Research Article

DOI: 10.4274/vhd.galenos.2023.2023-5-2
Viral Hepatitis Journal 2023;29(2):58-63

Sofosbuvir/Velpatasvir/Voxilaprevir Experience in Treatment-Naive Chronic Hepatitis C Patients: Preliminary Findings of Real World Data

Tedavi Naive Kronik Hepatit C Hastalarında Sofosbuvir/Velpatasvir/Voxilaprevir Gerçek Yaşam Verileri: Ön Sonuçlar

Tuba Damar Çakırca[1], Tansu Yamazhan[2], Esra Yüksekkaya[3], Fethiye Akgül[4], Behice Kurtaran[5], Ömer Karaşahin[6], Oğuz Karabay[7], Gülten Ünlü[8], İlkay Nur Can[1], Hüsnü Pullukçu[2], Yeşim Taşova[5], Süheyla Kömür[5], Yeşim Yıldız[9], Çiğdem Mermutluoğlu[10], Yakup Demir[10], Mustafa Kemal Çelen[10]

[1]*Şanlıurfa Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Şanlıurfa, Turkey*
[2]*Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, İzmir, Turkey*
[3]*Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Şanlıurfa, Turkey*
[4]*Batman Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Batman, Turkey*
[5]*Çukurova University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Adana, Turkey*
[6]*Erzurum Regional Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Erzurum, Turkey*
[7]*Sakarya University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Sakarya, Turkey.*
[8]*University of Health Sciences Turkey, Kocaeli Derince Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Kocaeli, Turkey*
[9]*Gazi University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey*
[10]*Dicle University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Diyarbakır, Turkey*

ABSTRACT

Objectives: The aim of this study was to present the preliminary findings of real-world data of sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) in treatment-naive chronic hepatitis C (CHC) patients, which was approved for the first time in treatment-naive patients in Turkey.

Materials and Methods: This retrospective, cross-sectional, multicenter and national study comprised treatment-naive CHC patients receiving SOF/VEL/VOX between June-December 2022 in ten centers from Turkey. The sustained virological response (SVR) was defined as undetectable hepatitis C virus (HCV)-RNA after at least 12 weeks or more from the end of antiviral therapy.

Results: Forty one patients initiating SOF/VEL/VOX were included in the study; median age 55 [interquartile range (IQR): 34.5-61 years], 63.4% males, and median HCV-RNA 521,644 IU/mL. Genotype distribution ranged from 1 to 4 in 28 patients who underwent genotype analysis, and genotype-1 was detected in 24 (85.7%) patients. The most common risk factor was substance

ÖZ

Amaç: Bu çalışmada tedavi naive kronik hepatit C (KHC) hastalarında sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) gerçek yaşam verilerinin ön sonuçlarının sunulması amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif, kesitsel, çok merkezli, ulusal çalışmaya Haziran-Aralık 2022 tarihleri arasında SOF/VEL/VOX tedavisi başlanmış tedavi naive KHC hastaları dahil edilmiştir. Kalıcı virolojik yanıt (SVR), antiviral tedavinin kesilmesinin ardından en az 12 hafta sonra saptanamayan hepatit C virüs (HCV)-RNA olarak tanımlanmıştır.

Bulgular: Çalışmaya SOF/VEL/VOX başlanan 41 tedavi naive KHC hastası dahil edildi. Hastaların medyan yaşı 55 [çeyrekler arası aralık (IQR) 34,5-61 yaş] olup, %63,4'ü erkekti. Medyan HCV-RNA 521.644 IU/mL saptandı. Genotip analizi yapılan 28 hastada genotip dağılımı 1 ile 4 arasında değişmekteydi ve hastaların 24'ünde (%85,7) genotip 1 saptandı. En sık görülen risk faktörü madde kullanımı (n=10, %24,4), en sık eşlik eden hastalık hipertansiyon (n=11, %26,8) idi. 3 (%7,3) hastada kompanse siroz ve 1 (%2,4)

