Research Article
Viral Hepatitis

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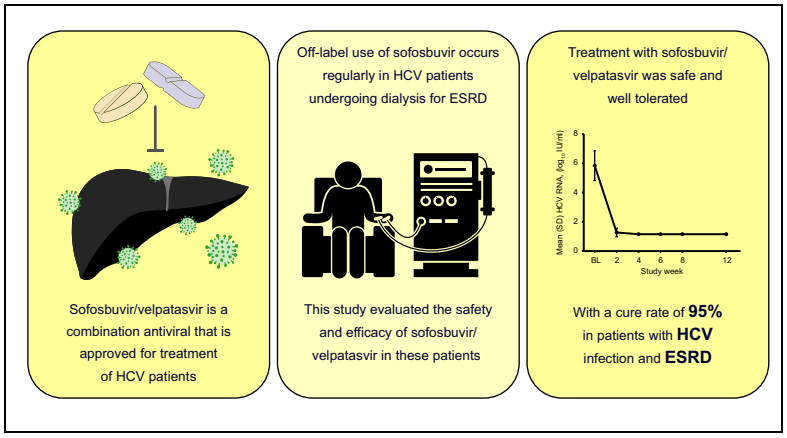
# Sofosbuvir/velpatasvir for 12 weeks in hepatitis C virus-infected patients with end-stage renal disease undergoing dialysis

## Graphical abstract




## Highlights

- Sofosbuvir/velpatasvir (SOF/VEL) is approved for patients with HCV infection.
- There is no dosing recommendation for SOF-based regimens for HCV-infected patients on dialysis.
- We evaluated SOF/VEL for 12 weeks in HCV-infected patients with end-stage renal disease on dialysis.
- SOF/VEL was safe and well tolerated, with a cure rate of 95% in our study.

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## Lay summary

Sofosbuvir/velpatasvir is a combination direct-acting antiviral that is approved for treatment of patients with hepatitis C virus (HCV) infection. Despite the lack of dosing recommendations, sofosbuvir-containing regimens (including sofosbuvir/velpatasvir) are frequently used for HCV-infected patients undergoing dialysis. This study evaluated the safety and efficacy of sofosbuvir/velpatasvir for 12 weeks in patients with HCV infection who were undergoing dialysis. Treatment with sofosbuvir/velpatasvir was safe and well tolerated, resulting in a cure rate of 95% in patients with HCV infection and end-stage renal disease.

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# Sofosbuvir/velpatasvir for 12 weeks in hepatitis C virus-infected patients with end-stage renal disease undergoing dialysis

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**Background & Aims**: Although off-label use of sofosbuvir-containing regimens occurs regularly in patients with hepatitis C virus (HCV) infection undergoing dialysis for severe renal impairment or end-stage renal disease (ESRD), these regimens are not licensed for this indication, and there is an absence of dosing recommendations in this population. This study evaluated the safety and efficacy of sofosbuvir/velpatasvir in patients with HCV infection with ESRD undergoing dialysis.

**Methods**: In this phase II, single-arm study, 59 patients with genotype 1–6 HCV infection with ESRD undergoing hemodialysis or peritoneal dialysis received open-label sofosbuvir/velpatasvir (400 mg/100 mg) once daily for 12 weeks. Patients were HCV treatment naive or treatment experienced without cirrhosis or with compensated cirrhosis. Patients previously treated with any HCV NS5A inhibitor were not eligible. The primary efficacy endpoint was the proportion of patients achieving sustained virologic response (SVR) 12 weeks after discontinuation of treatment (SVR12). The primary safety endpoint was the proportion of patients who discontinued study drug due to adverse events.

**Results**: Overall, 56 of 59 patients achieved SVR12 (95%; 95% CI 86–99%). Of the 3 patients who did not achieve SVR12, 2 patients had virologic relapse determined at post-treatment Week 4 (including 1 who prematurely discontinued study treatment), and 1 patient died from suicide after achieving SVR through post-treatment Week 4. The most common adverse events were headache (17%), fatigue (14%), nausea (14%), and vomiting (14%). Serious adverse events were reported for 11 patients (19%), and all were deemed to be unrelated to sofosbuvir/velpatasvir.

