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Research article

Effectiveness and Safety of Sofosbuvir/Velpatasvir and Barriers to Accessing Sofosbuvir/Velpatasvir among Patients with Hepatitis C Virus Infection: A Descriptive Study

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Abstract

Objective: To assess the effectiveness and safety of sofosbuvir/velpatasvir (SOF/VEL) in treating chronic hepatitis C infection and to identify barriers to accessing SOF/VEL. **Methods:** The study consisted of descriptive and qualitative research. In the descriptive study, subjects consisted of 288 patients with chronic infection with hepatitis C virus (HCV) receiving SOF/VEL, aged 18-70, treated at Maharaj Nakorn Chiang Mai or Nakornping Hospitals from January 1, 2020, to March 31, 2022. The effectiveness of SOF/VEL was assessed by measuring sustained virological response at 12 weeks (SVR12). The safety of the treatment was evaluated based on adverse events or reactions related to treatment, which were monitored from the start of treatment until discontinuing SOF/VEL. Data were collected for this study using an electronic data collection tool. In the qualitative study, 12 patients with HCV infection with no SOF/VEL treatment, 4 doctors, and 3 pharmacists were interviewed to gather insights about the barriers in accessing SOF/VEL. **Results:** In the descriptive study, 272 patients (94.4%) completed follow-up. SVR12 rate among patients completing follow-up was 90.8% (95% CI, 87.4–94.3%). Adverse events were observed in 8.1% of patients. Rash, headache, fatigue, abdominal pain, and nausea were the most common adverse events. In the qualitative study, 17 barriers to accessing SOF/VEL were identified. These barriers encompassed availability, affordability, acceptability, accessibility and other additional barriers. **Conclusion:** SOF/VEL is highly effective and safe, with commonly reported adverse events rated as mild. However, several barriers must be addressed to promote increased access to HCV treatment and contribute to reducing and eliminating HCV in Thailand.

Keywords: hepatitis C virus, sofosbuvir, velpatasvir, direct-acting antiviral, barriers to treatment, access to medicine

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บทความวิจัย

ประสิทธิผลและความปลอดภัยของยา sofosbuvir/velpatasvir และอุปสรรคในการเข้าถึงยา sofosbuvir/velpatasvir ในผู้ป่วยโรคไวรัสตับอักเสบซีเรื้อรัง: การศึกษาเชิงพรรณนา

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาประสิทธิผลและความปลอดภัยของยา sofosbuvir/velpatasvir (SOF/VEL) ในการรักษาโรคไวรัสตับอักเสบซีเรื้อรัง และค้นหาอุปสรรคในการเข้าถึงยา SOF/VEL **วิธีการ:** การศึกษาประกอบด้วยการวิจัยเชิงพรรณนาและการวิจัยเชิงคุณภาพ ในการวิจัยเชิงพรรณนา กลุ่มตัวอย่างคือผู้ป่วยไวรัสตับอักเสบซีเรื้อรังจำนวน 288 คนที่ได้รับยา SOF/VEL ซึ่งมีอายุ 18-70 ปี และได้รับการรักษา ณ โรงพยาบาลมหาราชนครเชียงใหม่หรือโรงพยาบาลนครพิงค์ ในช่วงวันที่ 1 มกราคม พ.ศ. 2563 ถึงวันที่ 31 มีนาคม พ.ศ. 2565 ประสิทธิผลของ SOF/VEL ประเมินจากผลการตรวจปริมาณไวรัสตับอักเสบซีในเลือดหลังจากหยุดการรักษาไปแล้ว 12 สัปดาห์ (SVR12) ความปลอดภัยของยาประเมินจากเหตุการณ์ไม่พึงประสงค์ที่เกี่ยวข้องกับยาโดยติดตามความปลอดภัยตั้งแต่วันที่เริ่มใช้ยาจนถึงวันที่ผู้ป่วยหยุดใช้ยา SOF/VEL การเก็บข้อมูลในการศึกษาใช้แบบเก็บข้อมูลอิเล็กทรอนิกส์ ส่วนในการวิจัยเชิงคุณภาพ เป็นการสัมภาษณ์ผู้ป่วยไวรัสตับอักเสบซีเรื้อรังที่ไม่ได้รับยา SOF/VEL จำนวน 12 คน แพทย์จำนวน 4 คน และเภสัชกรจำนวน 3 คนในประเด็นอุปสรรคในการเข้าถึงยา SOF/VEL **ผลการวิจัย:** ในการศึกษาเชิงพรรณนา ผู้ป่วยรับการติดตามการรักษาจนครบจำนวน 272 คน (ร้อยละ 94.4) มีผู้ป่วยที่ตรวจไม่พบไวรัสตับอักเสบซีในเลือดหลังจากหยุดการรักษาไปแล้ว 12 สัปดาห์ (SVR12) ร้อยละ 90.8 (95% CI, 87.4–94.3%) พบอาการไม่พึงประสงค์ในผู้ป่วยร้อยละ 8.1 โดยอาการไม่พึงประสงค์ที่พบมากที่สุดได้แก่ ผื่น ปวดศีรษะ อ่อนเพลีย ปวดท้อง และคลื่นไส้ งานวิจัยเชิงคุณภาพพบอุปสรรคในการเข้าถึงยา SOF/VEL ทั้งหมด 17 ประการ โดยอยู่ภายใต้หมวดการมียา ความสามารถในการจ่าย การยอมรับการใช้ยา การเข้าถึงแหล่งบริการ และหมวดอื่น ๆ **สรุป**: ยา SOF/VEL เป็นยาที่มีประสิทธิผลและความปลอดภัยที่สูงโดยอาการไม่พึงประสงค์ที่พบบ่อยเป็นอาการที่ไม่รุนแรง อย่างไรก็ตามยังมีอุปสรรคหลายประการที่ควรได้รับการแก้ไขเพื่อส่งเสริมให้เกิดการเข้าถึงยารักษาไวรัสตับอักเสบซีที่มากขึ้น และนำไปสู่การลดและกำจัดเชื้อไวรัสตับอักเสบซีในประเทศไทย