Address for Correspondence: Tuba Damar Çakırca MD, Şanlıurfa Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Şanlıurfa, Turkey
Phone: +90 414 317 17 17 **E-mail:** dr.tubadamar@gmail.com **ORCID ID:** orcid.org/0000-0002-1706-230X **Received:** 24.05.2023 **Accepted:** 07.07.2023

abuse (n=10, 24.4%) and the most common comorbidity was hypertension (n=111, 26.8%). 3 (7.3%) patients had compensated cirrhosis and one (2.4%) had hepatocellular carcinoma. While in the 1st month of treatment, HCV-RNA was negative in all patients except one patient, at the end of treatment all patients' viral load was negative. SVR12 results were available in 23 patients and SVR24 in 10 patients. SVR12 and SVR24 were achieved in all patients who could be evaluated (100%) (SVR12, 23/23; SVR24, 10/10). Adverse events were reported by two patients: Diarrhea (2.4%) and nausea (2.4%), but did not lead to a discontinuation of treatment.

Conclusion: The preliminary results of our study corroborated the efficacy and well tolerateability of SOF/VEL/VOX in treatment-naive CHC patients. High SVR rates were also observed across genotypes 1, 2, 3, 4 with the pangenotypic SOF/VEL/VOX.

Keywords: Hepatitis C treatment, sofosbuvir/velpatasvir/voxilaprevir, real-world data, direct acting antivirals

hastada hepatoselüler karsinom vardı. Tedavinin 1. ayında 1 hasta dışında tüm hastalarda HCV-RNA negatif iken, tedavi bitiminde tüm hastaların viral yükleri negatifti. SVR12 sonuçları 23 hastada ve SVR24 sonuçları 10 hastada mevcuttu. Değerlendirilebilen tüm hastalarda (%100) SVR12 ve SVR24 elde edildi (SVR12, 23/23; SVR24, 10/10). Hastaların birinde ishal (%2,4) ve birinde de mide bulantısı (%2,4) görüldü, ancak tedavinin kesilmesine neden olmadı.

Sonuç: Çalışmamızın ön sonuçları, daha önce tedavi görmemiş KHC hastalarında SOF/VEL/VOX'in etkin olduğunu ve iyi tolere edilebildiğini göstermektedir. Ayrıca pangenotipik SOF/VEL/VOX ile genotip 1, 2, 3, 4'te de yüksek SVR oranları gözlenmiştir.

Anahtar Kelimeler: Hepatit C tedavisi, sofosbuvir/velpatasvir/voxilaprevir, gerçek yaşam verileri, direkt etkili antiviraller

Cite this article as: Damar Çakırca T, Yamazhan T, Yüksekkaya E, Akgül F, Kurtaran B, Karaşahin Ö, Karabay O, Ünlü G, Can İN, Pullukçu H, Taşova Y, Kömür S, Yıldız Y, Mermutluoğlu Ç, Demir Y, Çelen MK. Sofosbuvir/Velpatasvir/Voxilaprevir Experience in Treatment-Naive Chronic Hepatitis C Patients: Preliminary Findings of Real World Data. Viral Hepatitis Journal 2023;29(2):58-63

Introduction

Hepatitis C virus (HCV) infection remains one of the most important public health problems worldwide, currently affecting 58 million people and 1.5 million newly infected patients each year (1). However, enhanced recognition of virus particles and understanding the pathophysiology of the disease, provided developments of direct-acting antivirals (DAA) pioneering improvements of therapy (2). After the first DAA was approved in 2011 by the US Food and Drug Administration, more than ten pharmaceuticals (including effective against all genotypes) are currently available for use (3). The World Health Organization proposes pan-genotypic DAAs for all adult patients infected with HCV (1).

Sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX); containing 400 mg sofosbuvir (NS5B polymerase inhibitor), 100 mg velpatasvir (NS5A inhibitor), and 100 mg voxilaprevir (NS3/4A protease inhibitor) is a pan-genotypic DAA introduced in treatment-experienced patients who were previously treated but failed with DAA-containing regimens. The product provides opportunity to patients using a single tablet once a day with good tolerability (4,5). Recently reported real-world data also endorses the effectiveness of SOF/VEL/VOX as a new option for treatment regimens for HCV patients who had previously experienced DAA failure (6,7).

Although the efficacy of the SOF/VEL/VOX combination is well established in treatment-naive patients in phase-3 trials, real world data is not available in the literature in such patients (8). SOF/VEL/VOX has been approved as a new option both in treatment-naive and prior experienced chronic hepatitis C (CHC) patients since June 2022 in Turkey (9). Thus, we were able to use SOF/VEL/VOX for the first time in real life in CHC patients who had not received any antiviral therapy previously.

In this study, we aimed to present the preliminary findings of real-world data of SOF/VEL/VOX in treatment-naive CHC patients, which was approved for the first time in treatment-naive patients in Turkey as well as in the world.

Materials and Methods

Patients and Study Design

This retrospective, cross-sectional, multicenter, and national study was conducted on patients who were administered SOF/VEL/VOX between June 2022 and December 2022 in ten centers from Turkey. The data of patients [sociodemographic features (age, sex, route of transmission), laboratory [viral load, HCV genotype-subtype, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gama-glutamyl transferase (GGT), alkaline phosphatase, platelet, International Normalized Ratio, alpha-fetoprotein, total bilirubin and radiological findings before and during treatment, treatment-related side effects and comorbidities] were collected retrospectively.

Patients who were older than 18 years, were infected with any genotype and subtype of HCV for more than 6 months and had never received antiviral therapy for HCV (treatment-naive) were included in the study.

Patients who were pregnant or breastfeeding and those who had experienced prior CHC treatment were excluded.

All patients were treated with one tablet SOF/VEL/VOX per day for eight weeks in non-cirrhotic patients and 12 weeks in patients with compensated cirrhosis in accordance with the manufacturer's and Social Security Institution of Turkey's recommendations (5,9). Patients were examined for clinical, virological, and biochemical improvements at the fourth, eighth, and, if any, twelfth weeks of treatment. The follow-up of the patients whose treatment was completed was continued every three months to determine the sustained virological response (SVR).

SVR was defined as undetectable HCV-RNA after at least 12 weeks or more from the end of antiviral therapy. The primary endpoint was an achievement of SVR. The secondary endpoints were determined as virologic responses at week four and the end of treatment (eighth or twelfth week).

This study was approved by the Harran University Faculty of Medicine Ethics Committee Commission (approval number: HRÜ/23.02.29, date: 23.01.2023).

Statistical Analysis

Statistical analyzes were performed using SPSS version 21 (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as frequencies, distributions, and percentages, and continuous variables as medians [interquartile range (IQR)]. The Kolmogorov-Smirnov test was used to assess the normality of the samples distribution. Friedman test and Wilcoxon signed-rank test were used to analyze variation of the recurrent laboratory parameters at the beginning of treatment, the 1st month of treatment, and the end of treatment for dependent groups. A value of $p<0.05$ was accepted statistically significant.

Results

This study included 41 treatment-naive CHC patients who were initiated SOF/VEL/VOX. Baseline characteristics and pretreatment laboratory results of all patients are presented in Table 1. The median age of the patients was 55 (IQR: 34.5-61 years) and 26 (63.4%) were male. The most frequently identified risk factor for CHC was substance abuse (n=10, 24.4%), while the most common comorbidity was hypertension (n=11, 26.8%). Three (7.3%) patients had compensated cirrhosis and one (2.4%) had hepatocellular carcinoma (HCC). The HCV genotype was evaluated in 28 (68.3%) patients. Genotype distribution was; genotype 1 in 24 (85.7%), genotype 2 in one (3.6%), genotype 3 in two (7.1%), and genotype 4 in one (3.6%) patient.

