Real-World Data from Turkey: Is Sofosbuvir/Ledipasvir With or Without Ribavirin Treatment for Chronic Hepatitis C Really Effective?

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Received: **August 1, 2019** *Accepted:* **March 21, 2020** *Available Online Date:* **April 30, 2020**

DOI: **10.5152/tjg.2020.19569**

Cite this article as: Demirtürk N, Aygen B, Çelik İ, *et al.* Real-world data from turkey: Is sofosbuvir/ledipasvir with or without ribavirin treatment for chronic hepatitis C really effective?. *Turk J Gastroenterol.* 2021; 32(2): 155-163.

ABSTRACT

Background: *In this study, we aimed to investigate the efficacy and safety of sofosbuvir-based therapies in the treatment of chronic hepatitis C in real-world clinical practice.*

Methods: *Data from patients with chronic hepatitis C treated with SOF/LDV ± RBV or SOF/RBV in 31 centers across Turkey between April 1, 2017, and August 31, 2018, were recorded in a nationwide database among infectious disease specialists. Demographics, clinical, and virological outcomes were analyzed.*

Results: *A total of 552 patients were included in the study. The mean age of the patients was 51.28 ± 14.2, and 293 (55.8%) were female. The majority had HCV genotype 1b infection (65%), 75.04% of the patients underwent treatment, and non-cirrhosis was present at baseline in 381 patients (72.6%). SOF/LDV ± RBV treatment was given to 477 patients and 48 patients received SOF/RBV according to HCV genotype. The total SVR12 rate was 99% in all patients. Five patients experienced disease relapse during the study and all of them were genotype 2. In patients infected with HCV GT2, SVR12 was 77.3%. SVR was 100% in all patients infected with other HCV genotypes. All treatments were well tolerated by patients without causing severe adverse events. Side effects and side effects-associated treatment discontinuation rates were 28.2% and 0.4%, respectively. Weakness (13.7%) was the common side effect.*

Conclusion: *The present real-world data of 525 patients with HCV genotypes 1, 1a, 1b, 3, 4, and 5 who underwent SOF/LDV ± RBV treatment in Turkey demonstrated a high efficacy and safety profile. HCV GT2 patients should be treated with more efficacious treatment.*

Keywords: *Chronic hepatitis C, sofosbuvir, ledipasvir, sustained virological response, genotype, real-world data*

INTRODUCTION

Hepatitis C virus infection is an important public health problem. It is a leading cause of chronic liver disease and hepatocellular carcinoma. According to the data of the World Health Organization, approximately 185 million people worldwide are chronically infected with hepatitis C virus (HCV).[1] In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy (GHSS) on viral hepatitis which proposes to eliminate viral hepatitis as a public health threat by 2030. Elimination of viral hepatitis as a public health threat requires 90% of those infected to be diagnosed and 80% of those diagnosed to be treated.[2] In the past, the only treatment option for chronic hepatitis C (CHC) was pegylated interferon plus ribavirin (RBV) combination therapy. But this treatment was not able to achieve a complete cure, and it was not enough for reaching the viral hepatitis elimination target of the World Health Organization (WHO).[3] Today, however, CHC can be accurately treated with direct-acting antiviral drugs (DAA).

Nowadays, there are three groups of DAA for the treatment of CHC. The first one inhibits the NS3-4 protease, the second inhibits NS5B polymerase, and the last one acts as an NS5A replication complex. A combination of two or more of these drugs is highly effective in treating CHC. One of these combination options is sofosbuvir/ledipasvir (SOF/LDV).[4]

Sofosbuvir is an oral nucleotide analogue HCV NS5B polymerase inhibitor, and ledipasvir is effective on the NS5A replication complex. A combination of SOF/LDV with and without RBV resulted in high rates of sustained virological response (SVR) in patients with CHC. Both phase studies and real-world data showed that SVR is 94-99% effective with a once-daily single-tablet regimen of SOF/LDV with or without RBV.[5-8]

In this study, we analyzed the data of 525 patients with CHC treated with SOF/RBV or SOF/LDV with or without RBV for 12 or 24 weeks.