คำสำคัญ: ไวรัสตับอักเสบซี โซฟอสบูเวียร์ เวลพาทาสเวียร์ ยาต้านไวรัสที่ออกฤทธิ์โดยตรง อุปสรรคการเข้าถึงการรักษา การเข้าถึงยา

Introduction

Hepatitis C is a widespread health issue affecting millions of individuals globally. According to estimates, 58 million people were infected with the disease, causing approximately 290,000 deaths yearly. Hepatitis C infection can lead to chronic hepatitis in 55 to 85% of patients, with 15 to 30% progressing to cirrhosis. A risk exists of developing liver cancer due to hepatitis C (1). When chronic hepatitis C leads to cirrhosis or liver cancer, it could significantly affect a person's quality of life and increase financial burden for the government in providing treatment. Treating cirrhosis or liver cancer costs from 170,000 to 600,000 THB per person annually (2-4).

Treatment for chronic hepatitis C usually involves antiviral drugs. The standard treatment was interferon with oral ribavirin. The treatment was ineffective in some strains of virus. Patients with HCV (hepatitis C virus) genotypes 1 and 4 experienced more difficulty in responding to interferon treatment (5). Interferon with ribavirin causes many adverse reactions, such as flu-like symptoms and bone marrow suppression. Furthermore, the cost of these drugs was high, with the average cost of medication alone ranging from 75,600 to 163,800 THB per course of treatment (4). Subsequently, direct-acting antivirals (DAAs) have been developed. These orally administered medications offer higher treatment effectiveness, shorter treatment durations and fewer adverse reactions.

Since 2012, Thailand has included peginterferon alfa-2a/2b and ribavirin in its National List of Essential Medicines (NLEM) category E (2) for treating HCV genotypes 1, 2, 3 and 6. By 2021, these medications were replaced by a more effective combined tablet of sofosbuvir and velpatasvir (SOF/VEL) (6).

Studies of SOF/VEL in other countries have demonstrated high efficacy and safety, with treatment effectiveness rates exceeding 90% and mild adverse reactions (7-9). However, populations studied in foreign research on SOF/VEL may differ from Thai populations in several ways such as the prevalence of co-infection with HIV, genotypes, and cirrhosis. These factors may affect the treatment's success. Furthermore, related studies in Thailand concerning SOF/VEL effectiveness, involved fewer than 100 patients (10, 11). Our study aimed to address this limitation by including over 200 patients from two different settings, thereby enhancing the generalizability of the results to a broader population.

Despite the high effectiveness and safety of SOF/VEL demonstrated in studies worldwide, according to statistics from the Faculty of Medicine Chiang Mai University and Nakornping Hospital, the access rate to SOF/VEL remained low with over 50% of patients unable to access the medication. To better understand the barriers preventing patients in Thailand from accessing SOF/VEL, we used the Access to Medicines framework (ATM framework) to guide the study (12-14). Access to medicines is a complex concept providing a comprehensive approach for analyzing access to medicine. Several frameworks have been developed to explain access to medicines, including the Management Sciences for Health Framework (13), the Frost and Reich Framework (12), and the Bigdeli Framework (14). After reviewing these frameworks, we found four components essential for accessing medicines, i.e., availability, accessibility, affordability, and acceptability.