**Conclusions**: Treatment with sofosbuvir/velpatasvir for 12 weeks was safe and effective in patients with ESRD undergoing dialysis.

**Lay summary**: Sofosbuvir/velpatasvir is a combination direct-acting antiviral that is approved for treatment of patients with hepatitis C virus (HCV) infection. Despite the lack of dosing recommendations, sofosbuvir-containing regimens (including sofosbuvir/velpatasvir) are frequently used for HCV-infected patients undergoing dialysis. This study evaluated the safety and efficacy of sofosbuvir/velpatasvir for 12 weeks in patients with HCV infection who were undergoing dialysis. Treatment with sofosbuvir/velpatasvir was safe and well tolerated, resulting in a cure rate of 95% in patients with HCV infection and end-stage renal disease.

**Clinical Trial Number:** NCT03036852.



Keywords: Direct-acting antiviral; ESRD; Severe renal impairment; Chronic hepatitis C infection; HCV, SVR12, drug safety.
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## Introduction

Hepatitis C virus (HCV) infection is a global health challenge with an estimated 71 million individuals infected worldwide.[1]

The disease burden of HCV infection is due to progression of chronic liver disease, which can lead to cirrhosis, liver failure, hepatocellular carcinoma, and death. Chronic HCV infection is also independently associated with the development of renal impairment referred to as chronic kidney disease (CKD) and has been shown to be more prevalent in patients with renal disease.[2,3] Chronic HCV infection has a significant negative impact on morbidity and mortality in patients undergoing dialysis.[4] HCV-infected patients with CKD have an accelerated rate of loss of kidney function, risk of progression to end-stage renal disease (ESRD), and increased risk of all-cause mortality when undergoing dialysis.[2,5–7]

Over the last 2 years, direct-acting antiviral agents have been approved for use in patients with HCV infection and CKD. However, approved HCV treatments for patients with ESRD are associated with drug-drug interactions, baseline resistance testing, risk of hepatotoxicity, and contraindication for those with decompensated liver disease.[8–10] Additionally, some of these regimens are not pangenotypic.

Treatment regimens containing the NS5B inhibitor, sofosbuvir, are the most widely prescribed treatments for HCV infection worldwide. The predominant circulating metabolite of sofosbuvir, GS-331007, is renally cleared and accumulates in patients with severe renal impairment or ESRD, which has resulted in the exclusion of this population in prior clinical trials, and consequently, a lack of dosing recommendations for patients with ESRD. However, real-world case series in patients with ESRD undergoing dialysis demonstrate substantial use of sofosbuvir-based regimens in this population, with no safety concerns identified.[11–17]

The fixed-dose combination of sofosbuvir and velpatasvir, an NS5A inhibitor, provides a treatment option for HCV-infected patients regardless of HCV genotype, patient demographics, and other disease characteristics.[18,19] The current study evaluated the safety and efficacy of sofosbuvir/velpatasvir in patients with ESRD who were undergoing dialysis to expand our knowledge regarding the use of sofosbuvir-based regimens in these patients with severe renal impairment and ESRD.

## Patients and methods

### Patients

Patients were enrolled between 19 April 2017 and 28 February 2018 at 22 sites in Canada, the United Kingdom, Spain, Israel, New Zealand, and Australia (ClinicalTrials.gov number, NCT03036852). Eligible patients were men and women, at least 18 years of age, with chronic genotype 1–6 HCV infection who were undergoing peritoneal dialysis or hemodialysis for ESRD. HCV treatment-naive or treatment-experienced patients without cirrhosis or with compensated cirrhosis were eligible. Patients previously treated with any HCV NS5A inhibitor were not eligible. The presence of cirrhosis was determined by a transient elastography (FibroScan® [Echosens, Paris, France]) result ≤12.5 kPa, liver biopsy (Metavir stage 4 or Ishak stage 5 or 6), or a FibroTest® (BioPredictive S.A.S., Paris, France) result ≥0.75 at screening. Patients with HIV infection were eligible if they were suppressed on a stable antiretroviral regimen for at least 8 weeks prior to screening. A full list of eligibility criteria is provided in the supplementary information. All patients provided written informed consent.