MATERIALS AND METHODS

The study was planned as retrospective, and multicentered between April 2017 and August 2018. Data were collected through the Turkish Society of Clinical Microbiology and Infectious Diseases (KLIMIK), The Study Group of Viral Hepatitis (VHCG). The study was approved by the local ethics committee (Clinical Research Ethics Committee of Afyon Kocatepe University, 2011-KAEK-2). Informed consent for the therapy was obtained from all subjects.

All patients older than 18 years, female or male, with chronic hepatitis C were treated with SOF/LDV or SOF/RBV were included in the study. Patients coinfected with hepatitis B virus (HBV) or human immunodeficiency virus (HIV) were also included in the study. CHC with liver transplantation or hepatocellular carcinoma were excluded from the study.

The CHC diagnosis was made using serum HCV RNA and ALT level and histological findings. Child-Pugh class A

score was considered compensated cirrhosis while class B or C was considered decompensated liver cirrhosis. Severity of liver disease was evaluated based on the history of ascites, encephalopathy, upper gastro-intestinal bleed secondary to varices, spontaneous bacterial peritonitis, or hepatorenal syndrome. In addition to laboratory findings (bilirubin and platelet levels), USG findings (increased echogenicity of the liver and nodularity on the liver surface) were also used in the diagnosis of cirrhosis.

The decision about treatment duration and the use or non-use of concomitant RBV was entirely at the discretion of the treating physician.

The study was conducted in a total of 31 specialized centers, such as university hospitals or the Ministry of Health, Training and Research hospitals.

At the time of study, LDV/SOF treatment was reimbursed for naïve cirrhotic patients and for all treatment-experienced patients for 12 weeks with RBV or 24 weeks without RBV in GT1, 4-6 CHC patients, including decompensated cirrhosis. For GT2 patients, 12 weeks of SOF/RBV treatment was reimbursed and for GT3 patients SOF/RBV was provided for 24 weeks, regardless of being cirrhotic or not, and just for GT3 cirrhotic patients SOF/LDV + RBV 24 weeks was also an alternative.

The duration of either SOF/LDV (400 mg/90 mg once daily, per oral) ± RBV (the RBV dose was adjusted according to body weight, 1000 mg/day, 1200 mg/day for <75 kg and ≥75 mg, respectively, per oral) or SOF/RBV treatments were 12 or 24 weeks. Patients were followed up for 12 weeks after the treatment to check SVR.

Demographic, clinical, biochemical, hematological, and virological data were recorded during the treatment and follow-up period. Quantitative HCV RNA assays were performed at treatment weeks 4, 8, 12, 24 (if workable), and 12 weeks after the end of treatment. Various commercial real-time PCR quantification kits with a threshold value of 15-25 IU/ml were used in these assays.

Efficacy and Safety Analysis

A virological response is described as undetectable HCV RNA in the fourth week of treatment (rapid virological response, *RVR*), at the end of treatment (12th or 24th treatment week, *EOT*), and at week 12 post-treatment (sustained virological response, *SVR*). If HCV RNA was negative at week 12 post-treatment, this is defined as SVR. Virological failure and virological relapse were defined as detectable HCV RNA at any time during treatment and post-treatment follow-up, respectively.

Safety data were evaluated according to adverse events during the treatment period and 12 weeks post-treatment. Serious adverse events were described as any life-threatening side effect, an event that led to hospital admission, prolonged and existing hospital stay, or event that resulted in mortality. Anemia was defined as hemoglobin <10 g/dL.

Statistical Analysis

Continuous variables are presented as the mean and standard deviation (SD), and categorical variables are expressed as frequency and percentage. Statistical analysis was applied using the Statistical Package for the Social Sciences (SPSS) software, version 21.0 for Windows (IBM Corp.; Armonk, NY, USA)..

RESULTS

As the choice of therapy, treatment duration, and the decision to add RBV were at the discretion of the physician, randomization according to matched baseline characteristics was not possible; therefore, the results of each sub-cohort categorized by treatment modality are presented individually.

A total of 552 patients were included in the study. However, 22 patients did not regularly check in, two patients died during the treatment period, treatment was discontinued for 3 patients because 1 of the patient developed pancreatic cancer during the therapy and the other 2 had side effects. Virological response was evaluated in 525 patients, and side effects were evaluated in 528 subjects.