Availability refers to having an adequate supply of medicines in terms of type and quantity. Accessibility refers to physical accessibility of the hospital, including the location of hospitals in relation to patients' residences. Affordability refers to factors related to the pricing of medicines, as well as the income and ability of patients to pay for healthcare services. Acceptability of medicines refers to the products' characteristics and attitudes and expectations of physicians and patients towards medicines (12-14). This study conducted interviews with patients, physicians, and pharmacists to gain a deeper understanding of the barriers of the access to SOF/VEL.

The study aimed to assess the effectiveness and safety of SOF/VEL in treating chronic HCV among Thai patients and to identify the barriers that hinder patients from accessing SOF/VEL.

Methods

The study protocol was approved by the Human Ethics Committee of the Faculty of Medicine, Chiang Mai University (No. 205/2022, Date of approval: June 20, 2022) and the Human Ethics Committee of Nakornping Hospital (No.053/65, date of approval 15 August 2022).

This mixed-methods study consisted of two components: a descriptive observational study and a qualitative study. The descriptive study aimed to investigate the effectiveness and safety of SOF/VEL. The qualitative study aimed to gather information from patients, physicians, and pharmacists about the barriers to accessing SOF/VEL treatment.

Effectiveness and safety of SOF/VEL

Settings, population and samples

The population comprised patients with chronic HCV infection receiving combined sofosbuvir 400 milligrams and velpatasvir 100 milligrams, with or without ribavirin once daily for 12 or 24 weeks. The duration of treatment depended on the physician's assessment.

The study recruited patients aged 18 to 70 with chronic hepatitis C receiving SOF/VEL, with or without ribavirin, daily for 12 or 24 weeks at Maharaj Nakorn Chiang Mai or Nakornping Hospitals between January 1, 2020 and March 31, 2022. Exclusion criteria encompassed patients with incomplete HCV RNA test results before or after initiating treatment; patients who did not complete their course of treatment and patients being lost to follow-up. The sample size was calculated using the ClinCalc calculator (15) for the comparison of a dichotomous variable in one study cohort with a known value published in previous literature. The known population percentage of patients recovering from HCV derived from related studies was 95.6% (8). The estimated percentage of patients expected to recover from HCV based on pilot data and findings from studies on SOF/VEL and others was 90%. Type I error (α) was set at 0.05, type II error (β) was set at 0.2. The calculated sample size was at least 137 patients. The actual number of patients participating in the study was 288.

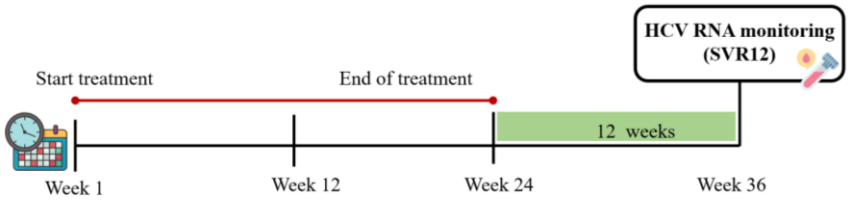
Outcome evaluation

The effectiveness of SOF/VEL was assessed by measuring sustained virological response at 12 weeks, also known as SVR12. SVR12 refers to achieving an undetectable level of HCV RNA using the Abbott m2000 RealTime System (with a lower limit of 12 IU/mL) at 12 weeks after completing either 12 or 24 weeks of HCV therapy (16) (Figures 1 A and B). The specific duration of treatment was determined by the physicians with the consideration of related factors such as liver cirrhosis and history of hepatitis C treatment. The safety of the treatment was evaluated based on adverse events related to treatment, which were monitored from the start of treatment until discontinuing SOF/VEL. Adverse events were collected from medical records and laboratory results (Hb, WBC, platelet, AST, ALT, albumin, total bilirubin, serum creatinine, and eGFR). Serious adverse reactions were also monitored and referred to as undesired effects that could lead to treatment termination, disability, hospitalization, or death.

Data collection

Data were collected for this study using an electronic data collection tool called Research Electronic Data Capture (REDCap), a web-based application developed by Vanderbilt University to capture data for clinical research and create databases and projects (17). This data storage tool provided access although restricted by a username and password provided by the software designer and meeting Health Insurance Portability and Accountability

A. Measurement of HCV RNA levels in the blood at week 12 after the end of treatment (SVR12) among patients treated for 12 weeks.



B. Measurement of HCV RNA levels in the blood at week 12 after the end of treatment (SVR12) among patients treated for 24 weeks.

Figure 1. Measurement of HCV RNA levels in the blood at week 12 after the end of treatment (SVR12)

Act, CFR Part 11, Federal Information Security Management Act, and international standards.