### Study design

In this phase II, open-label study, patients were enrolled to receive sofosbuvir/velpatasvir 400 mg/100 mg tablet[18,19] once daily for 12 weeks. Assessments were performed at screening and baseline; on-treatment Weeks 2, 4, 8, and 12; and post-treatment Weeks 4 and 12.

The study design was approved by an independent ethics committee at each participating site (supplementary information) and was conducted in compliance with the principles of the Declaration of Helsinki, Good Clinical Practice guidelines, and local regulatory requirements. The study was designed and conducted according to the protocol by Gilead Sciences in collaboration with the academic investigators.

### Study procedures and assessments

Serum HCV RNA was measured using the COBAS AmpliPrep/COBAS TaqMan HCV Quantitative Test, v2.0 (Roche Molecular Diagnostics, Pleasanton, CA, USA) with a lower limit of quantitation (LLOQ) of 15 IU/ml. HCV genotype and subtype were determined using the Siemens VERSANT HCV Genotype INNO-LiPA 2.0 assay (Siemens Healthcare GmbH, Erlangen, Germany) or NS5B Sanger sequencing methods. For patients who were unable to be genotyped using these methods, genotype and subtype were determined by basic local alignment search tool (BLAST) analysis of NS5A and NS5B sequences.

Deep sequencing of the HCV NS5A and NS5B coding regions was performed by DDL Diagnostic Laboratory (Rijswijk, the Netherlands) on all patients in the Resistance Analysis Population (*i.e.*, patients with virologic outcomes and at least 1 gene sequenced) to detect resistance-associated substitutions (RASs) present at baseline and again for patients with virologic failure to detect treatment-emergent RASs. RASs were defined as specific substitutions that either confer a reduced susceptibility to drugs of the given class with a >2.5-fold change in half-maximal effective concentration compared with a genotype-specific reference in a replicon model, or that commonly select in patients with virologic failure at the time of relapse (Table S1). All RASs are presented using a 15% assay cut-off.

Safety assessments included monitoring of adverse events, clinical laboratory tests, and vital sign measurements at baseline and all on-treatment and post-treatment visits. Physical examinations were performed at baseline, Week 12, and all post-treatment visits.

For pharmacokinetics (PK) evaluation, a single blood sample was collected from all patients at the on-treatment Weeks 2, 4, 6, 8, and 12 visits. For patients who consented to participate in an optional intensive PK substudy, blood samples were collected at the on-treatment Week 6, 8, or 12 visit at the following time points: predose and 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose. Plasma concentrations of sofosbuvir, sofosbuvir metabolites GS-566500 and GS-331007, and velpatasvir were determined using fully validated high-performance liquid chromatography-tandem mass spectroscopy bioanalytical methods.

### Statistical analyses

The primary efficacy endpoint was the proportion of patients who achieved sustained virologic response (SVR) (*i.e.*, HCV RNA <15 IU/ml) 12 weeks after discontinuation of sofosbuvir/velpatasvir (SVR12). The SVR12 rates and two-sided 95% exact CIs were calculated for study patients overall and by HCV

genotype and subtype using the Clopper-Pearson method.[20] The emergence of viral resistance was also evaluated. The primary safety endpoint was the proportion of patients who discontinued study drug due to adverse events. The steady-state, predialysis exposures of sofosbuvir, GS-331007, and velpatasvir were estimated based on population PK analysis. These PK exposure parameters were then compared to those observed in HCV-infected patients without renal impairment (estimated glomerular filtration rate >90 ml/min) who were treated with sofosbuvir/velpatasvir in phase II/III studies. Phoenix WinNonlin version 6.3 (Pharsight Corporation, Mountain View, CA, USA) was used to perform the PK data analyses.

SAS software version 9.4 (SAS Institute, Cary, NC, USA) was used to perform the statistical analyses.

Because of the exploratory nature of this study, no formal power calculations were performed to determine sample size; the sample size of 100 patients was selected for practical reasons.