The mean age of the patients was 51.28 ± 14.2, and 293 (55.8%) were female. The majority had HCV GT1b infection (65%) and 50 patients were infected with GT1a (9.5%). In 17 (3.2%) patients with infected HCV GT1, HCV subtyping failed. HCV GT2, 3, 4, and 5 were found in 22 (4.2%), 40 (7.6%), 53 (10.1%), and 1 (0.2%) patients, respectively. Only 1 patient had an infected dual genotype (GT3 + 4). At baseline, 144 (27.4%) patients developed cirrhosis. Baseline demographic characteristics and laboratory findings of patients, according to the treatment preference, are summarized in Table 1.

End of treatment response was obtained in all 525 (100%) patients, while SVR was found in 520 subjects

Table 1. Demographic Characteristics and Laboratory Findings of Patients According to Treatment Option

Characteristics	SOF/LDV, 12 weeks, *n* = 120 (%)	SOF/LDV + RBV, 12 weeks, *n* = 126 (%)	SOF/LDV, 24 weeks, *n* = 213 (%)	SOF/LDV + RBV, 24 weeks, *n* = 18 (%)	*SOF/RBV, 12 weeks, *n* = 24 (%)	*SOF/RBV, 24 weeks, *n* = 24 (%)	Total, *N* = 525 (%)
Age	56.93 ± 13.08	59.25 ± 11.93	59.42 ± 11.55	48.44 ± 7.87	41.36 ± 17.63	40.08 ± 16.61	51.28 ± 14.28
Female gender	77 (64.2)	72 (57.1)	117 (54.9))	7 (38.9)	11 (45.8)	9 (37.5)	293 (55.8)
HBV coinfection, (%)	1 (0.8)	2(1.6)	5(2.3)	0	1(4.2)	1(4.2)	10 (1.9)
HIV coinfection, (%)	0	1(0.8)	2(0.9)	2 (11.1)	-	-	5 (20.8)
Patient who inject drug (%)	-	-	-	3 (16.7)	-	-	3 (0.6)
**Fibrosis							
F0	6(5)	6(4.8)	3(1.4)	0	-	-	15 (2.9)
F1	18(15)	11(8.7)	12(5.6)	0	1(4.2)	5(20.8)	47 (8.9)
F2	15(12.5)	14(11.1)	18(8.5)	3(16.7)	4(16.6)	4 (16.6)	58 (11)
F3	18(15)	9(7.1)	19(8.8)	3(16.7)	8(33.3)	7(29.2)	64 (12.2)
F4	12(10)	15(11.9)	21(9.9)	2(11.1)	1(4.2)	1(4.2)	52 (9.9)
F5	7(5.8)	6(4.8)	21(9.9)	0	2(8.3)	0	36 (6.9)
F6	0	5(4)	17(8)	7(38.9)	1(4.2)	1(4.2)	31 (5.9)
Unknown	44(36.7)	60(47.6)	102(47.9)	3(16.7)	7(29.2)	6(25)	222 (42.3)
***Cirrhosis							
No cirrhosis	100(83.3)	89(70.6)	141(66.2)	8(44.4)	21(87.5)	22(91.7)	381 (72.6)
Compensated cirrhosis	20(16.7)	34(27)	59(27.7)	7(38.9)	3(12.5)	2(8.3)	125 (23.8)
[6]Decompensated cirrhosis	0	3(2.4)	13(6.1)	3(16.7)	-	-	19 (3.6)
Baseline HCVRNA, IU/ml							
≥ 800 000 IU/ml	64(53.3)	64(50.8)	106(49.8)	10(55.6)	13(54.2)	10(41.7)	267 (50.9)
HCVRNA, $\log_{10}$ IU/mL	4.18 ± 1.72	21.56 ± 12.78	3.94 ± 1.43	17.61 ± 6.33	5.07 ± 1.05	10.33 ± 3.57	10.94 ± 9.32
ALT, IU/ml	47.47 ± 27.45	58.38 ± 36.84	54.84 ± 38.83	72.00 ± 84.67	57.08 ± 46.70	56.50 ± 28.53	55.72 ± 18.54
AST, IU/ml	45.45 ± 30.19	56.37 ± 35.73	51.74 ± 36.29	75.72 ± 64.93	39.96 ± 18.43	39.29 ± 17.78	52.21 ± 65.83
Albumin, gr/dl	4.06 ± 0.6	4.14 ± 0.55	6.67 ± 0.06	7.60 ± 0.17	3.86 ± 0.91	4.42 ± 0.41	4.85 ± 087
Total bilirubin, mg/dl	0.71 ± 0.31	0.84 ± 0.40	0.61 ± 0.12	1.26 ± 0.92	1.05 ± 1.71	0.70 ± 0.28	0.92 ± 0.45
Hemoglobin, g/dL	13.67 ± 1.63	14.01 ± 1.63	14.44 ± 8.92	13.97 ± 1.64	14.04 ± 1.99	14.80 ± 1.48	15.14 ± 1.82
PLT, /1000 mm^3	228.67 ± 173.4	184.86 ± 61.95	194.40 ± 77.71	188.56 ± 83.19	226.67 ± 84.76	220.33 ± 47.34	216.67 ± 69.12
Antiviral treatment history							
Previous treatment regimens							
IFN/RBV	1 (1.2)	90 (83.3)	124 (68.5)	5 (55.6)	-	-	220 (55.8)
pegIFN/RBV	70 (82.4)	15 (13.9)	46 (25.4)	4 (44.4)	7 (100)	4 (100)	146 (37.1)
pegIFN/RBV/PI	14 (16.5)	3(2.8)	11 (6.1)	0	-	-	28 (7.1)
Previous treatment responses							
Non-responders	32 (37.6)	45 (45.9)	68 (37.5)	2 (22.2)	4 (57.1)	1 (25)	152 (38.6)
Relapsers	47 (55.3)	53 (54.1)	103 (56.9)	7 (77.8)	3 (42.9)	1 (25)	214 (54.3)
Treatment D/C	6 (7.1)	10 (10.2)	12 (6.6)	-	-	-	28 (7.1)

