)	116 (73.4)	54 (74.0)
Fatigue	156 (67.5)	97 (61.4)	59 (80.8)
Nausea	52 (22.5)	24 (15.2)	28 (38.4)
Arthralgia	49 (21.2)	21 (13.3)	28 (38.4)
Headache	48 (20.8)	26 (16.5)	22 (30.1)
Insomnia	40 (17.3)	28 (17.7)	12 (16.4)
Irritability	39 (16.9)	21 (13.3)	18 (24.7)
Rash	34 (14.7)	16 (10.1)	18 (24.7)
Pruritis	32 (13.9)	18 (11.4)	14 (19.2)
Cough	25 (10.8)	12 (7.6)	13 (17.8)
Diarrhea	19 (8.2)	13 (8.2)	6 (8.2)

[a] Data are number (percentage).
+ = and.

Table 4. Medication possession ratio (MPR) of 231 patients who received hepatitis C virus treatment with sofosbuvir and ribavirin (with or without Interferon)

Cohort Subgroups	MPR 80%-100%, n (%)	MPR 60%-79%, n (%)	MPR < 60%, n (%)
Overall patients (N = 231)	221 (95.7)	9 (3.9)	1 (0.0)
Patients with sustained virological response data (n = 213)	204 (95.8)	8 (3.8)	1 (0.0)
Achieved sustained virological response at 12 weeks posttreatment (n = 174)	168 (82.4)	6 (75.0)	0 (0.0)

who received dual therapy experienced high rates of drug-induced anemia and fatigue, but much less arthralgia, nausea, and headaches than those who received triple therapy. Sixty patients (26%) required ribavirin dose reduction, and 14 patients required erythropoietin alfa injections in addition to ribavirin dose reduction. Six patients discontinued therapy because of intolerable side effects (Table 3).

Seven (3%) patients experienced serious adverse events attributable to HCV treatment. Four patients taking dual therapy were seen in the ED for syncope (1), acute bronchitis (1), and chest pain (2), respectively. One patient taking triple therapy was seen in the ED for dizziness, fatigue, and clamminess and eventually discontinued therapy because of intolerability. One patient taking triple therapy was seen in the ED twice and admitted once for anxiety. One patient taking triple therapy was seen in the ED and admitted for an abdominal abscess.

Medication adherence was excellent; 221 patients had an MPR of at least 80%, 9 patients had an MPR of 60% to 79%, and 1 patient had an MPR lower than 60%. Of the 221 adherent patients, SVR12 data were available for 204 from the primary analysis, and 168 patients (82.4%) achieved SVR12. Of the 10 nonadherent patients, SVR12 data were available for 9 patients included in the primary analysis, and 6 patients (66.7%) achieved SVR12 (Table 4).

Multiple logistic regression analysis revealed that 2 factors were predictive of SVR12 outcomes. Female gender influenced higher SVR12 rates (odds ratio [OR] = 8.10, 95% confidence interval (CI) = 1.79-36.71). Baseline viral load exceeding 800,000 IU/mL influenced lower SVR12 rates (OR = 0.35, 95% CI = 0.13-0.93). Nonstatistically significant trends showed that patients with genotype 2 infection were more likely to achieve SVR12 (OR = 2.20, 95% CI = 0.86-5.62), and cirrhosis reduced the likelihood of achieving SVR12 (OR = 0.38, 95% CI = 0.14-1.01) (Table 5).

DISCUSSION

This retrospective study evaluated outcomes of KPSC patients with HCV who were treated with sofosbuvir-based dual

and triple therapy. We observed SVR rates of 72.9% for patients with genotype 1 infection, which is lower than the reported rate of 89% in clinical trials.[9] However, it is important to note that clinical trials reported SVR rates for treatment-naïve patients with genotype 1 infection who underwent triple therapy. Our SVR rates in treatment-naïve patients with genotype 1 infection who were treated with triple therapy are similar to (albeit lower than) rates reported in the NEUTRINO study; for genotype 1 infection, we observed an overall SVR rate of 80.8% and an SVR rate of 75% in the cirrhosis subgroup vs 89% and 80% rates reported in clinical trials.[9] These differences in overall SVR rate may be attributable to the higher number of patients with cirrhosis in our cohort (52.8% vs 17% in the NEUTRINO study).[9] In addition, our overall SVR rate of 72.9% for genotype 1 infection could be lower because we included treatment-experienced patients and interferon-intolerant patients. We observed an SVR rate of 64.7% in treatment-experienced patients with genotype 1 infection, 72.7% in treatment-experienced patients without cirrhosis, and 60.9% in the treatment-experienced subgroup with cirrhosis. For patients with genotype 1 infection, we observed higher SVR rates of 76.9% with triple therapy and 61.1% with dual therapy (a group of interferon-intolerant patients). No statistical analysis was conducted within subgroups of patients with genotype 1 infection because of the small numbers of patients in each subgroup.