Pre-treatment laboratory data and changes in parameters at the 1st month of treatment and at the end of treatment are presented in Table 2. The results of the patients whose laboratory parameters were recorded in all three time periods were analyzed. Changes in ALT, AST, GGT, and total bilirubin were found to be statistically significant at the beginning, 1st month, and the end of treatment. This significant difference in ALT, AST, and GGT changes was associated with a significant reduction in the 1st month of treatment compared to pre-treatment ($p<0.001$, $p= 0.001$ and $p=0.029$, respectively). A significant difference for the total bilirubin change was associated with a decrease in the 1st month of treatment compared with the end of treatment ($p=0.048$). The changes in ALT, AST, GGT and total bilirubin are shown in Figure 1. In the 1st month of treatment, HCV-RNA was negative in all patients except one patient; who had multiple preexisting diseases and had to use multiple medications and was also co-infected with syphilis and penicillin treatment had been administered concurrent with SOF/VEL/VOX. The patient's HCV-RNA at the end of treatment was negative.

The median pretreatment HCV-RNA of the patients was 521,644 IU/mL. HCV-RNA was evaluated in 35 patients in the 1st month of treatment and in 36 patients at the end of the treatment.

Table 1. Baseline characteristics of patients before treatment

	n=41
Age, year, median (IQR)	55 (34.5-61)
Sex, n (%)	
Male	26 (63.4)
Female	15 (36.6)
Risk factors, n (%)	
Substance abuse	10 (24.4)
Hemodialysis	1 (2.4)
Unknown	30 (73.2)
Comorbidities, n (%)	
Diabetes mellitus	4 (9.8)
Hypertension	11 (26.8)
Heart disease	8 (19.5)
Thyroid disease	1 (2.4)
Chronic renal failure	1 (2.4)
Asthma	3 (7.3)
Cirrhosis, n (%)	3 (7.3)
Hepatocellular carcinoma, n (%)	1 (2.4)
Splenomegaly, n (%)	1 (2.4)
Hepatosteatosis, n (%)	8 (19.5)
Pretreatment laboratory data	
HCV-RNA, IU/mL, median (IQR)	521,644 (177,630-2,668,048)
Platelets, x10^3/µL	248,000 (190,000-291,500)
Creatinin, mg/dL	0.82 (0.69-0.92)
Albumin, g/dL	4.2 (3.7-4.5)
ALT, U/L	58 (30-90)
AST, U/L	40 (27-61)
GGT, U/L	39 (26-77)
ALP, U/L	85 (62-111)
TB, mg/dL	0,60 (0.47-0.80)
AFP, IU/mL	3.0 (2.2-4.4)
INR	1.03 (1.00-1.10)
Genotype	
gp 1	24
Subtype 1a	4
Subtype 1b	14
Subtype unspecified	6
gp 2	1
gp 3	2
gp 4	1
Treatment duration	
8 weeks, n (%)	38 (92.7)
12 weeks, n (%)	3 (7.3)

IQR: Interquartile range, HCV: Hepatitis C virus, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transferase ALP: Alkaline phosphatase, TB: Total bilirubin, AFP: Alpha-fetoprotein, INR: International Normalized Ratio, gp: Genotype

Table 2. Pre-treatment, 1st month of treatment, and post-treatment laboratory data

Laboratory data, median (IQR)	n	Pre-treatment	Firstmonth of treatment	Post-treatment	p*
Platelets	24	237,500 (191,500-263,000)	230,500 (195,500-287,500)	240,500 (210,250-273,750)	0.284
Albumin	20	4.1 (3.7-4.4)	4.3 (3.9-4.4)	4.3 (3.7-4.7)	0.959
ALT	24	51 (27-83)	19 (14-26)	16 (11-26)	**<0.001**
AST	24	39 (27-57)	25 (17-30)	20 (17-29)	**<0.001**
GGT	16	34 (20-97)	26 (19-43)	27 (16-32)	**0.011**
ALP	15	85 (49-109)	78 (66-100)	78 (44-100)	0.526
TB	17	0.55 (0.35-0.93)	0.58 (0.40-0.95)	0.40 (0.27-0.80)	**0.014**
AFP	14	2.8 (2.0-3.3)	2.4 (1.7-3.2)	2.1 (1.8-3.3)	0.225
INR	17	1.03 (1.0-1.1)	1.0 (0.97-1.1)	1.0 (0.99-1.05)	0.167

