Role of **Sofosbuvir + Velpatasvir** fixed-dose combination in Hepatitis C

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Background and Objective of the Survey

The fixed-dose combination of sofosbuvir and velpatasvir has revolutionized the treatment landscape for hepatitis C virus (HCV) infection, offering a highly effective and convenient option for patients. Sofosbuvir is a nucleotide analog inhibitor of the HCV NS5B polymerase, while velpatasvir is a pan-genotypic inhibitor of the HCV NS5A protein.

The combination of sofosbuvir and velpatasvir provides potent antiviral activity against all major genotypes of HCV, making it suitable for the treatment of both treatment-naive and treatment-experienced patients. Its pan-genotypic efficacy eliminates the need for genotype testing, simplifying treatment decisions and ensuring broad accessibility.

Additionally, the fixed-dose combination of sofosbuvir and velpatasvir offers several advantages over previous HCV treatment regimens. Its once-daily dosing regimen and high barrier to resistance improve treatment adherence and reduce the risk of virologic failure. Furthermore, the combination therapy has a favorable safety profile, with few adverse effects and minimal drug interactions.

Clinical trials have demonstrated the high efficacy of sofosbuvir and velpatasvir combination therapy, with cure rates exceeding 95% across various patient populations, including those with compensated cirrhosis and HIV co-infection. The availability of generic formulations has further increased access to this life-saving treatment for patients in resource-limited settings.

In conclusion, the fixed-dose combination of sofosbuvir and velpatasvir represents a major advancement in the treatment of HCV infection, offering simplicity, efficacy, and safety in a single tablet regimen. Its widespread adoption has led to substantial progress towards the global elimination of HCV as a public health threat.

The objective of the survey is:

To evaluate the role of Sofosbuvir + Velpatasvir fixed-dose combination in Hepatitis C

Methodology of the Survey

A survey was conducted to evaluate the role of Sofosbuvir + Velpatasvir fixed-dose combination in Hepatitis C. A total of 50 doctors from India participated in the survey.

Step 1: A literature search was done on the topic. Below topics were covered in the literature search

- Introduction
- ASTRAL studies
- Efficacy across ASTRAL studies
- Safety across ASTRAL studies
- Health-related quality of life and work productivity analysis in the ASTRAL studies
- Review of the effectiveness of sofosbuvir/velpatasvir on chronic hepatitis C virus

Step 2: A survey questionnaire was prepared based on the literature search. The survey form was shared through the digital medium with physicians across India.

Step 3: Their responses were analyzed and the findings are provided in this survey analysis booklet.

Literature Review

Introduction

150 million people are infected worldwide by the Hepatitis C Virus (HCV), which is a single stranded RNA virus from the Flaviviridae family with 6 major genotypes (GTs). Progressive liver fibrosis is caused by chronic HCV infection, which can induce cirrhosis, hepatic decompensation, and hepatocellular carcinoma. It is estimated that the annual mortality rate of half a million people is due to liver disease associated with chronic HCV infection.

An estimated 35% of global HCV infections are caused by HCV GTs 2 and 3, which affect roughly 58 million people. Contrary to GT1, GTs 2 and 3 are diffused in low-income regions such as Latin America, Asia, sub-Saharan Africa and Eastern Europe. HCV GTs 2 and 3 were categorized together in treatment guidelines and were classified as easy to treat genotypes before the introduction of direct-acting antiviral agents. According to recent studies, HCV GT3 is linked to rapid disease progression and has lower rates of response to treatment compared to GT2, as particularly demonstrated in patients with cirrhosis and in patients who have not reacted to earlier treatment.

Patients with decompensated cirrhosis caused by HCV chronic infection is set to rise in the next decade. Liver transplantation was the only treatment option available to these patients until recently.

An additional challenge for clinicians is the eradication treatment in the HCV/HIV co-infected population. In fact, HCV/HIV-coinfected patients suffer from higher rates of cirrhosis and liver decompensation disease than their mono-infected counterparts.

HCV treatment has recently undergone a transformation with the development of drugs that directly impede HCV replication. Effective combinations of direct-acting antiviral agents are currently available. Clinicians must consider the patient's treatment history, HCV GT and subtype, stage of fibrosis, and patterns of antiviral resistance in specific cases in order to select a suitable regimen.

Regimens which include ribavirin (RBV) show a higher rate of side effects, mainly hematologic and RBV-free combinations would allow a better management of a wider range

of patients, including those with a low tolerance to RBV. This would in turn minimize the necessity for pretreatment testing and monitoring during therapy, aspects that could be especially beneficial in low-income countries.

Sofobusvir (SOF) is a nucleotide analogue inhibitor of the HCV NS5B polymerase approved for HCV treatment in conjunction with other agents, which include NS5A inhibitors, NS3/4A protease inhibitors (PI), RBV, and peginterferon-RBV. Velpatasvir (VEL) (also formerly known as GS-5816, Gilead Sciences) with antiviral activity against HCV replicons in GTs 1 to 6, is a last generation, pan-genotypic HCV NS5A inhibitor.

The SOF/VEL is a single tablet, once a day regimen that combines two pan-genotypic, high potency and high genetic barrier antiviral molecules, providing >95% of SVR across all GTs with favourable safety and tolerability across a broad patient population even for decompensated cirrhotic subjects.

The SOF/VEL pill is PI, gluten, and lactose free and can be used without RBV to address unmet needs in the HCV treatment paradigm.

ASTRAL studies

An evaluation of efficacy and safety on the combination of sofosbuvir and velpatasvir was reported in different patient populations by a series of Phase III clinical trials entitled ASTRAL (ASTRAL-1, ASTRAL-2, ASTRAL-3, ASTRAL-4, and ASTRAL-5).

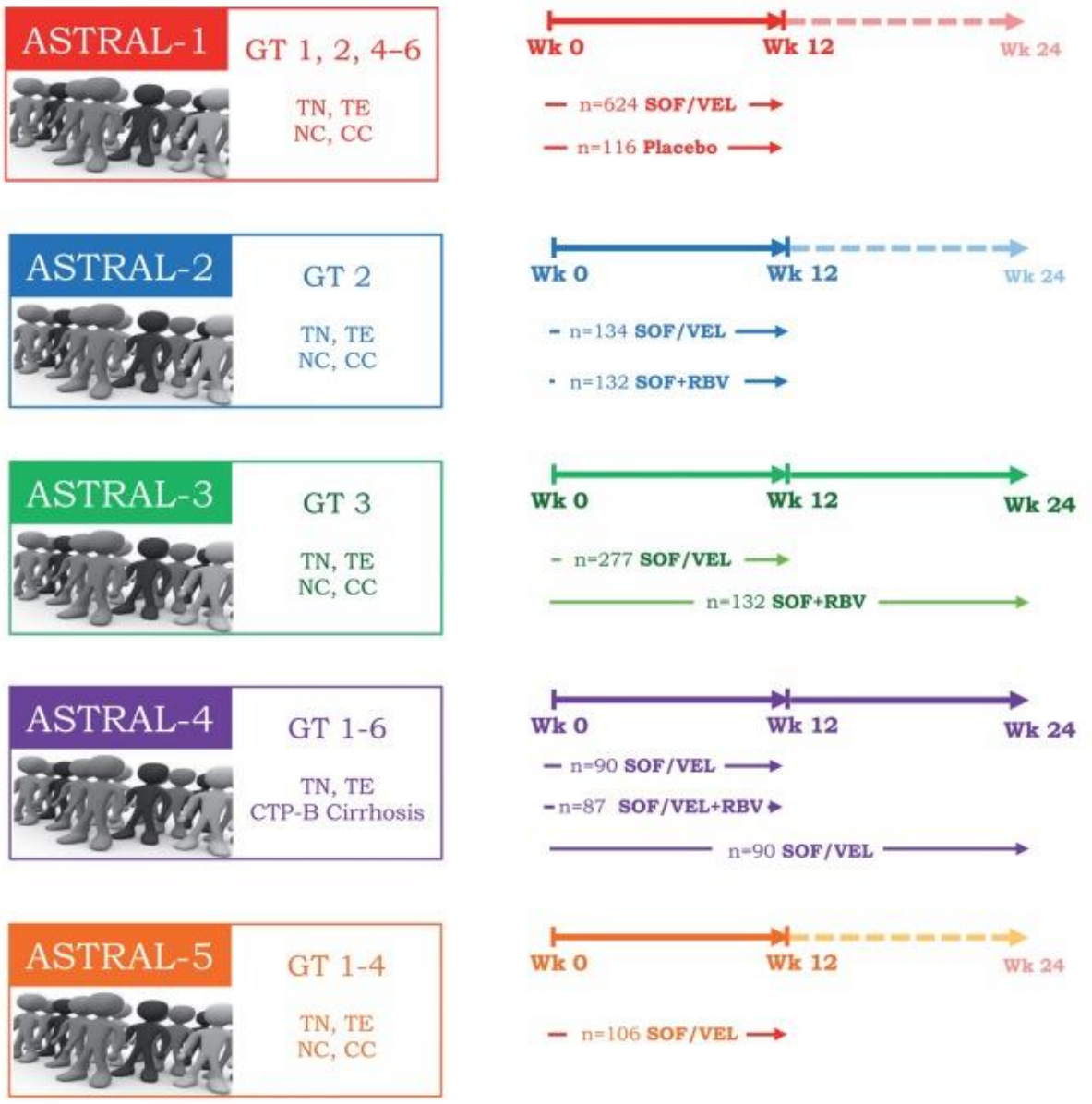

Figure 1. ASTRAL study design

Legend: SOF: Sofosbuvir; VEL: Velpatasvir; RBV: Ribavirin; GT: genotype; TN: Treatment Naive; TE: Treatment Experienced; NC: Non Cirrhotic; CC: Compensated Cirrhosis; CTP-B Cirrhosis: Child-Turcotte-Pugh B Cirrhosis.

The ASTRAL studies demonstrated that SOF/VEL is highly effective across all GTs and different stages of liver damage, and can therefore be defined as a pan-genotipic and pan-fibrotic regimen. The following ASTRAL studies were focused on particular patient settings, providing information with regard to the efficacy and safety of SOF/VEL in subpopulations of HCV-positive subjects, which were considered as difficult to treat until now.

ASTRAL populations and study design

ASTRAL-1 included patients infected with HCV GTs 1 to 6 with different stages of liver damage up to compensated cirrhosis, with the exclusion of GT3 infected patients. In the current DAA therapy era, GT3 infection has been relatively difficult to treat compared to other GTs, especially in subjects with cirrhosis or prior HCV treatment failure; therefore, a dedicated clinical trial study was set-up for those infected with GT3.

Patients were enrolled at 81 sites in North America, Europe, and Hong Kong. The study was double-blinded and placebo-controlled. Patients were randomized 5:1, with the exclusion of 35 patients infected with GT5, who only underwent SOF/VEL therapy, which was attributed to the low number. A total of 624 patients received at least one dose of the drug (116 patients received a placebo), 121/624 had compensated cirrhosis and 201/624 had experienced treatment.

The results of ASTRAL-2 and ASTRAL-3 studies are reported in the same manuscript, focused on HCV GT2 and HCV GT3 infected populations respectively. As mentioned in the introduction section, these two GTs, previously considered as easy to treat in the IFN-era, showed lower SVR rates for DAA-based therapies.

ASTRAL-2 and ASTRAL-3 studies shared identical inclusion/exclusion criteria, and about 20% of patients with compensated cirrhosis were enrolled. Patients who underwent previous treatment were also included (20%/total). Subjects with decompensated cirrhosis and those who interrupted previous therapy as a result of adverse events were excluded. Patients were randomized 1:1 in both of the studies, in order to receive different SOF/VEL-based regimens (12 weeks with or without RBV in ASTRAL-2, 12 weeks or 24 weeks without RBV in ASTRAL-3). ASTRAL-2, enrolled 266 patients to initiate treatment from 51 sites in the United States while in ASTRAL-3, 552 patients from centers in North America, Europe, and Australia initiated therapy.

ASTRAL-4 was dedicated to naïve and experienced HCV patients with decompensated cirrhosis (CHILD-Pugh-Turcotte class B). The study enrolled patients who did not receive a liver transplantation, or undergo antiviral treatment with any NS5A or NSB inhibitors, with a platelet count higher than 30,000/mm^3 and a creatinine clearance higher than 50 ml/min (Cockcroft-Gault equation). A total of 267 patients, recruited from 47 sites in the United States, initiated treatment with the following randomization: 90 patients received SOF/VEL for 12 weeks, 87 received SOF/VEL plus RBV for 12 weeks and 90 received SOF/VEL for 24 weeks. All of the HCV GTs except for GT 5 were represented.

