Real World Treatment of Hepatitis C with Second Generations Direct Acting Antivirals (DAAs): Initial Treatment Results from Diverse Treatment Centres in a North American Urban Referral Centre

Running Head: HCV Treatment Outcomes with Second Generation DAAs

Alex I. Aspinall[*#], Abdel Aziz Shaheen[*], Golasa Samadi Kochaksaraei[*], Breean Haslam[*], Samuel S. Lee[*], Gisela McPhail[§], Jeff Kapler[†], Oscar E. Larios[†], Kelly W. Burak[*], Mark. G. Swain[*], Meredith A. Borman, and Carla S. Coffin[*†]

Appointment of Authors:

AA: MD, PhD, Clinical Assistant Professor, Department of Medicine

AZS, GM, OL, MB: MD, Associate Professor, Department of Medicine

KB, SSL, MS: MD, Professor, Department of Medicine

CC: MD, Associate Professor, Department of Medicine

GSK: MD, Clinical Research Assistant

BH: Clinical Research Nurse Coordinator

JK: PharmD

[*]Calgary Liver Unit, Division of Gastroenterology and Hepatology, University of Calgary, [§]Calgary Urban Project Society, [†]Southern Alberta Clinic, Alberta Health Services, Calgary, Alberta, Canada.

Corresponding Author: Alex I. Aspinall, Calgary Liver Unit, Calgary Division of Gastroenterology and Hepatology, Department of Medicine. Email: aaspinal@ucalgary.ca

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Abstract

Background: High HCV cure rates have been observed in registration trials with second generation DAA. Real-world data in the USA and Europe has also demonstrated high sustained viral response (SVR) rates. **Aim**: To determine real-world SVR rates for HCV-infected patients treated with second generation DAA in the first 18 months of their availability in Canada. **Methods**: Four centres in a large Canadian city contributed their treatment data from a diverse HCV patient population including pre- and post-liver transplantation, HIV co-infected, and vulnerable populations. Multivariate analysis was used to determine independent predictors of treatment failure. **Results**: In 351 treated with DAAs, SVR rate was 92.9% (93.7%, 96.6% and 86.3% for Genotype 1a, 1b and 3 respectively, *P*=0.15). Independent predictors of not achieving SVR were male gender (Adjusted OR: 0.30, 0.10-0.89), older age (AOR: 0.95, 0.90-1.00), and in genotype 1a patients, history of hepatocellular carcinoma (HCC) (AOR: 0.13, 0.03-0.53). Presence of cirrhosis, genotype or HCC were not associated with a lower SVR. There were no differences in SVR rates according to treatment centre, HIV coinfection or liver

transplant. Decreased SVR was observed in Genotype 3 patients who received shorter treatment regimens (89.6% vs 33.3%, P=0.04). *De* novo HCC developed in 12 (3.4%) despite successful DAA therapy. **Conclusions**: We report high SVR rates for second generation DAA in a real world diverse cohort of HCV-infected patients. This study highlights the importance of conducting real-world analyses to elucidate clinical factors associated with poorer outcomes that may not be identified in registration trials.

Key words:

Canadian, Hepatitis C, directly acting antiviral agents, real-world data, retrospective cohort

Introduction

Unprecedented cure rates for people chronically-infected with the hepatitis C virus (HCV) have been achieved with the introduction of interferon (IFN)-free regimens, especially for HCV Genotypes of 1, 2 and 4. Phase III clinical trial results for sofosbuvir/ledipasvir and for paritaprevir, ritonavir, ombitasvir, dasabuvir (PrOD) ± ribavirin demonstrated SVR rates of 94-99% (1-3) and 97%-99.5% (4), respectively.

Historically, treatments for HCV in the real-world have not shown equal SVR rates to those achieved in clinical trials. This includes other interferon (IFN)-free regimens such as sofosbuvir in combination with simeprevir. Real world data from the HCV-Therapeutic Registry and Research Network (TARGET)observational cohort reported SVR rates of 81-87% (5). In comparison, the Phase II COSMOS clinical trial reported an overall SVR rate of 95% (6). The recently published phase III OPTIMIST-2 trial of sofosbuvir and simeprevir reported SVR rates of

88% and 79% in treatment naïve and treatment experienced cirrhotic patients respectively (7). For IFN-containing regimes, higher complication (8,9) and lower SVR rates (9) have been reported for the first generation directly acting antiviral agents (DAA) telaprevir and boceprevir, and was also shown in real-world data from sites involved in the current study (10).

