


Research Article

Efficacy of Sofosbuvir/Daclatasvir in a Single Tablet for Treating Chronic Viral Hepatitis C

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Background. Published data regarding the real-life application of the combination sofosbuvir/daclatasvir in Algeria are lacking. Therefore, we conducted an observational study to assess the efficacy and safety of this regimen in Algerian patients with chronic hepatitis C. **Methods.** We carried out a multicentric, observational, open-label study to assess the efficacy and safety of the generic fixed-dose combination (FDC) sofosbuvir/daclatasvir in patients with chronic hepatitis C. We included 100 patients with all genotypes for 12 or 24 weeks of treatment without ribavirin. The primary outcome was the proportion of patients with a sustained virologic response (SVR) 12 weeks after treatment cessation. The secondary outcome assessed the safety and occurrence of adverse events. This study is registered with ClinicalTrials.gov identifier: NCT05138523. **Results.** The full analysis set included 99 patients with a mean age of 51.4 ± 14.4 years and a sex ratio of M/F = 0.86. Our patients were infected with HCV genotype 1b ($n = 47$), 2 ($n = 17$), 1a ($n = 3$), 2a/2c ($n = 2$), 3 ($n = 2$), and 4 ($n = 1$). A total of 27 patients had missing genotype data. Most patients were naive noncirrhotic ($n = 70$) and took 12 weeks of treatment, 19 patients had cirrhosis, of which 68.42% ($n = 13$) were classified as Child–Pugh A, and 5 patients were treatment-experienced. Both cirrhotic and treatment-experienced patients took 24 weeks of treatment. Efficacy analysis was conducted on 95 patients, and the results showed that 91 patients achieved SVR12 with a response rate of 95.8% (95% CI: 92–100%). Six adverse events occurred and were minor and manageable. **Conclusion.** Our results demonstrate the efficacy and safety of sofosbuvir/daclatasvir in single tablets in treating Algerian HCV patients without ribavirin for 12 or 24 weeks. The promising results of this study warrant further trials to assess the efficacy and safety of this combination in treating special populations.

1. Introduction

Hepatitis C infection is a serious global health threat with around 1.5 million new infections occurring per year [1]. In 2021, the World Health Organization (WHO) estimated that approximately 58 million people were chronically infected with the hepatitis C virus (HCV) [1]. The distribution of HCV genotypes depends on geographic locations. HCV genotype 1 is the most prevalent worldwide (49.1%), followed by genotypes 3 (17.9%), 4 (16.8%), and 2 (11.0%), while genotypes 5 and 6 are responsible for less than 5% of the cases [2]. In Algeria, HCV infection prevalence is estimated at 1% [3]. In the northeastern geographical region of Algeria, genotype 1b was reported as the predominant type (86.2%) [4, 5]. However, more epidemiological studies are required to assess the exact prevalence of hepatitis C in Algeria.

Most HCV patients (around 70%) will develop chronic HCV infection with a 15–30% risk of developing cirrhosis and a 1–4% risk of developing hepatocellular carcinoma (HCC) [6]. The introduction of interferon-free regimens has positively changed the safety and efficacy of HCV treatment. It has been established that a combination regimen of direct-acting antiviral agents (DAAs) provides a sustained viral response (SVR) to HCV infections in more than 95% of the cases [7–12].

Sofosbuvir is an oral direct-acting antiviral that targets and inhibits the NS5B polymerase of HCV with high potency and a safety profile and the potential to be used in combination with other antivirals. Daclatasvir is an inhibitor of the HCV protein NS5A and is used in combination with sofosbuvir (with or without ribavirin) for the treatment of naïve patients with HCV genotypes 1, 2, or 3 [12]. Daclatasvir, when combined with sofosbuvir, has consistently demonstrated remarkable efficacy in the treatment of chronic hepatitis C in a wide range of patient demographics, demonstrating its potential as an effective and safe therapeutic choice [7–17].

In 2018, Algeria's national guidelines incorporated both medications as separate forms to be used as a backbone therapy for chronic HCV patients and deemed first-line treatment. Following this, BEKER Laboratories®, an Algerian pharmaceutical company, developed a fixed-dose combination (FDC) that contains the two direct antiviral agents sofosbuvir (400 mg) and daclatasvir (60 mg) [16–18].