Finally, to assess SOF/VEL efficacy and safety in HCV patients coinfected with HIV-1, ASTRAL-5, an open-label, single arm study, was performed. Patients were enrolled from 17 centers in the United States, and were required to be treated with an approved antiretroviral regimen, to acquire a HIV-1 viremia lower than 50 copies/mL and a CD4+ T-cell count higher than 100 cells/mL. Patients with compensated cirrhosis were also included, as well as experienced patients (excluding prior NS5A and NS5B inhibitors).

One hundred and six co-infected subjects initiated therapy consisting of a single pill of SOF/VEL once a day for 12 weeks (with the identical regimen and length for all the enrolled patients).

Efficacy across ASTRAL studies

The primary efficacy endpoint was common in all the ASTRAL studies, and was the rate of sustained virological response (SVR), defined as viremia lower than 15 IU/mL 12 weeks after therapy cessation in all the patients who received at least one dose of the drug after randomization. The secondary endpoints were different across the ASTRAL studies and depended on the specific enrolled populations and randomization.

ASTRAL-1 showed HCV infection and liver damage up to compensated cirrhosis in patients with GTs 1-6 (excluding GT3), and a SVR rate of 99% in patients who received SOF/VEL for 12 weeks, which is a significantly higher rate than the 85% value which was the pre-specified performance target. None of the subjects who received a placebo obtained an SVR.

The SVR rate was comparable among the different GTs (98% for GT1a, 99% for GT1b, 100% for GT2, 4, and 6, and 97% for GT5).

120/121 (99%) cirrhotic patients reached a SVR including 99.5% of experienced patients. Among non-cirrhotic patients 496/501 (99%) experienced a SVR.

ASTRAL-2 was a specifically required study by the Food and Drug Administration as a separated trial. The results showed a SVR rate of 99% in patients who received SOF/VEL for 12 weeks compared to 94% in those who underwent SOF plus RBV for 12 weeks. At the time the ASTRAL-2 study was performed, standard therapy showed a significant improvement in efficacy.

As reported in ASTRAL-3, HCV GT3 infected patients treated with SOF/VEL for 12 weeks reached a 95% SVR rate compared to 80% as shown by those receiving SOF plus RBV for 24 weeks, which is a highly significant difference in efficacy ($p<0.001$). Considering non-cirrhotic GT3 patients, SOF/VEL led to SVR in 191/197 subjects (97%, while SOF plus RBV determined an SVR in 163/187 subjects (87%).

The SVR rate with all oral DAAs in decompensated cirrhosis was lower than in patients with less advanced liver disease.

The phase 3 ASTRAL-4 study aimed to evaluate the efficacy of SOF/VEL in the difficult-to-treat HCV-infected population, showing an eradication rate of 83% after 12 weeks of SOF/VEL, 94% after 12 weeks of SOF/VEL plus RBV, and 86% after 24 weeks of SOF/VEL. The SVR rate obtained from the different SOF/VEL based regimens did not show any significant differences. However, in decompensated cirrhosis caused by HCV GT3 infection, a SVR rate of 71% was previously reported due to the fact that SOF/VEL plus RBV for 12 weeks resulted in 85% of the SVR.

The benefits of IFN-free therapy in advanced liver disease are still unclear. The secondary efficacy endpoints of ASTRAL-4 were linked to the improvement of liver damage, as the CPT and MELD scores changed at week 12 after therapy cessation. The analysis of CPT and MELD scores was performed on 250/267 patients; an improvement of CPT, compared to the baseline value, was observed in 47% of patients, and an improvement of MELD in 51% of those with a baseline value of less than 15, and in 81% of subjects with a MELD higher than 15. In general, such an improvement is due to a decrease in bilirubin levels and an increase in albumin levels. However, the long-term benefits on hepatic functions remain to be assessed.

Two efficacy endpoints were established in the ASTRAL-5 study, which was dedicated to the special population of HCV/HIV co-infected subjects. The first efficacy endpoint was common

in the other ASTRAL studies and showed 95% of SVR in 106 HCV/HIV patients who underwent SOF/VEL for 12 weeks. All of the patients with cirrhosis reached a SVR (100%) along with 94% of the black patients and 94% of the experienced patients.

The secondary endpoint was the assessment of the percentage of real virological failures in patients who had viremia lower than 15 IU/mL during treatment. In fact, among the 5/106 patients not included in the SVR group, only 2 patients were virological failures (at week 4 of post-treatment), while 2 were lost during the follow-up, and 1 withdrew consent.

An integrated post-hoc analysis on antiviral efficacy considering the main Astral trials (Astral-1, -2 and -3) has been recently performed. The SOF/VEL treatment for 12 weeks in 1035 patients showed an overall SVR rate of 98% with an intention-to-treat analysis. The high efficacy was consistent across all genotypes, with only 2 virological relapse in GT1 and 11 in GT3 patients.

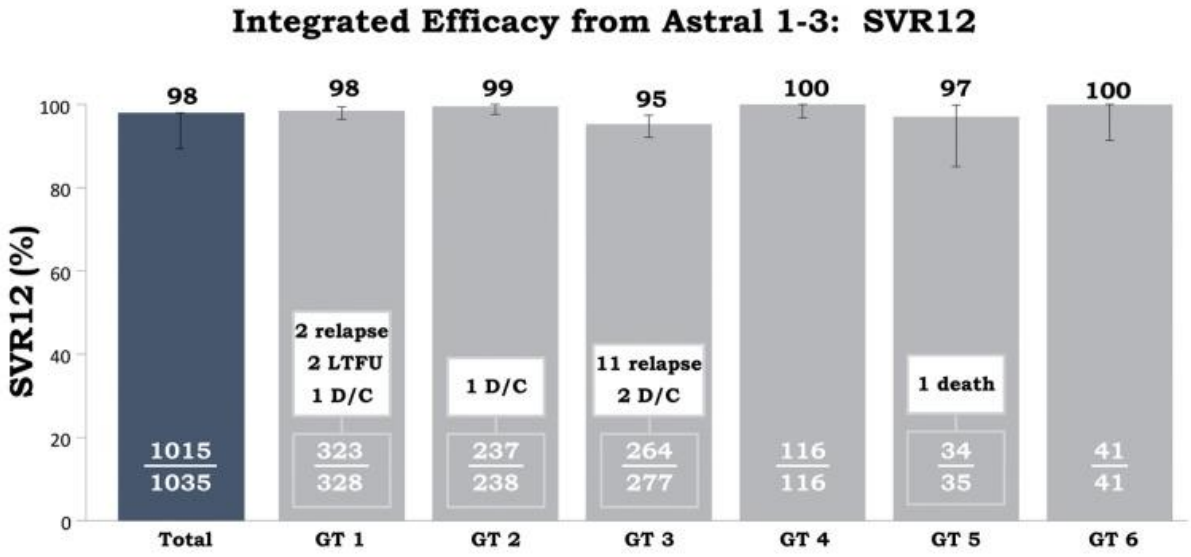

Figure 2. Integrated Intention To Treat Analysis of Efficacy from Astral 1-3: SVR12. SVR12: Sustained Virological Response 12

GT: Genotype; LTFU: Lost at Follow-Up; D/C: Discontinuation.

A retrospective analysis of efficacy results of SOF/VEL for 12 weeks for GT1–6 in phase 3 trials stratified by fibrosis stage has been recently proposed. The authors pooled patients data from SOF/VEL registration trials (ASTRAL-1 - , ASTRAL-2 , ASTRAL-3) and

SOF/VEL/VOX Polaris phase 3 studies (POLARIS-2 , and POLARIS-3), where SOF/VEL treatment was considered as comparative arm.

Authors identified 1567 patients enrolled in the ASTRAL and POLARIS programs and a METAVIR category was assigned according to the FibroTest score.

Table 1. Demographic features of F0-F2 patients, treated for 12 weeks, from the Integrated analysis (ASTRAL and Polaris studies)

Total n of F0-F2 patients		**887**
Mean age, y (range)		49 (18-79)
Male, n (%)		421 (47)
Mean BMI, kg/m^2 (range)		26 (17-48)
HCV GT, n (%)	1a	205 (23)
	1b	102 (11)
	2	196 (22)
	3	227 (26)
	4	101 (11)
	5	24 (3)
	6	31 (3)
Baseline HCV RNA log$_{10}$ IU/mL, mean (range)		6.3 (1.1-7.8)
Treatment Experienced, n (%)		177 (20)
F0, n (%)		337 (38)
F1, n (%)		160 (18)
F2, n (%)		390 (44)

Legend: BMI: Body Mass Index; GT: genotype; IU: International Units

Table 2. Demographic features of F3 and F4 patients, treated for 12 weeks, from the Integrated analysis (ASTRAL and Polaris studies)

		F3	F4
Total n of patients		236	444
Mean age, y (range)		57 (33-81)	58 (34-82)
Male, n (%)		162 (69)	355 (80)
Mean BMI, kg/m^2 (range)		28 (18-57)	28 (17-47)
HCV GT, n (%)	1a	67 (28)	107 (24)
	1b	26 (11)	48 (11)
	2	34 (14)	58 (37)
	3	77 (33)	164 (37)
	4	21 (9)	49 (11)
	5	5 (2)	5 (1)
	6	6 (3)	13 (3)
Baseline HCV RNA log$_{10}$ IU/mL, mean (range)		6.3 (4.0-7.4)	6.2 (4.1-7.5)
Treatment Experienced, n (%)		66 (28)	176 (40)

Legend: BMI: Body Mass Index; GT: genotype; IU: International Units

The F0-F2 population was largely represented (n=887), with a mean age of 49 yrs, younger than F3 and F4 groups (57 and 58 yrs, respectively), as expected. GTs distribution was homogeneous between the groups with GT1 as the most prevalent except for the cirrhotic subjects where 37% of patients was infected by GT3. F4 group showed a higher proportion of experienced patients (40%) when compared to patients with milder fibrosis (20% and 28% for F0-2 and F3, respectively).

In addition to the Intention-to-treat (ITT) analysis, that considered all patients who were randomized and received ≥1 dose of assigned study drug, the Completer analysis was also

performed, evaluating all patients who were randomized, completed assigned study treatment, and had HCV RNA data observed at post-treatment week 12 or imputed from a later time-point.

SOF/VEL for 12 weeks was highly effective across all GTs regardless of degree of fibrosis. Considering the Completer analysis, in the F0-F2 group almost all patients achieved an SVR (99.6%) with only 3 GT3 infected patients who relapsed out of 874 treated individuals. Similar high rates of response were registered also in patients with advanced fibrosis (F3: 232/234 SVR, 99.1%) and with cirrhosis (F4: 431/443 SVR, 97.2%). In this latter group, high rates of SVR were obtained also in GT3 patients (154/163, 94.4%) without the need for Ribavirin.

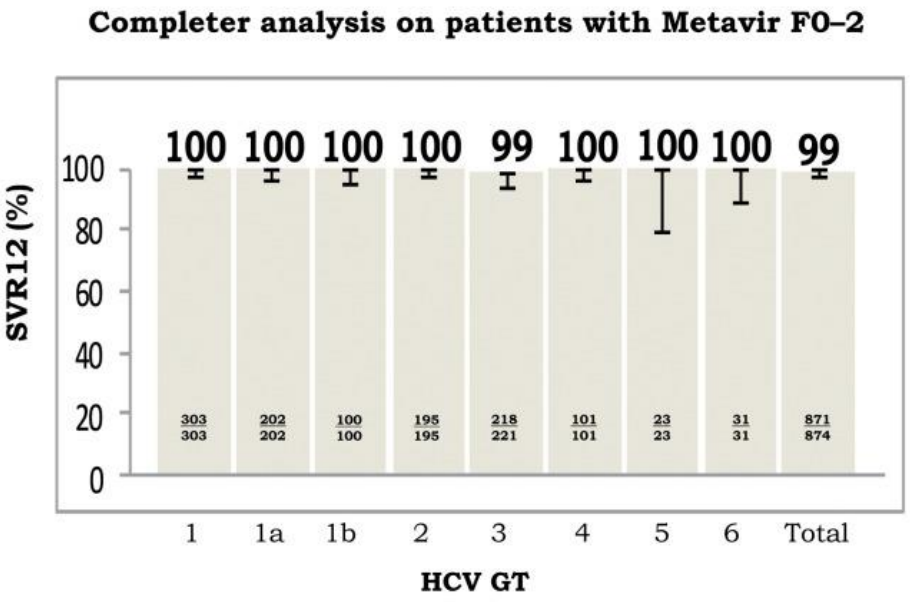

Figure 3. ASTRAL-1, -2, -3 and POLARIS-2, -3 combined retrospective analyses of efficacy in patients with METAVIR F0-F2, treated with Sofosbuvir/Velpatasvir for 12 weeks. Patients were treatment naïve and treatment experienced (including PI-failure)

SVR: Sustained Virological Response; GT: Genotype.