Data were collected by two clinical pharmacists, one being the primary researcher with extensive experience in Hepatitis C research and the other being a research assistant trained in data collection methods to ensure accuracy and minimize bias. The data comprised three parts: Part 1 comprised baseline patient characteristics, including sex, age, BMI, health insurance status, co-infection, genotype, baseline HCV RNA, fibrosis stage, cirrhosis, hepatocellular carcinoma, alcoholic liver disease, fatty liver, NASH (nonalcoholic steatohepatitis), prior antiviral treatment, treatment regimen, and treatment duration. Part 2 consisted of data on the effectiveness of SOF/VEL treatment, as measured using the SVR12. Part 3 constituted the assessment of safety of SOF/VEL treatment based on recorded symptoms, adverse events, and lab results. Computed tomography, ultrasound, and magnetic resonance imaging of patients were reviewed by physicians for accuracy in evaluation.

Statistical analysis

Electronically collected data exported to Excel were then analyzed using STATA, Version 14. Descriptive statistics was used to characterize the sample group. The SVR12 outcome and safety assessment were analyzed using descriptive statistics, with data presented as count and percentage.

Barriers in accessing SOF/VEL

Settings, and informants

The informants comprised 12 patients with chronic hepatitis C not receiving SOF/VEL medication, four physicians providing care to patients with chronic hepatitis C, and three pharmacists managing hepatitis C medication in Maharaj Nakorn Chiang Mai and Nakornping Hospitals. The number of informants depended on data saturation where no new barriers to medication were identified within the collected data.

Data collection

The structured qualitative interviews in this study concentrated on identifying barriers to accessing SOF/VEL treatment for chronic hepatitis C, based on ATM frameworks. Content accuracy was verified by a gastroenterology and liver disease specialist. The data were gathered by the first author with four years' experience as a clinical pharmacist and three years of research in hepatitis C. The first author received

comprehensive training from specialized hepatologists to ensure proficient clinical data collection.

Invitations to patients with HCV without SOF/VEL treatment were distributed through posters in Gastroenterology and Infectious Diseases Clinics (Maharaj Nakorn Chiang Mai and Nakornping Hospitals). Attending physicians or nurses provided research information documents to patients. For informants who were doctors and pharmacists, the researchers sent them an invitation letter to participate in the research, and an interview was scheduled when they agreed.

In the interview process, the researcher informed the participants about the research objectives, benefits, and potential risks. Participants with signed consent forms were interviewed. The researchers used an interview protocol divided in four themes based on the ATM framework: availability, accessibility, affordability, and acceptability. The detailed questions about each theme can be found in the appendix section. Duration of each interview was approximately 30 minutes.

Data analysis

The interviews were audio-recorded and transcribed verbatim. The content was analyzed using the ATM framework to organize the data systematically. The responses from the study participants were then subjected to thematic analysis based on the factors specified in the ATM framework, namely availability, affordability, acceptability, and accessibility. Data triangulation involved evaluating the data obtained from interviews with the data in medical records, along with using multiple perspectives in interpreting the data, including evaluations conducted by two clinical pharmacists. However, the researcher further assessed which dimensions' definitions aligned most with the responses provided by the study participants.

Results

Effectiveness and safety of SOF/VEL

Of 288 patients with chronic HCV infection who were under the treatment with SOF/VEL, 272 patients (94.4%) completed the follow-up (Figure 2). Most patients were male (62.1%), with a mean age of 54.0 years. The most common HCV genotype was genotype 3 (37.9%). Most patients had an HCV RNA level of less than 6,000,000 IU/mL (89.3%). The study's most commonly used HCV treatment regimen comprised SOF/VEL without RBV (93.4%), with most patients receiving a 12-week treatment course (98.5%) (Table 1).

The SVR12 rate was 90.8% (95% CI, 87.4 to 94.3%) among patients with complete follow-up. Those with genotype 1 HCV infection exhibited the highest SVR12 rate (when not considering genotype 2 which had only one patient), while those with genotype 6 HCV infection had the lowest rate. Furthermore, patients without cirrhosis demonstrated a higher SVR12 rate

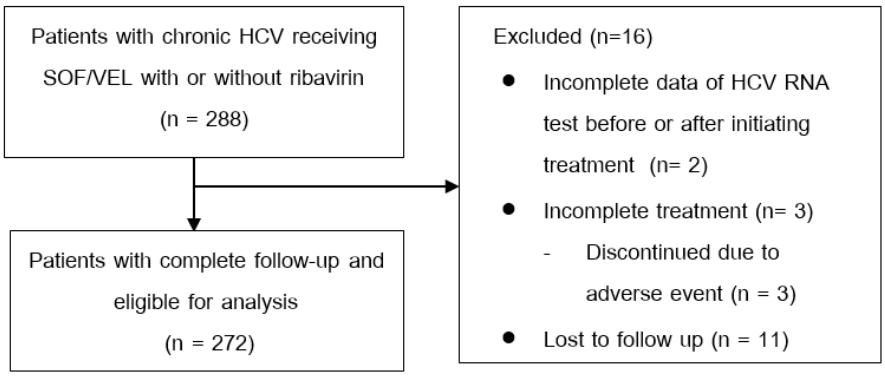


Figure 2. Flowchart of patients included in data analysis; the effective population includes all patients with complete follow-up and eligible for data analysis.

