Hepatitis C virus (HCV) infection is more common in patients with chronic kidney disease stage 4 or 5 than in the general population.\(^1,2\) HCV transmission might be either nosocomial within the dialysis unit, or from (mostly past) blood transfusions, or occasionally from an infected graft.\(^2,3\) HCV infection is a strong independent risk factor for death in patients on dialysis.\(^4\) With (peg) interferon and ribavirin, sustained viral response (SVR) rates are low, around 35% in dialysis patients, and tolerance is poor.\(^5,6\) However, anti-HCV treatments have changed dramatically over the past 5 years. With direct-acting antiviral agents, SVR rates now exceed 95% in patients without chronic kidney disease.\(^3\) Unfortunately, patients with chronic kidney disease stages 4 and 5 have been excluded from virtually all controlled trials with direct-acting antiviral agents.

In *The Lancet*, David Roth and colleagues\(^7\) report the first results of C-SURFER, a phase 3 study. They recruited 235 patients with chronic HCV genotype 1 infection (the most prevalent genotype in dialysis patients\(^6\)) and chronic kidney disease stage 4 or 5 (76% were on haemodialysis, 6% were cirrhotic, and 80% were treatment naive). Patients were randomly assigned to either immediate (n=111) or delayed (n=113) treatment with an oral once-daily combination of grazoprevir (100 mg) and elbasvir (50 mg) for 12 weeks. Additionally, 11 patients were assigned to an immediate intensive pharmacokinetic group. The authors did not request a liver biopsy at baseline to assess the extent of liver fibrosis: biochemical non-invasive markers or transient elastography were sufficient, in line with recent practice changes.\(^8\) The removal of a significant hurdle, the risk of liver biopsy, should facilitate the treatment of HCV in dialysis patients.

Roth and colleagues’ report on the immediate treatment group, with or without intensive pharmacokinetic study (n=122): the SVR at 12 weeks (SVR12) was 99% (95% CI 95·3–100·0). Thus, the cure of HCV infection (at least for genotype 1) now appears at hand in chronic kidney disease stage 4 or 5. The tolerance of the study regimen was also impressive, with no withdrawals due to side-effects. Despite some selection bias for healthier patients, as suggested by their younger age (mean 56 years) and somewhat lower comorbidity than the typical western dialysis patient, the results appear generalisable to candidates for a kidney transplant. Only a small minority of these patients are treated as yet for HCV,\(^4\) despite the poor prognosis associated with the virus. The single pill grazoprevir and elbasvir regimen appears attractive in a population facing polypharmacy.\(^7\) Both grazoprevir and elbasvir are substrates of CYP3A/P-glycoprotein, whereas grazoprevir is also a substrate for the organic anion transporter protein 1B. Furthermore, both drugs are intestinal breast cancer resistance protein inhibitors.\(^10\) These characteristics imply a significant risk of drug–drug interactions, needing careful attention.

Roth and colleagues’ excluded patients with a failed kidney allograft but still under treatment with ciclosporin, an inhibitor of the organic anion transporter protein 1B. This point is relevant. The effect of the grazoprevir and elbasvir regimen in prevalent kidney graft recipients (some of whom, transplanted decades ago, are still receiving ciclosporin) remains to be studied. The risk of similar drug–drug interactions might be even greater with several other direct-acting antiviral agents, apart from grazoprevir and elbasvir.\(^11\)

Overall, the report from Roth and colleagues’ makes an important contribution to the battle against both HCV and the dire prognosis of dialysis patients worldwide. After registration and reimbursement of grazoprevir and elbasvir, a much greater fraction of patients with chronic kidney disease stages 4 and 5 should soon be treated. By contrast with the expected residence of HCV
for decades in dialysis units, it is now time to envision eradication of HCV from such units. Needless to say, this goal should best be achieved by the combination of prevention and cure, rather than by cure only. The long-awaited availability of highly active anti-HCV drugs should be no reason for complacency regarding the application of basic cost-effective hygiene precautions within haemodialysis units.

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