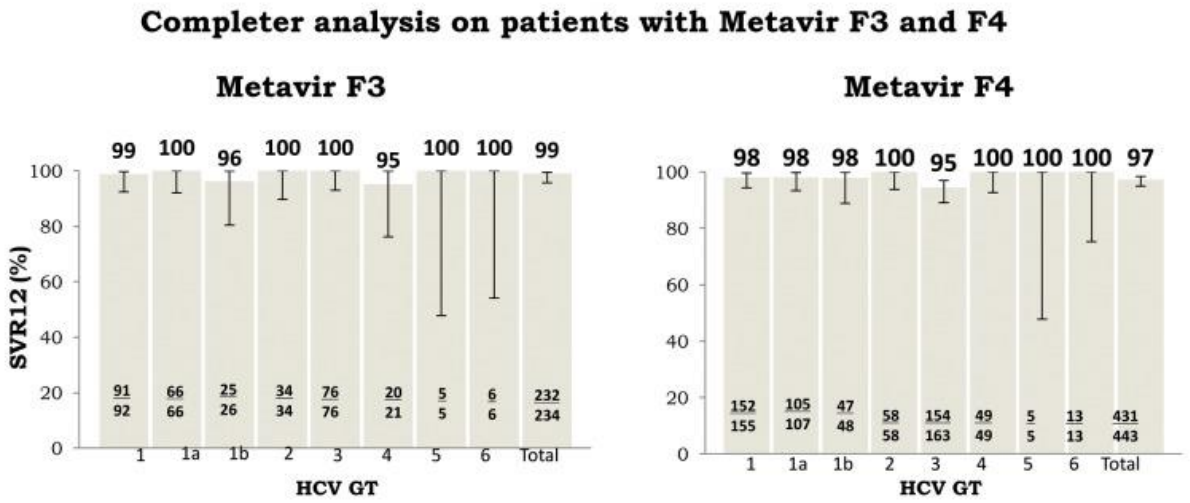

Figure 4. ASTRAL-1, -2, -3 and POLARIS-2, -3 combined retrospective analyses of efficacy in patients with METAVIR F3 and F4, treated with Sofosbuvir/Velpatasvir for 12 weeks. Patients were treatment naïve and treatment experienced (including PI-failure)

SVR: Sustained Virological Response; GT: Genotype.

Safety across ASTRAL studies

Rate of adverse events (AEs) and treatment discontinuation because of AEs was the secondary end point of the ASTRAL-1 study. Treatment was interrupted by 1 patient (<1%) in the SOF/VEL group and by 2 patients (2%) in the placebo group. Serious AEs occurred in 15 patients (2%) treated with SOF/VEL and in none of the patients who received a placebo. Overall, AEs (mostly headache, nausea, fatigue and nasopharyngitis) were recorded in 78% of subjects who underwent SOF/VEL therapy, and in 77% of those in the placebo group, without any significant difference.

In the ASTRAL-2 and ASTRAL-3 studies, a patient included in the ASTRAL-2 study interrupted treatment after the first pill due to anxiety and a headache. In ASTRAL-3, RBV was only discontinued by 9 patients (3%) as a result of AEs. In the ASTRAL-2 study, the percentage of serious AEs was the same in those who received and those who did not receive RBV (1%); in the ASTRAL-3 study, 2% of subjects who did not receive RBV experienced serious AEs compared to 15% of those who received RBV. Considering both studies, AEs were generally frequent in patients who underwent RBV-including regimens and the types of AEs were typical of RBV (anemia, insomnia, irritability and coughing). Two ASTRAL-2 patients

died during the post-treatment follow-up and 3 ASTRAL-3 patients died during treatment. All the deaths seemed to be due to causes unrelated to therapy or were categorized as unknown.

As expected for the severe condition of the study population in terms of liver damage, the serious AEs rate was higher in the three groups of the ASTRAL-4 study with hepatic encephalopathy and sepsis being the most frequent and serious AEs. For the same reason, the nine deaths that occurred during the study were thought to be unrelated to treatment and were possibly ascribable to the end-stage of liver disease. Anemia was very common in 30% of patients who received RBV, and was experienced at a different level of severity.

ASTRAL-5 had a proportion of patients who interrupted treatment due to AEs as a primary safety end-point. In fact, 71% of patients experienced at least one AE, which was serious in only 2 cases (2%) and led to therapy discontinuation in one case. Another patient interrupted therapy as a consequence of a mild adverse event (a single vomiting episode) at day 48 and reached SVR12 regardless. None of the patients died and in none of the cases, the ARV was modified. Pruritus was not observed in any patient of the ASTRAL studies among the AEs.

Overall, the SOF/VEL regimens demonstrated a very good safety profile in all the ASTRAL studies, which covered a wide range of the different features that are typical of HCV-chronically infected patients. Nevertheless, in the case of other concomitant treatments, caution is required in order to avoid drug-to-drug interactions (DDI). SOF/VEL is not recommended for patients treated with amiodarone due to the risk of severe symptomatic bradycardia if taken together. Other drugs reduce SOF/VEL efficiency (antacids and proton pump inhibitors, some anticonvulsants, antimycobacterials, and chemotherapy topotecan). However, the SOF/VEL regimen presents a very good DDI profile, which represents the best option in multi-treated patients with co-morbidities, in women of child-bearing potential, and in active drug users or in opioid substitution therapy. This makes SOF/VEL regimen suitable also for patients using recreational drugs, generally not mentioned during the anamnestic evaluation.

SOF/VEL can also be administered in patients with mild or moderate renal impairment, even if it is not recommended for patients with more severe renal damage (eGFR\30 mL/min/1.73 m^2).

The tolerability of SOF/VEL for 12 weeks was retrospectively assessed by an integrated safety analysis in more than 1000 patients treated in the ASTRAL-1, ASTRAL-2, and ASTRAL-3 studies. SOF/VEL was well tolerated in HCV-infected patients with similar incidence and severity as in placebo treated subjects. The most common AEs emerging in SOF/VEL group

from the integrated analysis were headache, fatigue, nausea, and nasopharyngitis, whose incidence was similar in placebo undergoing patients.

Table 3. Retrospective integrated analysis of data from 1,035 SOF/VEL for 12 Weeks patients and control/placebo patients in ASTRAL-1, -2, and -3

Patients, n (%)	SOF/VEL 12 weeks N=1035	Placebo 12 weeks N=116
AEs	821 (79)	89 (77)
Grade 3 or 4 AEs	33 (3)	1 (<1)
SAEs	23 (2)*	0
AE leading to treatment D/C	2 (<1)^	2(2)
Death	3 (<2)**	0)

Table 4. More frequent adverse events from the retrospective integrated safety analysis of data from 1,035 SOF/VEL for 12 Weeks patients and control/placebo patients in ASTRAL-1, -2, and -3

Patients, n (%)	SOF/VEL 12 weeks N=1035	Placebo 12 weeks N=116
Headache	296 (29)	33 (28)
Fatigue	217 (21)	23 (20)
Nausea	135 (13)	13 (11)
Insomnia	87 (8)	11 (9)
Nasopharyngitis	121 (12)	12 (10)
Cough	57 (6)	4 (3)
Irritability	49 (5)	4 (3)
Pruritus	33 (3)	5 (4)
Dyspepsia	33 (2)	4 (3)

Health-related quality of life and work productivity analysis in the ASTRAL studies

Patients with chronic HCV infection, usually have a poor health-related quality of life and impaired work productivity. The patients reported outcomes are directly described by the patient and pertain to the patient's health, quality of life, or functional status associated with health care or treatment. The effect of SOF/VEL on PROs in HCV-patients included in the ASTRAL studies was performed, and a comparative analysis between patients with and without cirrhosis was also conducted.

The analysis performed on the ASTRAL-1 patient groups showed that patients treated with SOF/VEL experienced a significant improvement in PROs during treatment and after SVR. In the placebo group, only one PRO improved by week 4 of treatment, and no further improvements were noted.

ASTRAL-2 and ASTRAL-3 populations were analyzed with regard to PROs in a dedicated study with a total of 818 HCV patients. As previously mentioned, the overall rates of all adverse events were lower in the RBV-free SOF/VEL group (all $p<0.03$) and, therefore, patients who received RBV-free SOF/VEL regimens, reported significantly higher PRO scores during treatment compared to those who received the RBV-containing regimen (SOF plus RBV). At post-treatment week 12, changes from baseline levels were no longer different between the two treatment arms.

Finally, a comparative analysis of PROs during and after SOF/VEL treatment in HCV patients with and without cirrhosis, from ASTRAL studies (1 to 4) was performed by Younossi and co-workers. As expected, baseline PROs were lower in patients with cirrhosis, but, during SOF/VEL treatment and after reaching the SVR, subjects with and without cirrhosis experienced a significant improvement in the scores.

In general, the administration of SOF/VEL produced a significant improvement in patients' quality of life, resulting in a benefit for the patients going beyond the SVR, as demonstrated by the PROs analysis of patients' perception of the treatment.

Review of the effectiveness of sofosbuvir/velpatasvir on chronic hepatitis C virus

Worldwide, there are six hepatitis C virus (HCV) genotypes that exist. A recent systemic review estimated that globally genotype 1 (GT1) is responsible for 49% of all adult HCV infections, followed by genotype 3 (GT3) (18%), genotype 4 (GT4) (17%), genotype 2 (GT2) (11%), genotype 5 (GT5) (2%), and genotype 6 (GT6) (1%).

The nonstructural protein 5B (NS5B) nucleotide inhibitor sofosbuvir (SOF) is authorized for use in conjunction with other direct-acting antivirals (DAA's) to treat HCV infection. Velpatasvir (VEL) is an investigational inhibitor of the HCV NS5A protein with antiviral efficacy against all HCV genotypes (previously known as GS-5816, Gilead Sciences, Foster City, USA). The combination of VEL and SOF, administered orally and daily as a single tablet (400 mg SOF and 100 mg VEL combination) with or without ribavirin (RBV), has demonstrated excellent effectiveness in patients with all HCV genotypes. To assess the efficacy of HCV treatment, we use the sustained virology response (SVR) rate. SVR means that an undetectable viral load (HCV RNA <15 IU/mL) is observed at 12 weeks after completing treatment (SVR12).

Feld et al. carried out a clinical trial to examine the efficacy of sofosbuvir/velpatasvir (SOF/VEL) in 740 patients with chronic HCV-GT 1, 2, 4, 5, and 6 (624 patients received treatment, and 116 patients had placebo). These patients are initially treated or untreated, and some of them had compensated cirrhosis. The SVR12 was 99% (95% confidence interval [CI], 98 to >99) in the 624 patients who received SOF/VEL therapy, which was significantly higher than the prescribed 85% ($p<0.001$) performance target . Neither of the 116 placebo patients had SVR. SVR rates were similar regardless of HCV genotype ranging from 97% (95% CI, 85 to >99) to 100% (95% CI 97-100). Of the 121 patients with cirrhosis, 120 (99% [95% CI, 95 to >99) had an SVR regardless of genotype. An SVR is seen in 496/501 (99%) of non-cirrhotic individuals.

In a meta-analysis, Ahmed et al. investigated 1427 patients who took either SOF/VEL or SOF/VEL + RBV, found that a single-tablet of SOF/VEL regimen is highly efficient in chronic HCV (GT 1-6) patients, with SVR12 rates >97%. Cirrhotic or non-cirrhotic, naïve, and treatment-experienced patients also showed high SVR12 rates.