Later, Bristol Myers Squibb carefully considered the possible impact of stopping daclatasvir, which has been available since 2015, and decided that there would be no clinical impact given the availability of multiple recommended alternative HCV treatments. Daclatasvir was then discontinued due to marketing reasons and not because of any quality, safety, or effectiveness problems with the treatment [19, 20].

However, daclatasvir has been manufactured in several generic variants and is still widely available. In many low- and middle-income countries where the new pangenotypic DAA combinations are expensive and not available, it is advised by the international guidelines from the American

Association for the Study of Liver Diseases (AASLD), the Infectious Diseases Society of America (IDSA), and the European Association for the Study of the Liver (EASL) to continue using the cost-effective combination of sofosbuvir/daclatasvir [21–23].

Furthermore, the WHO Model List of Essential Medicines, which is designed to serve as a reference for nations or regional authorities in adopting or adapting therapies based on local priorities, supports the use of the combination of sofosbuvir and daclatasvir [24].

Although these individual drugs were already recommended in our national guidelines, the locally developed fixed-dose combination “Sofosdac®” and its efficacy and safety profile needed to be evaluated in the local context to assess the specific outcomes associated with this particular combination. Therefore, we conducted a multicentric, observational, open-label study to assess the efficacy and safety of the locally developed single-pill combination of sofosbuvir/daclatasvir in Algerian patients with chronic hepatitis C.

2. Patients and Methods

2.1. Study Design. This study was a multicentric, observational, prospective, cohort, open-label study to assess the efficacy and safety of the combination of sofosbuvir/daclatasvir (400 mg of sofosbuvir and 60 mg of daclatasvir) treatment in patients with chronic HCV. Eligible patients were recruited from 6 sites covering east, west, and central regions of Algeria: Centre Hospitalo-Universitaire Mustapha, Algiers, with two departments: hepatology and gastroenterology, Etablissement Public Hospitalier Nouvel Hôpital, Khenchela Department of Internal Medicine, Centre Hospitalier et Universitaire Benaouda Benzerdjeb, Department of Hepatogastro-Enterology, Oran, Etablissement Hospitalier Universitaire, Department of Hepatogastro-Enterology, Oran, and Etablissement Public Hospitalier Boufarik, Department of Infectious Diseases. The first patient in (FPI) date was 21 November 2019, and the last patient last visit (LPLV) was on 18 November 2020. Patients received the treatment as part of their routine medical care (noncirrhotic patients were prescribed one tablet daily for 12 weeks, and cirrhotic patients were prescribed one tablet daily for 24 weeks). We included 99 patients with HCV chronic infection and genotypes 1, 2, 3, and 4, in line with the study's inclusion and exclusion criteria. Patients were followed-up during the study until 12 weeks after the cessation of the treatment and for one year out of protocol.

2.2. Participants. Patients with the following eligibility criteria were included in this study: men and women aged 18 years and above with a confirmed HCV chronic infection, genotypes 1, 2, 3, 4, 5, or 6, and treatment-naïve or treatment-experienced (pegIFN-RBV failure, tritherapy 1st generation telaprevir and boceprevir, and sofosbuvir-pegIFN-RBV failure).

Fibrosis was evaluated either by noninvasive methods (fibro scan, fibrosis 4 score (Fib 4), and AST to platelet ratio index (APRI)) during the preinclusion period (of at least one month) or a liver biopsy puncture of at least 24 months before the inclusion visit. Fibrosis has been defined according to the METAVIR score: F0, F1, F2, F3, and F4. Also, compensated cirrhosis Child–Pugh A or decompensated cirrhosis has been included. Laboratory tests including liver function, WBC, hemoglobin, platelets, and creatinine were performed.

Patients with the following criteria were excluded: pregnant and/or breastfeeding females, patients unable to use effective masculine or feminine contraception during the study and 6 months after the end of treatment, patients with advanced cardiopulmonary pathology, malignant neoplasia, or performing haemodialysis, patients with levels of creatinine <30 ml/min, patients with HCC, patients with a personal or family history of torsade de pointes, patients using amiodarone, having QT prolongation >450 ms, and/or medications triggering conduction disturbances with long QT, 30 days before inclusion, patients allergic to nucleoside analogues, and patients who took anticonvulsants (carbamazepine, eslicarbazepine, fosphenytoin, phenytoin, oxcarbazepine, pentobarbital, phenobarbital, primidone, or the antimycobacterial agents: rifabutin and rifampicin) [16, 17]. All patients provided written informed consent.

