VIRAL HEPATITIS

Is it the end of the line for interferon therapy for hepatitis C?

Results from two clinical trials have added to the body of evidence demonstrating the efficacy of interferon-free treatment regimens for hepatitis C. “The treatment of HCV is rapidly evolving towards interferon-free regimens,” explains Greg Everson, corresponding author of one of the studies, published in *Gastroenterology*. “One reason for this movement away from interferon is the toxicity and numerous adverse effects associated with this agent; ribavirin also has significant toxicity, especially haemolytic anaemia and rash.” Everson and colleagues therefore conducted a phase IIa, open-label study examining the safety and efficacy of an interferon-free and ribavirin-free regimen of daclatasvir, asunaprevir and BMS-791325 in treatment-naïve patients with HCV genotype 1 infection without cirrhosis.

66 patients were included in four study arms that consisted of two doses of BMS-791325 and two different durations of treatment (12 versus 24 weeks). Optimal doses of daclatasvir and asunaprevir have already been established. The researchers found that all regimens and durations of treatment achieved sustained virological response rates at 12 weeks (SVR12) of $\geq 90\%$. In addition, the triple regimen was well tolerated, with few adverse effects and low rates of discontinuation of treatment.

“This research indicates that the triple therapy used in this study warrants additional study; the phase IIb study has been expanded to include larger numbers of patients, and additional arms will be added to examine efficacy in treatment-experienced patients, patients with cirrhosis and patients infected with HCV genotype 4,” concludes Everson.

In the other phase II, open-label study, published in *The Lancet*, Eric Lawitz and colleagues investigated the combination of sofosbuvir and ledipasvir with or without ribavirin in 100 treatment-naïve or previously treated patients with HCV genotype 1 infection.

Five treatment groups were included in the trial: in cohort A, 60 non-cirrhotic, treatment-naïve patients received sofosbuvir plus ledipasvir for 12 weeks (group 1), sofosbuvir plus ledipasvir and ribavirin for 8 weeks (group 2) or sofosbuvir and ledipasvir for 8 weeks (group 3); in cohort B, 40 previously treated patients (22 of whom had compensated cirrhosis) received sofosbuvir plus ledipasvir for 12 weeks (group 4) or sofosbuvir plus ledipasvir and ribavirin for 12 weeks (group 5). The primary end point of the study was SVR12.

“97 of the 100 patients were cured,” reports Lawitz. “These are really outstanding results.” Two patients had viral relapse and one patient in group 5 had a serious adverse event of anaemia (thought to be related to ribavirin treatment). The researchers conclude that the combination of ledipasvir and sofosbuvir with or without ribavirin “has the potential to cure most patients with HCV genotype 1 infection, irrespective of treatment history or the presence of compensated cirrhosis.”

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Original articles Everson, G. T. *et al.* Efficacy of an interferon- and ribavirin-free regimen of daclatasvir, asunaprevir, and BMS-791325 in treatment-naïve patients with HCV genotype 1 infection. *Gastroenterology* doi:10.1053/j.gastro.2013.10.057 | Lawitz, E. *et al.* Sofosbuvir and ledipasvir fixed-dose combination with and without ribavirin in treatment-naïve and previously treated patients with genotype 1 hepatitis C virus infection (LONESTAR): an open-label randomised, phase 2 trial. *Lancet* doi:10.1016/S0140-6736(13)62121-2