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## Research Article

# Daclatasvir Plus Sofosbuvir With and Without Ribavirin for Previously Treated or Untreated Chronic HCV Infection Genotype 1, 2 and 4 in Togo

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### ABSTRACT

**Background:** Daclatasvir (DCV) is a potent, pangenotypic nonstructural protein 5A inhibitor with demonstrated antiviral efficacy when combined with sofosbuvir (SOF) with or without ribavirin (RBV) in patients with chronic hepatitis C virus (HCV) infection. We are using SOF-DCV combination for large scale treatment.

**Objectives:** The aim of the current study was designed to investigate the efficacy and safety of sofosbuvir/daclatasvir, with or without ribavirin for previously treated or untreated in treatment of HCV genotype 1, 2 and 4, as well as their effect on the liver fibrosis.

**Methods:** One hundred twenty-seven patients with chronic HCV infection were categorized into 2 groups. The group 1 comprised treatment naïve patients, with total serum bilirubin  $\leq 1.2\text{mg}/10^{-1}\text{L}$ , serum albumin  $\geq 3.5\text{g}/10^{-1}\text{L}$ , ALAT  $\geq 3\text{N}$ , ASAT  $\leq 2\text{N}$  and platelets count  $150 \times 10^9/\text{L}$ . The group 2 included Peg-INF- $\alpha$  or sofosbuvir treatment-experienced patients or patients having at least 2 of the following characteristics: total bilirubin  $\leq 1.2\text{mg}/10^{-1}\text{L}$ , serum albumin  $\geq 3.5\text{g}/10^{-1}\text{L}$ , ALAT  $\geq 3\text{N}$ , ASAT  $\leq 2\text{N}$  and platelets count  $150 \times 10^9/\text{L}$ . The first group was treated with sofosbuvir/daclatasvir for 12 weeks except sofosbuvir treatment experienced patients, who were treated with sofosbuvir/daclatasvir + ribavirin for 24 weeks, with generic medications: DCV 60 mg plus SOF 400 mg  $\pm$  ribavirin (RBV) within the treatment of hepatitis C virus infection. Efficacy and safety were assessed, and baseline factors associated with sustained virological response at post-treatment week 12 (SVR12) were explored.

**Results:** Sustained virological response (SVR12), was 95,8% in group 1 and 93,8% in group 2. Such high efficacy was accompanied with tolerable adverse effects as well as with significant improvement in liver fibrosis.

**Conclusion:** SOF plus DCV with or without ribavirin achieved high efficacy and safety in HCV genotypes 1,2 and 4 patients. Their effect was accompanied with attenuation of liver fibrosis. Further wider-scale studies are needed to evaluate the actual role of IL 18 polymorphism in treatment response with Sofosbuvir/Daclatasvir.

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## Background

Chronic hepatitis C infection is a major public health problem with an estimated 71 million people chronically infected with hepatitis C worldwide and it is the most common cause of hepatocellular carcinoma (HCC), with an annual incidence of HCC is approximately 3-8% in patients with cirrhosis [1-3]. The availability of highly effective direct-acting antivirals (DAAs) with excellent safety profiles, even in with advanced hepatic fibrosis and liver cirrhosis has completely revolutionized the treatment landscape of patients with CHC and led to the treatment of patients with CHC being dramatically scaled up in last years [3]. The goal of antiviral treatment is to eradicate the virus, defined as a viral RNA that is undetectable [2, 4-7]. There is considered to be a sustained viral response (SVR), if this RNA remains undetectable 12 weeks after ceasing treatment (SVR12) [6, 8]. Sofosbuvir (SOF) is a nucleotide analogue inhibitor of HCV NS5B polymerase with activity against all HCV genotypes [9]. Daclatasvir (DCV) is a potent, pan-genotypic inhibitor of the HCV NS5A protein [10]. The aim of the current study was designed to investigate the efficacy and safety of sofosbuvir/daclatasvir, with or without ribavirin for previously treated or untreated in treatment of HCV genotype 1, 2, and 4, as well as their effect on the liver fibrosis.