For additional details regarding the methods used, please refer to the Supplementary CTAT Table.

## Results

### Patient characteristics

Seventy-eight patients were screened from 22 March 2017 through 14 February 2018 at 22 sites in Canada, the United Kingdom, Spain, Israel, New Zealand, and Australia. Fifty-nine patients were enrolled and received at least 1 dose of sofosbuvir/velpatasvir, including 46 (78%) treatment-naive and 13 (22%) treatment-experienced patients (Table 1). Of the 19 patients who were screened and not enrolled, 17 patients did not meet eligibility criteria, and 2 patients met eligibility criteria but were not enrolled because their screening visits were outside the visit window (Table S2). The mean (range) age of patients was 60 (33–91) years; 59% of patients were male, and 29% had cirrhosis. Most patients had genotype 1 (46% [25% 1a and 19% 1b]) or 3 (32%) HCV infection; 12% had genotype 2, 7% had genotype 4, and 3% had genotype 6 HCV infection. The mean (range) baseline HCV RNA level was 5.8 (3.1–7.7) $\log_{10}$ IU/ml. Fifty-four of the 59 patients enrolled (92%) were undergoing hemodialysis, with a mean (range) dialysis duration of 7 (0–40) years, while the other 5 patients (8%) were undergoing peritoneal dialysis. As expected in this population, the majority of patients had multiple comorbidities. Overall, 90% of patients had underlying vascular disorders, primarily hypertension; 37% had underlying cardiac disorders, including coronary artery disease, cardiac failure, or cardiomyopathy; and 32% had diabetes mellitus. During the study, 53% of patients were taking calcium channel blockers and 47% of patients were taking beta blockers. Additionally, 37% of patients were taking proton-pump inhibitors during the study, which is also common in the dialysis population.

**Table 1. Baseline demographics and disease characteristics.**

| | Sofosbuvir/velpatasvir for 12 weeks (n = 59) |
|---|---|
| Mean age (range), yr | 60 (33–91) |
| Male, n (%) | 35 (59) |
| Race, n (%) | |
| White | 31 (53) |
| Asian | 18 (31) |
| Black or African American | 6 (10) |
| American Indian or Alaska Native | 2 (3) |
| Native Hawaiian or Pacific Islander | 2 (3) |
| Mean body mass index (range), kg/m$^2$ | 26 (17–39) |
| HCV genotype, n (%) | |
| 1 | 27 (46) |
| 1a | 15 (25) |
| 1b | 11 (19) |
| Other | 1 (2) |
| 2 | 7 (12) |
| 3 | 19 (32) |
| 4 | 4 (7) |
| 6 | 2 (3) |
| Cirrhosis, n (%) | 17 (29) |
| Mean HCV RNA level (range), $\log_{10}$ IU/ml | 5.8 (3.1–7.7) |
| Prior HCV treatment experience, n/N (%) | 13/59 (22) |
| Direct-acting antiviral-naive | |
| Pegylated interferon + ribavirin | 6//13 (46) |
| Other | 7/13 (54) |
| Type of dialysis, n (%) | |
| Hemodialysis | 54 (92) |
| Peritoneal dialysis | 5 (9) |
| Mean duration of dialysis (range), yr | 7 (0–40) |
| Prior renal transplant, n (%) | 19 (32) |

HCV, hepatitis C virus.

### Efficacy

Overall, 56 of 59 patients achieved SVR12 (95%; 95% CI 86–99%) following 12 weeks of once-daily treatment with sofosbuvir/velpatasvir (Table 2). Of the patients who achieved SVR12, 53 patients had study drug adherence rates of ≥90% as measured by pill counts, and 3 patients, who did not return all their study drug bottles, had study drug adherence rates of <90% due to the imputation of missed pills. Of the 3 patients who did not achieve SVR12, 2 patients had virologic relapse determined at post-treatment Week 4, including 1 treatment-experienced patient with genotype 3a HCV and cirrhosis and 1 treatment-naive patient with genotype 1b HCV without cirrhosis (this patient was discontinued from the study after 11 weeks of treatment due to nonadherence with study drug). The latter patient had a study drug adherence rate of 48% as measured by pill counts and low plasma concentrations of GS-331007 at on-treatment Week 8, consistent with nonadherence with study drug dosing. The third patient who did not achieve SVR12 died from suicide after achieving viral suppression at the post-treatment Week 4 visit.

