Treatment of HCV patients on hemodialysis with daclatasvir and asunaprevir

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The treatment of chronic hepatitis C virus (HCV) infection has improved dramatically with the advent of direct-acting antiviral agents (DAAs). Daclatasvir + asunaprevir was the first approved interferon- and ribavirin-free combination regimen in Japan [1–4]. Although recently developed DAAs have shown quite high rates of sustained virological response (SVR), there are some patients for whom it is unclear whether the therapy is appropriate or likely to be effective due to co-existing clinical conditions, such as patients with renal failure, especially end-stage renal failure, on dialysis or decompensated liver cirrhosis, and organ transplant recipients. Two papers appear in the recent issue of *Journal of Gastroenterology* which report on the treatment of patients on hemodialysis with combined daclatasvir + asunaprevir therapy [5, 6]. Suda et al. [5] treated and evaluated 21 patients on hemodialysis, including four patients with compensated cirrhosis who were treated for 24 weeks with daclatasvir + asunaprevir combination therapy. These authors found that 95 % (20/21) of their patients achieved SVR for ≥ 12 weeks after the end of treatment (SVR12). Only one patient who experienced relapse had a pre-existing NS3 D168E resistance-associated variant (RAV), whereas there were three

patients with pre-existing NS5A Y93 RAVs who nonetheless achieved SVR. Only one patient discontinued the therapy with elevated alanine aminotransferase (ALT) levels (about tenfold the upper limit of normal) and decreased platelet counts ($7.5\text{--}4.4 \times 10^4/\mu\text{l}$) at week 12, but this patient also achieved SVR. Serious adverse events were seen in only one patient who was found to have hepatocellular carcinoma at the end of the therapy. The authors concluded that the therapy was highly effective and well tolerated. Toyoda et al. [6] also evaluated the efficacy and safety of 24 weeks of daclatasvir + asunaprevir combination therapy in 28 patients receiving hemodialysis and compared them with 56 propensity score-matched control patients without renal dysfunction [6]. They reported that all 28 patients on hemodialysis achieved SVR, in contrast to 94.6 % of the control patients who achieved SVR. Initial reduction of HCV RNA at week 1 was significantly greater in the hemodialysis patients and the disappearance of serum HCV RNA occurred significantly earlier than in control patients. No serious adverse events were noted in either group of patients, and ALT elevation was comparable between the two groups of patients. These authors thus concluded that the therapy is safe and effective in patients receiving hemodialysis. Recently, Kawakami et al. [7] also reported early kinetics in 18 patients on hemodialysis treated with the same regimen and reported that the reduction of HCV RNA was greater in hemodialysis patients. Although all three of these studies show that patients on hemodialysis responded better to the therapy, the reason for this outcome is unknown. Kawakami et al. [7] compared blood asunaprevir and daclatasvir concentrations and showed that the area under the curve of asunaprevir was significantly lower in hemodialysis patients than in controls, while the trough concentration of daclatasvir was slightly higher in

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hemodialysis patients. These differences might affect the response of patients to the therapy, but this trend should be analyzed in a larger number of patients.

As all studies reported to date have shown high SVR rates and safety in this patient population, daclatasvir + asunaprevir combination therapy should be recommended for patients on hemodialysis.

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Compliance with ethical standards

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