## Methods

### I Patients

A total of 127 patients having chronic HCV genotype 1, 2 and 4 infections, who were scheduled to receive combined Sofosbuvir/daclatasvir with or without ribavirin, were chosen from NGO ASADH (Association Sauvons l'Afrique Des Hépatites). All patients volunteered to participate in the study and were prospectively followed up for the full duration of the study, which was 3 months during which the patients were evaluated every 4 weeks. Patients were subjected to thorough history taking, clinical examination and laboratory investigations including serum transaminases, total serum albumin, bilirubin, platelets, as well as abdominal ultrasound. Eligible patients had chronic infection with genotype 1, 2 and 4 HCV, aged between 20 and 80 years, with plasma HCV RNA  $\geq \log 5.8$ . Exclusion criteria included patients co-infected with HBV and HIV.

### II Study Design

This work was conducted conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained from all patients. Patients were categorized into 2 groups; group 1 was characterized by being treatment-naïve patients with total serum bilirubin  $\leq 1.2\text{mg}/10^{-1}\text{L}$ , serum albumin  $\geq 3.5\text{g}/10^{-1}\text{L}$ , ALT  $\geq 3\text{N}$ , AST  $\leq 2\text{N}$  and platelets count  $150 \times 10^9/\text{L}$ . Group 2 included Peg-INF-alpha or sofosbuvir treatment-experienced patients and at least two of the following: total bilirubin  $\leq 1.2\text{mg}/10^{-1}\text{L}$ , serum albumin  $\geq 3.5\text{g}/10^{-1}\text{L}$ , ALT  $\geq 3\text{N}$ , AST  $\leq 2\text{N}$  and platelets count  $150 \times 10^9/\text{L}$ . Group 1 Patients were treated with sofosbuvir/daclatasvir for 12 weeks, treatment experienced patients, were treated with sofosbuvir/daclatasvir + ribavirin for 24 weeks. The effect of therapies on liver fibrosis was assessed by fibrosis score 4 (FIB-4), a noninvasive technique employing

4 parameters according the following equation:  $\text{Age}(\text{years}) * \text{AST}(\text{UI/L}) / (\text{platelets count}(10^9/\text{L}) * \sqrt{\text{ALT}}(\text{UI/L})$  [11]. Both sofosbuvir and daclatasvir were administered, orally once daily in a dose of 400 mg and 60 mg, respectively. The dose of ribavirin was 800-1000 mg in divided doses according to patient tolerability. The treatment regimen was in consistence with the protocol of the guidelines of European Association for the Study of liver (ESAL).

### III Assessment of Virological Response

Virological response was assessed by HCV-RNA PCR using commercial laboratory in (Paris) France, which has an LLOQ of 15UI/mL. HCV-RNA PCR was done at 4 weeks as well as at 12 weeks after the end of treatment. If HCV-RNA was undetectable 12 weeks after the end of treatment, the patient was considered to have SVR12. Virologic relapse was defined as the presence of serum HCV-RNA  $\geq 15\text{UI}/\text{mL}$  at any time during post-treatment follow-up period. Treatment failure was defined as inability of the patient to complete the treatment regimen due to intolerance of adverse effects.

### IV Assessment of Drugs Safety

Safety data were collected monthly during treatment and 4 weeks after stoppage of treatment. Collected data reported the adverse events and clinical laboratory tests, as liver function tests, serum creatinine and complete blood count.

### V Assessment of Liver Fibrosis

Liver fibrosis was assessed in all studies patients using FIB-4 test before starting the treatment and at 12 weeks after the end of therapy.

### VI End Points and Statistical Analysis

Primary endpoint was SVR12 defined as HCV RNA below the lower limit of quantification (LLOQ) or undetectable at least 12 weeks after treatment was discontinued. The collected data were revised, organized tabulated and statistically analysed using statistical package for social sciences (SPSS) version 21 (IBM Corporation, Armonk, NY, USA). All patients who started the protocol were included for the efficacy of the analysis. Data were presented as the mean  $\pm$  standard deviation (SD), mean  $\pm$  standard error of mean (SEM), frequency and percentage. Chi-square and Fisher's exact test were used for comparison of categorical data. Description analysis was performed to compare genotype frequency using the Chi-square test for qualitative data and mean  $\pm$  SD for quantitative data. Odd ratios (OR) were calculated where and when applicable. Results were considered statistically significant when the p-value was less than 0,05.