Curry et al. conducted a multicenter, open-label trial on 268 patients randomly assigned to one of three arms: SOF/VEL + RBV once daily for 12 weeks; SOF/VEL once daily for 24 weeks; or SOF/VEL once daily for 12 weeks. SVR rates were 83% (95% CI, 74-90) in patients treated

with SOF/VEL for 12 weeks, 94% (95% CI, 87 to 98) in those treated with SOF/VEL plus RBV for 12 weeks, and 86% (95% CI, 77 to 92) in those treated with SOF/VEL for 24 weeks . Therefore, all three treatment groups with rates of SVR significantly superior to the expected spontaneous HCV clearance rate of 1% at 12 weeks after therapy ($p<0.001$ for all three comparisons) reached the adjusted primary efficacy endpoint. In addition, SVR rates were also successfully high in patients with chronic HCV infection and decompensated cirrhosis mainly due to decreases in bilirubin and an increase in albumin.

Pisaturo et al. conducted meta-analysis research in naïve individuals with chronic HCV infection and mild fibrosis. They found that a SOF/VEL single-tablet regimen without RVB is very effective in chronic, non-cirrhosis HCV patients (SVR12=98%) and in HCV patients without advanced hepatic-fibrosis (SVR12=96%).

All the authors mentioned above agreed that in chronic HCV patients with genotypes 1-6, including treatment-experienced and cirrhotic individuals, the SOF/VEL therapy combination was highly successful. Therefore, SOF/VEL single tablet results to be effective against all HCV genotypes with minimal risk of resistance if taken for 12 or 24 weeks.

The treatment of hepatitis C virus genotype 3

Genotype 3 (GT3) is the second most common hepatitis C virus (HCV) genotype globally, accounting for 18% of all HCV infections in adults. However, there are significant geographical differences in rates; GT3 is most common in South Asia (67%), with 54% and 79% in India and Pakistan, respectively. GT3 is also common in Australia (36%) and Tropical Latin America (30%), as well as Western Europe (29%). These figures show that HCV GT3 infection affects many people and requires care since it increases the risk of hepatic steatosis, hepatic fibrosis and cirrhosis development, and hepatocellular cancer.

Pegylated-interferon (Peg-IFN) + ribavirin (RBV) was previously the treatment standard for HCV GT3. However, current guidelines such as those of the European Liver Studies Association (EASL) recommend either velpatasvir + sofosbuvir + ribavirin (VEL + SOF ± RBV) or daclatasvir (DCV) + SOF ± RBV as first-line therapy, dependent on the therapy experience and cirrhotic status with the RBV administration. Initially, most direct-acting antivirals (DAAs) were developed using genotype 1 (GT1) replicon models. However, full-length GT1 and genotype 2 (GT2) HCV genomes have only recently been capable of

replicating the whole virus life cycle in vitro . Consequently, the first protease and NS5A inhibitors showed relative inadequacies in treatment results with GT3 compared to GT1 and GT2. In addition, GT3 is a genotype that is harder to cure than GT1 or GT2. Because the biology of GT3 differs from that of GT1, with faster progression, steatosis, and more significant risks of cirrhosis and primary liver cancer, the best treatments are needed.

Fathi et al. focused on a subset of the data comprising existing HCV GT3 therapy. They assessed the efficacy of present and future HCV treatment regimens. These treatments included licensed DAAs such daclatasvir (DCV), elbasvir (EBR), grazoprevir (GZR), pegylated interferon (Peg-IFN), ledipasvir (LDV), ombitasvir (OBV), sofosbuvir (SOF) or SOF-containing, velpatasvir (VEL), as well as new, unlicensed treatments for HCV GT3, such as glecaprevir (GLE), pibrentasvir (PIB), MK-3682 (uprofosbuvir), ruzasavir (RZR) and vocilaprevir (VOX). The analysis examined combinations of these medicines with and without RBV. For treating GT3 infections, the authors discovered that regimens incorporating newer DAAs (pibrentasvir + glecaprevir or grazoprevir + ruzasvir + uprofosbuvir) are more successful than those containing older DAA. In addition, the study shows that DAA regimens can treat GT3 infection instead of Peg-IFN-based treatments .

Ahmed et al. concluded in his meta-analysis of 1427 patients who took either SOF/VEL or SOF/VEL + RBV that the use of RBV was significantly beneficial among GT3 patients than in other genotypes. It resulted in a relapse risk (RR) of 0.89, 95% confidence interval (CI) [0.80, 0.99], p=0.04, in 132 patients. In patients with GT3 HCV and the role of RBV, Berden et al. studied the most effective DAA regimen among 3415 patients. The highest rates of sustained virology response (SVR) were estimated among non-cirrhotic patients receiving SOF+VEL with RBV 99% (95% CI, 90%-100%) and without RBV 97% (95% CI, 95%-99%), SOF + DCV + RBV (96% (90% CI, 92%-99%) and SOF+ Peg-IFN + RBV (95%; 95% CI, 91%-98%). For cirrhotic patients, the highest levels of SVR were estimated for SOF + VEL for 24 weeks (96%; 95% CI, 92%-99%), in the group of SOF+ DCV + RBV for 24 weeks (94%; 95% CI, 87%-98%) and in patients who received SOF + VEL + RBV for 12 weeks (94%, 95% CI, 86%-98%). Ribavirin improves efficacy in both cirrhotic and noncirrhotic individuals (odds ratio, 2.6-4.5).

In light of the research above, the authors have shown that the treatment of RBV with SOF-containing patterns, including newer DAA in HCV infection in GT3 patients, is more effective than previous regimens. Furthermore, when RBV adds to SOF/VEL, HCV GT3 demonstrated

a greater SVR. However, its efficacy when combined with novel DAAs remains a matter of debate.

Safety of the treatment of chronic hepatitis C virus infection

Since Peg-IFN alfa plus ribavirin (P+R) is a definitive treatment for chronic hepatitis C virus (HCV), it yields a high sustained virologic response (SVR) but with more significant side effects and poor tolerance, resulting in a suboptimal SVR rate. On the other hand, sofosbuvir (SOF)-containing regimens produce better SVR rates and fewer side effects than P+R regimens, according to several randomized controlled trials (RCTs).

Fan et al. analyzed eighteen randomized controlled studies (RCT) studying the safety of sofosbuvir-containing regimen versus pegylated interferon + ribavirin (P+R) on 2975 patients with varying therapy duration, regimens, therapy history, cirrhotic and non-cirrhotic. The patients took a SOF-containing regimen or a P+R regimen. In addition, safety-related adverse events (AE) are tested. For the overall AEs, the P+R regimen was 97.1% (95% confidence interval (CI): 94.2%-98.8%), which was significantly higher than all sofosbuvir-containing regimens.

According to Zignego et al., 1567 patients in a series of phase III clinical trials entitled ASTRAL (ASTRAL-1, ASTRAL-2, ASTRAL-3, ASTRAL-4, and ASTRAL-5) were assessed for the safety sofosbuvir/velpatasvir (SOF/VEL) and ribavirin (RBV). Patients who received SOF/VEL + RBV had a higher rate of side effects overall and a substantially higher rate of certain events known to be associated with RBV therapy than those who received SOF/VEL alone . When used with amiodarone, SOL/VEL might cause severe bradycardia. Other drugs reduce SOF/VEL efficiency (antacids and proton pump inhibitors, some anticonvulsants, anti-mycobacterial, and chemotherapy.

Stokes et al. conducted a systemic review and meta-analysis studying the side effects of sofosbuvir/ledipasvir/ribavirin (SOF/LDV/RBV) and sofosbuvir/ledipasvir (SOF/LDV) in 1179 patients with chronic HCV genotype 1 (GT1). Patients who got SOF/LDV/RBV experienced considerably more adverse events than those who only received SOF/LDV. When comparing LDV/SOF vs. LDV/SOF/RBV, the pooled relative risk of any adverse event (AE) was 0.11 (95% CI: 0.04-0.29). There were differences in adverse effects linked with ribavirin, such as fatigue/asthenia, rash, irritability, cough/bronchitis, and anemia. There were four

serious adverse events linked to study therapy, all of which occurred in the SOF/LDV/RBV groups. Hemolytic anemia, nonfatal myocardial infarction, morbilliform rash, and cardiac arrest were among the complications.

Finally, SOF/VEL is safer with minimal side effects than with Peg-INF alpha and ribavirin. Nevertheless, caution is required to avoid drug-to-drug interactions (DDI) in the case of other concomitant treatments with SOF/VEL.

Duration of retreatment in chronic hepatitis C virus patients with relapse

Patients treated for shorter durations (four-eight weeks) with all-oral non-structural protein 5A (NS5A) direct-acting antiviral (DAA) had higher re-treatment sustained virologic response (SVR) rates than those initially treated for longer durations (10-12 weeks). The brief therapy ends in treatment failure owing to the treatment-emergent hepatitis C virus (HCV) NS5A resistance-associated variants (RAVs).

Izumi et al. evaluated in an open-label study the efficacy and safety of sofosbuvir-velpatasvir (SOF/VEL) plus ribavirin (RBV) for 12 or 24 weeks. The study involved 117 Japanese patients with genotype 1 hepatitis C virus (HCV) infection who are treated before with NS5A inhibitor (DAA)) or genotype 2 HCV infection with any DAA-containing regimen. SVR rates were higher with 24 weeks versus 12 weeks of treatment. In the 12 and 24 weeks treatment groups, 82% (47/57; 95% confidence interval (CI) 70%-91%) and 97% (58/60; 95% CI 88%-100%) of patients achieved SVR, respectivel. In comparison, the difference in SVR rates for the treatment groups was statistically significant (24 weeks vs. 12 weeks for all patients, p=0.023). 95% of the previously treated patients with NS5A inhibitor-based DAA for a longer duration (12-14 weeks) had NS5A or non-structural protein 5B (NS5B) resistant associated substitutions (RASs) at baseline. These RASs do not have any negative effect on the treatment results . Thus SOF/VEL + RBV is highly influential among this population of longer retreatment duration (24 weeks).

Ruane et al. conducted an open-label trial to assess the efficacy of sofosbuvir/velpatasvir/vocilaprevir (SOF/VEL/VOX) for 12 weeks in chronic HCV patients who previously did not achieve SVR receiving SOF/VEL containing regimen. They studied 31 cirrhotic or non-cirrhotic patients with different HCV genotypes 1-5 (GT1-5). These patients received SOF/VEL/VOX for eight weeks or SOF/VEL for 12 weeks. At baseline, 32% of

patients had NS5A resistance-associated substitutions (RASs), and 26% had nonstructural protein 3 (NS3) RASs. No patients had both NS5A and NS3 RAS. With the re-treatment of SOF/VEL/VOX for 12 weeks, 31 of 31 patients with chronic HCV infection had an SVR rate of 100% (95% CI: 89% to 100%) in patients who had not obtained an SVR with earlier SOF and VEL exposure. For NS5A inhibitor-experienced patients, a 12-week treatment of SOF/VEL/VOX is an authorized salvage treatment. Few patients who failed therapy with SOF/VEL/VOX for eight weeks developed treatment-emergent resistance-associated substitutions (RASs) (one of 23 virologic failures), implying that re-treatment with the same regimen for a longer period of time may be more effective .

The results further support the use of SOF/VEL-containing regimen either with ribavirin (24 weeks) or VOX (12 weeks) as a salvage regimen for patients who have failed prior therapy with NS5A inhibitor-containing regimens. With a longer re-treatment duration, HCV resistance will be diminished.

References:

1. Zignego AL, Monti M, Gragnani L. Sofosbuvir/Velpatasvir for the treatment of Hepatitis C Virus infection. Acta Biomed. 2018;89(3):321-331.
2. Ahmed R, Kareem R, Venkatesan N, et al. Sofosbuvir/Velpatasvir - A Promising Treatment for Chronic Hepatitis C Virus Infection. *Cureus*. 2021;13(8):e17237.