2.3. Treatment Regimen. Sofosdac® single pills (including 400 mg of sofosbuvir and 60 mg of daclatasvir), developed by BEKER Laboratories®, an Algerian pharmaceutical company, were administered orally once daily. Noncirrhotic patients were prescribed one tablet daily for 12 weeks, and cirrhotic patients were prescribed one tablet daily for 24 weeks or for 12 weeks if administered with ribavirin. The latter was not prescribed due to its unavailability in the Algerian market.

2.4. Efficacy and Safety Monitoring. Patients were monitored through a clinical assessment and laboratory tests at D0, D7, D15, D21, W4, W8, W12, W24, and W36 of treatment initiation. Quantitative real-time PCR for HCV RNA was performed at 12 weeks after treatment to confirm SVR. The primary outcome was the proportion of patients with SVR12 weeks after treatment cessation. The rate of SVR12 and the 95% confidence interval were based on all evaluable patients and were also reported by the patients' group. Treatment failure was also reported. The secondary outcome was the assessment of the safety of FDC sofosbuvir/daclatasvir by reviewing the collected safety data. Adverse events were evaluated during the study at scheduled visits with laboratory tests, physical examinations, and electrocardiographic monitoring.

2.5. Statistical Analysis. The sample size was calculated using Epi Info and StatCalc software by the Centers for Disease Control and Prevention (CDC). Considering a marginal error of 5%, a confidence level of 95%, and a success rate of

95% (based on previous studies [8–15]), the minimum required sample size was 73 patients. By adding a 30% dropout rate to compensate for the loss of follow-up during the study follow-up period, the obtained sample size was 95 patients.

Following our local authorities' recommendation, we chose to include a total of 100 patients in the study. However, the full analysis set included 99 patients since one patient's file was lost. The efficacy analysis set included all patients who took at least one dose of the study medication and had an evaluable primary endpoint (viral load at week 12 posttreatment cessation). This set included 95 patients as four patients were lost to follow-up with no evaluable primary endpoint (SVR12).

Numerical variables were presented as the mean, standard deviation, minimum, and maximum if normally distributed. Nonnormally distributed data (e.g., laboratory results) were presented as a median and interquartile range. Counts and percentages were used to present categorical variables. SVR12 with a 95% confidence interval (95% CI) was calculated for the efficacy population (overall and per treatment group). The chi-square test (χ^2) was used to compare the rate of SVR12 achievement between the different subgroups. The Friedman test was used to compare the laboratory data throughout the three visits. All statistical tests were conducted considering a 0.05 level of significance. Statistical analysis was conducted using IBM-SPSS, version 28.

2.6. Ethics. The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki. Good Clinical Practice (GCP) Guidelines were followed during study conduction. Compliance with BEKER Laboratories® and regulatory standards provides assurance that the rights, safety, and well-being of patients participating in noninterventional studies are protected and consistent with the principles that have their origin in the Declaration of Helsinki and that the study data are credible and responsibly reported. The study was reviewed by the Independent Ethics Committee (IEC) of Centre Hospitalo-Universitaire (CHU) Mustapha. Eligible patients were only included in the study after providing written (witnessed, where required by law or regulation) informed consent approved by the General Department of Pharmacy and Health Equipment/Ministry of Health, Population, and Hospital Reform that complies with the International Council for Harmonisation ICH GCP guideline and regulatory requirements and is considered appropriate for this study. Informed consent was obtained before collecting any data described in this study protocol. Patients received the treatment as part of their medical routine prescription. This study is registered with ClinicalTrials.gov (ID: NCT05138523) and accessible at: <https://rb.gy/zblalq>.

3. Results

3.1. Patient Characteristics. A total of 100 patients with chronic HCV infection were enrolled in this study and received treatment at five different centers in Algeria

between November 21, 2019, and November 18, 2020. The efficacy analysis population included 95 patients as four patients were lost to follow-up with no evaluable primary endpoint (SVR12), and one patient's file was lost. More details about patients' disposition and distribution based on the prescribed treatment duration are shown in Figure 1.