All data are presented as mean ± standard deviation (range).

*These treatment options were used only for patients with CHC infected HCV GT2 and GT3. **Ishak scoring system. ***Determined by clinical findings. [6]If there is at least one of the symptoms such as ascites, variceal bleeding, encephalopathy, spontaneous bacterial peritonitis, or hepatorenal syndrome.

SOF, Sofosbuvir; LDV, ledipasvir; RBV, ribavirin; HCV, hepatitis C virus; PegINF, pegylated interferon; INF, interferon; PI, first-generation protease inhibitors (telaprevir or boceprevir); D/C, discontinuation; F, fibrosis; GT, genotype; ALT, alanine transaminase; AST, aspartate aminotransferase; PLT, platelet; HBV, hepatitis B virus; HIV, human immunodeficiency virus.

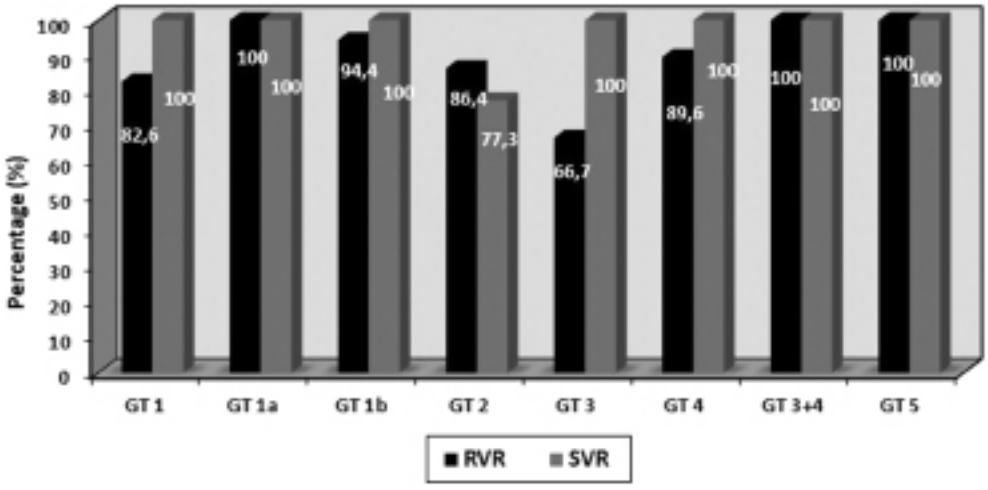

Figure 1. Virological responses according to genotypes.