Survey Form

1) Which of the following guidelines/recommendation do follow pertaining to diagnosis and management of Hepatitis C?

a. World Health Organization (WHO) recommendations

b. European Association of study of Liver (EASL)

c. American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA)

2) Which of the following factors do you consider while selecting the antiviral treatment in your patients with Hepatitis C?

a. Severity of disease (cirrhosis/no cirrhosis)

b. Complications (compensated/decompensated status)

c. Genotype of HCV

3) Which of the following treatment options do you prefer in your patients with Hepatitis C?

a. Interferons

b. Pegylated interferons

c. Direct acting antivirals (DAA)

4) According to you, which of the following are advantages of direct-acting antivirals?

a. virological efficacy

b. ease of use

c. safety and tolerability

d. IFN-free treatment option

e. Ribavirin free treatment option

f. pangenotypic activity

5) Which one of the following is your most preferred treatment option (DAA) in patients with hepatitis C infection (without cirrhosis or compensated cirrhosis)?

a. Sofosbuvir monotherapy

b. Sofosbuvir + Velpatasvir

c. Sofosbuvir + Ledipasvir

d. Sofosbuvir + Declatasvir

6) How long do you use Sofosbuvir velpatasvir combination in patients with hepatitis c (those without cirrhosis or compensated cirrhosis)?

a. 8 weeks

b. 12 weeks

c. 24 weeks

7) Which one of the following is your most preferred treatment option (DAA) in patients with hepatitis C infection with decompensated cirrhosis?

a. Sofosbuvir + Ribavirin

b. Sofosbuvir + Velpatasvir

c. Sofosbuvir + Velpatasvir + Ribavirin

d. Sofosbuvir + Declatasvir + Ribavirin

e. Sofosbuvir + Ledipasvir + Ribavirin

8) How long do you use Sofosbuvir velpatasvir combination in patients with hepatitis c with decompensated cirrhosis?

a. 8 weeks

b. 12 weeks

c. 24 weeks

9) Which of the following patient profiles are suitable for the treatment of sofosbuvir velpatasvir FDC?

a. Treatment naïve patients

b. Previously treated (with DAA/interferon/ribavirin)

c. Both

10) In what all indications do you prefer sofosbuvir velpatasvir FDC?

a. HCV patients without cirrhosis

b. HCV patients with compensated cirrhosis

c. HCV patients with decompensated cirrhosis

11) Do you prefer sofosbuvir velpatasvir FDC in your patients with HCVinfection who are currently on dialysis?

a. Yes

b. No

12) According to your experience, sofosbuvir velpatasvir FDC is effective in which of the following HCV genotypes?

a. Genotype 1

b. Genotype 2

c. Genotype 3

d. Genotype 4

e. Genotype 5

f. Genotype 6

g. Effective across all genotypes (Pangenotypic)

13) What are the important factors according to you that gives a competitive advantage to Sofosbuvir velpatasvir FDC over other drugs and combinations?

a. Efficacy

b. Safety and tolerability

c. pangenotypic activity

d. IFN-free treatment option

e. Ribavirin free treatment option

14) In the past, have you used Sofocure-V (sofosbuvir velpatasvir FDC) in your practice?

a. Yes

b. No

15) How would you rate your experience (in terms of efficacy) with Sofocure-V solution on a scale of 1-10 (1 being worst, 10 being best)?

a. 1

b. 2

c. 3

d. 4

e. 5

f. 6

g. 7

h. 8

i. 9

j. 10

16) In the past, have you used Sofocure-V (sofosbuvir velpatasvir FDC) in your practice?

a. Yes

b. No

17) How would you rate your experience (in terms of safety) with Sofocure-V solution on a scale of 1-10 (1 being worst, 10 being best)?

a. 1

b. 2

c. 3

d. 4

e. 5

f. 6

g. 7

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i. 9

j. 10

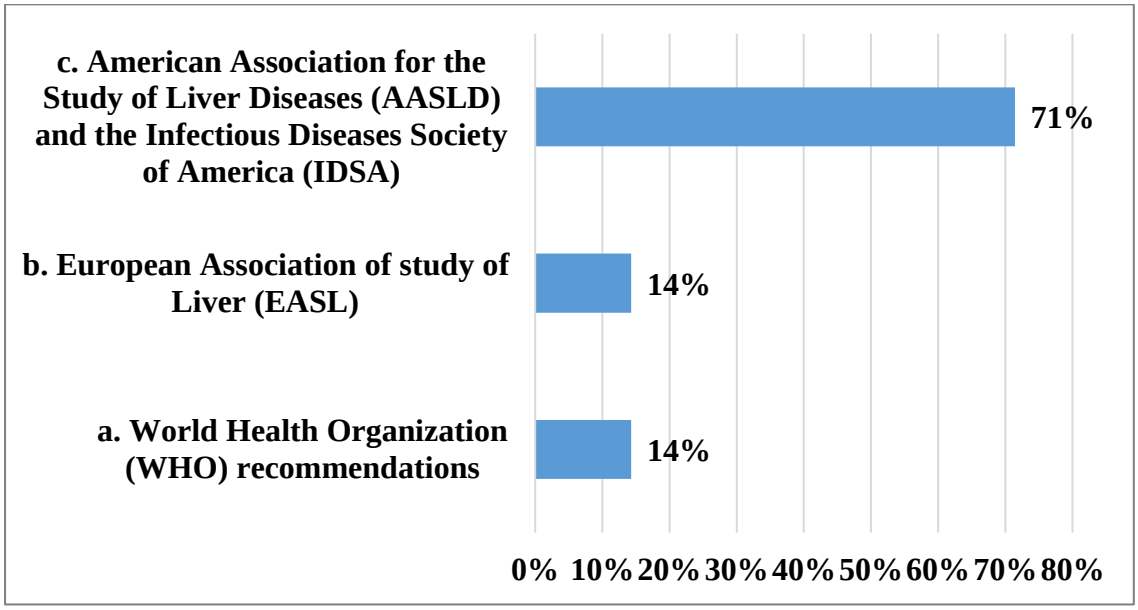
Survey Findings

1) Which of the following guidelines/recommendation do follow pertaining to diagnosis and management of Hepatitis C?

a. World Health Organization (WHO) recommendations

b. European Association of study of Liver (EASL)

c. American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA)



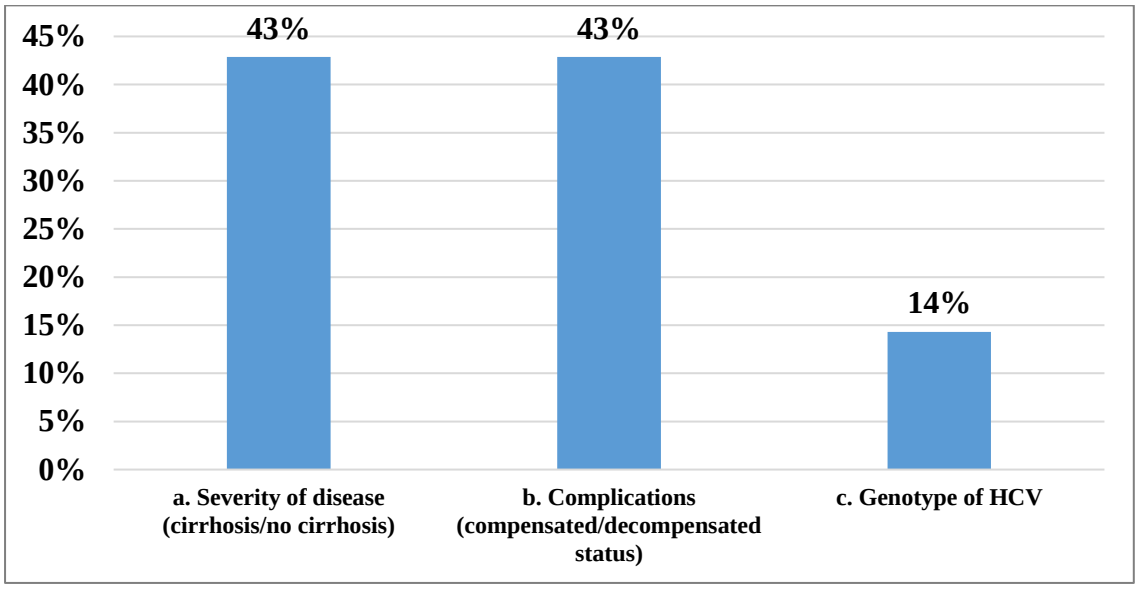
According to 71% of doctor, American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) follow pertaining to diagnosis and management of Hepatitis C.

2) Which of the following factors do you consider while selecting the antiviral treatment in your patients with Hepatitis C?

a. Severity of disease (cirrhosis/no cirrhosis)

b. Complications (compensated/decompensated status)

c. Genotype of HCV



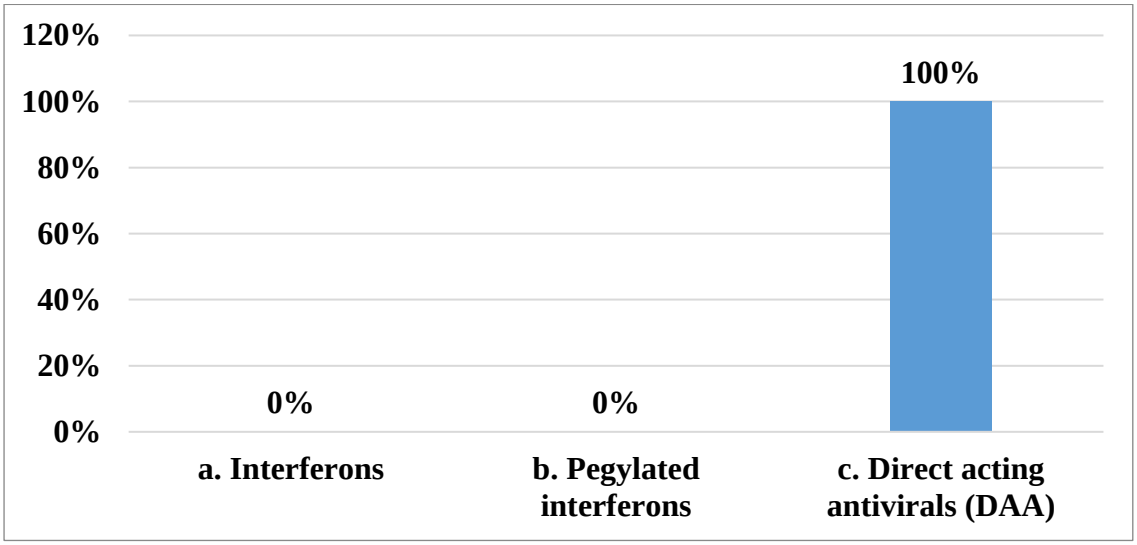
As per 43% of doctor, severity of disease (cirrhosis/no cirrhosis) and complications (compensated/decompensated status) are the factors they consider while selecting the antiviral treatment in their patients with Hepatitis C.

3) Which of the following treatment options do you prefer in your patients with Hepatitis C?

a. Interferons

b. Pegylated interferons

c. Direct acting antivirals (DAA)



According to majority of doctors, 100%, they prefer direct acting antivirals (DAA) in their patients with Hepatitis C.

4) According to you, which of the following are advantages of direct-acting antivirals?

a. virological efficacy

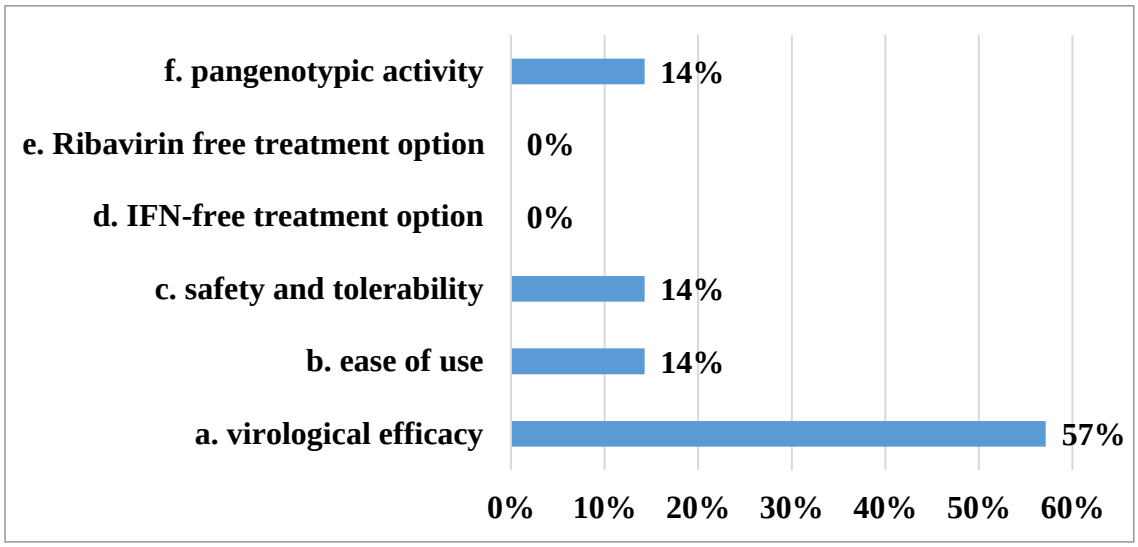
b. ease of use

c. safety and tolerability

d. IFN-free treatment option

e. Ribavirin free treatment option

f. pangenotypic activity



According to 57% of doctor, the most important advantage of direct-acting antivirals is virological efficacy.