The mean age of the study participants was 51.4 ± 14.4 years. The gender distribution was almost equal with a slightly higher rate of female participation (53.5%) with a sex ratio of M/F = 0.86. Out of 99 patients, 80 patients (80.8%) were noncirrhotic, and 19 patients (19.2%) were cirrhotic, of which 13 had Child–Pugh classification A. Most included patients were treatment-naïve, and only five patients were treatment-experienced (5.1%), with pegIFN-RBV failure ($n = 4$) or boceprevir-pegIFN-ribavirin failure ($n = 1$). A total of 72 patients had their genotypes tested. Most of them ($n = 47$) were infected with HCV genotype 1b, 3 had genotype 1a, 19 had genotype 2, two patients had genotype 3, and one patient had genotype 4. A total of 27 patients had missing genotype data. (See Table 1).

A total of ten patients (10.1%) reported alcohol consumption with a median (IQR) quantity of 140 (124) g/week. The reported duration of alcohol consumption ranged from 3 to 20 years with a median (IQR) duration of 5 (4) years. Almost one-quarter of the study population (25 patients, 25.2%) reported that they are current or previous tobacco smokers with a median (IQR) smoking duration of 11 (26.6) years. The most frequently reported methods of contamination included dental care (75 patients, 75.8%), while other methods were reported with varying frequencies. Most patients reported discovering their infection through systematic and preoperative blood testing, while other methods of HCV infection discovery were reported with less frequency.

3.2. Efficacy Results. The primary outcome of the FDC of sofosbuvir/daclatasvir treatment at 12 or 24 weeks was detected by SVR12, as shown in Table 2. There were 95 patients with an evaluable primary endpoint (viral load at week 12 posttreatment cessation). Four patients were lost to follow-up, and one patient's file was lost. Efficacy analysis was conducted on 95 patients, and the results showed that out of 95 patients, 91 patients achieved SVR 12 with a response rate of 95.8% (95% CI: 92–100%). The same response rate was achieved among the subgroup of patients who received sofosbuvir/daclatasvir tablets for 12 weeks (95.8%; 95% CI=91–100%) and among those who received the treatment for 24 weeks (95.8%; 95% CI= 87–100%).

Noncirrhotic naïve patients ($n = 70$) were treated for 12 weeks, and SVR12 was achieved in 67 patients (95.7%). Noncirrhotic and treatment-experienced patients ($n = 5$) and cirrhotic naïve patients ($n = 19$) were both treated with sofosbuvir/daclatasvir for 24 weeks without ribavirin. SVR12 was achieved in all five noncirrhotic and treatment-experienced patients (100%) and in 18 cirrhotic naïve patients (94.7%). The SVR12 rates of patients according to their cirrhosis status and treatment history are shown in Table 2.

In our study, four genotypes were present in the population. The majority of patients had genotype 1b ($n = 47$), and all achieved SVR12 with a response rate of 100%, followed by patients with genotype 2 ($n = 17$) whose response rate was 94.1%. The remaining patients with genotype 1a ($n = 3$), 2a/2c ($n = 2$), 3 ($n = 2$), and 4 ($n = 1$) responded to treatment with a response rate of 66.7%, 50%, 50%, and 100% respectively. A total of 27 patients had missing genotype data; however, 23 of them achieved SVR12 with a response rate of 95.8%. SVR12 rates for genotypes are shown in Table 3.

3.3. Safety Results. Throughout the study treatment and follow-up period, a total of 6 adverse events were reported by 3 patients (with an attack rate of 6.1% and an incidence rate of 3.0%). The adverse events were vertigo, digestive hemorrhage, oesophageal varices rupture, asthenia, headache, and retinal bleeding. Out of these 6 events, two events (oesophageal varices rupture and retinal bleeding) were considered serious but not associated with the treatment. The final outcome of the six events was positive.

Patients were monitored through a clinical assessment and laboratory tests at D0, D7, D15, D21, W4, W8, W12, W24, and W36 of treatment initiation. Laboratory tests including liver function, WBC, hemoglobin, platelets, and creatinine are shown in Table 4.

However, being an observational trial, our study did not require clinical assessment, and not all patients turned in their laboratory results, which left a lot of missing data.

Due to the missing data at week 24, no significant results can be reported for noncirrhotic patients (both naïve and pretreated).

Cirrhotic patients ($n = 19$) presented with median ALT results of 78.5 at D0. At W24 after treatment initiation, the ALT median dropped to 24.1 and stabilized at 29.7 at W36 posttreatment ($p < 0.005$).

As shown in Table 4, the results for the remaining tests (WBC, hemoglobin, platelets, and creatinine) were not statistically significant.