(99%) based on per-protocol analysis. When all the patients included in the study were evaluated, the EOT response was 95.1% (525/552), and the SVR was 94.2% (520/552) based on ITT analysis. In 5 patients (1%) relapse was seen. The presence of a high viral load or cirrhosis before treatment, previous treatment experience, the presence of comorbidity, a combination of treatments, and the duration of treatment did not change the treatment response of the patients.

SVR rate was found to be 100% in patients infected with all genotypes except GT2. Only one patient was infected with HCV GT5; he was treated with SOF/LDV for 12 weeks. One patient had an infection with a double genotype (GT3 + GT4); he was treated with SOF/LDV + RBV for 24 weeks. The treatment responses according to HCV genotype are shown in Figure 1.

All 5 patients who relapsed were infected with HCV genotype 2. Four of them had received 12-week SOF/RBV treatment and 1 of them had received 12-week SOF/LDV + RBV therapy. All patients complied well with treatment. All patients were treatment-experienced, one of them experienced disease relapse and four of them did not respond to the treatment. The characteristics of these patients are given in Table 2.

Of the 22 patients infected with HCV GT2 evaluated in our study, three were treated with SOF/LDV + RBV for 12 weeks, 14 were treated with only SOF/RBV for 12 weeks, and the remaining 5 were treated with only SOF/RBV for 24 weeks (Table 1). Relapse occurred in 1 (33.3%) of 3 patients who received SOF/LDV + RBV for 12 weeks and in 4 (28.6%) of 14 patients who received SOF/RBV for 12 weeks. SVR was obtained in all patients

Table 2. Characteristics of Patients With Relapse

Patient	Age	Gender	Cirrhosis	ALT, IU/mL	HCV RNA, $\log_{10}$, IU/mL	Previous treatment/response	Treatment
1	52	Male	Compensated cirrhosis	22	7.44	PegIFN + RBV, 48w/relaps	SOF/LDV + RBV, 12 weeks
2	57	Female	Compensated cirrhosis	34	1.63	PegIFN + RBV, 24w/ nonresponse	SOF/RBV, 12 weeks
3	52	Male	Compensated cirrhosis	25	7.140	PegIFN + RBV, 24w/ nonresponse	SOF/RBV, 12 weeks
4	56	Female	Decompensated cirrhosis	57	1.62	PegIFN + RBV, 24w/ nonresponse	SOF/RBV, 12 weeks
5	66	Male	Decompensated cirrhosis	31	3.15	PegIFN + RBV, 24w/ nonresponse	SOF/RBV, 12 weeks

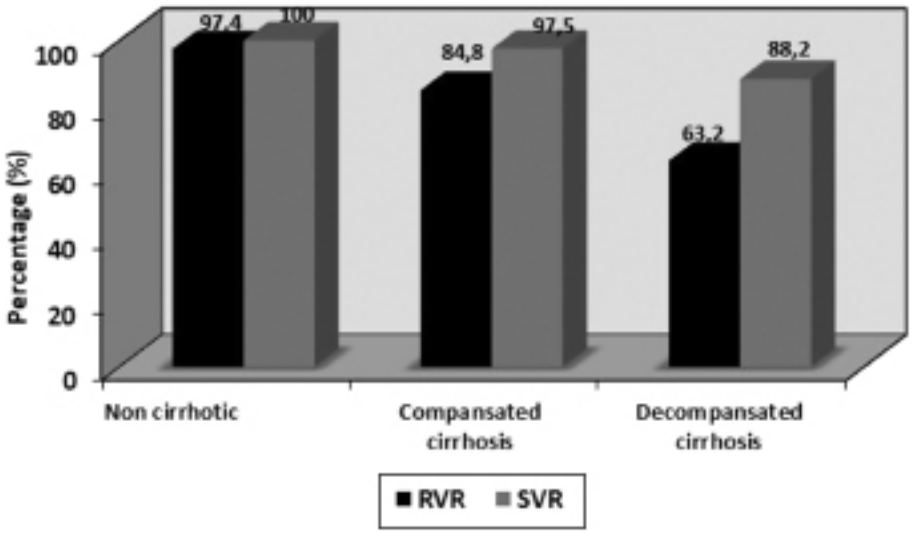

Figure 2. Virological responses according to cirrhosis.

treated with SOF/RBV for 24 weeks. When treatment responses were evaluated in HCV GT2 infected patients, SVR was detected in 17 (77.3%) of 22 patients (Figure 1).