Table 1. Baseline characteristics of the overall cohort (n=272)

characteristic	
sex, n (%)	
male	169 (62.1)
female	103 (37.9)
age, year, mean (SD)	54.0 ± 13.0
BMI, kg/cm^2, mean (SD)	23.7 ± 4.6
health insurance schemes, n (%)	
universal coverage scheme	138 (50.7)
social security scheme	47 (17.3)
civil servant medical benefit scheme	76 (27.9)
uninsured[1]	11 (4.0)
HIV co-infection, n (%)	56 (20.6)
HBV co-infection, n (%)	10 (3.7)
HBV HIV triple infection, n (%)	2 (0.7)
genotype, n (%)	
1	79 (29.0)
2	1 (0.4)
3	103 (37.9)
6	62 (22.8)
N/A	27 (9.9)
HCV RNA <6,000,000 IU/mL[2]	243 (89.3)
HCV RNA ≥6,000,000 IU/mL[2]	29 (10.7)
HCV RNA, $\log_{10}$ IU/mL, median (IQR)	5.9 (5.2 -6.4)
fibrosis stage, n (%)	
F0	6 (5.1)
F1	49 (41.9)
F2	5 (4.3)
F3	22 (18.8)
F4	32 (27.4)
N/A	158 (58.0)
cirrhosis, n (%)	146 (53.7)
Child–Pugh A	123 (91.2)
Child–Pugh B	23 (8.8)
Child–Pugh C	-
hepatocellular carcinoma, n (%)	26 (9.6)
alcoholic liver disease, n (%)	24 (8.8)
fatty liver, n (%)	53 (19.5)
NASH, n (%)	4 (1.5)
prior antiviral treatment, n (%)	
naïve	255 (93.8)
experienced	17 (6.3)
peginterferon plus ribavirin regimen	11 (64.7)
DAA regimen	6 (35.3)
treatment regimen, n (%)	
SOF/VEL	254 (93.4)
SOF/VEL plus ribavirin	18 (6.6)
treatment duration, n (%)	
12 weeks	268 (98.5)
24 weeks	4 (1.5)

1: No health insurance coverage

2: A threshold at 6 million IU/mL has been proposed to best discriminate treatment outcomes on sofosbuvir-based regimens (18).

compared with those with Child-Pugh class A and B cirrhosis (Table 2). Of 272 patients, 22 (8.1%) experienced adverse events, without any patient experiencing serious adverse events. No deaths were reported. The most reported adverse events were rash (1.5%), headache (1.0%), abdominal pain (1.0%), and nausea (1.0%) (Table 3).

Barriers in accessing SOF/VEL

The qualitative study identified 17 barriers to accessing SOF/VEL within 8 themes as presented in Table 4.

1. Availability

Inefficient medication procurement system: Physician A emphasized how the inefficient medication procurement system led to multiple hospital visits for patients, resulting in missed doses and ineffective treatment. Physician D highlighted the close tie between medication availability and the procurement system,

Table 2. Effectiveness at 12 weeks after treatment completion (n=272)

	SOF/VEL	SOF/VEL plus RBV	SOF/VEL	SOF/VEL plus RBV	total
duration of treatment[1]	12 weeks	12 weeks	24 weeks	24 weeks	-
n	252	16	2	2	272
overall SVR12[2]	227/252 (90.1)	16/16(100.0)	2/2 (100.0)	2/2 (100.0)	247/272(90.8)
genotype					
1	73/74 (98.7)	4/4 (100.0)	1/1 (100.0)	-	78/79 (98.7)
2	1/1 (100.0)	-	-	-	1/1 (100.0)
3	89/97 (91.8)	5/5 (100.0)	1/1 (100.0)	-	95/103(92.2)
6	42/54 (77.8)	6/6 (100.0)	-	2/2 (100.0)	50/62 (80.7)
N/A	22/26 (84.6)	1/1 (100.0)	-	-	23/27 (85.2)
baseline CPT class[3]					
noncirrhotic	116/123(94.3)	3/3 (100.0)	-	-	119/126 (94.4)
class a	103/117 (88.0)	3/3 (100.0)	1/1 (100.0)	2/2 (100.0)	109/123 (88.6)
class b	8/12 (66.7)	10/10(100.0)	1/1 (100.0)	-	19/23 (82.6)
class c	-	-	-	-	-

1: The specific duration of treatment was determined by the physician's decision.