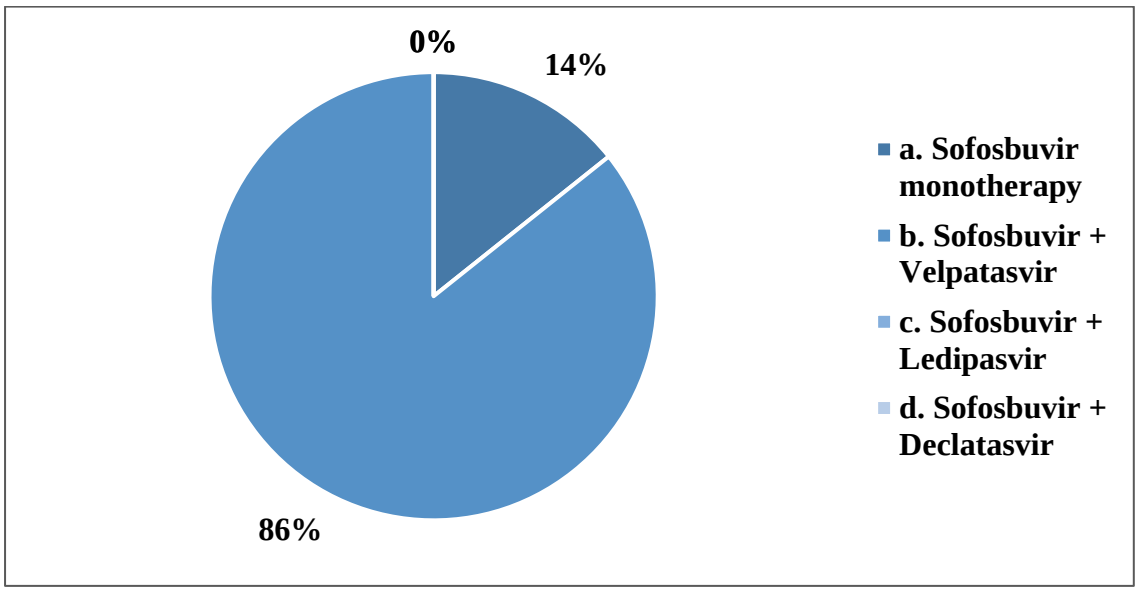
5) Which one of the following is your most preferred treatment option (DAA) in patients with hepatitis C infection (without cirrhosis or compensated cirrhosis)?

a. Sofosbuvir monotherapy

b. Sofosbuvir + Velpatasvir

c. Sofosbuvir + Ledipasvir

d. Sofosbuvir + Declatasvir



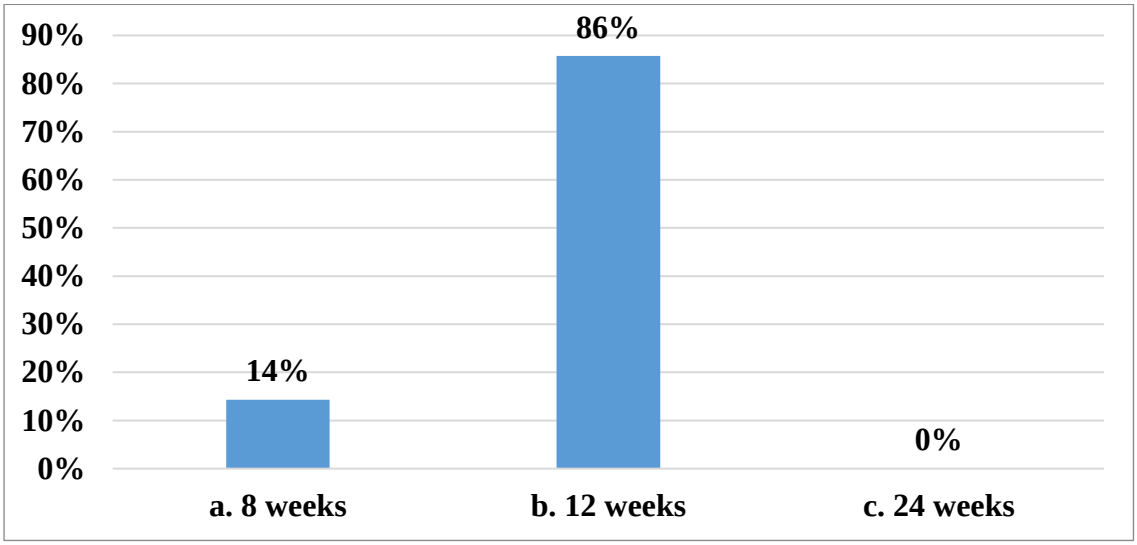
According to majority of doctors, 86%, Sofosbuvir + Velpatasvir is their most preferred treatment option (DAA) in patients with hepatitis C infection (without cirrhosis or compensated cirrhosis).

6) How long do you use Sofosbuvir velpatasvir combination in patients with hepatitis c (those without cirrhosis or compensated cirrhosis)?

a. 8 weeks

b. 12 weeks

c. 24 weeks



As per 86% of doctor, they use Sofosbuvir velpatasvir combination in patients with hepatitis c (those without cirrhosis or compensated cirrhosis) for 12 weeks.

7) Which one of the following is your most preferred treatment option (DAA) in patients with hepatitis C infection with decompensated cirrhosis?

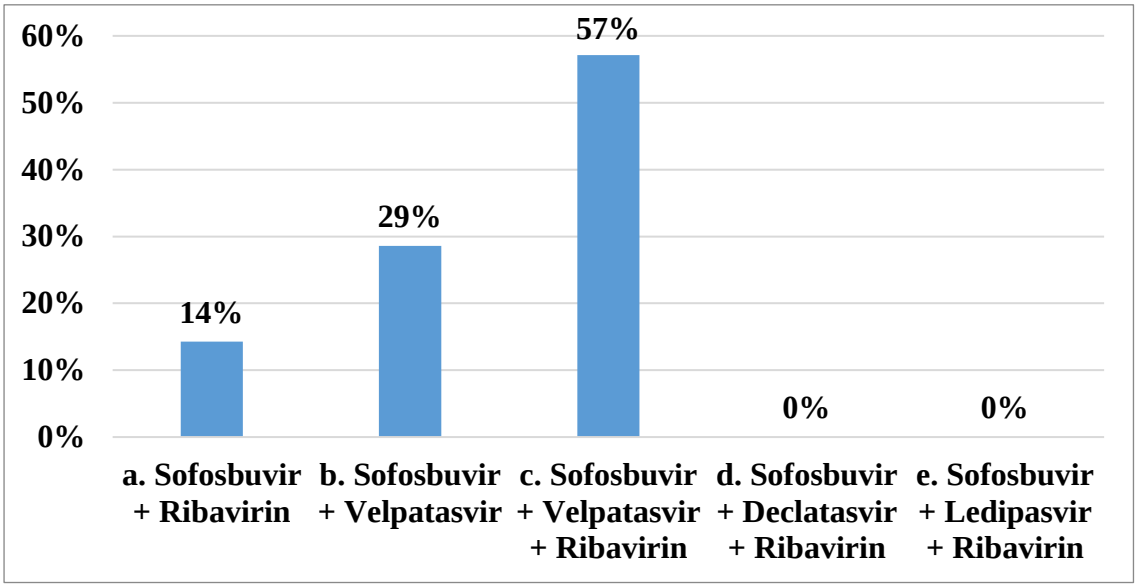
a. Sofosbuvir + Ribavirin

b. Sofosbuvir + Velpatasvir

c. Sofosbuvir + Velpatasvir + Ribavirin

d. Sofosbuvir + Declatasvir + Ribavirin

e. Sofosbuvir + Ledipasvir + Ribavirin



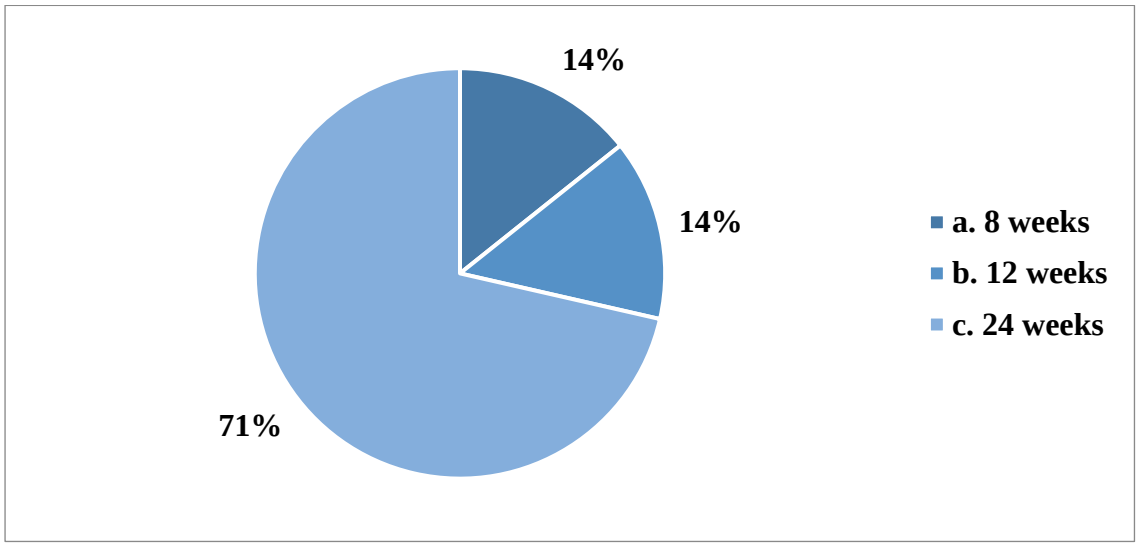
According to 57% of doctor, Sofosbuvir + Velpatasvir + Ribavirin is their most preferred treatment option (DAA) in patients with hepatitis C infection with decompensated cirrhosis.

8) How long do you use Sofosbuvir velpatasvir combination in patients with hepatitis c with decompensated cirrhosis?

a. 8 weeks

b. 12 weeks

c. 24 weeks



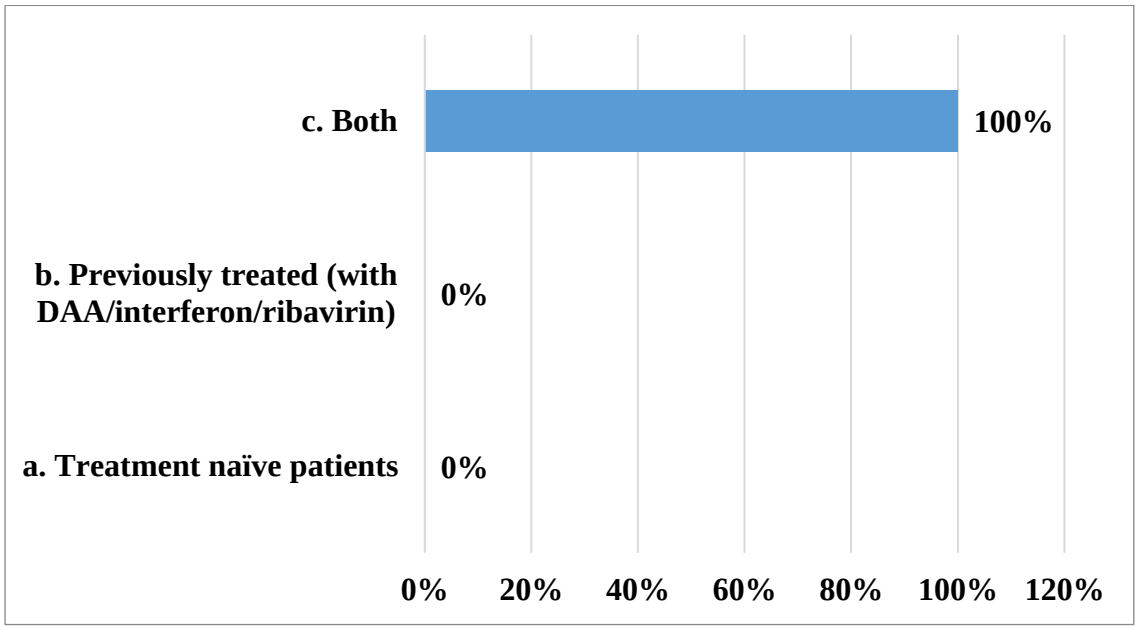
According to majority of doctor, 71%, they use Sofosbuvir velpatasvir combination in patients with hepatitis c with decompensated cirrhosis for 24 weeks.

