Second Generation of Direct Acting Antivirals (DAAs) for HCV Infection

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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 second 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. Currently, numerous novel agents in the pipeline, which have broader and potent antiviral activities across different HCV genotypes and early viral decline, are now under active investigation.

Despite the surprising advances of HCV treatment in the recent years, the optimal treatment in HCV patients still need further confirmation and refinement. In the near future, the patients will benefit their clinical outcomes from more potent and simple DAAs.