When RPR and SVR are evaluated in patients, according to previous treatment status, these were found to be 79.7% and 99.2% in treatment-naive patients and 97.1% and 99% in treatment-experienced patients, respectively.

The rates of SVR according to the presence or absence of cirrhosis and treatment options in patients are shown in Figures 2 and 3, respectively.

Adverse Events

At the end of the study, observed side effects were evaluated in 528 patients. No serious side effect was observed in any patient. The number of patients with any adverse event was 148 (28.03%). The most common side effects were weakness (13.6%), headache (8.9%), and insomnia (4.7%). Other recorded side effects were nausea, fatigue, pruritus, abdominal pain, anorexia, increased appetite and weight gain, dizziness, arthralgia, and rash.

In terms of laboratory results, two patients had minimal total bilirubin elevation (maximum threefold; normal limits 0.2-1.2 mg/dL), 18 had anemia (hemoglobin <10 g/dL), and up to fivefold transaminase increase in

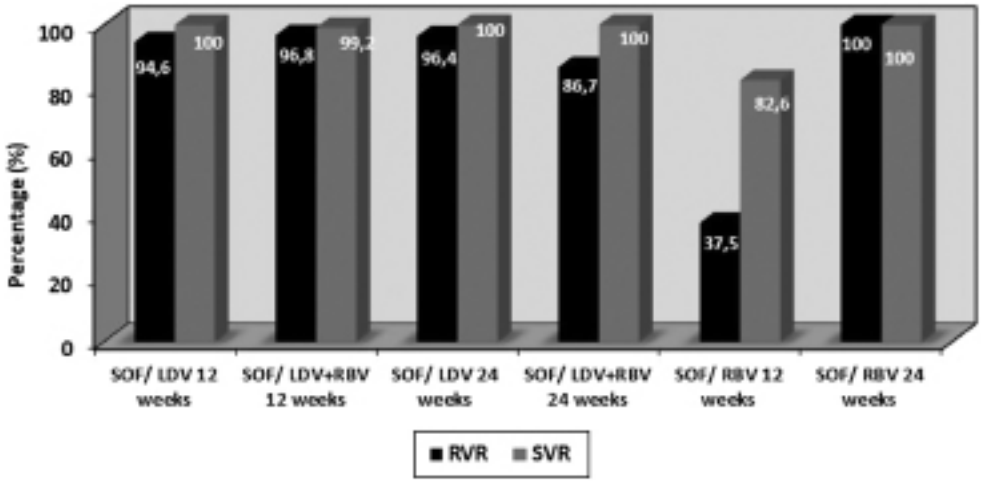

Figure 3. Virological responses according to treatment options.

8 patients (normal limits for AST and ALT 0-40 IU/mL and 0-41 IU/mL, respectively). In the group that was planned to be treated with SOF/LDV for 12 weeks, for 1 patient, the treatment was terminated early due to purplish discoloration of the tongue in the fourth week of treatment and in 1 patient, treatment was terminated early due to severe fatigue in the eighth week of treatment. In 10 out of 192 patients (5.2%) who received RBV treatment, RBV dose was decreased due to anemia, and in 5 (2.6%) patients RBV treatment was stopped.