9) Which of the following patient profiles are suitable for the treatment of sofosbuvir velpatasvir FDC?

a. Treatment naïve patients

b. Previously treated (with DAA/interferon/ribavirin)

c. Both



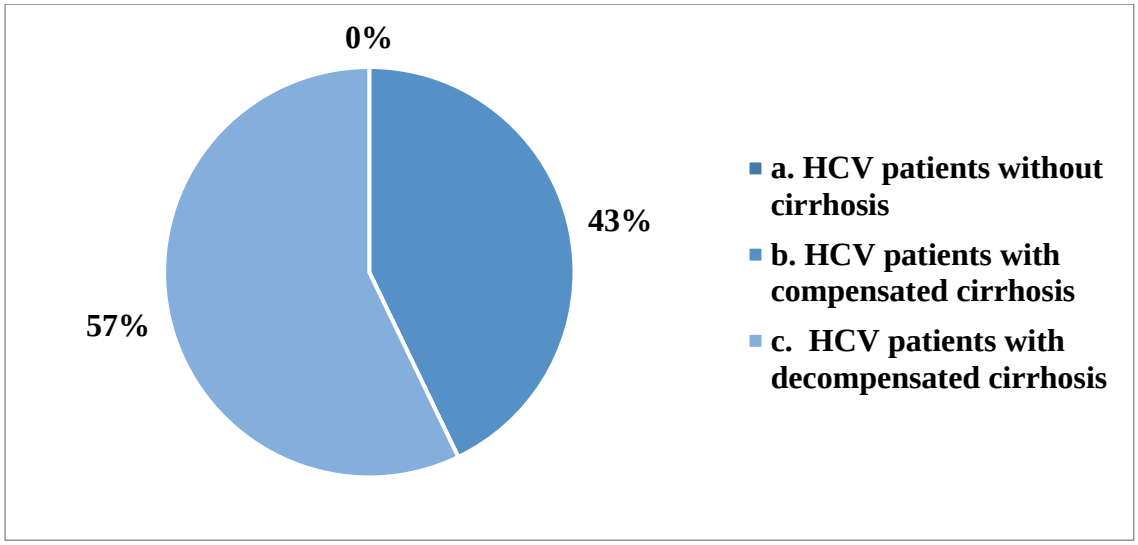
All the doctors (100%) unanimously agree that naïve patients and previously treated (with DAA/interferon/ribavirin) patients – both are suitable for the treatment of sofosbuvir velpatasvir FDC.

10) In what all indications do you prefer sofosbuvir velpatasvir FDC?

a. HCV patients without cirrhosis

b. HCV patients with compensated cirrhosis

c. HCV patients with decompensated cirrhosis

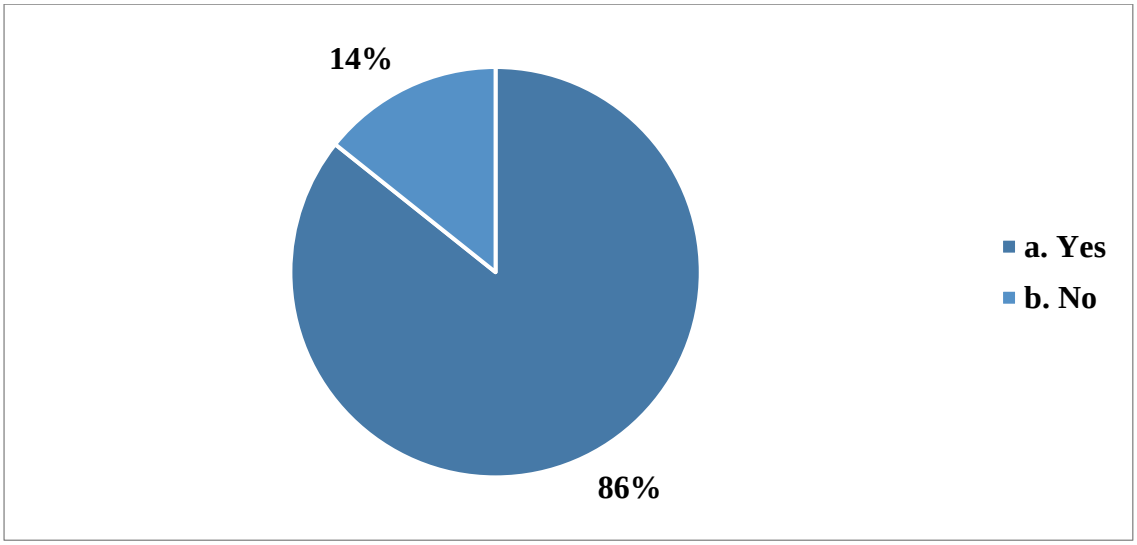


As per 57% of doctor, they prefer sofosbuvir velpatasvir FDC in HCV patients with decompensated cirrhosis.

11) Do you prefer sofosbuvir velpatasvir FDC in your patients with HCVinfection who are currently on dialysis?

a. Yes

b. No



According to majority of doctors, 86%, they prefer sofosbuvir velpatasvir FDC in their patients with HCVinfection who are currently on dialysis.

12) According to your experience, sofosbuvir velpatasvir FDC is effective in which of the following HCV genotypes?

a. Genotype 1

b. Genotype 2

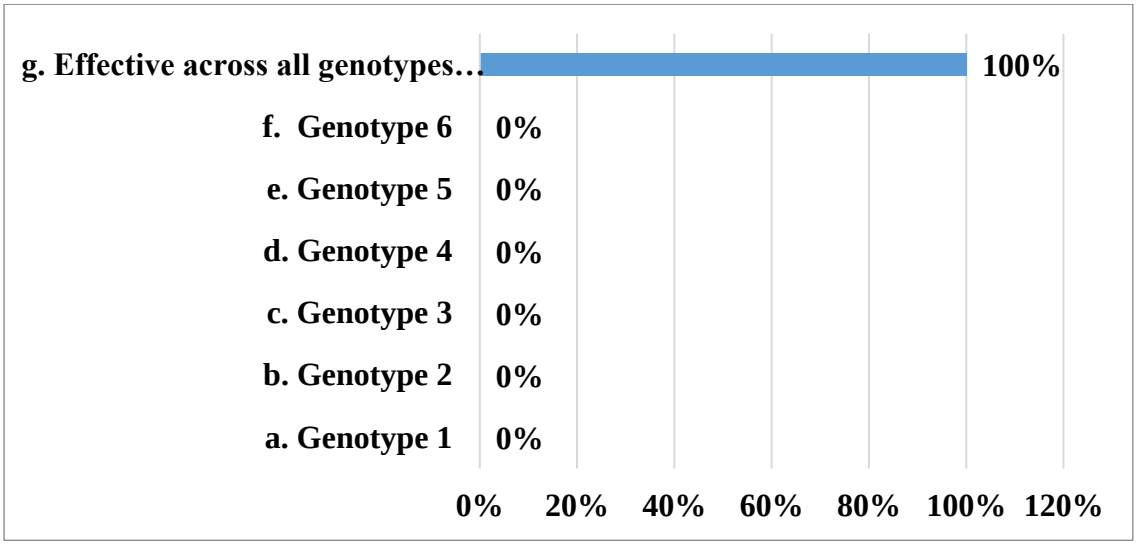
c. Genotype 3

d. Genotype 4

e. Genotype 5

f. Genotype 6

g. Effective across all genotypes (Pangenotypic)



According to majority of doctors, 100%, sofosbuvir velpatasvir FDC is effective across all HCV genotypes (Pangenotypic).

13) What are the important factors according to you that gives a competitive advantage to Sofosbuvir velpatasvir FDC over other drugs and combinations?

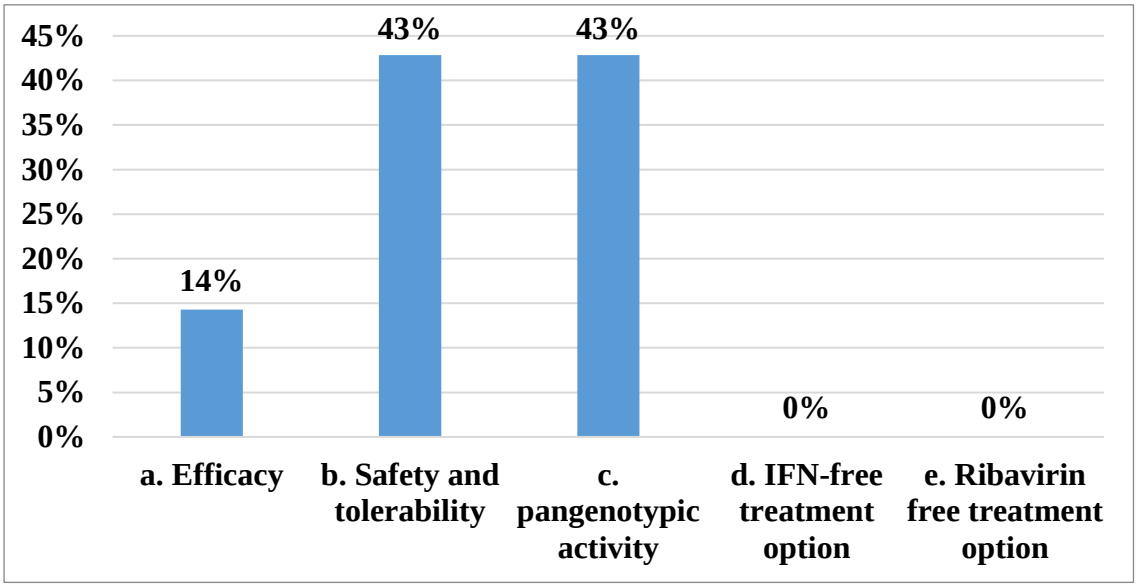
a. Efficacy

b. Safety and tolerability

c. pangenotypic activity

d. IFN-free treatment option

e. Ribavirin free treatment option

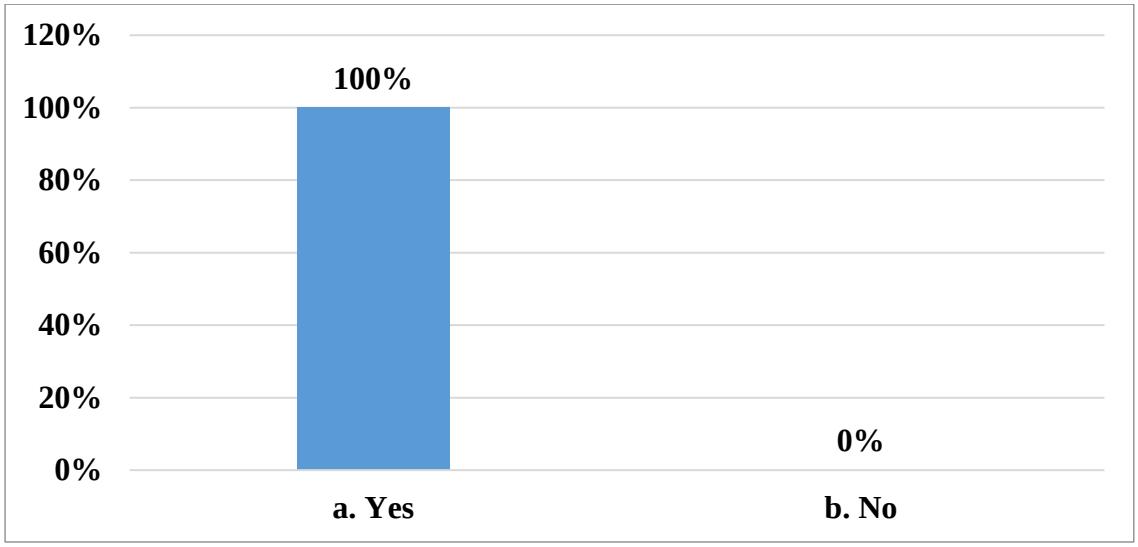


As per 43% of doctor, safety and tolerability is the important factor that gives a competitive advantage to Sofosbuvir velpatasvir FDC over other drugs and combinations whereas other 43% of doctors believe that it is the pangenotypic activity which gives it competitive advantage.