IQR: Interquartile range, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamil transferaz, ALP: Alkaline phosphatase, TB: Total bilirubin, AFP: Alpha-fetoprotein, INR: International Normalized Ratio, *Friedman test

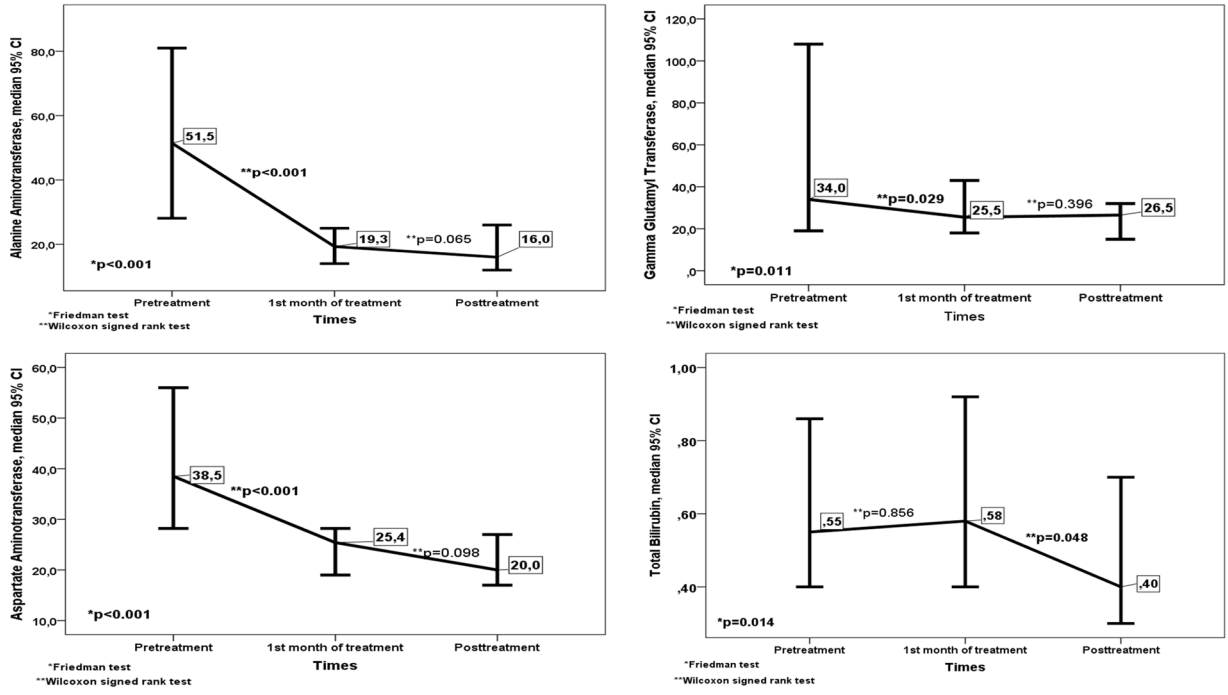

Figure 1. Change of laboratory parameters during treatment

While only one patient had detectable HCV-RNA (2375 IU/mL) in the 1st month of treatment, all patients were negative for HCV-RNA at the end of treatment. SVR12 results were available in 23 patients and SVR24 in 10 patients. SVR12 and SVR24 were achieved in all patients who could be evaluated (100%) (SVR12, 23/23; SVR24, 10/10). Diarrhea was detected in one patient (2.4%) and nausea in another patient (2.4%) in the first month of treatment. The complaints of the patient who had nausea continued throughout the treatment, but the treatment was completed successfully.

