HCV Infection

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Abstract Hepatitis C virus (HCV) infection, the leading cause of cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC), affects approximately 170 million people worldwide. With the introduction of dual combination therapy by peginterferon and ribavirin, the overall sustained virologic response (SVR) rates can reach 50-60% in hepatitis C virus genotype 1 (HCV-1) and HCV-4 infection, and about 80% in HCV-2 and HCV-3 infection with 48 and 24 weeks of therapy. However, there is still substantial proportion of patients not responsive to the dual combination therapy.

Recently, the first generation direct acting antivirals (DAAs), including telaprevir and boceprevir which target the HCV non-structural protein 3 and 4A (NS3/4A), in combination with peginterferon and ribavirin further improve the overall SVR rates in treatment-naïve (63-75%) and treatment-experienced (59-66%) HCV-1 patients. The triple combination therapy has been approved by FDA in 2011 and been the new standard of care (SOC) to treat HCV-1 patients. However, these agents had increased rates of adverse events and increased pill and financial burdens. Furthermore, these agents showed poor antiviral activity for HCV-2 or HCV-3 patients. These limitations restricted the unselected use of the novel agents. The use of next-wave generation of DAAs, which target more HCV domains (NS3/4A, NS5B, NS5A, nucleocapsid protein etc…), are aimed to further increase the SVR rates, and decrease the pill burdens as well as the potential adverse events. Until recently, many clinical trials focusing on the DAA based treatment in combination with peginterferon plus ribavirin or interferon-free DAA therapies have further improving the overall treatment response to more than 80%. Furthermore, the corresponding safety profiles are more favorable. Among these novel therapeutic agents, some of them possess pan-genotypic effects for HCV.

Despite the surprising advances of HCV treatment in the recent years, the regimens for the optimized treatment are needed to be validated in clinical practice. Long-term efficacy and safety evaluation should also be needed for these novel therapeutic agents.