

Efficacy and safety of ombitasvir/paritaprevir/ritonavir/ribavirin in management of Egyptian chronic hepatitis C virus patients with chronic kidney disease

A real-life experience

Sherief Abd-Elsalam, MD, PhD^{a,*}, Yousry Esam-Eldin Abo-Amer, MD, PhD^b, Mohamed El-Abgeegy, MD, PhD^c, Samah A. Elshweikh, MD, PhD^d, Heba Fadl Elsergany, MD, PhD^c, Rehab Ahmed, MD, PhD^c, Mahmoud Elkadeem, MD, PhD^a, Nehad Hawash, MD, PhD^a, Shaimaa Soliman, MD, PhD^e, Rehab Badawi, MD, PhD^a, Ayman Mohammed Abdou Elguindy, MD, PhD^f, Moataz Yousry Soliman, MD^b, Ahmed Abdelhaleem Mohamed, MD^c, Loai Mansour, MD, PhD^a

Abstract

Treatment of hepatitis C virus (HCV) infection in patients with chronic kidney disease was difficult in the past because of the use of interferon (IFN). It was associated with high risk IFN-related adverse reactions due to reduced renal clearance of IFN. This study aimed to evaluate the antiviral efficacy, safety, and tolerability of ombitasvir/paritaprevir/ritonavir/ribavirin in chronic kidney disease patients infected with chronic HCV.

This observational, open-label prospective study was carried out on 103 patients infected chronic HCV with different grades of renal impairment. Paritaprevir/ritonavir and ombitasvir (75/50/12.5 mg) twice daily plus ribavirin were given to the patients for 12 weeks. Dose adjustment of ribavirin was done according to degree of renal impairment.

Sustained virological response (12 weeks after the end of treatment) occurred in 101 patients (98.1%). Anemia occurred in 48 patients. No serious adverse events were observed in any patient.

Paritaprevir/ritonavir and ombitasvir plus ribavirin for 12 weeks was considered to be safe and effective in the treatment of chronic HCV infected patients with varying degrees of renal impairment.

Abbreviations: ALT = alanine transferase, AST = aspartate transferase, CKD = chronic kidney disease, ESRD = end-stage renal disease, HCV = hepatitis C virus, IFN = interferon, SVR = sustained virological response.

Keywords: Egypt., end-stage renal disease, end-stage renal disease, hepatitis C virus, Renal impairment, Sustained virological response

1. Introduction

Hepatitis C virus (HCV) infection is highly prevalent in Egypt.^[1,2] Genotype 4 (and in particular subtype 4a) dominates

the HCV epidemic in Egypt.^[1-6] The prevalence of chronic kidney disease (CKD) including end stage renal disease (ESRD) is recognized to be significantly higher in HCV-seropositive patients than in HCV-seronegative subjects.^[7-9]

Editor: Dominik Steubl.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request; The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

^a Department of Tropical Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt, ^b Hepatology, Gastroenterology and Infectious Diseases Department, Mahala Hepatology Teaching Hospital, Gharbia, ^c National Hepatology and Tropical Medicine Research Institute in Cairo, Cairo, Egypt, ^d Internal Medicine Department, Tanta University, Tanta, ^e Department of Public health and Community medicine, Menofia University, Menofia, Egypt, ^f College of Dental Medicine, Basic & Clinical Oral Sciences, Umm al-qura University, Saudia Arabia.

* Correspondence: Sherief Abd-Elsalam, Tropical Medicine Department, Tropical Medicine Department, Tanta University, Tanta, Egypt, 35127 (e-mail: sherif_tropical@yahoo.com).

Copyright © 2020 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Abd-Elsalam S, Abo-Amer YE, El-Abgeegy M, Elshweikh SA, Elsergany HF, Ahmed R, Elkadeem M, Hawash N, Soliman S, Badawi R, Elguindy AM, Soliman MY, Mohamed AA, Mansour L. Efficacy and safety of ombitasvir/paritaprevir/ritonavir/ribavirin in management of Egyptian chronic hepatitis C virus patients with chronic kidney disease: A real-life experience. *Medicine* 2020;99:42(e21972).

