

Update in Infectious Diseases

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Hepatitis C virus (HCV) infection is an important cause of chronic liver disease, cirrhosis and hepatocellular carcinoma. According to the WHO, between 130 and 170 million people worldwide are chronically infected, representing 3% of the world's population, and more than 350,000 people die annually from HCV related causes (1,2,3). Most acute HCV infections are asymptomatic and therefore go unrecognized and 50-90% of patients subsequently develop chronic infection. Liver disease can slowly progress to cirrhosis in 10-40% of the patients (4). HCV infection is also the leading cause of primary hepatic cancer in Europe (4). There are some important extrahepatic manifestations of chronic HCV infection including cryoglobulinemia, non-Hodgkin lymphoma and metabolic disturbances (4).

Until recently the standard of care for chronic HCV infection was combination therapy with pegylated interferon-alpha (pegIFN) and ribavirin. However treatment response was disappointing, especially in patients infected with HCV genotype 1, with sustained virologic response (SVR) rates of 40-54% after a 48-week course of therapy. Patients who relapsed or did not respond to treatment can be re-treated, with even lower SVR rates of 32-53% and 4-14%, respectively (4).

In 2011 two new drugs for the treatment of chronic hepatitis C were approved by the FDA. Boceprevir, marketed as Victrelis, and telaprevir (Incivo) are directly-acting NS3/4A protease inhibitors (PI). In July 2011 EMA approved boceprevir for use in the European Union in combination with pegIFN and ribavirin in patients with HCV genotype 1 infection who were pre-

viously untreated or who had failed therapy. Telaprevir is still pending a decision by the European Commission and has not yet been approved in Europe (5). Phase III clinical trials with the two new agents showed encouraging results. Tripe therapy including a PI was associated with 27-31% higher SVR rates in treatment-naïve patients. Patients who had previously relapsed had SVR rates of 75-86%, but non-responders had considerably lower SVR rates (33% for telaprevir) (4). There are, however, some concerns related to PI treatment like an increase in the frequency of anemia and the rapid emergence of PI resistance, especially in cases with previous non-response, non-adherence and patients unable to tolerate full doses of pegIFN and ribavirin (4).

Other therapeutic options, still in development, are other NS3/4A PIs, NS5B polymerase inhibitors, directly-acting antiviral combinations, cyclophilin inhibitors, pegIFN lambda, therapeutic vaccines designed to boost the immune system of patients on therapy, and monoclonal antibodies (6). In addition to the new drugs, novel tools have been discovered in recent years to aid in predicting SVR. Polymorphisms located upstream of the IL28B gene have been shown to be associated with SVR to treatment (4) and an increased insulin resistance estimated using the homeostasis model assessment (HOMA-IR) has also been shown to be linked to treatment failure, although insulin-sensitising agents with pioglitazone and metformin have not yet proven effective in randomized controlled trials (7).

This year has brought new options that hopefully will be of great use for patients with chronic HCV genotype 1 infection.

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