SUMMARY

With the great diversity of HCV and its ability to rapidly mutate to escape targeted therapeutics, strategies to design the proper combination of inhibitors will be critical; however, the development the HCV experimental systems needed to elucidate the molecular mechanisms that mediate HCV infection have greatly advanced our understanding of the viral life cycle, resulting in the identification of unprecedented number of putative HCV inhibitors. With many of these HCV antiviral compounds already inclinical development, it is clear that we are about to witness a great change in HCV patient care.

The search for new therapies for chronic hepatitis C virus (HCV) is ongoing. These can be divided conceptually into: derivatives of current treatment; treatments targeting HCV-encoded proteins; treatments targeting host-encoded proteins; and therapeutic and preventive vaccines.

Characterization of HCV-encoded proteins and their functions has permitted development of strategies aimed at interrupting HCV replication. Key potential drug targets include the NS2/3 autoprotease, the NS3 RNA helicase, the NS3/4A serine protease, the NS5A protein, and the NS5B RNA-dependent RNA polymerase.

NS3/4A protease inhibitors are the first direct acting antiviral (DAA) agents approved for clinical use in combination with peginterferon and ribavirin. It is anticipated that these treatment regimens will increase SVR rates in treatment-naïve patients and in those patients who have previously failed peginterferon/ribavirin therapy. Relapsers appear to do much better than nonresponders when re-treated with telaprevir or boceprevir plus peginterferon and ribavirin.

Once available, we suggest that protease inhibitor-containing regimens be considered in treatment-naïve patients as well as in patients who relapsed or experienced viral breakthrough during prior attempts at treatment.

Another approach to HCV therapy is to target the host proteins that the virus uses for its own life cycle. A theoretical advantage of this strategy is that the genetic barrier for viral resistance may be higher than for DAA therapy.

Hepatitis C virus genotype 4 (HCV-4) is the most common type of hepatitis C virus (HCV) in the Middle East and Africa, in particular Egypt. Since the development of new protease inhibitors, the response of HCV-4 to the standard regimen of treatment (pegylated interferon/ribavirin) lags behind other genotypes and has become the most resistant type to treat.

The development of therapeutic strategies for all patients with HCV-4 is still a considerable challenge. New types of interferon (Consensus Interferon, Y-shaped, Albinterferon…) and new direct action antiviral drugs (RG7128,Alisporivir,Nitazoxanide….) may improve the treatment of patients with HCV-4 .