2: An undetectable level of HCV RNA at 12 weeks after completing either 12 or 24 weeks of HCV therapy (16).

3: CPT Child–Pugh Turcotte

causing treatment delays when drugs became scarce.

Limitations of hospital level and prescribing physicians: Physician D highlighted not having gastroenterologists as one reason for patients' inaccessibility to medication and treatment delay. He suggested allowing general medicine physicians to prescribe medications due to limited gastroenterologists. From the patient's perspective, Patient I experienced unavailability in a small hospital that lacked medication for hepatitis C treatment.

Limitations of prescribing criteria: Physician A emphasized the need for revising the NLEM drug approval criteria. Flexibility and reliance on physicians' judgment were essential. Removing certain criteria, like an HCV viral load >5000 IU/mL, ensured treatment for individuals at any stage of fibrosis.

Complex processes for prescribing medication in universal health coverage and social security systems scheme: Physician C observed complex processes in medication access for patients with universal healthcare and social security schemes. This group experienced delayed treatment initiation, necessitating referral letters.

2. Affordability

Financial burden for SOF/VEL: Physician A and Pharmacist B mentioned financial burden as a barrier to accessing SOF/VEL for foreign patients or those without healthcare coverage. From the patient's perspective, Patient I, a non-Thai national without health insurance, expressed concern that she might be unable to afford the medication if its cost was high.

Financial burden of transportation: Patient B faced problems with treatment costs, including transportation to the hospital. Multiple comorbidities and coordination among physicians caused delays in starting hepatitis C treatment.

Table 3. Adverse events among patients treated with SOF/VEL with or without ribavirin (n=272)

adverse event	number (%)
any adverse event	22 (8.1)
serious adverse events[1]	0
adverse event leading to discontinuation of SOF/VEL	0
disability	0
hospitalization	0
death	0
common adverse events	
rash	4 (1.5)
headache	3 (1.0)
abdominal pain	3 (1.0)
nausea	3 (1.0)
fatigue	2 (0.7)
anemia	2 (0.7)
dyspnea	1 (0.4)
insomnia	1 (0.4)
dry cough	1 (0.4)
nasopharyngitis	1 (0.4)
rising serum creatinine	1 (0.4)

[1]Serious adverse events was defined as events that result in the discontinuation of treatment, disability, hospitalization, or death (19).

3. Acceptability

Patient's concern of adverse effects of SOF/VEL: Patient B worried about its effectiveness and safety, while Patient H, a patient with thalassemia, feared potential blood-thinning effects and preferred a medication without anemia risks.

Patient's concern on drug interactions: Patient K encountered difficulties starting SOF/VEL due to drug interactions with his antiretroviral medications. The process of switching to a different regimen required consultations among specialists, resulting in delayed treatment.

4. Accessibility

Stigmatization: Patient K experienced stigma, making him afraid to seek HCV treatment, leading to delayed treatment. However, he eventually realized the importance of overcoming his fear and sought treatment despite the stigma.

Barriers on transportation and referral system: Patient F faced barriers on transportation and referral system due to living far from the hospital and having multiple appointments. Physician C highlighted the inefficient HCV patient referral system as a barrier, resulting in delayed treatment for patients under universal coverage or social security schemes. They suggested establishing a systematic approach for referring patients to nearby hospitals.

5. Limited awareness and knowledge about HCV treatment among patients: Physician B emphasized the patients' inadequate knowledge about HCV treatment hindered their engagement in the treatment process. She recommended implementing community-level campaigns to improve treatment access and knowledge.

6. Insufficient knowledge among medical providers regarding the diagnosis and treatment of HCV: Physician A mentioned that some medical providers still believed that HCV could not be treated, indicating inadequate understanding of recommended treatment approaches for Hepatitis C. From the patient's perspective, Patient F mentioned an experience where a physician at a hospital nearby his home mistakenly believed that HIV medication also covered HCV treatment, leading to delayed treatment.

7. Lack of communication from healthcare providers: Patient L did not receive updates on available hepatitis C medication and was unaware of new free medications. She regretted not knowing earlier and seeking treatment before experiencing severe liver symptoms.