In Canada, sofosbuvir/ledipasvir has been available since October 2014 and PrOD became available in 2015. Both regimens were included on the provincial drug benefits list (i.e. public reimbursement) in Alberta in 2015. These HCV treatments have been available for a longer period of time in most western countries including the USA and in Europe. Some of those jurisdictions have recently reported their real world HCV treatment experiences with the second generation DAAs (10) (11), but Canadian real-world treatment data in both non-cirrhotic and cirrhotic patients is lacking .

In the current study, our main objectives were; to determine HCV treatment SVR rates using second generation HCV DAA in the first 18 months of their availability in Canada, and to evaluate SVR rates among different demographic and clinical characteristics. Our secondary objective was to assess predictors of SVR in this cohort. Our data includes a diverse cohort of patients treated at four treatment centres in a large Canadian City. Our study highlights the relevance of obtaining real-world data in assessing responses to novel HCV treatment regimens.

Materials and Methods

Patient Population

In this retrospective cohort study, patient and treatment data was extracted and analyzed from a database for all HCV patients who received antiviral therapy. A manual chart

review was required to extract transient elastography (TE) values using Fibroscan® (Echosens, France). Patients were seen at four treatment centres in Calgary, Canada, serving a referral catchment area of approximately 2 million people. The clinics included a diverse cohort of patients seen at a University referral liver clinics at two hospitals (Calgary Liver Unit), a community clinic treating vulnerable populations (i.e., Calgary Urban Project Society) and a HIV co-infected clinic (Southern Alberta Clinic). The primary intention-to-treat (ITT) outcome was SVR with a modified ITT (mITT) outcome that excluded the very small number deaths during treatment period (n=2 patients) and patients lost to follow up (n=4). HCV viral load at baseline was determined by Abbott real-time PCR assay (lower limit of detection, LLOD 12 IU/ml, Missasauga, Ontario).

One author (AA) reviewed all data to determine whether the patients had been treated within or outside Health Canada-recommended labelling. Prescriptions outside Health Canada-labelling were noted. Canadian product monographs published during the period of the study and recommendations based on registration trials for the DAA were considered to be standard of care (SOC) (12,13).

The SOC for treatment-naïve genotype 1 non-cirrhotic patients with low viral load, i.e., <6 $\log^{10}$ international units (IU) / mL was 8 weeks of sofosbuvir and ledipasvir, compared to 12 weeks for either treatment-naïve patients with a high baseline HCV RNA viral load (≥6 $\log^{10}$ IU/mL) or compensated cirrhotic patients. For treatment-experienced genotype 1, SOC was accepted as either 24 weeks of therapy with sofosbuvir/ ledipasvir or 12 weeks of therapy with sofosbuvir/ ledipasvir and ribavirin. These treatment guidelines were based on the preliminary

results of the SIRIUS study for difficult to treat chronic HCV patients, which became available during the period of this study (15).

For genotype 1b patients treated with PrOD, 12 weeks of therapy was considered SOC and 12 weeks with PrOD and ribavirin was recommended for genotype 1a. Cirrhotic patients or previous null responders to IFN-based therapy did not receive PrOD. For patients treated with simeprevir in combination with sofosbuvir, either 12 or 24 weeks of therapy was accepted as SOC, based on published data showing no difference treatment outcomes with shorter treatment duration (i.e., COSMOS trial) (6). Further, there was no Canadian recommendation for the duration of this off-label therapy during the current study period.

For HCV genotype 2 patients, the SOC for duration of therapy was 12 weeks of sofosbuvir/ribavirin in non-cirrhotic patients versus either 12 or 16 weeks of sofosbuvir/ribavirin therapy in patients with cirrhosis. The recommendation to extend treatment of cirrhotic genotype 2 patients to 16 weeks was based on results from the FUSION trial, which became available during the course of this study (16). For genotype 3 patients, 24 weeks of therapy with sofosbuvir/ribavirin was accepted as standard of care.