Received: 13 December 2019 / Received in final form: 2 July 2020 / Accepted: 26 July 2020

<http://dx.doi.org/10.1097/MD.00000000000021972>

In the past, treating HCV infection in patients with CKD was difficult because of toxicities associated with the use of interferon (IFN) and reduced its renal clearance; so that, the risk of IFN-related toxicity might increase.^[10,11] This toxicity was aggravated by the concomitant use of renal excreted ribavirin (RBV), which is minimally eliminated by hemodialysis including hematologic toxicity in a population already at risk for anemia.^[12]

Ombitasvir/paritaprevir/ritonavir plus dasabuvir (OBV/PTV/r +DSV) are mainly metabolized by the liver. They have got FDA approval for the treatment of HCV patients with severe renal disease.^[13] This regimen was associated with high sustained virological response (SVR) at post-treatment week 12 (SVR12) in patients with genotype 1 infection, synonymous with viral cure.^[14] Pharmacokinetics of these DAAs were evaluated in HCV seronegative persons with mild (creatinine clearance 60–89 mL/min), moderate (creatinine clearance 30–59 mL/min), and severe (creatinine clearance 15–29 mL/min) renal impairment. The plasma exposures observed support the use of this regimen in HCV-infected patients with renal impairment with no need for dose adjustments.^[15] This study aimed to evaluate the antiviral efficacy, safety, and tolerability of ombitasvir/paritaprevir/ritonavir/ribavirin in CKD patients infected with chronic HCV infection.

2. Patients and methods

This observational, open-label prospective study was carried in the national hepatology and tropical medicine research institute; outpatient clinics in internal medicine and tropical medicine departments in Tanta University Hospital and El-obour clinic in Kafr-Elsheikh during the period between January and September 2018 on 103 chronic HCV infected patients with varying degrees of renal impairment with estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m². Institutional ethical committee approval was obtained and a written consent was taken from every participant.

Patients younger than 18 years old, with decompensated cirrhosis, organ transplantation, severe anemia (Hb level less than 10 g/dl), and severe uncontrolled morbidity e.g. cardiac disease, malignant tumors, HIV, or hepatitis B virus co-infection were excluded from the study. Moreover, pregnant and lactating females and patients receiving contraindicated concomitant drugs for ombitasvir/paritaprevir/ritonavir were excluded from the study.

All patients enrolled in this study were evaluated by Complete blood count (CBC), liver function tests, liver enzymes including alanine transferase (ALT) and aspartate transferase (AST), Fasting blood sugar, serum creatinine and estimated glomerular filtration rate, HBs-Ag testing, α -fetoprotein as well as abdominal ultrasonography.

Renal function was assessed in our patients by estimating serum creatinine, blood urea and eGFR calculation for all patients with serum creatinine more than 1.2 mg/dL by CKD-EPI equation^[16] as eGFR is considered to be an important indicator of kidney function that is vital for recognition, assessment and management of CKD.^[17–20] All patients received paritaprevir/ritonavir and ombitasvir (75/50/12.5 mg) film-coated table twice daily plus ribavirin for 12 weeks. RBV was given 200 mg 4 hours before dialysis 3 times weekly. In patients without dialysis, the dose of ribavirin was calculated according to eGFR with eGFR < 30 mL/

min; RBV dose was 200 mg daily. RBV was stopped in patients who developed severe anemia or intolerant to it.

Patients were followed up routinely every 4 weeks. Side effects were recorded. Complete blood count, liver, and kidney function tests (serum creatinine and blood urea), quantitative PCR for HCV RNA and eGFR were performed before the start of therapy and at weeks 4, 8, and 12 during antiviral treatment. The primary end point was a SVR at 12 weeks after end of treatment determined by quantitative PCR for HCV RNA that was also estimated at weeks 4, 12 (end of therapy). The secondary end point was to evaluate the side effects and the safety of this regimen in our patient groups.

2.1. Statistical analysis

Results were statistically analyzed using SPSS statistical package version 23 (SPSS Inc. Released 2015. IBM SPSS statistics for windows, version 23.0, Armonk, NY: IBM Corp.). Number (No), percentage (%) means (\bar{x}) and standard deviation was used for description of data. Repeated measures ANOVA (with Bonferoni correction) with Mauchly test for sphericity test were used for comparison among 3 or more consecutive measures in the same group of quantitative variables. Assumed sphericity was used for normally distributed data while Greenhouse-Geisser was used for not normally distributed data.

3. Results

The mean age of the patients included in the study was 58.49 \pm 6.92 years; fifty-four (52.4%) patients were males and fifty-five (53.4%) patients were on dialysis. Baseline demographic and clinical characteristics are shown in (Table 1).

No significant change was observed in the level of follow up of serum creatinine (p value=0.11), white blood cells (p value=0.10), platelets (p value=0.067), total bilirubin (p value=0.54), and eGFR (p value=0.076); while, there was a significant decrease in ALT and AST (P value < 0.001) (Table 2).