14) In the past, have you used Sofocure-V (sofosbuvir velpatasvir FDC) in your practice?

a. Yes

b. No



According to majority of doctors, 100%, they have used Sofocure-V (sofosbuvir velpatasvir FDC) in their practice.

15) How would you rate your experience (in terms of efficacy) with Sofocure-V solution on a scale of 1-10 (1 being worst, 10 being best)?

a. 1

b. 2

c. 3

d. 4

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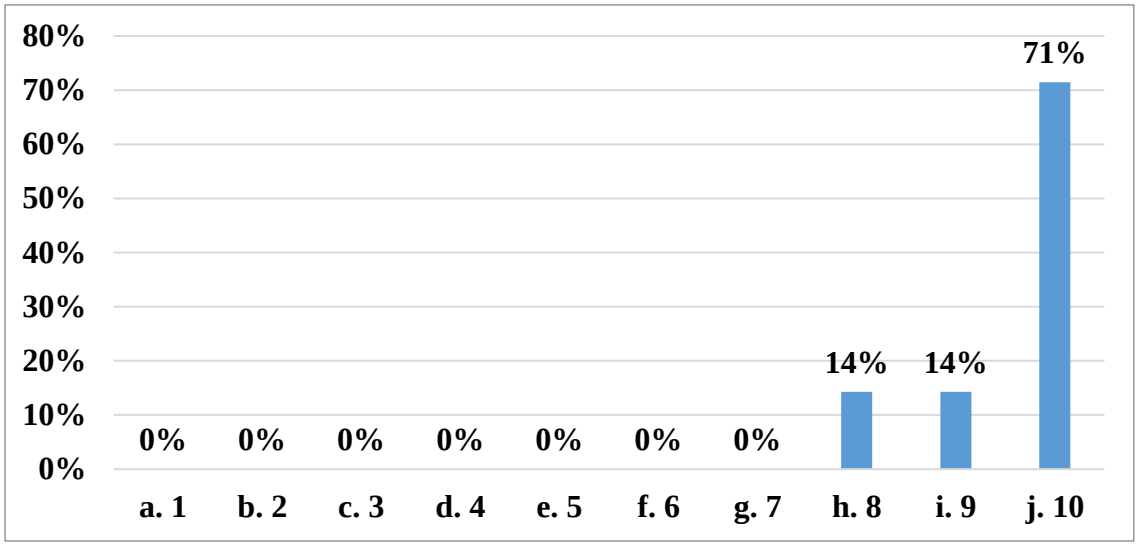
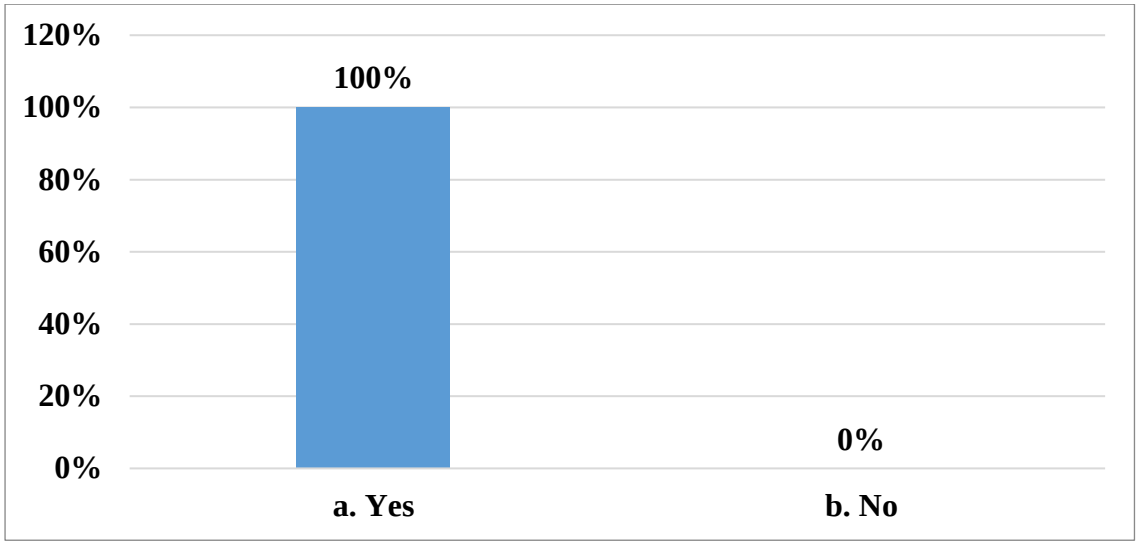


71% of doctor, rate their experience (in terms of efficacy) with Sofocure-V solution as 10 on a scale of 1-10 (1 being worst, 10 being best).

16) In the past, have you used Sofocure-V (sofosbuvir velpatasvir FDC) in your practice?

a. Yes

b. No



According to majority of doctors, 100%, they have used Sofocure-V (sofosbuvir velpatasvir FDC) in their practice.

17) How would you rate your experience (in terms of safety) with Sofocure-V solution on a scale of 1-10 (1 being worst, 10 being best)?

a. 1

b. 2

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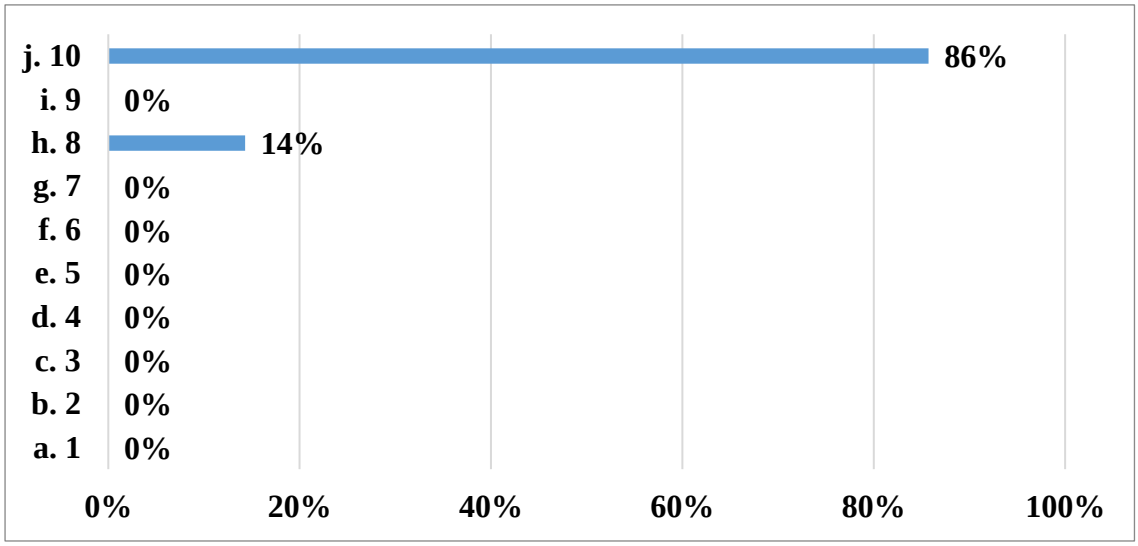

Majority of doctors, 86%, rate their experience (in terms of safety) with Sofocure-V solution on a scale of 1-10 (1 being worst, 10 being best) as 10.

Summary

- According to 71% of doctor, American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) follow pertaining to diagnosis and management of Hepatitis C.
- As per 43% of doctor, severity of disease (cirrhosis/no cirrhosis) and complications (compensated/decompensated status) are the factors they consider while selecting the antiviral treatment in their patients with Hepatitis C.
- According to majority of doctors, 100%, they prefer direct acting antivirals (DAA) in their patients with Hepatitis C.
- According to 57% of doctor, the most important advantage of direct-acting antivirals is virological efficacy.
- According to majority of doctors, 86%, Sofosbuvir + Velpatasvir is their most preferred treatment option (DAA) in patients with hepatitis C infection (without cirrhosis or compensated cirrhosis).
- As per 86% of doctor, they use Sofosbuvir velpatasvir combination in patients with hepatitis c (those without cirrhosis or compensated cirrhosis) for 12 weeks.
- According to 57% of doctor, Sofosbuvir + Velpatasvir + Ribavirin is their most preferred treatment option (DAA) in patients with hepatitis C infection with decompensated cirrhosis.
- According to majority of doctor, 71%, they use Sofosbuvir velpatasvir combination in patients with hepatitis c with decompensated cirrhosis for 24 weeks.
- All the doctors (100%) unanimously agree that naïve patients and previously treated (with DAA/interferon/ribavirin) patients – both are suitable for the treatment of sofosbuvir velpatasvir FDC.
- As per 57% of doctor, they prefer sofosbuvir velpatasvir FDC in HCV patients with decompensated cirrhosis.

- According to majority of doctors, 86%, they prefer sofosbuvir velpatasvir FDC in their patients with HCVinfection who are currently on dialysis.
- According to majority of doctors, 100%, sofosbuvir velpatasvir FDC is effective across all HCV genotypes (Pangenotypic).
- As per 43% of doctor, safety and tolerability is the important factor that gives a competitive advantage to Sofosbuvir velpatasvir FDC over other drugs and combinations whereas other 43% of doctors believe that it is the pangenotypic activity which gives it competitive advantage.
- According to majority of doctors, 100%, they have used Sofocure-V (sofosbuvir velpatasvir FDC) in their practice.
- 71% of doctor, rate their experience (in terms of efficacy) with Sofocure-V solution as 10 on a scale of 1-10 (1 being worst, 10 being best).
- According to majority of doctors, 100%, they have used Sofocure-V (sofosbuvir velpatasvir FDC) in their practice.
- Majority of doctors, 86%, rate their experience (in terms of safety) with Sofocure-V solution on a scale of 1-10 (1 being worst, 10 being best) as 10.

Consultant Opinion

Based on the survey analysis regarding the management of Hepatitis C, here are some recommendations and opportunities for improving patient care and potential strategies for pharmaceutical companies:

Market Opportunities:
Recognize the widespread preference for direct-acting antivirals (DAA) among healthcare professionals as an opportunity for pharmaceutical companies to invest in the development and marketing of innovative DAA formulations.

Value for Healthcare Professionals:
Provide healthcare professionals with continued education and training on the latest guidelines and recommendations from organizations such as the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) regarding the diagnosis and management of Hepatitis C.

Adverse Effect Management:
Focus on developing DAA formulations with improved safety and tolerability profiles, addressing concerns related to adverse effects and enhancing patient adherence to treatment regimens.

Withdrawal Management:
Implement protocols and guidelines for the safe and effective withdrawal management of existing antiviral treatments, ensuring smooth transitions to new DAA regimens as recommended by healthcare professionals.

Market Positioning:
Position DAA formulations with proven virological efficacy, such as Sofosbuvir + Velpatasvir, as preferred treatment options for patients with Hepatitis C across different disease stages and genotypes, emphasizing their pangenotypic activity and competitive advantages.

Personalized Treatment Decisions:

Encourage healthcare providers to consider individual patient factors, such as diseasezseverity, comorbidities, and treatment history, when selecting the most appropriate DAA regimen, facilitating personalized treatment decisions and optimizing patient outcomes.

Improving Patient Outcomes:

Collaborate with healthcare providers to monitor treatment responses and patient outcomes systematically, leveraging real-world data to evaluate the effectiveness and safety of DAA formulations in diverse patient populations and clinical settings.

Innovation and Research:

Invest in ongoing research and development initiatives to advance the field of Hepatitis C treatment, exploring novel DAA combinations, formulations, and treatment strategies aimed at further improving treatment efficacy, safety, and patient convenience.

By addressing these aspects, both healthcare professionals and pharmaceutical companies can work together to optimize the management of Hepatitis C, ultimately leading to improved patient outcomes and enhanced quality of care for individuals affected by this condition.

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