Table 4. Barriers to accessing SOF/VEL

theme	barrier	reported by		
		physicians	pharmacists	patients
availability	inefficient medication procurement system	●	●	
	limitations of hospital level and prescribing physicians	●		●
	limitations of prescribing criteria	●	●	●
	complex processes for prescribing medications	●	●	
affordability	the financial burden of SOF/VEL	●	●	●
	the financial burden of transportation cost			●
acceptability	patient's concern of adverse effect			●
	patient's concern of drug interaction			●
accessibility	stigmatization			●
	patients face inconvenience in traveling to hospitals	●		●
	inefficient HCV patient referral system	●		
patient's knowledge and awareness	limited awareness and inadequate knowledge about HCV treatment among patients.	●	●	●
healthcare providers' knowledge	insufficient knowledge among medical providers regarding the diagnosis and treatment of HCV	●		●
communication issues	lack of communication from healthcare provider			●
hospital system	limitations of small hospitals in conducting laboratory testing for diagnosing and treating HCV	●		
	inefficient HCV patient tracking system.	●	●	
	lack of widespread HCV screening.	●		●

8. Hospital system

Limitations of small hospitals in conducting HCV laboratory testing: Physician A mentioned limitations in laboratory testing at small hospitals. Necessary tests, such as HCV antigen, were difficult to access in small hospitals.

Inefficient tracking system for patients with HCV: Physician B pointed out that patients receiving a diagnosis with hepatitis C in the past might have been forgotten, leading to a lack of follow-up and treatment. Pharmacist A noted that some patients were lost to follow-up, and the hospital lacked any system to monitor whether the patients completed the treatment.

Lack of widespread HCV screening: Physician D recommended increasing community-level screening and raising public awareness of the virus. Patient J, who underwent community-level screening, proposed implementing a government policy for HCV screening in the community to enable more people to enter the treatment process.

Discussion

Effectiveness and safety of SOF/VEL

The results of the descriptive study indicate that SOF/VEL is an effective treatment for HCV, with an overall SVR12 rate of 90.8%. The high SVR12 rates

observed in this study are consistent with those reported in related studies at the rates of 90 to 100% with SOF/VEL treatment among patients with HCV genotypes 1 to 6 and various stages of liver disease (7-9, 20). The study also found that HCV genotype 1 exhibited the highest SVR12 rate (98.7%), consistent with that reported in related studies that HCV genotype 1 exhibited a high response rate to SOF/VEL treatment (9, 10, 20, 21). The research findings also indicate that patients with HCV genotype 3 responded well to SOF/VEL treatment with a high SVR rate of 92%. This outcome was consistent with those reported in related studies with similarly high SVR rates (22-25). Due to its association with a higher incidence of liver steatosis (26), fibrosis progression (27), and liver cirrhosis (28), HCV genotype 3 merits additional consideration.

This study found that HCV genotype 6 had lower SVR rates than those in the ASTRAL-1 clinical trial (20) and Wei et al.'s study (29). The SVR rate in our study was 80.7%, in contrast to 100 and 99.0% reported by ASTRAL-1 and Wei et al., respectively. Differences in genotype 6 subtypes might explain this discrepancy, but the specific impact of these subtypes on treatment response to SOF/VEL is currently understudied. Further research is needed to explore this. Another reason that may have contributed to the difference in effectiveness of SOF/VEL observed in real-world practice compared with that in clinical trials was the level of monitoring and follow-up by medical providers. In clinical trials, patients were closely monitored and supervised, which might have led to better adherence to the treatment regimen. This included closely tracking medication use and managing the other co-administered medications. However, in real-world settings, medical providers might not have the same level of close monitoring for each patient, which could have potentially affected treatment outcomes.

The SVR12 rate was higher among patients with in non-cirrhotic HCV than that among those with Child-Pugh class A or B cirrhosis, aligning with the result in existing studies (20, 29). Cirrhosis can potentially lower the drug response rate due to reduced liver drug concentration (30), necessitating early HCV detection and treatment to prevent advanced liver disease.

In our study, 8.1% of the 272 patients reported experiencing mild adverse events such as headaches, abdominal pain, fatigue, nausea, and rash, consistent with those in related studies (20, 31, 32). The incidence of adverse events reported in this study (8.1%) was lower than that reported in other clinical studies. For instance, a multi-center clinical trial by Curry et al. in 2015 (32) reported that 14% of patients experienced adverse events during their treatment with SOF/VEL.