One hundred patients (97.1%) had undetectable PCR for HCV-RNA at week 4; meanwhile; at the end of treatment; the response reached 100%. However; 12 week after treatment; (SVR) occurred in 101 patients (98.1%) while 2 patients had viral relapse.

Regarding the safety of antiviral treatment; Side effects were observed in 62 patients. Forty-eight patients had anemia: (44 patients had reduction of RBV dose, 48 patients received erythropoietin and 4 patients received packed RBCs), while 3 patients presented by pruritus and insomnia. GIT disturbances were noticed in 3 patients also. However, no serious adverse events were observed in any patient (Tables 3 and 4).

4. Discussion

The treatment of HCV in patients with renal impairment was a challenge till the last few years because these patients could not benefit from INF containing regimen and they were at risk of liver disease progression. However, this is changed by the era of IFN-free treatment regimen as these drugs offered a chance for the cure of these patients.

In this study; 103 patients with chronic HCV infection and severe renal impairment were enrolled, all these patients had received ombitasvir/paritaprevir/ritonavir plus ribavirin for 12

Table 1
Baseline characteristics (n=103).

Variable	Pre-treatment	
	Mean \pm SD, range, median	
Age (yr)		
Mean \pm SD	58.49 \pm 6.92	
Range	28-75	
Median	62	
FBG (mg/dL)		
Mean \pm SD	134.86 \pm 43.93	
Range	78-221	
HbA1c		
Mean \pm SD	6.52 \pm 0.47	
Range	5.8-7.4	
eGFR (mL/min/1.73m ²)		
Mean \pm SD	21.63 \pm 2.57	
Range	19-26	
AFP (ng/l)		
Mean \pm SD	4.27 \pm 2.79	
Range	1.5-8.9	
INR		
Mean \pm SD	1.08 \pm 0.07	
Range	1-1.2	
Serum albumin (g/dL)		
Mean \pm SD	3.81 \pm 0.51	
Range	3-4.61	
	No. (%)	
Sex:		
Male	54 (52.4)	
Female	49 (47.6)	
Hypertension:		
YES	64 (62.1)	
NO	39 (37.90)	
DM		
YES	14 (13.6)	
NO:	89 (86.4)	
Dialysis:		
Yes	55 (53.4)	
No	48 (46.6)	
HBsAg:		
Positive	0 (0.0)	
Negative	103 (100.0)	

*AFP = alfa-fetoprotein, DM = diabetes mellitus, FBS = fasting blood sugar, HB = hemoglobin, HBsAg = hepatitis B surface antigen, INR = International normalized ratio, SD = standard deviation.

weeks, only 3 patients did not achieve virologic response; However; all our patients were PCR negative at week 12 of treatment; then ultimately; 2 patients had relapsed at 12 weeks post treatment (SVR 98.1%).

Table 2
Baseline and follow up laboratory investigations of the studied group (n=103).

Variable	Pre-treatment	wk4	wk8	wk12	wk12 Post	P value
	Mean \pm SD	Mean \pm SD	Mean \pm SD			
Serum creatinine	5.08 \pm 2.42	5.11 \pm 2.66	5.00 \pm 2.32	4.82 \pm 2.12	4.79 \pm 2.09	.11
WBCs	7269.12 \pm 2976.20	7936.99 \pm 3006.74	7480.58 \pm 2861.25	8983.49 \pm 9414.80	7307.00 \pm 2566.28	.10
HB	11.82 \pm 1.72	10.43 \pm 1.56	10.46 \pm 1.67	10.52 \pm 1.50	11.22 \pm 1.59	<.001
Plt	175.87 \pm 64.03	178.90 \pm 65.78	173.58 \pm 59.17	178.39 \pm 52.72	185.82 \pm 48.53	.067
ALT	38.15 \pm 23.14	28.23 \pm 20.06	31.55 \pm 16.03	29.44 \pm 10.93	28.99 \pm 9.81	<.001
AST	37.12 \pm 24.71	25.18 \pm 12.32	28.28 \pm 14.66	27.86 \pm 11.68	27.24 \pm 10.19	<.001
Total bilirubin	0.84 \pm 0.39	0.87 \pm 0.32	0.83 \pm 0.23	0.84 \pm 0.19	0.86 \pm 0.19	.549
eGFR	21.63 \pm 2.57	22.45 \pm 2.19	21.96 \pm 3.01	22.42 \pm 2.98	21.69 \pm 2.61	.076

*ALT = alanine transferase, AST = aspartate transferase, GFR = glomerular filtration rate, HB = hemoglobin, N = number, PLT = platelets, SD = standard deviation, WBCs = White blood cells.