Plasma levels of HCV RNA declined rapidly with treatment, with all patients (100.0%; 95% CI 94–100%) having HCV RNA < LLOQ after 4 weeks of treatment (Fig. 1). No patients experienced on-treatment virologic failure.

### Viral resistance

A total of 58 patients (98%) were included in the resistance analysis population. At baseline, 32% of patients had NS5A RASs, and

**Table 2. Treatment response.**

| | Sofosbuvir/velpatasvir for 12 weeks (n = 59) |
|---|---|
| SVR12, n (%) | 56 (95) |
| Overall virologic failure, n (%) | 2 (3) |
| Relapse | 2 (3) |
| On-treatment virologic failure | 0 |
| Other, n (%) | 1 (2) |

SVR12, sustained virologic response rate 12 weeks after discontinuation of treatment.

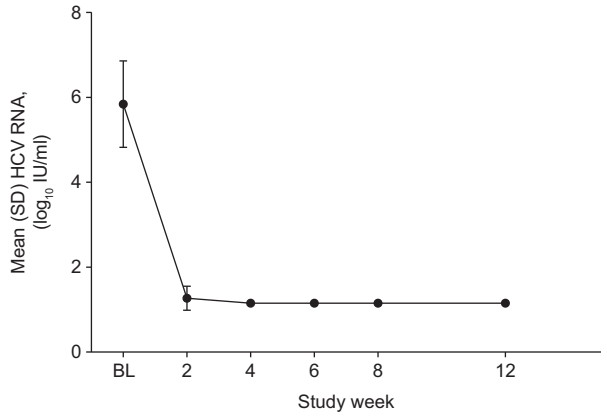


**Fig. 1. Mean (± SD) HCV RNA levels from baseline through end of treatment.** BL, baseline.

12% of patients had NS5B nucleoside inhibitor (NI) RASs (Table S3). Overall, 94% of patients with baseline NS5A RASs and 97% of patients without baseline NS5A RASs achieved SVR12. The treatment-experienced patient with genotype 3a HCV infection and cirrhosis with virologic failure had the NS5A RAS Y93H at baseline and Y93H/Y at the time of relapse, with no NS5B NI RASs detected at baseline or relapse. The treatment-naive patient with genotype 1b HCV infection without cirrhosis with virologic failure (who had poor adherence with study drug) did not have NS5A or NS5B NI RASs detected at baseline or relapse. No NS5A or NS5B NI RASs emerged in either patient at the time of relapse.

### Safety

Most patients experienced an adverse event (80%), the majority of which were mild or moderate in severity (Table 3). The most common adverse events (reported for ≥10% of patients) were headache (17%), fatigue (14%), nausea (14%), vomiting (14%), and insomnia (10%). Serious adverse events were reported for 11 patients (19%), and none were assessed as related to study treatment. No adverse events associated with renal dysfunction were reported. The only renal adverse events in this study included Grade 1 increased daytime urinary frequency and Grade 1 renal colic (1 patient each). No patients prematurely discontinued sofosbuvir/velpatasvir due to adverse events. Two deaths occurred during the study. One patient, who had a history of anxiety, died from suicide 79 days after completing study treatment, and 1 patient, who achieved SVR12 and had a history of tobacco use, died of metastatic lung cancer 111 days after completing study treatment.

The incidence of Grade 3 and 4 laboratory abnormalities was consistent with patients with ESRD undergoing dialysis. The only Grade 3 laboratory abnormalities observed in more than 1 patient were decreased hemoglobin (4 patients), hyperglycemia (5 patients), and hyperkalemia (2 patients). All 5 patients with hyperglycemia had diabetes, and 4 of these patients were taking medication for diabetes. The only Grade 4 laboratory abnormality observed in more than 1 patient was increased creatinine (14 patients), and abnormalities in creatinine are anticipated in patients with ESRD undergoing dialysis.