Barriers to accessing SOF/VEL

The qualitative study identified 17 barriers to accessing SOF/VEL. Some fell under the ATM framework, while others were not included in the framework. Regarding the availability of SOF/VEL, the study indicated that inadequate SOF/VEL supply could delay treatment and negatively impact patient care. Other studies have raised concerns about the government's procurement and distribution system for the high cost medicines in E (2) access program under the NLEM. The E (2) access program required all three insurance schemes to provide subsidies for specific items of high cost medicines for patients meeting the eligibility criteria (33). Issues surrounding organizational structure, internal processes, and support systems make timely and adequate medication distribution challenging, often resulting in temporary shortages that undermine confidence among healthcare professionals. Furthermore, each health insurance scheme has varying regulations, reimbursement models, and support systems for the E (2) medication; thereby, increasing the complexity and workload for hospitals. Differences in medication authorization processes among schemes require extensive documentation, further complicating the management process for healthcare providers (34). The study highlights

medication procurement, distribution, prescribing complexity and challenges across hospitals. To address these issues, the government should refine the system. The National Health Security Office (NHSO) ought to review the medication reservation process and initial reserved quantities tailored to the needs of different healthcare facilities. Streamlining processes and reducing the number of involved units or departments could speed up procurement. Further barriers noted in similar studies encompass hospital capacity limitations, physician prescribing practices, and restrictive prescribing criteria (35, 36).

The study reveals that the patient's health coverage schemes influences SOF/VEL affordability. Under Thailand's universal coverage, Thai citizens can access NLEM-listed medications and healthcare services. However, ancillary costs, like transportation, can pose affordability barriers, as shown in Huan-Keat Chan et al.'s study in Malaysia (37). For non-Thai patients, barriers might include the cost of SOF/VEL and laboratory expenses, corroborating other studies linking lack of insurance to reduced HCV treatment access (38). As HCV can be transmitted via several routes, including blood and sexual contact, treating non-Thai patients is critical for Thailand's 2030 hepatitis C elimination goal (39). Government strategies should address screening, awareness raising, knowledge dissemination, and preventive measures for foreigners.

Regarding the acceptability of SOF/VEL, the study shows that while physicians perceive SOF/VEL as an effective and safe HCV treatment, patients' acceptability is often marred by concerns over potential adverse effects and drug interactions. This echoes findings from Grebely et al. (40), where fears about adverse effects deterred patients from initiating treatment. Comprehensive patient education, transparent communication, and detailed information about SOF/VEL's adverse effects and drug interactions are essential to address these concerns. Regular medication reviews using interaction databases can help identify and alleviate conflicts, enhancing treatment acceptance and adherence.

The study identifies patient-related stigmatization and travel inconvenience as barriers to accessibility. The findings aligned with those reported in related research (37). Stigma can deter patients from seeking HCV treatment, while those in remote areas may face travel-related challenges. Another obstacle lies in the inefficient patient referral system, which could delay SOF/VEL access. To mitigate these barriers, recommendations include improving geographic treatment access, possibly through establishing local treatment facilities, refining the referral system for timelier treatment access, and considering telehealth solutions, which have been successful in enhancing HCV treatment access in other studies, such as the study by Arora et al. (41).

The study emphasizes barriers to SOF/VEL access beyond the ATM framework, such as limited patient awareness and knowledge about HCV treatment and insufficient knowledge among healthcare providers about HCV diagnosis and treatment. These are consistent with related research findings (37, 42). These barriers underline the need for patient education and provider training. The lack of communication from healthcare providers was identified as another barrier in this study, which aligns with related research findings (35), stressing the need for comprehensive patient information about their conditions and treatment options.

Structural barriers, such as inefficiencies in patient tracking and insufficient HCV screening, echo earlier findings (37, 42), emphasizing the need for robust healthcare infrastructure, efficient tracking systems, and comprehensive screening programs. These elements are crucial for facilitating access to HCV treatment and ensuring early detection and timely intervention.

This study encountered some limitations that need to be considered. Firstly, it did not assess the long-

term outcomes of SOF/VEL treatment. Secondly, participants' varying health literacy levels may have influenced their understanding and responses to the survey. Thirdly, the study focused only on patients who completed treatment, potentially missing insights from those discontinuing treatment due to adverse events. Fourthly, adverse events were based on physician documentation, potentially leading to underreporting when patients did not deem them significant. This may have resulted in underestimated incidence rates. Lastly, recall bias is possible as patients relied on memory for their experiences with HCV treatment, affecting the accuracy and completeness of their responses.

Conclusions

In summary, the research findings affirm the effectiveness of SOF/VEL in suppressing the HCV and its high safety profile with minimal adverse effects. We identified 17 barriers to accessing SOF/VEL, namely, availability, affordability, acceptability, accessibility, and four other categories. To mitigate these barriers, we recommend several strategic measures. These encompass streamlining the medication procurement and distribution process, revising the criteria for medication prescribing, simplifying the process of dispensing medication, employing telemedicine services, facilitating convenient patient transportation, augmenting the expertise of healthcare professionals, implementing robust educational campaigns, establishing efficient centralized referral systems, and developing comprehensive screening programs. By integrating these measures, we aim to increase access to hepatitis C treatment and further the goal of eliminating HCV in Thailand.

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