Table 3
Side effects in the studied patients.

Side effects	No (%) (n=103)
*No side effects	41 (39.8)
*Have Side effects	62 (60.2)
Anemia	48 (46.6)
Pruritus	3 (2.9)
headache	1 (0.9)
Fatigue	1 (0.9)
Insomnia	3 (2.9)
Diarrhea	2 (1.9)
Nausea	1 (0.9)
Cough	2 (1.9)
Myalgia	1 (0.9)

*No = number.

This was similar to the results obtained by Atsukawa et al., who studied 31 patients suffering from HCV infection and ESRD and concluded that rates of rapid virologic response, end-of-treatment response, and SVR12 were 93.5% (29/31), 100% (31/31), and 96.8% (30/31), respectively.^[21] Also, Pockros et al., 2016^[22] concluded that 18 of 20 HCV positive patients with CKD who received ombitasvir co-formulated with paritaprevir and ritonavir, administered with dasabuvir for 12 weeks have achieved SVR with 1 patient relapsed after treatment. In addition, “Muñoz-Gómez et al., 2017”^[23] stated that 46 patients suffering from CKD stage 4 and 5 who received ombitasvir/paritaprevir/ritonavir(OBV/PTV/r) \pm dasabuvir (DSV) \pm ribavirin (RBV) had 95.7% SVR12.

However, as dasabuvir is not available in Egypt. The Egyptian protocol recommends ombitasvir/paritaprevir/ritonavir with ribavirin in management of HCV patients with renal impairment.^[24] As this study was a real life experience in daily HCV management practice in Egypt, it reported that Paritaprevir/ritonavir and ombitasvir plus ribavirin for 12 weeks was considered to be safe and effective in the treatment of chronic HCV infected patients with varying degrees of renal impairment.

There was a significant decline in hemoglobin in our patient group. This could be explained as patients with ESRD suffer from anemia due to inadequate erythropoietin production and hemolysis due to decreased RBV excretion. Most of hemoglobin decline occurred during the first month of treatment. Despite, 48 patients had erythropoietin from the start of therapy they showed significant decline in hemoglobin. No 1 had to stop RBV and 4 patients had packed RBCs transfusion. Our results were similar to “Muñoz-Gómez et al, 2017”^[23] who concluded that the

Table 4
Anemia in studied patients and management.

Anemia	No. (%)
Grade (10 – 8)g/dL	48 (46.6)
Grade (8 – 6)g/dL	0 (0.0)
RBV dose reduction	44 (42.7)
RBV Discontinuation	0 (0.0)
Erythropoietin	48 (46.6)
Blood transfusion	4 (3.9)

*RBV = ribavirin.

overall incidence of anaemia in their 2 studied groups was 47.8% either they were taking RBV or not. On the other hand 9 of the patients enrolled by Pockros et al, 2016^[22] had to stop RBV as they reached prespecified values for its stoppage.

Both ALT and AST can be considered as surrogate markers of hepatocellular injury. It was demonstrated that persistent elevation of ALT and AST was associated with progression of CHC and increasing risk for cirrhosis.^[25–27] So that, follow up of liver enzymes had been done and there was significant decrease in ALT and AST until reaching base line at 12 week of therapy and this decrease was sustained at week 12 post treatment. This was in agreement with results obtained by Huynh et al, 2018^[28] who studied 115 HCV patients and found that 85.5% and 83.9% of patients had normal ALT and AST as early as week 2 of therapy and this percentage increased to 90.8% at post treatment weeks 12 (18). In addition, the study done by Atsukawa et al,^[21] showed marked decrease in patients ALT at 12 weeks post treatment. Additionally, Khan et al, 2017^[29] had concluded that enzyme levels (particularly AST and AST:ALT ratio) were a viable alternative to HCV RNA, with strong predictive value in determining treatment success of DAA therapies.

