INRTRODUTION:

The World Health Organization (WHO) estimates 170 million individuals worldwide are infected with hepatitis C virus (HCV).For example, ***Frank et al., in 2000*** *reported that Egypt had the highest number of reported infections, largely attributed to the use of contaminated parenteral antischistosomal therapy. This led to a mean prevalence of HCV antibodies in persons in Egypt of 22%.*

Egypt has the largest epidemic of hepatitis C virus (HCV) in the world. The recently released Egyptian Demographic Health Survey [EDHS] tested a representative sample of the entire country for HCV antibody. The sample included both urban and rural populations and included all 27 governorates of Egypt. Over 11,000 individuals were tested. The overall prevalence (percentage of people) positive for antibody to HCV was 14.7% ***(El-zanaty et al., 2009)****.*

Chronic infection with HCV is one of the most important causes of chronic liver disease and the most common indication for orthotopic liver transplantation (LT) in the United States ***(Davis et al., 1989).***

With the current standard care, a combination therapy of pegylated interferon-alfa plus weight based ribavirin for 24 to 72 weeks, only half of all patients with chronic hepatitis C can be cured ***(Zeuzem et al., 2004).***

The chance to achieve a sustained virologic reponse (SVR) by such regimens differs significantly between HCV genotypes with SVR rates of 40–50% in patients infected with genotype 1, contrasted by SVR rates

of approximately 80% in those infected with genotypes 2 or 3 ***(Hadziyannis et al., 2004).***

In addition, treatment with pegylated interferon-alfa and ribavirin is long (up to 72 weeks) and associated with numerous side effects like anaemia, flu-like symptoms or depression ***(Fried et al., 2002).***

The exploding knowledge of the HCV life cycle and of structural features of the HCV proteins has supported the development of many promising directly acting anti-viral agents, also named 'specifically targeted anti-viral therapy for hepatitis C' (STAT-C) compounds ***(Poordad et al., 2008).***

Many of these direct anti-virals are currently in phase I–III development and will significantly change treatment options for HCV infection in the near future ***(Sarrazin and Zeuzem, 2009).***

A number of recent discoveries have allowed for the development of these agents, ranging from the ability to grow HCV in tissue culture and develop infectious molecular clones of the virus, to crystallographic analyses that have identified the 3-dimensional structure of HCV ***(Sheehy et al., 2005).***

The two most promising agents currently under development are directed against a serine protease (NS3/NS4A), which is necessary for cleaving viral polypeptides, and against an RNA-dependent polymerase inhibitor (NS5B) ***(Harrison,2007).***

Protease Inhibitors

Replication of the hepatitis C virus initially results in the synthesis of a polyprotein that is then cleaved into structural and nonstructural proteins. The nonstructural proteins are mainly enzymes essential for the HCV life cycle ***(Lindenbach et al., 2005)***

These nonstructural proteins are progressively cleaved from the polyprotein by a number of proteasesthis enzyme is an obvious candidate target for drug development ***(Harrison, 2007).***

The most advanced compounds are telaprevir and boceprevir that are both inhibitors of the HCV NS3 protease and that have been shown to significantly enhance SVR rates in HCV genotype 1 patients, when applied in addition to pegylated interferon-alfa and ribavirin ***(McHutchison et al., 2009).***

The most advanced compounds are telaprevir and boceprevir that are currently under phase III evaluation and are expected to be approved in 2011/2012.

Polymerase Inhibitors

In addition to protease inhibitors, RNA-dependent RNA polymerase (NS5B) inhibitors are also being actively developed against HCV. Studies of valopicitabine (NM283) have been suspended because of gastrointestinal toxicity at the 800-mg dose ***(Lawitz et al., 2007).***

However, another agent, R1626, a prodrug of a nucleoside analogue (R1479) that targets the HCV RNA polymerase, is currently generating enthusiasm as an alternative option in this class ***(Pockros et al., 2007).***