DISCUSSION

Treatment with DAA drugs in CHC patients was included in the guidelines in 2015 for the first time.[9] In this guideline SOF/LDV combination therapy was one of the first-line treatment options for CHC patients infected with HCV genotypes 1, 4, 5, and 6. SOF/RBV therapy was also recommended for CHC patients infected with HCV genotypes 2 and 3. In Turkey, the costs of the CHC treatment regimen including SOF/LDV and SOF/RBV were to be paid by the state social security institutions from June 2016. Therefore, CHC treatment with the DAA drugs was widespread, but the payment provision by state social security was only passed in the second half of 2016 in Turkey. This study was based on the CHC treatment guidelines of 2015 and 2016 in the treatment choices of the evaluated patients and whether or not the DAA drugs in Turkey were covered by social security.[9-11] Today, most of the costs of the first-line drug recommended for use in the treatment of CHC in Turkey are still not covered by the state. Therefore, DAA medications included in the first-line therapy recommended in the current guidelines cannot be easily accessed in our country.[12] In our study, the treatment results of patients receiving SOF/LDV + RBV or SOF/RBV in 2016 were evaluated retrospectively between 2017 and 2018. Our study contains real-world data reported from Infectious Disease Clinics in Turkey, the first evaluation of SOF/LDV ± RBV and SOF/RBV treatment outcomes in CHC patients.

In this study, SVR was obtained in all patients infected with HCV GT1 (patients who could not be subtyped), GT1a, GT1b, GT3, and GT4. In the literature, a meta-analysis on 2626 HCV GT1-infected CHC patients was performed to evaluate the results of SOF/LDV, SOF/LDV + RBV treatment, and SVR was determined in about 96%. In the same study, it was reported that the presence of cirrhosis or treatment experience in patients did not affect SVR rates. In addition, adding RBV to SOF/LDV treatment did not increase SVR rates.[13] The results of our study are consistent with these real-world data. We also obtained 100% SVR with 12-week treatment with SOF/LDV in HCV GT1, GT1a, and GT1b infected patients.

Based on LDV/SOF's indication, results from 2 treatment arms of 12 weeks with RBV or 24 weeks without RBV did not differ. However, our study was retrospective, and the treatment groups included different numbers of patients. Therefore, a comparison of the effects of treatment options on SVR could be limited. On the other hand, in many studies in which real-world data were reported with 12-week SOF/LDV ± RBV treatment in CHC patients, it was noted that the efficacy ranged from 92% to 100% in conformance with phase studies and that addition of RBV or utilizing 24 weeks of treatment did not have a positive effect on SVR.[7,14-17] Therefore, in the current guidelines, SOF/LDV treatment is still among the first-line treatments for HCV GT1-infected CHC patients.[12]

Nowadays, SOF/LDV treatment is recommended for 12 weeks in treatment-naive patients infected with HCV GT4 but it is not the first choice in treatment-experienced patients.[12] However, in the Turkish Society of Clinical Microbiology and Infectious Diseases (KLIMIK) consensus report on the treatment and follow up of CHC published in our country, the SOF/LDV ± RBV combination was recommended for 12-24 weeks in the treatment of patients with HCV GT4 infection.[11] In the literature, SVR rates are reported to be 100% in phase 2 studies and 95.4% in real-world data, regardless of the presence of cirrhosis, in treatment-naive or treatment-experienced patients infected with HCV GT4 who were treated with the combination of SOF/LDV ± RBV.[7,18] In this study, SVR was obtained in all CHC patients with HCV GT4 infection who were treated with SOF/LDV for 12 or 24 weeks and SOF/LDV + RBV for 12 weeks. As a result, the SOF/LDV regimen is an effective option in the treatment of CHC patients infected with HCV GT4.

In the current guidelines, sofosbuvir/velpatasvir or glecaprevir/pibrentasvir combinations are recommended as the first choice for the treatment of CHC patients infected with HCV GT2 and HCV GT3.[12] Although SOF/LDV + RBV treatment is not recommended in any guidelines for these patients, SOF/LDV + RBV combination was also used in HCV GT2 and GT3 infected patients in our country because this was the only treatment option which was reimbursed for cirrhotic patients. In the reports that evaluate both phase studies and real-world data, the rates of SOF/RBV in HCV GT2 infections ranged from 86% to 100% with 12-week RBV treatment, the duration of treatment was increased to 16 weeks, and SVR

rates were increased; therefore, SOF/RBV treatment was effective in HCV GT2 infections.[19-21] In the same studies, it was reported that the SOF/RBV combination was not effective in HCV GT3 infected patients for 12 weeks and that SVR could be increased to 85% after 24 weeks of treatment.[20,21] In our study, all of the patients with relapse who were infected with HCV GT2 received treatment for 12 weeks and were treatment-experienced patients. Interestingly, unlike the literature, none of the patients infected with HCV GT3 showed non-response or relapse. This may be because the duration of treatment was 24 weeks, and the number of patients was low. Nevertheless, it can be concluded that the SOF/RBV 24-week treatment scheme may be used in patients infected with HCV GT3 in countries where the first-line treatment recommendations according to current guidelines cannot be reached.