## Results

### I Baseline Characteristic of the Patients

This study included 127 patients, where 96 patients were allocated in the group 1 and 32 in the group 2. The mean age was  $47,8 \pm 9,6$  in group 1 and  $45,6 \pm 11,5$  in group 2. Concerning the gender 60 were female and 67 were male with ratio sex 1.1, From the total number of patients 7 had

diabetes, 10 had hypertension, 7 had previously received interferon-alpha based therapy, 4 had previously received sofosbuvir + ribavirin therapy. For viral load ( $\log_{10}$ IU/mL), the mean was  $5,81 \pm 0,76$  in group 1 and  $5,84 \pm 0,69$  in group 2. The genotype 2 unknown subtype was

predominating 28,4%, followed by genotypes 2a (23,2%), genotypes 2a/2c (16,8%). 2 cases of cirrhosis were detected in group 2. For fibrosis score, 14 had mild fibrosis and 16 had moderate fibrosis (FIB-4 < 1.45), 2 had severe fibrosis (FIB-4 > 3.25).

**Table 1:** Demographic data and baseline characteristics.

Characteristic	SOF+ DAC (n= 95)	SOF+DAC+RBV (n= 32)
<b>Demographic characteristics</b>		
Age (M, SD)	47,8 ± 9,6	45,6 ± 11,5
Male, n (%)	50 (52,6%)	17 (53,1%)
Diabetes n (%)	4 (4,2%)	3 (9,4%)
Hypertension, n (%)	9 (9,5%)	1 (3,1%)
<b>HCV disease-related characteristics</b>		
Traitement naïve, n (%)	94 (98,9%)	-
Treatment-experienced, n (%)	-	7 (21,9%)
<b>Genotype, n (%)</b>		
1	1 (1,1%)	3 (9,4%)
1a	8 (8,4%)	2 (6,3%)
1b	9(9,5%)	4 (12,5%)
2a	22 (23,2%)	10 (31,3%)
2b	4 (4,2%)	-
2a/2c	16 (16,8%)	6 (18,8%)
2c	1 (1,1%)	1 (3,1%)
2d	1 (1,1%)	-
2e	1 (1,1%)	-
2m	2(2,1%)	-
Unknown genotype	1 (1,1%)	1(3,1%)
2 unknown subtype	27 (28,4%)	4 (12,5%)
4	2 (2,1%)	1 (3,1%)
Plasma VHC RNA, $\log_{10}$ IU/ml, (M, SD)	5,81±0,76	5,84±0,69
<b>Cirrhosis, N (%)</b>		
Absent	30 (31,6%)	4 (12,5%)
Not reported	65 (68,4%)	26 (81,3%)
Present	-	2 (6,3%)
ALT (M, SD)	46,3±33,7	43,2±24,8
AST (M, SD)	43,2±35,4	42,2±38,4
Albumin (M, SD)	53,7±10,2	49,2±10,8
Total Bilirubin (M, SD)	11,7±1,4	11,9±0,4
Platelets count (M, SD)	155±342	159±321

## II Effect of Sofosbuvir/Daclatasvir with or without Ribavirin on Virological Response

In the group 1, 91 patients (95,8%) achieved SVR12 while 30 (93,8%) achieved SVR12 in the group 2 (Table 2). Both protocols, 121 patients (95,3%) achieved SVR12 while 2 patients relapse within 4 weeks' post treatment. Four patients didn't complete the study; 2 patients from each

of the first and second group, but were included in the statistics, one of them had severe fibrosis and developed hepatic decompensation one month after initiation of therapy, she was a female. There were 6 relapsers, 4 in group 1 and 2 in the group 2. Four of the relapsers were males and two were females. Two of the relapsers had moderate fibrosis (pre-treatment), 4 had severe fibrosis (pre-treatment) and one patient was diabetic and hypertension.