### Pharmacokinetics

Exposures ($AUC_{tau}$) of sofosbuvir, GS-331007, and velpatasvir were 81%, 1,719%, and 41% higher, respectively, in HCV-infected patients with ESRD undergoing dialysis compared with HCV-infected patients with normal renal function (estimated glomerular filtration rate >90 ml/min) evaluated in the sofosbuvir/velpatasvir phase II/III population (Table 4).

**Table 3. Adverse events and laboratory abnormalities.**

| | Sofosbuvir/velpatasvir for 12 weeks (n = 59) |
|---|---|
| Any adverse event, n (%) | 47 (80) |
| Grade 3 adverse events, n (%)[a] | 7 (12) |
| Serious adverse events, n (%)[b] | 11 (19) |
| Adverse events leading to sofosbuvir/velpatasvir discontinuation, n (%) | 0 |
| Deaths, n (%) | 2 (3) |
| Adverse events occurring in ≥ 10% of patients, n (%) | |
| Headache | 10 (17) |
| Fatigue | 8 (14) |
| Nausea | 8 (14) |
| Vomiting | 8 (14) |
| Insomnia | 6 (10) |
| Grade 3 or 4 laboratory abnormalities in > 1 patient, n (%) | |
| Creatinine | |
| Grade 3 | 1 (2) |
| Grade 4 | 14 (24) |
| Hyperglycemia[c] | |
| Grade 3 | 5 (9) |
| Hemoglobin | |
| Grade 3 | 4 (7) |
| Hyperkalemia | |
| Grade 3 | 2 (3) |
| Grade 4 | 1 (2) |

[a] Cardiac failure congestive, device-related infection, headache, insomnia, neurilemmoma benign, pneumonia, and pubis fracture; all unrelated to study treatment.
[b] Anxiety, atrial fibrillation, cardiac failure congestive, cellulitis, depression, device-related infection, neurilemmoma benign, pneumonia, post procedural hemorrhage, post procedural swelling, pubis fracture, respiratory tract infection, and streptococcal bacteremia; all unrelated to study treatment.
[c] All in patients with ongoing diabetes.

## Discussion

In this multicenter, open-label study, treatment with sofosbuvir/velpatasvir for 12 weeks in HCV-infected patients with ESRD undergoing dialysis resulted in an SVR12 rate of 95%. Two patients had virologic failure: 1 patient relapsed with NS5A resistance before and after completing treatment, and 1 patient, who was discontinued from study treatment due to nonadherence with study drug dosing as assessed by pill counts and PK data, relapsed without NS5A resistance. Treatment with sofosbuvir/velpatasvir was generally safe and well tolerated, with a safety profile consistent with that expected for patients with ESRD undergoing dialysis. There were no treatment-related discontinuations or serious adverse events.

Overall, the safety and efficacy results from this study are consistent with those observed in the ASTRAL-1, ASTRAL-2, ASTRAL-3, ASTRAL-5, POLARIS-2, and POLARIS-3 clinical trials of sofosbuvir/velpatasvir, which demonstrated that treatment with sofosbuvir/velpatasvir for 12 weeks was well tolerated and resulted in high SVR rates across HCV genotypes in patients with or without compensated cirrhosis.[21–23] The safety profile and response rates are also consistent with results from a phase IIb study, which demonstrated that treatment of ledipasvir (an NS5A inhibitor) combined with sofosbuvir once daily for 12 weeks in HCV-infected patients with ESRD was well tolerated and resulted in an SVR12 rate of 100%.[24]