All genotype 1 patients evaluated for or undergoing liver transplantation who received sofosbuvir/ledipasvir/ribavirin for any duration between 12 and 24 weeks were considered to have been treated within existing guidelines. The results of the SOLAR-1 and SOLAR-2 studies in decompensated and LT recipients were published after the study was completed (17). For any patient treated with an IFN (i.e., pegylated Interferon) regimen that also contained sofosbuvir, 12 weeks was considered the SOC duration based on the NEUTRINO trial results (18).

Ethics approval was obtained through the University of Calgary Conjoint Ethics Review Board (CHREB) and Alberta Health Services Institutional Review Board.

Outcomes

The primary outcome of interest was undetectable virus 12 weeks after then end of therapy (SVR12).

Study variables

Patients' demographics including age in years and gender (male/female) were obtained. Clinical and laboratory data including previous HCV treatment (yes/no); liver stiffness measurement by transient elastography (TE) (kPa) at baseline and follow-up; change of TE (follow up-baseline measurement); baseline HCV RNA (IU/ml); previous history of HCC (yes/no); HCC development after starting treatment (yes/no); coinfection with hepatitis B (yes/no); coinfection with HIV (yes/no); HCV genotype; baseline glomerular filtration rate; having kidney disease (yes/no) and cirrhosis at baseline (Fibroscan ≥12.5kPa and/or biopsy showing Metavir F4 fibrosis) (yes/no); histology by Metavir score when available (stage 1-4); model for end stage liver disease (MELD) at baseline; MELD-Na at baseline; treatment according to guidelines (yes/no); and medical care centers were all recorded.

Statistical Analysis

Bivariate analyses were performed using Fisher's exact test or Wilcoxon rank sum test for categorical and continuous data respectively. Categorical data were expressed as

percentage and continuous data were demonstrated as medians with interquartile ranges (IQR). A logistic regression model was created to evaluate variables (age, gender, previous treatment, genotype, baseline TE, baseline HCV RNA, MELD, MELD-Na, presence of cirrhosis, previous history of HCC, and treatment according to guidelines) that independently predicted SVR. Sensitivity analyses were done to assess the latter regression model among different genotypes. Adjusted odds ratios (AOR) with 95% confidence intervals (CI) are reported. All statistical analyses were performed using STATA (Stata Statistical Software: Release 14. College Station, TX, USA). A priori significance level of 0.05 was used in all analyses.

Results:

In total, 357 HCV patients were enrolled and outcome data was available in 98.3% (351/357 patients) treated with a second generation DAA containing-regimen between October 2014 and April 2016. Among the six patients for whom SVR information was not available, two died on treatment and four were lost to follow up. Three of the four that were lost to follow up had undetectable HCV RNA at the end of treatment (EOT). Overall, by ITT 91.3% (326/357) and by mITT 92.9% (326/351) of patients achieved an SVR. Patients who achieved SVR were likely to be younger (age 57 vs. 60 yr, *P*=0.02), female (SVR 97.0% vs. 90.3% for male gender, *P*=0.02), non-cirrhotic (95.5% vs. 89.3%, *P*=0.03) and no history of HCC at diagnosis (80% vs. 93.7%, p=0.04), Table 1. Six patients died (4 males, 66.7%; median age: 60) during post treatment follow up period. Those who died had significant lower SVR rates (50.0%, compared to 93.6% SVR rate among remaining patients, P <0.01). There was no impact of baseline MELD, history of HCC or liver transplant on patient survival. *De* novo HCC developed in 12 patients (3.4%).

Majority of them (n=11) achieved SVR. Demographic, clinical and laboratory characteristics of our cohort are presented in table 1.