4. Discussion

We assessed the efficacy and safety of a generic fixed-dose combination of sofosbuvir 400 mg/daclatasvir 60 mg in naïve and treatment-experienced patients with genotypes 1, 2, 3, and 4 for 12 or 24 weeks without ribavirin. We found that the sofosbuvir/daclatasvir regimen was safe and effective in achieving SVR12 with a response rate of 95.8% in Algerian patients with chronic HCV. These results are in accordance with those of previous studies that reported a high sustained viral response rate (>95%) for the combination of sofosbuvir/daclatasvir in patients with chronic HCV [8–15]. A comparable response rate is observed for other antiviral treatments currently used [25].

We observed no significant adverse effects among our patients' group with only 6 events reported by 3 patients that were minor and manageable. Several other studies reported a low rate of adverse events in patients using the

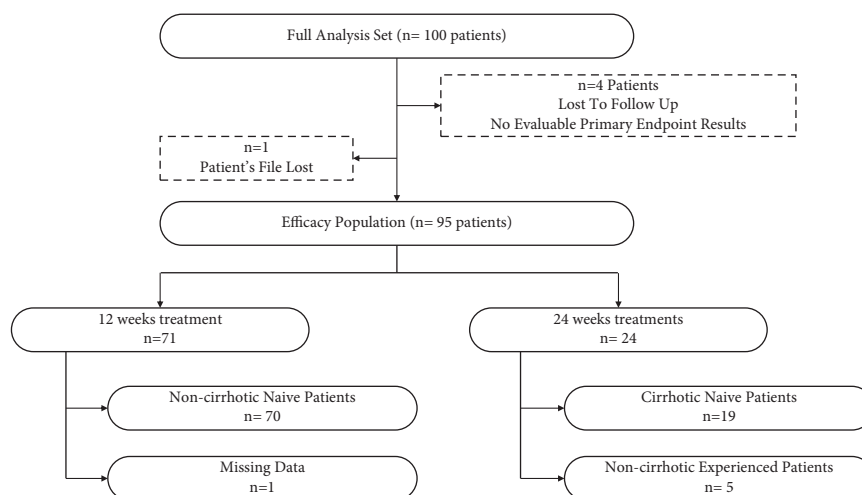


FIGURE 1: Patients' disposition.

TABLE 1: Baseline demographic characteristics and laboratory data of the study patients.

Age	Mean	SD
	51.4	14.4
Variables	Number (n = 99)	%
<i>Sex</i>		
Female	53	53.5
Male	46	46.5
<i>Genotype</i>		
1a	3	03.03
1b	47	47.47
2	17	17.17
2a/2c	2	2.0
3	2	2.0
4	1	1.0
Missing data	27	27.27
<i>Liver status</i>		
Cirrhotic	19	19.19
Noncirrhotic	80	80.80
<i>Fibrosis score</i>		
F4	19	19.19
<i>History of treatment</i>		
Treatment-naïve	93	93.93
Treatment-experienced	5	05.05
<i>Medical history</i>		
Obesity	24	24.2
Diabetes	17	17.2
<i>HBV results</i>		
Positive	1	01.01
Negative	98	98.98
<i>Laboratory data (mean ± SD)</i>		
ALT (IU/L)	54.41 (50.3)	—
WBC ($\times 10^3$)/mm ³	7.06 (4.8)	—
PN	4.8 (7.5)	—
Hb (g/dL)	13.5 (1.9)	—
Platelet ($\times 10^3$)/mm ³	223.05 (75.6)	—

combination of sofosbuvir/daclatasvir [8–13]. In our study, one patient reported vertigo and asthenia which are considered common side effects of the treatment. The second patient experienced digestive hemorrhage through rupture of oesophageal varices secondary to portal hypertension

which was not related to the used treatment. The third patient reported the common side effects of vertigo and headache but also experienced blurred vision and retinal bleeding secondary to incidental findings of arterial hypertension which is not related to the regimen used in the

TABLE 2: Variables associated with an SVR rate: cirrhosis status and treatment history.

Variables	Count	SVR (<i>n</i>)	SVR (%)
Noncirrhotic naive patients	70	67	95.7
Cirrhotic naive patients	19	18	94.7
Noncirrhotic experienced patients	5	5	100
Missing data	1	1	100
Total	95	91	95.8

SVR, sustained viral response.

TABLE 3: Sustained virological response (SVR) by genotype.