One patient who is cirrhotic died during treatment because of underlying disease pancreatic adenocancer, and thus could not be evaluated for SVR. Another patient developed novel HCC six months after the cessation of treatment while examining for SVR24. He achieved SVR24 and underwent transarterial chemotherapy (TACE).

Discussion

This study presented preliminary results of real-world data of treatment - naive CHC patients treated with SOF/VEL/VOX and supports that SOF/VEL/VOX is effective and tolerable in treatment-naive CHC patients. Also, limited data show that SVR rates are high, favoring the results of clinical trials.

SOF/VEL/VOX, the efficacy of which has been demonstrated in phase-3 trials, was introduced as a reliable salvage treatment option especially in patients nonresponding to DAA treatment. POLARIS-1 and POLARIS-4 phase-3 trials included DAA-experienced patients and consistent with these trials real world settings showed high SVR rates in patients who failed from DAA course (6,7,10,11,12). On the other hand, real-world data are scarce about the efficacy and safety of SOF/VEL/VOX in patients who have never received HCV therapy.

POLARIS-2 and POLARIS-3, phase-3 open-label trials, in which the efficacy of SOF/VEL/VOX was investigated primarily in DAA-naive CHC patients, comprised patients who had not received any antiviral therapy previously, besides interferon-based regimen experienced patients. Cirrhotic and noncirrhotic patients from all genotypes were included in the POLARIS-2 study, except genotype-3 cirrhotic patients. Genotype-3 cirrhotic patients who were excluded from POLARIS-2 were included in POLARIS-3. In the SOF/VEL/VOX treatment arm; 76% (n=383) of the patients included in the POLARIS-2 study and 68% (n=75) of the patients included in the POLARIS-3 study were treatment-naive patients who had never received any HCV therapy previously. In these trials, SOF/VEL/VOX for 8 weeks compared with SOF/VEL for 12 weeks. Albeit the SOF/VEL/VOX arm could not be shown to be non-inferior to the SOF/VEL arm in POLARIS-2, high overall SVR rates were obtained in both arms, 95% versus 98% (13). In the present study 41 treatment-naive CHC patients with genotype 1-4 were included, and the majority of our patients were noncirrhotic (92,7%); therefore, except three patients, they received SOF/VEL/VOX for 8 weeks. All patients' response to treatment was excellent and HCV-RNAs were negative at the 1st month of treatment except one patient. The patient who had detectable HCV-RNA in the first month of treatment had multiple preexisting diseases and had to use multiple medications concomitant with HCV treatment. Also, he was co-infected with syphilis and penicillin treatment had been administered in addition to SOF/VEL/VOX. However, the patient's viral load was negative at the end of treatment. SVR12 results were available in 23 patients during the article submission, and SVR rates were 100%.

In this evaluation, one patient with chronic renal failure who was on dialysis three times a week received SOF/VEL/VOX, despite the fact that it has not been studied in patients with end-stage renal disease (ESDR) requiring dialysis. Since the patient was a Syrian refugee and there was no HCV treatment approved for refugees in Turkey, SOF/VEL/VOX was used which obtained by the patient's own resources. SOF/VEL/VOX was used with no dose adjustment in accordance with the manufacturer's recommendation (5). The patient completed the treatment with no complications and achieved SVR. To the best of our knowledge, this is the first case of receiving SOF/VEL/VOX in a patient with ESDR requiring dialysis. SOF/VEL/VOX was given to a patient with HCC and viral load was negative at the first month of treatment. Follow-up continues for virological response.

Clinical studies and postmarketing experience revealed that the most common gastrointestinal adverse reactions related to SOF/VEL/VOX are diarrhea and nausea (4,11,12,13,14). In this study, diarrhea was detected in one patient (2.4%) and nausea in another patient (2.4%) in the first month of treatment. The complaints of the patient, who had nausea, continued throughout the eight weeks but did not lead to a discontinuation of treatment. Serious adverse events were determined in two patients. One patient developed current HCC six months after the cessation of treatment while examining for SVR24. He achieved SVR24 and underwent TACE for HCC. Another patient who was cirrhotic died during treatment because of underlying disease pancreatic adenocancer, which was not related to the SOF/VEL/VOX treatment.