**Table 2:** Virological response among studied population, Total n=127.

Studied group	Regimen of treatment	Total No.	SVR 12	Relapsers plus patients stopped treatment
Group 1	SOF/DAC	95	91 (95,8%)	4 (4,2%)
Group 2	SOF/DAC+RIB	32	30 (93,8%)	2 (6,2%)

### III Safety of Sofosbuvir/Daclatasvir with or without Ribavirin

In group 1 and group 2, the reported adverse events were fatigue (20% and 21,9%), headache (16,8% and 31,3%), Dizziness (16,8% and 3,1%), fever (9,5% and 9,4%), insomnia (8,4% and 15,6%), in group 2 patients had a serious adverse effect. In both groups, we did not noted death, respectively (Table 3). The results of our study showed that only 6 patients (out of 127) did not reach SVR12. Four patients didn't complete

the study; 2 patients from each of the first and second group, but were included in the statistics, one of them had severe fibrosis and developed hepatic decompensation one month after initiation of therapy, she was a female. There were 6 relapsers, 4 in group 1 and 2 in the group 2. Four of the relapsers were males and two were females. Two of the relapsers had moderate fibrosis (pre-treatment), 4 had severers fibrosis (pre-treatment) and one patient was diabetic and hypertension.

**Table 3:** Side effect among studied group.

Parameters	SOF+ DAC (n= 95)	SOF+DAC+RBV (n= 32)
<b>Patient with any adverse effect</b>	19 (20,0%)	3 (9,4%)
<b>Patient with a serious adverse effect</b>	0 (0%)	4 (12%)
<b>Death</b>	0 (0%)	0 (0%)
<b>Anorexia</b>	6 (6,3%)	5 (15,6%)
<b>Fatigue</b>	19 (20,0%)	7 (21,9%)
<b>Fever</b>	9 (9,5%)	3 (9,4%)
<b>Insomnia</b>	8 (8,4%)	3 (9,4%)
<b>Headache</b>	16 (16,8%)	3 (9,4%)
<b>Dizziness</b>	16 (16,8%)	1 (3,1%)
<b>Decreased hemoglobin (&lt;10 g/dL)</b>	2 (2,1%)	7 (21,9%)
<b>Increased serum bilirubin</b>	6 (6,3%)	30 (93,8%)

### Discussion

Hepatitis C virus (HCV) infection accounts for the most common cause of chronic liver disease [12]. It can be associated with many several hepatic and extrahepatic disorders. Of patients with chronic infection, many develop cirrhosis and HCC. Before 2011, the standard antiviral therapy was pegylated interferon-alpha and RBV for 24-48wk [6, 13]. After a few years, unremitting research had led to the discovery of several DAA<sub>s</sub> that target several molecular targets. DAA-based regimens can greatly increase the efficacy and shorten the duration of HCV therapy. Since about 2015, DAA<sub>s</sub> have had access to the (Togolese market), and (Togolese patients) with hepatitis C have been treated with legal DAA regimens. Since this is such a short amount of the time, the real-world data on the use of DAA drugs in (Togo) has not been sufficient [14].

This study is a large, prospective, real-world study evaluating the efficacy and safety of sofosbuvir plus daclatasvir, with or without ribavirin regimens in patients infected with genotype 1, 2, and 4 observed from 2015 to 2019. A total of 127 patients have received the treatment based of generic DAA<sub>s</sub> and allocated in two groups (1 and 2). We noticed that in our study, the patients have the same years old, and most of the patients had the genotypes 2, which basically reflects the prevalence of the genotypes among HCV circulated in Togo [15]. We constated that, patients with the higher viral load (> 6 log) had more than 50 years old. Also, we found that the patients with cirrhosis were not old and were allocated in group 2. One of them had higher levels of ALT, AST, total bilirubin and mild fibroses score 4, diabetes. The had lower levels of platelets, albumin and viral load.