The majority of our study cohort was genotype 1a (n=206, 82.0%), compared to genotype 1b (n=59), 2 (n=25), 3 (n=51) and other genotypes (n=9). There was no significant difference in SVR rates between different genotypes (*P*=0.15). The baseline TE was similar among patients who achieved SVR12 compared those who did not (median: 10.2 vs. 12.5 kPa, *P*=0.13). SVR12 rates were not influenced by baseline renal function, previous treatment, baseline HCV viral load, MELD, MELD-Na, history of liver transplantation nor coinfection with HIV, Table 1. Although the location of the four treating sites (i.e., academic vs community) did not impact SVR rates (*P*=0.73), all health care providers were considered local experts in HCV treatment.

Most patients were treated with a sofosbuvir-containing regimen (96.3%, n=338), while only 24 patients (6.8%) were treated with IFN-based regimen (in combination with a second generation DAA).

SVR12 rates for Genotype 1a patients (n=206) treated with sofosbuvir/ledipasvir (n=158, SVR: 93.0%), sofosbuvir/ledipasvir/ribavirin (n=13, SVR: 92.3%) were comparable to patients treated with simeprevir and sofosbuvir (n=17, SVR: 100%), Peg-IFN based therapy (n=13, SVR: 92.3%) and paritaprevir, ombitasvir, ritonavir, dasabuvir (PrOD) ± ribavirin (n=5, SVR:100%), *P*=0.82. Similarly, genotype 1b patients (n=59) who were treated with sofosbuvir/ledipasvir (n=48, SVR: 95.8%), were comparable to all other regimens (n=9, SVR 100%), P=1.00, Table 2.

For genotype 3 patients (n=51) treated with sofosbuvir and ribavirin (n=45), the SVR rate was 84.4% compared to 100% to other regimens, P=0.58, Table 2. In this group, 28 patients (54.9%) had cirrhosis compared to 121 patients (40.5%) in all other genotypes, *P*=0.07.

All regimens and durations of therapy were analyzed to determine whether they were within treatment guidelines established during the period of this study. Most patients were treated within established treatment guidelines (Supplementary Table 1). For the majority of non-genotype 3 patients, treatment within or outside of treatment guidelines did not impact SVR rates (Supplementary Table 1). However, for the small number of patients with genotype 3 who were treated outside of established guidelines, a significantly lower SVR was noted (89.6% vs 33.3%, p=0.04).

In 183 patients, we calculated TE change through the treatment period (difference between TE measured in follow-up period compared to baseline). Patients who achieved SVR had similar reduction of TE compared to patients did not achieve SVR (-2.8 vs. -2.7 kPa), *P*=0.31. A significant reduction in TE was observed in HCV patients with G1a infection, who achieved SVR compared to G1a patients who failed HCV therapy (-2.9 vs. -0.3), *P*=0.02.

Significant predictors of SVR identified by univariate analysis were older age, male gender, the presence of baseline cirrhosis and previous history of HCC. However, in multivariate model, only older age (AOR: 0.95, 0.90-1.00) and male gender (AOR: 0.30, 0.10-0.89) were associated with not achieving SVR (Table 3). In a sensitivity analysis limiting the cohort to Genotype 1a patients, only male gender (AOR: 0.12, 0.02-0.98) and previous history of HCC (AOR: 0.13, 0.03-0.53) were associated with not achieving SVR.

Discussion:

In this multi-site retrospective Canadian cohort study, we observed high SVR rates in a real-world diverse cohort of HCV infected patients treated with second-generation DAA regimens. The overall SVR of 92.1% across all treatment regimens and genotypes (93.8% for Genotype 1 and 86.5% for Genotype 3) is comparable to SVR rates reported in other real-world cohorts that included cirrhotic patients with multiple genotypes (82.2%-85.9%) (14). For patients treated with sofosbuvir/ledipasvir ± ribavirin, the observed SVR rate of 93.8% was comparable to other real-world studies (TRIO: 94-97% (11) and HCV-TARGET: 95-97% (10)). The SVR rate that we observed was comparable to those seen in the registration trials that led to the approval of current DAA regimens (ION-1: 98-99%, ION-2: 94-99%, ION-3: 93-95%) (1-3). All 11 patients treated with PrOD ± ribavirin achieved an SVR, consistent with results from registration trials (SAPPHIRE-I: 95-98% TURQUOISE-II: 92-96% (15), (16)).