SVR12 rates in our patients with genotype 2 infection were comparable to findings from the POSITRON, FISSION, FUSION, and VALENCE clinical trials.[9-11] Observed SVR rates in our population were 1% to 5% lower than SVR rates reported in clinical trials, which is expected and commonly described as the gap between efficacy and effectiveness; efficacy describes sofosbuvir performance under clinical trial settings, whereas effectiveness describes how the drug performs in real-world settings.[17,18] Selection into clinical trials is not random and results in study populations that are highly motivated and overall healthier.[14] The differences in observed SVR rates (compared with reported SVR rates) likely are attributable to our study's inclusion and exclusion criteria, which resulted in a broader demographic.

Because only 19 patients with genotype 3 infection were included in our study, findings were limited. However, our observed SVR12 rates for patients who received triple therapy were higher than rates reported in the literature. We did not conduct statistical analysis on patients with genotype 4, 5, and 6 infections due to low number of patients in each subgroup.

Rates of side effects (95.7%), serious adverse events (3%), and discontinuations (3%) in our study were comparable to rates reported in the clinical trials.[9-11] Most patients (66.7%) who discontinued therapy early because of side effects received triple therapy. Ribavirin was the main cause of anemia and fatigue. Our findings correlate with current HCV treatment guidelines; interferon-based regimens are no longer recommended, and ribavirin-based therapy is only considered in very specific circumstances.[1]

Patients in our cohort predominantly had genotype 2 infection (55.9%), which does not correlate with HCV genotype distribution at KPSC or the reported distribution in the US; genotype 1 infection accounts for 70% of all infections, whereas genotypes 2 and 3 only account for 14% and 13%, respectively.[19] This discrepancy occurs because the standard of care for genotype 1 infection at the time of this study was triple therapy. Many patients had contraindications or were unable to tolerate interferon therapy and possibly were waiting for the newer all-oral regimens. Patients with genotype 1 infection were treated in our cohort if they insisted on treatment or if postponing treatment was not advisable. This explains the high proportion of patients with cirrhosis and treatment experience in our genotype 1 subgroup (60% and 48.6%, respectively). Meanwhile, SVR rates for interferon-sparing regimens for genotype 2 infection were reported in the 90-plus percentile in all cases except for treatment-experienced patients with cirrhosis.[9-11] For these reasons, it is not surprising that our cohort genotype distribution does not reflect the overall genotype distribution in the US.

Standardized measurements of medication adherence for short-term treatments such as new DAA had not been proposed

Table 5. Multiple logistic regression analysis of patients with genotypes 1 and 2 infection who received hepatitis C virus treatment with sofosbuvir and ribavirin (with or without interferon)

Variable	Odds ratio	95% confidence interval
Genotype		
1	1	
2	2.20	(0.86-5.62)
Sex		
Men	1	
Women	8.10	(1.79-36.71)
Age		
Per year	1.03	(0.98-1.09)
Cirrhosis		
No	1	
Yes	0.38	(0.14-1.01)
Treatment-naïve		
No	1	
Yes	1.89	(0.73-4.89)
Previral load > 800,000 IU/mL		
No	1	
Yes	0.35	(0.13-0.93)
Medication possession ratio		
< 80%	1	
≥ 80%	2.28	(0.31-16.78)

at the time of this study. Among adherent patients, 82.4% achieved SVR (vs 66.7% of nonadherent patients).

Our study had several limitations. Despite use of our 2 largest groups (70 patients with genotype 1 infection and 119 patients with genotype 2 infection), our multiple logistic regression analysis was still limited. Most of our findings were not statistically significant, which was likely because of the small sample size.

The assessment and documentation of patients varied among Medical Centers within the KPSC region. Patients' cirrhosis status was obtained via chart review, which reflects the real-world practice of diagnosing disease in various ways. Clinical trials suggest therapeutic efficacy in optimal conditions, whereas real-world observations describe events that actually happen in practice. Side effects, either reported by patients or assessed by practitioners, were possibly interpreted differently depending on practitioner status (physician, nurse, or pharmacist). As a result, side effects could not be clearly differentiated as being treatment related or associated with underlying disease. Approximately 8% of patients did not provide SVR12 data many weeks after it was due. This led to an incomplete accounting of all patients taking sofosbuvir during the study period. Because of the short treatment duration and the nature of the ways in which medication adherence is calculated, MPR calculation can overestimate adherence, whereas an alternative calculation using proportion of days covered can underestimate adherence. Finally, triple therapy for genotype 1 infection is no longer first-line and has been replaced by interferon and ribavirin-free regimens.[1]

This study's strength is its ability to demonstrate the value of research on real-world patients. We suggest similar studies be conducted on newer DAA-based regimens. Future real-world studies should aim to identify patient factors that influence SVR rates within various HCV subgroups.

CONCLUSION

In this study, sofosbuvir-based regimens were highly effective in the treatment of patients with genotype 2 chronic HCV. We observed lower SVR12 rates for patients with genotype 1 infection than rates reported in registered clinical trials. Lower SVR12 rates may be a direct result of our study's broad inclusion criteria, which allowed for inclusion of patients with advanced disease progression (vs patients enrolled in clinical trials). We observed higher SVR12 rates for patients with genotypes 1 and 3 infection who received triple therapy. Real-world patients tolerated sofosbuvir-based therapy very well and with high rates of adherence. Serious adverse events and discontinuation rates were similar to reported rates from clinical trials. Women and patients with a lower baseline HCV viral load were more likely to achieve SVR12. ❖

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