The results of this study suggest that sofosbuvir/daclatasvir with or without ribavirin were successful in treating pan-genotypes [16, 17]. Ninety fifty percent of the patients reached the primary endpoint of

SVr12 in either naïve or treatment-experienced patients. In the Abdel-Aziz *et al.* study, the demonstrated this same SVR12 but in this study the work with patients with genotypes 4 [11]. The SVR rates were consistently high in all the two groups: (95,8%) for the naïve and (93,8%) for the treatment-experienced patients. No statistically significant different in SVR was found among patients' groups (1 and 2) with different genotype and with different liver statuses. In other study, of HCV genotype, two clinical trials had evaluated the effect of sofosbuvir in combination with daclatasvir, one was for treatment-naïve patients with HCV genotype, 1,2 and 3 which reported that SVR12 was 100% of the patients had genotype 1 and 86-100% in patients with genotype 2 and 3, this study similar to ours, although we did not study genotype 3 [18].

In our study, the safety profiles of sofosbuvir/daclatasvir with or without ribavirin therapy. In patients who completed the study, there were no clinically significant treatment-emergent adverse events in patients receiving sofosbuvir/daclatasvir without ribavirin. The low incidence of adverse event might attribute, at least in part, to short duration of treatment as compared to INF-based therapy. In patients receiving sofosbuvir/daclatasvir +ribavirin, increased serum bilirubin and decreased hemoglobin were related to ribavirin drug. These findings previously reported by Abdel-aziz *et al.*, and Wu *et al.*, suggested that ribavirin is a triggering factor of hemolytic anemia [11, 19]. On the other hand, the current study reported that 2 patients from developed hepatic decompensation one month after initiating therapy, such findings were supported by Dyson *et al.*, who suggested a possible hepatotoxic effect caused by an unknown interaction or reaction to the drug combination; though the association with the DAA was not proven [20].

These results indicated that close monitoring is essential while on DAA therapy; especially in patients with advanced liver disease [11]. Daclatasvir is eliminated by hepatic metabolism and direct biliary

excretion with 88% being excreted in faeces. Biliary excretion of these drug could be impaired in the setting of advanced liver disease or secondary to a bile transporter defect. This potential mechanism needs further evaluation [21]. This study had a limitation. However, our study provided data from the real-life experience of using DAAs in Togo and confirmed the safety and efficacy, thus providing physicians with the data needed for potential positive treatment outcomes.

## Conclusion

The data of this study are encouraging, the combination of sofosbuvir plus daclatasvir, with or without ribavirin is an important option for use in treatment-naïve or treatment experienced patients with chronic HCV genotype 1,2 and 4 infection. The SVR12 achieved high efficacy (more than 94%) and well tolerated in the genotype. View this SVR rates, it should prompt to use of next generation regimens. Real-world data are consistent with the efficacy and tolerability profile of sofosbuvir plus daclatasvir with or without ribavirin seen in clinical trials.

## Limitations

The effect of tested drugs on liver fibrosis was limited because liver biopsy in the standard test for accurate assessment of liver fibrosis. Further studies are essential to confirm such results. Also, we don't do the viral load in Togo to the strains, it will do in commercial laboratory in France.

## Author Contributions

Study concept and design: Folly Anyovi, Simplice D. Karou, Jacques Simpore. Analysis and interpretation of data: Folly Anyovi. Critical revision: of the manuscript for important intellectual content: Reham Soliman, Gamal Shiha.

## Conflicts of Interest

None.