Our cohort had a high frequency of cirrhotic patients (43.1%) likely, stemming from the "warehousing" of patients that occurred prior to October 2014 when the first Health Canada approved all oral regimen (sofosbuvir with ledipasvir) became available. Prior to their approval, there was reticence to treat patients with advanced disease with IFN-based regimens due to the poor outcomes and risk factors identified through the French multicenter prospective study (i.e., the CUPIC study) (9). In our cohort, we identified that the presence of cirrhosis as well as older age, male gender and a past history HCC were all significant risks for not achieving an SVR. These observations are a departure from the findings of registration trials, and emphasize the clinical relevance and importance of conducting real-world analyses. In this study, SVR rates in patients with advanced liver disease were not as high as those seen in registration trials, a

finding that has also been supported by the findings of other recently published real-world cohorts (11,14).

Prior to the availability of sofosbuvir/ledipasvir, several patients were treated with the off label regimen of sofosbuvir in combination with simeprevir, based on the results of the Phase II COSMOS trial (6). In the current study, although all 17 patients who received simeprevir /sofosbuvir achieved an SVR (Table 1), this is not representative of our entire treatment experience with this regimen. In an ongoing retrospective study, preliminary data analysis has shown that there are a significant number of cases who had previously failed this regimen that were subsequently successfully re-treated with sofosbuvir/ledipasvir/RBV. Thus, the overall SVR rate was only 86.4% with this combination (data unpublished, abstract presentation 6th annual Canadian HCV meeting, Banff 2017). This was in contrast to the high SVR rate of 90-94% that was observed in that Phase II COSMOS trial (6). The lower observed SVR rate was consistent with that seen in the recently published Phase III OPTIMIST-II trial in which treatment-naïve, cirrhotic patients achieved an SVR 88% of the time, and in treatment-experienced, cirrhotic patients, 79% achieved an SVR (7).

A relatively small number of patients were treated with PEG-IFN, ribavirin and a second-generation protease inhibitor. Higher than expected SVR rates were seen in this group with 97% (23/24) patients achieved an SVR, in contrast to only 90% SVR among treatment-naïve patients based on registration trial data (i.e, NEUTRINO) (17).

We observed no differences in SVR were between the four treatment centres, including the single centre that treated HCV and HIV co-infected patients. Similarly, all liver transplant recipients achieved an SVR. We observed that our overall SVR rate of 92.1% was lower than

reported in registration trials. Treatment outside of established SOC (i.e., Health Canada guidelines) did not impact SVR in most patients. However, a small number of HCV genotype 3 infected patients who received a shortened course of therapy, outside of current SOC guidelines, had a significantly lower SVR. At that time, there were no up to date Canadian consensus guidelines for sofosbuvir-containing regimens (18), and there was anecdotal difficulty in obtaining appropriate courses of therapy through private insurers according to Health Canada recommendations.

A total of 31.8% of genotype 1 patients that could have been treated for 8 weeks with sofosbuvir/ledipasvir received 12 weeks of therapy. Results from the ION-3 trial (2) indicated that there would be no expected decrement in SVR for selected patients. Thus, this is an area for improvement and potential significant cost savings.

We identified 12/356 (3.3%) of patients treated with a DAA who developed *de novo* HCC in up to 6 months of follow up after therapy. This is consistent with other observations (19) that have noted up to 3.2% of patients developing *de novo* HCC within 24 weeks of follow up. This highlights the need for vigilance and screening for HCC after HCV treatment, especially among cirrhotic patients. Thus, the data also highlight the fact that the risk of HCC was not abrogated by successfully treating HCV among cirrhotic patients in our cohort.