**Table 4. Steady-state sofosbuvir, GS-331007, and velpatasvir plasma pharmacokinetic parameters and statistical comparisons in HCV-infected patients with ESRD undergoing dialysis *vs.* HCV-infected patients with normal renal function.**

| PK parameter | Mean (%CV) | | %GMR (90% CI) |
|---|---|---|---|
| | ESRD population | Phase II/III population with normal renal function | |
| Sofosbuvir | n = 21 | n = 693 | |
| $AUC_{tau}$, h·ng/ml | 2,382 (24) | 1,372 (41) | 181 (158–207) |
| $C_{max}$, ng/ml | 1,041 (17) | 578 (34) | 188 (166–213) |
| GS-331007 | n = 59 | n = 940 | |
| $AUC_{tau}$, h·ng/ml | 230,989 (35) | 12,334 (26) | 1,819 (1,717–1,926) |
| $C_{max}$, ng/ml | 9,776 (35) | 793 (27) | 1,203 (1,132–1,278) |
| Velpatasvir | n = 59 | n = 939 | |
| $AUC_{tau}$, h·ng/ml | 4,279 (51) | 3,187 (55) | 141 (125–160) |
| $C_{max}$, ng/ml | 227 (41) | 276 (61) | 93 (81–107) |

%CV, percentage coefficient of variation; %GMR, percentage geometric mean ratio; ESRD, end-stage renal disease; HCV, hepatitis C virus; PK, pharmacokinetic.

Plasma exposures of sofosbuvir, GS-331007, and velpatasvir were higher in HCV-infected patients with ESRD undergoing dialysis compared with HCV-infected patients with normal renal function. The increased exposure of GS-331007, the predominant circulating metabolite of sofosbuvir, was expected, as it is renally cleared. These observations are also consistent with results from a phase I study in HCV-negative patients with varying degrees of renal impairment and ESRD, which showed increased exposures of GS-331007 in patients with severe renal impairment, and even higher exposures in patients with ESRD. These increases in exposure were not considered clinically relevant as no exposure-response relationships for safety metrics were observed. Additionally, real-world case series have demonstrated substantial use of sofosbuvir-based regimens in patients with ESRD with no safety concerns identified.[11–17]

Over the last few years, several HCV treatments have been approved for use in patients with HCV infection and CKD, and each regimen has limitations. For example, some of these treatments require the addition of ribavirin for optimal efficacy in many populations, and ribavirin-induced toxicities are exacerbated in patients with ESRD.[8] Some components of these approved treatments are associated with the potential for drug-drug interactions, which adds increasing complexity to the management of HCV-infected patients with ESRD who frequently have multiple comorbid conditions and concomitant medications.[8] Some treatments also require baseline resistance testing for patients with genotype 1a infection.[10] Additionally, these regimens involve the use of protease inhibitors, which carry the risk of alanine aminotransferase elevations or hepatotoxicity, especially in patients with hepatic decompensation. These HCV protease inhibitor-containing regimens also have drug-drug interaction potential with other substrates/inhibitors of cytochrome P450, including some HIV antiretroviral therapies and immunosuppressive medications, which are of clinical relevance to the renal dialysis population.[8–10] Finally, indications for some of these regimens are limited to patients with HCV genotypes 1 and/or 4. Sofosbuvir/velpatasvir offers a single-tablet, once daily, pangenotypic treatment for HCV in patients with ESRD who are undergoing dialysis, including those with hepatic decompensation.

The relatively low number of patients in some subgroups and the exclusion of patients with decompensated liver disease may limit the generalizability of our findings (supplementary information). Another limitation was the absence of a placebo-controlled group to assist in distinguishing between adverse events that were related to treatment from those arising as sequelae of HCV infection, ESRD, or underlying comorbidities. Additionally, the high SVR rate observed in this study precludes meaningful analysis of patient subgroups.

The data collected in this study provide information to support the use of sofosbuvir/velpatasvir in HCV-infected patients with ESRD. The results from this study also support the applicability of this data in patients with severe renal impairment and the use of sofosbuvir/velpatasvir in this population with no additional safety risks. In conclusion, the single-tablet, pangenotypic regimen of sofosbuvir/velpatasvir for 12 weeks is a safe, well tolerated, and highly effective treatment option for HCV-infected patients undergoing dialysis for ESRD.

## Financial support

This study was funded by Gilead Sciences, Inc.