In studies reported from Korea and Japan where the prevalence of HCV GT2 is high, it has been reported that treatment-naive and treatment-experienced patients infected with HCV GT2 had SVR at rates ranging from 92.8% to 100% with SOF/RBV treatments for 12-16 weeks.[22,23] In our study, SVR was 77.3% in HCV GT2-infected patients. This may be because the treatment period is 12 weeks because, in cirrhotic patients infected with HCV GT2, it is recommended that the treatment period should be at least 16 weeks.[24] In our study, all patients who relapsed were identified as cirrhotic patients.

SOF/LDV ± RBV and SOF/RBV combinations were found to have a very good safety profile in clinical trials. Real-world data showed that the rate of serious side effects ranged from 1.7% to 4.6%.[7,14,16] In our study, 28.03% of the patients reported at least one side effect, but no serious side effects were seen. Most of the side effects were weakness, headache, and insomnia. The frequency of discontinuation due to side effects in the current trial was very low (0.4%).

In the current guidelines for the treatment of CHC patients, combinations of pangenotypic sofosbuvir/velpatasvir or glecaprevir/pibrentasvir are recommended as the first choice. The studies carried out with these treatment options, especially in non-cirrhotic patients, reduced the duration of treatment up to 8 weeks, and SVR reached 100%.[2,12] Therefore, especially in HCV GT1a, HCV GT3, and HCVGT2 infections and cirrhotic patients, lower SVR with SOF/LDV or SOF/RBV combinations and the need for longer treatment periods have led to the removal of these treatments as first options.[1,10,12]

Limited data using real-world trials exist on the treatment response of SOF-based DAA in CHC patients with compensated cirrhosis . In some studies, it has been reported that the presence of compensated cirrhosis does not affect response to SOF/LDV therapy in CHC patients especially infected with GT1.[25,26] In our study SVR was also found to be 97.5% in CHC patients with compensated cirrhosis. SOF/LDV treatment is one of the options recommended by the guidelines for the treatment of CHC patients with decompensated cirrhosis. But in these patients, SVR is lower.[2,11,12] In our study, SVR was found to be 88.2% in CHC patients with decompensated cirrhosis, although treatment compliance was good in these patients. Therefore, it is important to treat hepatitis C patients before decompensated cirrhosis develops.

The present study has some limitations. First, it was uncontrolled, retrospective, and there was no external monitoring of the collected data. Therefore, a comparison of the effects of treatment options on SVR could be limited. Second, the quantification of HCV viral load and genotyping were conducted at several laboratories. Nevertheless, this study is of great value, as it is reports on the effectiveness and safety outcomes in real-world clinical practice in our country.

In conclusion, SOF/LDV or SOF/RBV treatments are still considered as effective options in CHC patients considering the results of our study which included real-world data with a large number of patients reported from our country. Therefore, in cases where the first choice of DAAs, such as in our country, cannot be available, especially in GT1 and GT4 patients, SOF/LDV can still be used as effective and safe treatment options. The validity of this result can be evaluated with new real-world data on this treatment choice in future studies.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Afyon Kocatepe University, Date: 07.04.2017 and Number 2017/4. Decision:81

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.D., B.A.; Design -N.D., B.A.; Supervision - N.D.; Resource - All authors; Materials - B.A., N.D.; Data Collection and/or Processing - All authors; Analysis and/or Interpretation - N.D.; Literature Search - N.D.; Writing - N.D.; Critical Reviews - All authors.

Acknowledgments: We thank the Study Group for Viral Hepatitis of the Turkish Society of Clinical Microbiology and Infectious Diseases for their contribution to the study conduct and data collection.

Conflict of Interest: No conflict of interest for any of the authors.

Financial Disclosure: There isn't financial support.

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