Interestingly, although 49/356 (13.8%) patients who had a positive EOT viral load at or below the level of quantification, the majority of them (81.6%) ultimately achieved an SVR. Whether this is an epiphenomenon of all oral DAA regimens or of a more sensitive assay than those used in previous PEG-IFN eras is unknown. Nonetheless, the finding of a positive EOT PCR is anxiety-provoking for both patient and physician alike, as in previous eras such a finding

would imply treatment failure. While all such patients also undergo SVR12 testing, it is worthy to note, and helpful when counselling such patients, that the majority of individuals who had a positive EOT PCR treated with all oral DAA ultimately achieved an SVR. Additionally, we did not observe any cases of hepatitis B virus reactivation despite recent data showing reactivation of HBV in HCV co-infected patients (either HBV core antibody or HBV surface antigen positive individuals) undergoing DAA therapy (24).

In summary this is the largest real world Canadian study published on treatment outcomes with second generation DAA's. Our data show overall high SVR rates even in difficult to treat complex HCV patients in academic and community treatment centers. Our study also highlights risk factors for HCV treatment failures and identifies areas for optimizing HCV management (i.e., either extending or reducing duration of therapy, relevance of EOT viral load testing, need for HCC surveillance) and hence illustrates the clinical relevance of obtaining real-world treatment data.

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Table 1: Characteristics of patients according to SVR status

Characteristic	Achieved SVR	Not achieved SVR	*P*-value
	n=326 (92.9%)	n=25 (7.1%)	
Age at treatment	57 (50-61)	60 (56-64)	0.02
Gender			
Male (n=220)	90.3%	9.7%	0.02
Female (n=136)	97.0%	3.0%	
Having previous treatment	91.9%	8.1%	0.65
Genotype			
1 a (n=206)	93.7%	6.3%	
1 b (n=59)	96.6%	3.4%	0.15
2 (n=25)	88.0%	12.0%	
3 (n=51)	86.3%	13.7%	
4 & 6 (n=9)	100%	0%	
Fibroscan baseline	10.2 (6.7-20.4)	12.5 (7.6-26.3)	0.13
HCV PCR baseline	701,684 (158,376-1,677,684)	500,000 (94,082-1,500,000)	0.47
CKD at baseline (n=16)	100%	0%	0.62
Baseline eGFR	94 (81-101)	96 (83-99)	0.61
Coinfection			
HIV (n=12)	100%	0%	1.00
HBV (n=1)	100%	0%	1.00
Cirrhosis at baseline			
Yes (n=149)	89.3%	10.7%	0.03
No (n=201)	95.5%	4.5%	
Previous history of HCC (n=20)	80%	20%	0.04
Post liver transplant (n=9)	100%	0%	1.00
Site			
Site # 1 (n=11)	100%	0%	
Site # 2 (n=40)	92.5%	7.5%	0.73

Site # 3 (n=110)	90.9%	9.1%	
Site # 4 (n=190)	93.7%	6.3%	
Mortality in follow up period (n=6)	50%	50%	<0.01
Developed HCC in follow up (n=12)	91.7%	8.3%	0.58
MELD	6 (6-6)	6 (6-6)	0.98
MELD_Na	7 (5-8)	6 (5-8)	0.94

Table 2: SVR by treatment regimen and genotype

Characteristic	Achieved SVR n=326 (92.9%)	Not achieved SVR n=25 (7.1%)	*P*-value
Regimen			
Genotype 1a (n=206)	93.7%	6.3%	0.53
SOF/LDV (n=158)	93.0%	7.0%	
SOF/LDV+RBV (n=13)	92.3%	7.7%	
SIM+SOF (n=17) *	100%	0%	0.82
SOF+RBV (n=0)	NA	NA	
IFN based (n=13)	92.3%	7.7%	
Holkira (n=5)	100%	0%	
Genotype 1b (n=59)	96.6%	3.4%	0.20
SOF/LDV (n=48)	95.8%	4.2%	
SPF/LDV+RBV (n=1)	100%	0%	
SIM+SOF (n=2)	100%	0%	1.00
SOF+RBV (n=0)	NA	NA	
IFN based (n=3)	100%	0%	
Holkira (n=5)	100%	0%	
Genotype 2 (n=25)	88.0%	12.0%	0.41
SOF/LDV(n=0)	NA	NA	
SOF/LDV+RBV (n=0)	NA	NA	
SIM+SOF (n=0)	NA	NA	1.00
SOF+RBV (n=23)	87.0%	13.0%	
IFN based (n=2)	100%	0%	
Holkira (n=0)	NA	NA	