## REFERENCES

- World Health Organization. WHO. Global hepatitis report (2017) Geneva.
- Pawlotsky JM, Negro F, Aghemo A, Berenguer M, Dalgard O et al. (2016) EASL Recommendations on Treatment of Hepatitis C 2016. *J Hepatol* 69: 461-511. [[Crossref](#)]
- Galle PR, Forner A, Llovet JM, Mazzaferro V, Piscaglia F et al. (2018) EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol* 69: 182-236. [[Crossref](#)]
- Kohli A, Shaffer A, Sherman A, Kottlilil S (2014) Treatment of Hepatitis C. *JAMA* 312: 631-640. [[Crossref](#)]
- Hessel MHM, Cohen AF, Rissmann R (2016) Sofosbuvir and daclatasvir. *Br J Clin Pharmacol* 82: 878-879. [[Crossref](#)]
- González G R, Jiménez P M, González A C, Mostazo T J (2016) New approaches in the treatment of hepatitis C. *World J Gastroenterol* 22: 1421-1432. [[Crossref](#)]
- Castells L, Llaneras J, Campos Varela I, Bilbao I, Crespo M et al. (2017) Sofosbuvir and Daclatasvir in Mono- and HIV-coinfected Patients with Recurrent Hepatitis C After Liver Transplant. *Ann Hepatol* 16: 86-93. [[Crossref](#)]
- Lagging M, Wejstål R, Norkrans G, Karlström O, Weiland O et al. (2017) Treatment of hepatitis C virus infection: updated Swedish Guidelines 2016. *Infect Dis (Lond)* 49: 561-575. [[Crossref](#)]
- Asselah T (2014) Sofosbuvir for the treatment of hepatitis C virus. *Expert Opin Pharmacother* 15: 121-130. [[Crossref](#)]
- Stedman C (2014) Sofosbuvir, a NS5B polymerase inhibitor in the treatment of hepatitis C: A review of its clinical potential. *Therap Adv Gastroenterol* 7: 131-140. [[Crossref](#)]
- Abdel aziz AM, Ibrahim MA, El sheikh AA, Kamel MY, Zenhom NM et al. (2018) Effect of Sofosbuvir Plus Daclatasvir in Hepatitis C Virus Genotype-4 Patients: Promising Effect on Liver Fibrosis. *J Clin Exp Hepatol* 8: 15-22. [[Crossref](#)]
- Abdelqader A, Kabacam G, Woreta TA, Hamilton JP, Luu H et al. (2017) Pre- Versus Posttransplant Treatment of Hepatitis C Virus With Direct-Acting Antivirals in Liver Transplant Recipients: More Issues to be Solved. *Exp Clin Transplant* 15: 1-5. [[Crossref](#)]
- Carter W, Connelly S SK (2017) Reinventing HCV Treatment: Past and Future Perspectives. *J Clin Pharmacol* 57: 287-296. [[Crossref](#)]
- Yang Y, Wu F, Wang W, Shi J, Li Y et al. (2019) Real life efficacy and safety of direct-acting antiviral therapy for treatment of patients infected with hepatitis C virus genotypes 1, 2 and 3 in northwest China. *World J Gastroenterol* 25: 6551-6560. [[Crossref](#)]
- Assih M, Ouattara AK, Diarra B, Yonli AT, Compaore TR et al. (2018) Genetic diversity of hepatitis viruses in West-African countries from 1996 to 2018. *World J Hepatol* 10: 807-821. [[Crossref](#)]
- Bunchorntavakul C, Reddy KR (2015) Alimentary Pharmacology and Therapeutics Review article: the efficacy and safety of daclatasvir in the treatment of chronic hepatitis C virus infection. *Aliment Pharmacol Ther* 42: 258-272. [[Crossref](#)]
- Poordad F, Schiff ER, Vierling JM, Landis C, Fontana RJ et al. (2016) Daclatasvir with sofosbuvir and Ribavirin for Hepatitis C Virus Infection With Advanced Cirrhosis or Post-Liver Transplantation Recurrence. *Hepatol* 63: 1493-1505. [[Crossref](#)]
- Sulkowski MS, Gardiner DF, Torres MR, Reddy KR, Hassanein T et al. (2014) Daclatasvir plus Sofosbuvir for Previously Treated or Untreated Chronic HCV Infection. *New Engl J Med* 370: 211-221. [[Crossref](#)]
- Wu LS, Jimmerson LC, Macbrayne CE, Kiser JJ, D'Argenio DZ (2016) Modeling ribavirin-induced anemia in patients with chronic Hepatitis C Virus. *CPT Pharmacometrics Syst Pharmacol* 5: 65-73. [[Crossref](#)]
- Dyson JK, Hutchinson J, Harrison L, Rotimi O, Tiniakos D et al. (2016) Liver toxicity associated with sofosbuvir, an NS5A inhibitor and ribavirin use. *J Hepatol* 64: 234-238. [[Crossref](#)]
- Lee C (2013) Daclatasvir: Potential role in hepatitis C. *Drug Des Devel Ther* 7: 1223-1233. [[Crossref](#)]