

## **Grazoprevir-elbasvir effective for hepatitis C in advanced chronic kidney disease**

By Will Boggs MD

NEW YORK (Reuters Health) - The combination of grazoprevir and elbasvir is effective for treating hepatitis C virus (HCV) genotype 1 infection in patients with stage 4-5 chronic kidney disease (CKD), according to the C-SURFER trial.

"Patients with chronic kidney disease should be screened for HCV infection if not already done," Dr. David Roth from University of Miami Miller School of Medicine told Reuters Health by email. "Many of these patients would benefit from therapy in some extrahepatic outcomes, such as progression of CKD, quality of life outcomes, glucose intolerance. These are, of course, in addition to any benefit on the further injury to the liver of untreated HCV infection and risk of hepatocellular carcinoma."

HCV infection accelerates the decline in kidney function in patients with CKD and increases mortality among patients on hemodialysis.

Dr. Roth and colleagues investigated the effects of an all-oral HCV regimen combining grazoprevir and elbasvir in a phase 3 trial of 235 patients with stage 4-5 CKD who were infected with HCV genotype 1.

The treatment group received grazoprevir 100 mg and elbasvir 50 mg once daily for 12 weeks. Beginning four weeks after this phase, the deferred-treatment group (originally assigned to placebo) underwent 12 weeks of the same treatment.

All but one of the patients in the immediate-treatment group (99%) achieved sustained virological response (SVR) at 12 weeks, a rate significantly better than the historical control rate of 45%. One noncirrhotic patient relapsed 12 weeks after the end of treatment.

HCV RNA was undetectable in one of 113 deferred treatment patients four weeks after the initial 12 weeks, and the patient denied taking any HCV therapy outside the study.

SVR was achieved by all 36 patients who had NS3/4A resistance-associated variants and in 16 of 17 (94.1%) patients who had the NS5A resistance-associated variant, the team reports in *The Lancet*, online October 6.

There were no serious drug-related adverse events in the immediate-treatment group, and the frequencies of renal system adverse events were comparable between the two groups. Neither group experienced significant changes in mean eGFR or creatinine.

"I believe that nephrologists and hepatologists will need to determine which of the chronic kidney disease population would be best treated and when," Dr. Roth said. "The issue of pre versus post kidney transplant treatment might have a very large impact on patient waiting time on the deceased donor waiting list if the patient were to accept a kidney from a HCV positive donor."

"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," write Dr. Michel Jadoul and Dr. Yves Horsmans from Université Catholique de Louvain in Brussels, Belgium, in a related editorial.

"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 hemodialysis units," they caution.

Dr. Ravindra A. Prabhu from Manipal University in Karnataka, India, who recently reviewed interventions for dialysis patients with HCV infection, told Reuters Health by email, "The main message here is the emergence of an oral therapy of three months' duration with less adverse effects and almost complete response at least in the short term in the advanced chronic kidney disease population where treatment options are limited and less tolerated."

Dr. Prabhu added, "This would allow these patients to be placed on kidney transplant waiting lists after start of treatment. Whether these patients can receive this combination after kidney transplant would need further study."

Merck Sharp & Dohme Corp. funded the trial, employed six of the 19 authors, and had various relationships with 11 of the other authors.

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