Entry inhibitors show promise as drugs with new MOA for treatment of HBV and HDV infection

April 2 2011

Promising new viral hepatitis data presented today at the International Liver CongressTM show that entry inhibitors --a new mechanism of action for drugs to treat viral hepatitis -- could provide the first new hepatitis B and hepatitis D treatments for many years.[1,2]

Most current approved therapies directly target viral replication (e.g. nucleotide/side analogues), and can lead to the development of viral resistance or viral rebound after the end of treatment. Entry inhibitors prevent the virus from entering the cell and forming a stable replication complex, limiting the issue of viral rebound and resistance development.

Professor Heiner Wedemeyer, EASL's Secretary General, commented: "The current treatments available for hepatitis B & D are limited. These novel drugs are the first promising treatments for many years. The shift in the mechanism of action of these drugs from inhibiting the virus's replication directly to inhibiting its entry into the cell, and thus its replication – means they are less likely to produce viral resistance; a huge problem faced by many of today's clinicians."

One study1 showed that treatment of ex-vivo liver cells with synthetic anti-lipopolysaccharide peptides (SALPs) during and prior to HBV infection was highly effective and dose dependent in inhibiting infection – reducing markers of HBV infection (e.g. HBV RNA, HBV antigens) in the concentration range of 4-5 µg/mL by 90% and 0.5-2 µg/mL by 50%.

The study also demonstrated that SALPs showed activity against other viral (e.g. HIV, herpes) and microbial (e.g. peritonitis, colitis and pneumonia) infections. Therefore, SALPs represent a very promising therapeutic strategy to treat viral hepatitis infection and concomitant bacterial infection – which often leads to life threatening systematic complications.

Other studies[2,3] illustrated the enormous value of the chimaeric mouse model of chronic HBV and HDV infection for the preclinical evaluation of antiviral drugs. The study demonstrated that the HBV entry inhibitor Myrcludex-B was able to completely block the spread of HBV from cell to cell and to prevent de-novo HDV infection of human hepatocytes.

Professor Wedemeyer commented: "Although there are 35 million people around the world with HDV infection there is currently little to offer them therapeutically. I am therefore delighted to see these new drug developments."

More information: References

1. Lucifora J et al. Novel peptide-based microbiocides inhibiting hepatitis b virus entry by preventing virus interaction with the cell surface. Abstract presented at The International Liver CongressTM 2011. www1.easl.eu/easl2011/program/Orals/338.htm

2. Lutgehetmann M et al. Block of hepatitis delta infection by the entry inhibitor myrcludex b in upa mice: establishment of an efficient mouse model for human HBV/HDV infection. Abstract presented at The International Liver CongressTM 2011. www1.easl.eu/easl2011/program/Orals/390.htm

3. Ben M et al. Administration of the entry inhibitor Myrcludex-B after establishment of Hepatitis B Virus infection prevents viral spreading

among human hepatocytes in uPA mice. Abstract presented at The International Liver CongressTM 2011.
www1.easl.eu/easl2011/program/Orals/337.htm

Provided by European Association for the Study of the Liver