Genotype 3 (n=51)	86.3%	13.7%	0.07
SOF/LDV (n=0)	NA	NA	
SOF/LDV+RBV (n=1)	100%	0%	
SIM+SOF (n=0)	NA	NA	0.58
SOF+RBV (n=45)	84.4%	15.6%	
IFN based (n=5)	100%	0%	
Holkira (n=0)	NA	NA	
Other genotypes (n=9)	100%	0%	1.00
SOF/LDV (n=4)	100%	0%	
SOF/LDV+RBV (n=1)	100%	0%	
SIM+SOF (n=0)	NA	NA	
SOF+RBV (n=2)	100%	0%	1.00
IFN based (n=1)	100%	0%	
Holkira (n=1)	100%	0%	

Table 3: Predictors of achieving SVR among all patients

	Univariate analysis	Multivariate analysis

	Univariate Odds Ratio of achieving SVR (95% CI)	Adjusted Odds Ratio of achieving SVR (95% CI)
Age, in years	0.95 (0.90-0.99)	0.95 (0.90-1.00)
Male gender	0.28 (0.10-0.84)	0.30 (0.10-0.89)
Previous treatment	0.82 (0.34-1.97)	NA
Genotype 1a	1.34 (0.59-3.03)	NA
Baseline Fibroscan (per kpa)	0.99 0.97-1.02)	NA
Viremia (per 1000 IU)	1.00 (0.99-1.02)	NA
Cirrhosis at baseline	0.39 (0.17-0.91)	0.56 (0.23-1.36)
Treated according to guidelines	1.09 (0.36-3.32)	NA
Previous history of HCC	0.27 (0.08-0.88)	0.37 (0.11-1.28)
Baseline MELD	1.76 (0.35-8.97)	
Baseline MELD Na	1.01 (0.78-1.31)	

Supplementary Table 1: SVR by following guidelines

Characteristic	Achieved SVR	Not achieved SVR	*P*-value
	n=326 (92.9%)	n=25 (7.1%)	
Treatment within guidelines			
Yes (n=292)	93.2%	6.9%	0.78
No (n=54)	92.6%	7.4%	
Genotype			
Genotype 1a			
Treatment within guidelines			
Yes (n=166)	94.0%	6.0%	1.00
No (n=38)	94.7%	5.3%	
Genotype 1b			
Treatment within guidelines			
Yes (n=50)	96.0%	4.0%	1.00
No (n=7)	100.0%	0%	
Genotype 2			
Treatment within guidelines			
Yes (n=22)	86.4%	13.6%	1.00
No (n=3)	13.6%	0%	
Genotype 3			
Treatment within guidelines			
Yes (n=48)	89.6%	10.4%	0.04
No (n=3)	33.3%	66.7%	

Genotype 4 and 6			
Treatment within guidelines			
Yes (n=6)	100%	0%	NA
No (n=3)	100%	0%	

Table 1 Footnote:

*Data is presented as percentage for categorical data or median and interquartile range for contentious data

Table 2 footnote:

*Complete data on all SIM + SOF treated individuals were not captured in the current study. Prior treatment failures with this regimen were excluded if they subsequently received a SOF/LDV based regimen. Preliminary data from an ongoing retrospective study has identified overall SVR rate of only 86% with SIM/SOF (data not shown).

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Statement of Interests:

- A.I. Aspinall has served as a speaker, advisory board member and/or has received research support from AbbVie, Gilead, Merck
- SS Lee has served as a speaker, advisory board member and/or has received research support from AbbVie, BMS, GSK, Janssen, Gilead, Novartis, Merck, Roche and Vertex.
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- OE Larios has no funding interests to declare.
- KW Burak has served as a speaker, advisory board member and/or has received research support from Bayer, Verlyx, Lupin, Astellas, Gilead, Amgen and Merck
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- AA Shaheen, G Samadi Kochaksaraei, B Haslam and J Kapler have no funding interests to declare.