Genotypes	Count	SVR (<i>n</i>)	SVR (%)
1a	3	2	66.7
1b	47	47	100
2	17	16	94.1
2a/2c	2	1	50
3	2	1	50
4	1	1	100
Missing data	27	23	95.8

SVR, sustained viral response.

TABLE 4: Clinical assessment and laboratory tests.

Laboratory tests	<i>n</i>	Day 0		<i>n</i>	Week 24		<i>n</i>	Week 36		<i>P</i> value
		Median	IQR		Median	IQR		Median	IQR	
<i>Naïve noncirrhotic patients</i>										
ALT	68	36.50	25.53	26	15.00	12.50	2	20.65	.	1.000
WBCs	65	5800.00	6575.82	25	7500.00	2985.00	2	12290.00	.	0.223
Hemoglobin	67	13.50	2.40	25	13.50	2.50	2	12.50	.	0.607
Platelets	68	213500	248925	25	254000	134550	2	305000	.	1.000
Creatinine clearance	17	66.20	92.1415	6	9.38	3.11	1	—	—	0.368
<i>Naïve cirrhotic patients</i>										
ALT	19	78.50	71.31	18	24.00	19.30	12	29.75	17.30	0.005
WBCs	19	5490.00	2560.00	18	5265.00	2285.00	12	6170.00	2343.00	0.076
Hemoglobin	19	13.40	3.30	18	13.20	2.10	12	14.00	1.80	0.920
Platelets	19	156000	98000	18	151500	95550	12	197000	107750	0.529
Creatinine clearance	13	10.01	84.21	8	11.53	85.22	7	10.15	4.25	0.022
<i>Pretreated noncirrhotic patients</i>										
ALT	5	32.40	25.01	3	16.60	.	3	16.40	.	0.097
WBCs	5	7470.00	6255.00	3	9820.00	.	3	8400.00	.	0.717
Hemoglobin	5	16.30	2.55	3	15.30	.	3	14.60	.	0.097
Platelets	5	268000	139000	3	276000	.	3	285000	.	0.717
Creatinine clearance	—	—	—	—	—	—	—	—	—	—

study. The three patients finished their treatment and achieved SVR12.

Many clinical studies proved that the combination of sofosbuvir/daclatasvir is pangenotypic [8–10, 13]. In Algeria, we lack data on HCV prevalence; however, it has been estimated that 1% of the population might carry HCV, with genotype 1b as the most prevalent, especially in the northeastern regions of the country [3–5].

Genotype 1b was the most prevalent in our study and was carried out by 47 patients who achieved SVR12 with response rates of 100%. The second most prevalent type in our study was genotype 2 (*n* = 17) with a reported SVR12 of 94.1%. Other studies report a similar response rate for these two genotypes [8–10, 13]. Taken together, our results

confirm the pangenotypic potential of the FDC of sofosbuvir/daclatasvir in Algerian patients with chronic HCV; however, further studies are needed with a higher number of patients with all genotypes to support these findings.

Most of our patients were noncirrhotic naive patients (*n* = 70) and followed 12 weeks of treatment achieving a response rate of 95.7%. Two noncirrhotic naive patients who presented with an F2 level of fibrosis were prescribed a 24-week regimen as per the investigator's recommendation and achieved SVR12. In our study, cirrhotic patients (of which the majority were classified as Child–Pugh A) followed a 24-week regimen without ribavirin due to its unavailability in the Algerian market and achieved high SVR12 with a response rate of 94.7%. Cirrhosis is not strongly

associated with treatment failure but with a lower rate of SVR [9]; however, it was not the case in our study which can be explained by the low number of patients in this group. Nonetheless, these results support the efficacy of the FDC of sofosbuvir/daclatasvir in cirrhotic patients without ribavirin which will spare patients from its numerous side effects [14, 15].

Furthermore, an alanine aminotransferase (ALT) increase is common with chronic HCV infection and is linked to necroinflammation; nevertheless, up to 25% of patients consistently maintain normal ALT values [26]. Following DAA therapy, ALT values return to normal, as a result of a high SVR. Previous studies showed comparable SVR rates for patients presenting normal and elevated ALT while using DAAs, which is similar to what was observed for patients treated with interferon [27]. In our study, cirrhotic patients presented with elevated ALT levels that significantly decreased after treatment initiation and stabilized post treatment ($p < 0.005$).