## Conflicts of interest

Sergio M. Borgia has received honoraria from AbbVie, Gilead Sciences, and Merck, and his institution has received funding from AbbVie, Gilead Sciences, and Merck. Janet Dearden has nothing to disclose. Eric M. Yoshida has been an investigator of clinical trials sponsored by Gilead Sciences, Merck, AbbVie, and Janssen, and has received honoraria for continuing medical education and advisory board lectures from Gilead Sciences Canada, Merck Canada, and AbbVie Canada. Stephen D. Shafran has received honoraria from Gilead Sciences, Merck, and Pfizer, and his institution has received funding from AbbVie, Gilead Sciences, Janssen, and Merck. Ashley Brown has received grant funding from Gilead Sciences, has served as an advisor/investigator for AbbVie, Gilead Sciences, and Merck, and has received speaking honoraria from AbbVie, Gilead Sciences, and Merck. Ziv Ben-Ari has received honoraria from AbbVie, Gilead Sciences, and Merck, and his institution has received funding from AbbVie, Gilead Sciences, and Merck. Matthew E. Cramp has been an investigator/advisory board member and has received honoraria for speaking from AbbVie, Gilead Sciences, Merck, and Janssen. Curtis Cooper has received honoraria from AbbVie, Gilead Sciences, and Merck, and his institution has received funding from AbbVie, Gilead Sciences, and Merck. Matthew Foxton has received honoraria for speaking from Gilead Sciences and BMS, and is an advisory board member for Norgine. Conrado Fernandez Rodriguez has received honoraria from Gilead Sciences, AbbVie, and MSD, and his institution has received funding from AbbVie and MSD. Rafael Esteban has received funding and honoraria from AbbVie, Gilead Sciences, and Merck. Robert Hyland, Sophia Lu, Brian J. Kirby, Amy Meng,

Svetlana Markova, Hadas Dvory-Sobol, and Anu O. Osinusi are employees of Gilead Sciences and hold stock interests in the company. Rafael Bruck has been an investigator of clinical trials sponsored by AbbVie, Merck, BMS, and Gilead Sciences, and has received honoraria for lectures from AbbVie and Merck Israel. Javier Ampuero has nothing to disclose. Stephen D. Ryder has attended paid advisory boards for Gilead Sciences, AbbVie, and MSD. Kosh Agarwal has received research grants from MSD and Gilead Sciences, and has received honoraria for speaking and serving on advisory boards from Arbutus, Gilead Sciences, MSD, and Vir. Raymond Fox has nothing to disclose. David Shaw has been an investigator of clinical trials sponsored by Gilead Sciences and AbbVie. Shariq Haider is an advisory board member for Gilead Sciences, Merck, and AbbVie, and a speakers bureau member for Merck. Bernard Willems has served as a consultant and on advisory boards for Gilead Sciences, AbbVie, BMS, and Intercept, and has received research grants from Gilead Sciences and AbbVie. Yoav Lurie has nothing to disclose. Jose Luis Calleja is an advisory board member for Gilead Sciences, AbbVie, and MSD. Edward J. Gane is an advisory board member for Gilead Sciences, Merck, AbbVie, Janssen, and Roche, and a speakers bureau member for Gilead Sciences and AbbVie.

Please refer to the accompanying ICMJE disclosure forms for further details.

## Authors' contributions

Sergio M. Borgia, Edward J. Gane, Robert Hyland, and Anu O. Osinusi designed the study. Sergio M. Borgia, Janet Dearden, Eric M. Yoshida, Stephen D. Shafran, Ashley Brown, Ziv Ben-Ari, Matthew E. Cramp, Curtis Cooper, Matthew Foxton, Conrado Fernandez Rodriguez, Rafael Esteban, Rafael Bruck, Javier Ampuero, Stephen D. Ryder, Kosh Agarwal, Raymond Fox, David Shaw, Shariq Haider, Bernard Willems, Yoav Lurie, and Jose Luis Calleja served as study investigators and collected data. Robert Hyland, Sophia Lu, Brian J. Kirby, Amy Meng, Svetlana Markova, Hadas Dvory-Sobol, and Anu O. Osinusi analyzed and interpreted the data. All authors provided critical revision and approval of the manuscript.

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## Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2019.05.028.

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