Study Limitations

The strength of this study is that it is the first study examining SOF/VEL/VOX for the first time in treatment-naive CHC patients in a real-life setting. On the other hand, the major limitation of our study was the relatively small patient size. Also, the number of patients with cirrhosis was low. Another limitation is that data of if any resistance-associated substitutions of patients not be eligible due to the insufficient resources of our country.

Conclusion

The preliminary results of our study corroborated the efficacy and well tolerateability of SOF/VEL/VOX in treatment-naive CHC patients. We also observed high SVR rates across genotypes 1, 2, 3, 4 with the pangenotypic SOF/VEL/VOX. Consequently, SOF/VEL/VOX may be another choice with the easy-to-use (once-daily, fixed-dose combination and short-duration regimen) in all genotypes of treatment-naive CHC patients. Additional studies with high sample sizes are required to support our data.

Ethics

Ethics Committee Approval: This study was approved by the Harran University Faculty of Medicine Ethics Committee Commission (approval number: HRÜ/23.02.29, date: 23.01.2023).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.D.Ç., Concept: T.D.Ç., T.Y., E.Y., F.A., B.K., Ö.K., O.K., G.Ü., İ.N.C., H.P., Y.T., S.K., Y.Y., Ç.M., Y.D., M.K.Ç., Design: T.D.Ç., T.Y., E.Y., F.A., B.K., Ö.K., O.K., G.Ü., İ.N.C., H.P., Y.T., S.K., Y.Y., Ç.M., Y.D., M.K.Ç., Data Collection or Processing: T.D.Ç., T.Y., E.Y., F.A., B.K., Ö.K., O.K., G.Ü., İ.N.C., H.P., Y.T., S.K., Y.Y., Ç.M., Y.D., M.K.Ç., Analysis or Interpretation: T.D.Ç., Literature Search: T.D.Ç., Writing: T.D.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare no financial support.

References

1. https://www.who.int/news-room/fact-sheets/detail/hepatitis-c
2. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2018. J Hepatol. 2018;69:461-511.
3. AASLD-IDSA HCV Guidance Panel. Hepatitis C Guidance 2018 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2018;67:1477-1492.
4. Bourlière M, Gordon SC, Flamm SL, Cooper CL, Ramji A, Tong M, Ravendhran N, Vierling JM, Tran TT, Pianko S, Bansal MB, de Lédinghen V, Hyland RH, Stamm LM, Dvory-Sobol H, Svarovskaia E, Zhang J, Huang KC, Subramanian GM, Brainard DM, McHutchison JG, Verna EC, Buggisch P, Landis CS, Younes ZH, Curry MP, Strasser SI, Schiff ER, Reddy KR, Manns MP, Kowdley KV, Zeuzem S; POLARIS-1 and POLARIS-4 Investigators. Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection. N Engl J Med. 2017;376:2134-2146.
5. Vosevi [prescribing information]. Foster City, CA: Gilead Sciences, Inc; 2017.