Renal function tests were stable during treatment and at 12 weeks after therapy. Our results were in accordance with the results of Muñoz-Gómez et al.^[23]; On the contrary, previous studies showed that SOF-based therapies in patients suffering from renal function impairment (eGFR < 45 mL/min) were associated with high risk of renal function deterioration and adverse events.^[30]

While recent Egyptian study conducted by Eleterby et al had studied the efficacy of sofosbuvir based regimen in chronic HCV patients with CKD with eGFR of less than 60 mL/min/1.73 m², and they concluded that SVR was achieved in 97.5% of their study population, and that 18 patients of their patients had improved renal function at end of therapy, they also documented that patients group with more severe renal disease and those on dialysis showed lower SVR (80%) and they concluded that these regimens are safe and effective in treating patients suffering from chronic HCV with moderate to severe renal impairment.^[31]

In all our recovered patients who are on dialysis precautions are taken to prevent reinfection of those patients according to CDC recommendations to prevent transmission of HCV which is available since 2001.^[32]

One of the strength points of our study is that it was a prospective study that allowed us to directly follow our patients' renal function.

The limitation of the study is the limited sample size. So, larger studies on larger number of patients are recommended to document these findings.

In conclusion, The use of paritaprevir/ritonavir and ombitasvir (75/50/12.5 mg) daily plus ribavirin for 12 weeks was safe and

effective in the treatment of chronic HCV genotype 4 infected patients with varying degrees of renal impairment.

Acknowledgments

We would like to acknowledge the contributions of Egypt's national committee for control of viral hepatitis for the great efforts for control of hepatitis C in Egypt. Special thanks to Dr. Manal Negm consultant of nephrology in Tanta University and Prof. Mohammad Safi Ullah for their commitment and support.

Author contributions

S.A.-E., Y.A.-A and M.E.-A designed the study. S.A.-E., M. U. and R.B. developed the methodology. S.A.-E., M.U. and A.M. A. E wrote the article. S.A.-E., Y. E.-A., M.E.-A., S. A. E, H.F.E., R.A., M.E., N.H., S. S, R. B, M. Y. S., A.A.M and L. M collected the data. S.S., S.A.-E. and A.M. A. E performed the analysis. All the authors participated sufficiently in the work and approved the final version of the article.

References

- [1] Blach S, Zeuzem S, Manns M, et al. global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modeling study. *Lancet GastroenterolHepatol* 2017;2:161–76.
- [2] Ahmed OA, Kaisar HH, Hawash N, et al. Efficacy of sofosbuvir plus ribavirin with or without peginterferon-alfa in treatment of a cohort of Egyptian patients with hepatitis C virus infection. *Infect Disord Drug Targets* 2017;17:95–100.
- [3] Abd-Elsalam S, Sharaf-Eldin M, Soliman S, et al. Efficacy and safety of sofosbuvir plus ribavirin for treatment of cirrhotic patients with genotype 4 hepatitis C virus in real-life clinical practice. *Arch Virol* 2018;163: 51–66.
- [4] Ahmed OA, Kaisar HH, Badawi R, et al. Efficacy and safety of sofosbuvir-ledipasvir for treatment of a cohort of Egyptian patients with chronic hepatitis C genotype 4 infection. *Infect Drug Resist* 2018; 11:295–8.
- [5] Ahmed OA, Elsebaey MA, Fouad MHA, et al. Outcomes and predictors of treatment response with sofosbuvir plus daclatasvir with or without ribavirin in Egyptian patients with genotype 4 hepatitis C virus infection. *Infect Drug Resist* 2018;11:441–5.
- [6] Ahmed OA, Safwat E, Khalifa MO, et al. Sofosbuvir plus daclatasvir in treatment of chronic hepatitis C genotype 4 infection in a cohort of Egyptian patients: an experiment the size of Egyptian village. *Int J Hepatol* 2018;2018:9616234.
- [7] Satapathy SK, Lingisetty CS, Williams S. Higher prevalence of chronic kidney disease and shorter renal survival in patients with chronic hepatitis C virus infection. *Hepatol Int* 2012;6:369–78.
- [8] Tsui JJ, Vittinghoff E, ShlipakMG, et al. Association of hepatitis C seropositivity with increased risk for developing end-stage renal disease. *Arch Intern Med* 2007;167:1271–6.
- [9] Goodkin DA, Bieber B, Gillespie B, et al. Hepatitis C infection is very rarely treated among hemodialysis patients. *Am J Nephrol* 2013;38: 405–12.
- [10] Fabrizi F, Dulai G, Dixit V, et al. Meta-analysis: interferon for the treatment of chronic hepatitis C in dialysis patients. *Aliment Pharmacol Ther* 2003;18:1071–81.
- [11] Russo MW, Goldsweig CD, Jacobson IM, et al. Interferon monotherapy for dialysis patients with chronic hepatitis C: an analysis of the literature on efficacy and safety. *Am J Gastroenterol* 2003;98:1610–5.
- [12] Rebetol (ribavirin USP) capsules, for oral use [package insert]. Whitehouse Station, NJ: Merck. Revised on May 2015. Available at: https://www.merck.com/product/usa/pi_circulars/r/rebetol/rebetol_mg.pdf.
- [13] American Association for the study of Liver Disease/Infectious Disease Society of America/International Antiviral Society. Recommendations for testing, managing, and treating hepatitis C virus. 2015. Available at: <https://www.hcvguidelines.org/>.
- [14] Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research(CDER). Guidance for