We reported two particular cases of cirrhotic patients who deviated from the protocol and took only 12 weeks of treatment yet achieved SVR12.

Our study included only five noncirrhotic treatment-experienced patients who took 24 weeks of treatment and achieved SVR12 with a response rate of 100%. Treatment-experienced patients are known to respond less to treatment and require the addition of ribavirin, which was not the case in our study [14, 15, 28]. However, the low number of patients in this category is not significant to support the high response rate of this group.

The sanitary conditions during the COVID-19 pandemic prevented some patients from attending scheduled consultations which led to protocol deviations. However, we report the results for the total efficacy population who have evaluable postdose efficacy endpoint (SVR12) to reflect real-life scenarios and provide unbiased efficacy outcomes.

In many low- and middle-income countries, the new pangenotypic DAA combinations are expensive and not available [13, 18, 29–32]. Therefore, the combination of generic forms of sofosbuvir/daclatasvir is often used as a first-line treatment, and international guidelines support its use as a cost-effective alternative [22–24].

In Africa, HCV is a substantial public health problem, with prevalence rates varying greatly throughout the continent, ranging from 1 to 1.6% in some areas to more than 10% in others [33, 34]. Thus, to evaluate the effectiveness of DAAs in this local setting, it is crucial to consider the experience of African countries with these treatments [18, 32, 34–37].

With one of the highest HCV prevalences, Egypt doubled its efforts to achieve HCV control using several DAA regimens [32–38]. Many clinical trials sought to assess the efficacy and safety of the combination of sofosbuvir/daclatasvir in the country, and the findings reported the high effectiveness and tolerance of the combination in the treatment of chronic HCV [30, 31, 36, 38, 39]. Moreover, a generic combination of sofosbuvir-daclatasvir proved to be safe and is associated with a high SVR12 rate in Egyptian patients with chronic HCV [29, 32].

In 2016, WHO planned an ambitious program to eliminate viral hepatitis by 2030, through national screening campaigns and treatment implementation programs [1, 32, 35, 40]. To join in these efforts, Algerian sanitary authorities and the medical community established a national guideline for the treatment of HCV and HBV and adopted the locally developed fixed-dose combination “Sofosdac®” as the backbone therapy for HCV patients which is considered a cost-effective, pangenotypic treatment used in resource-limited countries [24, 41]. Since 2018, Algeria have conducted periodic HCV screening campaigns, and with the availability of a pangenotypic therapy that does not require genotyping testing, patients may now get treatment swiftly, allowing Algeria to meet WHO goals by 2030.

5. Conclusion

Our observational study supports the safety and efficacy of pangenotypic FDC sofosbuvir/daclatasvir in treating Algerian HCV patients with an SVR12 response rate of 95.8%. Nonetheless, the lack of data on HCV in Algeria require further studies to estimate the prevalence. Furthermore, our study did not include difficult-to-treat patients and special populations. The promising results of this study warrant further trials to assess the efficacy and safety of the FDC of sofosbuvir/daclatasvir in treating these patients and to better assess the prevalence of HCV in Algeria.

Data Availability

The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

Disclosure

The results of the study were presented as oral communication at the 33rd National Conference of SAHGEED (Algerian Society of Hepato-Gastro-Enterology and Digestive Endoscopy) [42], as well as in the conference (Uruguay without hepatitis C- Hepcity Free Cities program) on 29th March 2022 [43]. A poster of the study was presented in the virtual event of the World Hepatitis Summit on June 2022 [44].

Conflicts of Interest

N.D. has served as a principal investigator for BEKER Laboratories®. A.S.M.B., I.B., L.N., and S. Helal are employees of BEKER Laboratories®. Statistical support for this study was provided by Maha Abulfetoh from PRU (Pharmaceutical Research Unit PRU, Jordan). The study drug was provided by BEKER Laboratories® as a donation. All the other authors declare no conflicts of interest.

Authors' Contributions

N.D., S. B, C.M., N.A., S. Hemmam., M.Y., A.S.M.B., I.B., L.N., and N. Afredj. designed the study. N.D., S.B., C.M.,

N.A., S. Hemmam., M.Y., A.T., N.G., R.K., I.O.C., O.D., H.A.B., S.G., I.F., A.K.L., M.K., and N. Afredj. helped with patient management and care. S. Helal wrote the first draft of the manuscript. N.D. and A.S.M.B. helped with the preparation of the manuscript. All the authors confirmed the final published version.

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