6. Belperio PS, Shahoumian TA, Loomis TP, Backus LI. Real-world effectiveness of sofosbuvir/velpatasvir/voxilaprevir in 573 direct-acting antiviral experienced hepatitis C patients. J Viral Hepat. 2019;26:980-990.
7. Da BL, Lourdusamy V, Kushner T, Dieterich D, Saberi B. Efficacy of sofosbuvir/velpatasvir/voxilaprevir in direct-acting antiviral experienced patients with hepatitis C virus. Eur J Gastroenterol Hepatol. 2021;33:859-861.
8. Younossi ZM, Stepanova M, Jacobson IM, Asselah T, Gane EJ, Lawitz E, Foster GR, Roberts SK, Thompson AJ, Willems BE, Welzel TM, Pearlman B, Younossi I, Racila A, Henry L. Sofosbuvir and velpatasvir with or without voxilaprevir in direct-acting antiviral-naïve chronic hepatitis C: patient-reported outcomes from POLARIS 2 and 3. Aliment Pharmacol Ther. 2018;47:259-267.
9. https://www.sgk.gov.tr/Duyuru/Detay/01062022-SUT-Degisiklik-Tebligi-Islenmis-Guncel-2013-SUT-2022-06-16-10-29-43
10. Onofrio FQ, Cooper C, Borgia SM, Vachon ML, Ramji A, Lilly LB, Wong A, Booth J, Sattar I, Morales H, Lee S, Conway B, Feld JJ. Salvage Therapy with Sofosbuvir/Velpatasvir/Voxilaprevir in DAA-experienced Patients: Results from a Prospective Canadian Registry. Clin Infect Dis. 2021;72:e799-e805.
11. Degasperi E, Spinetti A, Lombardi A, Landonio S, Rossi MC, Pasulo L, Pozzoni P, Giorgini A, Fabris P, Romano A, Lomonaco L, Puoti M, Vinci M, Gatti F, Carolo G, Zoncada A, Bonfanti P, Russo FP, Aghemo A, Soria A, Centenaro R, Maggiolo F, Rovere P, Pasin F, Paon V, Faggiano G, Vario A, Grossi G, Soffredini R, Carriero C, Paolucci S, Noventa F, Alberti A, Lampertico P, Fagiuoli S; NAVIGATORE-Lombardia and Veneto Study Groups. Real-life effectiveness and safety of sofosbuvir/velpatasvir/voxilaprevir in hepatitis C patients with previous DAA failure. J Hepatol. 2019;71:1106-1115.
12. Llaneras J, Riveiro-Barciela M, Lens S, Diago M, Cachero A, García-Samaniego J, Conde I, Arencibia A, Arenas J, Gea F, Torras X, Luis Calleja J, Antonio Carrión J, Fernández I, María Morillas R, Rosales JM, Carmona I, Fernández-Rodríguez C, Hernández-Guerra M, Llerena S, Bernal V, Turnes J, González-Santiago JM, Montoliu S, Figueruela B, Badia E, Delgado M, Fernández-Bermejo M, Iñarrairaegui M, Pascasio JM, Esteban R, Mariño Z, Buti M. Effectiveness and safety of sofosbuvir/velpatasvir/voxilaprevir in patients with chronic hepatitis C previously treated with DAAs. J Hepatol. 2019;71:666-672.
13. Jacobson IM, Lawitz E, Gane EJ, Willems BE, Ruane PJ, Nahass RG, Borgia SM, Shafran SD, Workowski KA, Pearlman B, Hyland RH, Stamm LM, Svarovskaia E, Dvory-Sobol H, Zhu Y, Subramanian GM, Brainard DM, McHutchison JG, Bräu N, Berg T, Agarwal K, Bhandari BR, Davis M, Feld JJ, Dore GJ, Stedman CAM, Thompson AJ, Asselah T, Roberts SK, Foster GR. Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials. Gastroenterology. 2017;153:113-122.
14. Liu CH, Peng CY, Liu CJ, Chen CY, Lo CC, Tseng KC, Su PY, Kao WY, Tsai MC, Tung HD, Cheng HT, Lee FJ, Huang CS, Huang KJ, Shih YL, Yang SS, Wu JH, Lai HC, Fang YJ, Chen PY, Hwang JJ, Tseng CW, Su WW, Chang CC, Lee PL, Chen JJ, Chang CY, Hsieh TY, Chang CH, Huang YJ, Kao JH. Sofosbuvir/velpatasvir/voxilaprevir for patients with chronic hepatitis C virus infection previously treated with NS5A direct-acting antivirals: a real-world multicenter cohort in Taiwan. Hepatol Int. 2023;17:291-302.