

Oral Hepatitis C Drug Found Safe in Patients With Renal Failure

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The fixed dose oral combination of glecaprevir and pibrentasvir (Mavyret) demonstrated efficacy across genotypes and was found safe in patients with severe renal impairment, in a recently published phase 3 trial.

Lead author of the study report, Edward Gane, MD, of the Liver Unit in Auckland City Hospital, New Zealand, commented on the study drug to *MD Magazine*.

"The new fixed dose combination of glecaprevir and pibrentasvir provides a safe and effective treatment for patients with hepatitis C infection who have severe renal impairment," Gane said. "Because neither drug is cleared by the kidney, no dose adjustment is required even in people on dialysis."

Gane and colleagues found that HCV infection is more prevalent among patients with chronic kidney disease (CKD) than among those without the disease; and those with concomitant HCV infection are at higher risk for progression to end-stage renal disease, as well as for compensated cirrhosis and hepatocellular carcinoma.

With no other all-oral direct acting antiviral (DAA) yet approved for patients with severe renal impairment and HCV genotype 2,3,5 or 6 infection, the only other available approved option for this population is interferon with ribavirin.

"However, the negative side-effect profile of interferon is well documented in this population, and ribavirin is excreted in the urine, (and) accumulates systemically in patients with severe renal impairment," researchers wrote.

The NS3/4A protease inhibitor glecaprevir and the NS5A inhibitor pibrentasvir are both excreted through the biliary system rather than through renal clearance, and the fixed dose oral combination has been approved for treatment of HCV genotype 1,2,3,4,5 or 6 with or without compensated cirrhosis, and in genotype 1 previously treated with an NS5A inhibitor or an NS3/4A protease inhibitor but not both.

In the open-label single-group phase 3 trial (EXPEDITION-4) the researchers provided 12 weeks of Mavyret to 104 patients with stage 4 or 5 CKD (82% dependent on hemodialysis) and concurrent infection with HCV genotype 1 (52%), 2 (16%), 3 (11%), 4 (19%), 5 or 6 (2%).

A total of 19% of patients had compensated cirrhosis, and 42% had received previous treatment for HCV infection, most with a combination of interferon and ribavirin.

Gane and colleagues reported that sustained virologic response (SVR) at 12 weeks, consistent with cure, was attained in 98% of patients. There were no instances of virologic failure during treatment or of virologic relapse during 12 weeks of follow-up after the end of treatment.

The side effect profile of the regimen was characterized as acceptable, which was particularly notable for this population with numerous coexisting conditions. The most common adverse events were pruritus, fatigue and nausea. There was a similar rate of adverse events in patients undergoing dialysis as in those who were not on dialysis.

"In the phase 3 study in patients with severe renal impairment including those on dialysis, all patients who received 12 weeks treatment were cured and there was no toxicity seen," Gane said. "The lack of significant drug interactions and no need for ribavirin makes this an ideal treatment regimen in this patient population."

The study, "Glecaprevir and Pibrentasvir in Patients with HCV and Severe Renal Impairment," was published online in the *New England Journal of Medicine* last month.