- Industry Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment. Available at: <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm225333.pdf>
- [15] Khatri A, Dutta S, Marbury TC, et al. The pharmacokinetics and safety of the direct acting antiviral regimen of ABT-450/r, ombitasvir with/without dasabuvir in subjects with mild, moderate and severe renal impairment compared to subjects with normal renal function. *Hepatology* 2014;60:320A.
- [16] National kidney foundation. CKD-EPI CREATININE EQUATION, 2009. Available at: <https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>, Accessed in January 2018.
- [17] National Kidney, Foundation, K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002;39:S1–266.
- [18] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604–12.
- [19] Stevens LA, Schmid CH, Zhang Y, et al. Development and validation of GFR-estimating equations using diabetes, transplant and weight. *Nephrol Dial Transplant* 2009;25:449–57.
- [20] Abdelmoemen G, Khodeir SA, Abou-Saif S, et al. Prevalence of occult hepatitis C virus among hemodialysis patients in Tanta university hospitals: a single-center study. *Environ Sci Pollut Res Int* 2018;25:5459–64.
- [21] Atsukawa M, Tsubota A, Koushima Y, et al. Efficacy and safety of ombitasvir/paritaprevir/ritonavir in dialysis patients with genotype 1b chronic hepatitis C. *Hepatol Res* 2017;47:1429–37.
- [22] Pockros PJ, Reddy KR, Mantry PS, et al. Efficacy of direct-acting antiviral combination for patients with hepatitis C virus genotype 1 infection and severe renal impairment or end-stage renal disease. *Gastroenterology* 2016;150:1590–8.
- [23] Muñoz-Gómez R, Rincón D, Ahumada A, et al. Therapy with ombitasvir/paritaprevir/ritonavir plus dasabuvir is effective and safe for the treatment of genotypes 1 and 4 hepatitis C virus (HCV) infection in patients with severe renal impairment: a multicentre experience. *J Viral Hepat* 2017;24:464–71.
- [24] El-Gendy NA, EL-Raey FM, Nassibi SA, et al. Efficacy of ombitasvir/paritaprevir/ritonavir plus ribavirin in treatment of chronic hepatitis C patients with end stage renal disease on regular hemodialysis. *IJMA* 2020;2:313–9.
- [25] Lynch SM, Wu GY. Hepatitis C virus: a review of treatment guidelines, cost effectiveness, and access to therapy. *J ClinTranslHepatol* 2016;4:310–9.
- [26] González-Grande R, Jiménez-Pérez M, González Arjona C, et al. New approaches in the treatment of hepatitis C. *World J Gastroenterol* 2016;22:1421–32.
- [27] Zampino R, Marrone A, Restivo L, et al. Chronic HCV infection and inflammation: clinical impact on hepatic and extra-hepatic manifestations. *World J Hepatol* 2013;5:528–40.
- [28] Huynh T, Zhang J, Hu K. Hepatitis C virus clearance by direct-acting antiviral results in rapid resolution of hepatocytic injury as indicated by both alanine aminotransferase and aspartate aminotransferase normalization. *J Clin Transl Hepatol* 2018;6:258–63.
- [29] Khan ST, McGuinty M, Corsi DJ, et al. Liver enzyme normalization predicts success of Hepatitis C oral directacting antiviral treatment. *Clin Invest Med* 2017;40:E73–80.
- [30] Saxena V, Korashy FM, Sise ME, et al. Safety and efficacy of sofosbuvir-containing regimens in hepatitis C-infected patients with impaired renal function. *Liver Int* 2016;36:807–16.
- [31] Eletreby R, El-Serafy M, Anees M, et al. Sofosbuvir-containing regimens are safe and effective in the treatment of HCV patients with moderate to severe renal impairment. *Liver Int* 2020;40:797–805.
- [32] Centers for Disease Control, Prevention, Recommendations for preventing transmission of infections among chronic hemodialysis patients. *MMWR Recomm Rep* 2001;50(RR-5):1–43.