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Pharmacokinetics, safety and efficacy of a full dose sofosbuvir-based regimen given daily in hemodialysis patients with chronic hepatitis C

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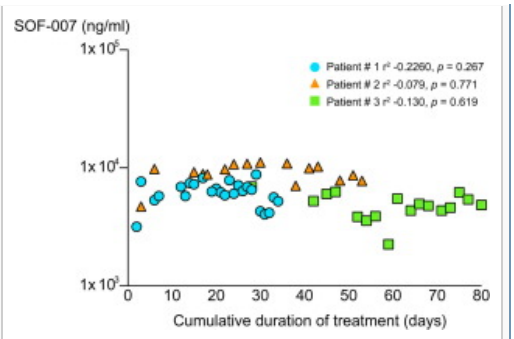
Background & Aims

Hepatitis C virus (HCV) infection is an independent risk factor for chronic kidney disease and leads to faster liver disease progression in patients requiring hemodialysis than in those with normal renal function. Little is known about the use of a sofosbuvir-containing regimen for infected patients on hemodialysis. We aimed to describe the pharmacokinetics, safety and efficacy of sofosbuvir in 2 dosing regimens and associated antiviral agents in



HCV-infected patients requiring hemodialysis.

Methods

Multicenter, prospective and observational study of patients receiving sofosbuvir, 400 mg once daily (n = 7) or 3 times a week (n = 5), after hemodialysis with simeprevir, daclatasvir, ledipasvir or ribavirin was conducted. Drug plasma concentrations were determined by liquid chromatography-tandem mass spectrometry before and after a 4 h hemodialysis and 1.5 h after last drug intake at the end of hemodialysis.

Results

Plasma concentrations of sofosbuvir or its inactive metabolite sofosbuvir-007 did not accumulate with either regimen between hemodialysis sessions or throughout the treatment course. Sofosbuvir-007 extraction ratio (52%) was consistent with historical data. In one patient receiving the once daily regimen, sofosbuvir-007 half-life was slightly higher (38 h) than for patients with normal renal function receiving a full dose. Hemodialysis did not remove any other associated anti-HCV agents. Clinical and biological tolerance was good for all patients. Two relapses occurred with the 3 times a week regimen and none with the once daily.

Conclusions

A regimen including sofosbuvir, 400 mg once daily, could be proposed for HCV-infected patients requiring hemodialysis and should be associated with close clinical, biological, cardiovascular, and therapeutic drug monitoring.

Lay summary

Hepatitis C Virus (HCV) infection in hemodialysis patients is prevalent and aggressive. Effective anti-HCV treatment in these patients may stabilize their renal disease. However, sofosbuvir, the cornerstone of most anti-HCV–containing regimens, should not be administered to these patients until more data is available. In this pharmacokinetic study, sofosbuvir full dose (400 mg once daily) administered every day with another direct antiviral agent did not accumulate in hemodialysis patients and was safe and effective.

Abbreviations:

HCV (hepatitis C Virus), ESRD (end-stage renal disease), DAAs (direct-acting anti-HCV agents), SOF (sofosbuvir), LDV (ledipasvir), SOF-007TP (sofosbuvir uridine-triphosphate), SOF-007 (predominant sofosbuvir inactive metabolite GS-331007), QD (once daily), TIW (three times a week), DCV (daclatasvir), SMV (simeprevir), RBV (ribavirin), PegIFN (pegylated interferon), ALT (alanine aminotransferase), AST (aspartate aminotransferase), GGT (gamma-glutamyl transferase), pre-HD (blood samples collected just before 4-h hemodialysis), post-HD (blood samples collected just after 4-h hemodialysis), C1.5h (blood samples collected 1.5h after hemodialysis and dose intake), SVR (sustained virologic response)

Keywords:

Sofosbuvir, Hepatitis C Virus, Hemodialysis, Pharmacokinetics

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