Data suggest liver experts should take care when prescribing novel antiviral HCV drugs

April 2 2011

Data presented at the International Liver Congress highlight the fact that new novel antiviral compounds for the treatment of hepatitis C virus (HCV) must be prescribed and monitored by experts and specialists to ensure resistance is minimised.[1,2,3,4,5,6]

Several studies observed the rapid onset of HCV resistance in patients treated with NS3-protease, NS5b-polymerase and NS5a inhibitors. Although these direct anti-virals are effective in both treatment-naive HCV patients and those who've been previously unresponsive to current treatment options, the development of resistant viral variants may cause problems in the future. In fact, two studies found HCV strains resistant to novel antiviral compounds pre-existed in patients who had never previously been exposed to the new antiviral compounds. In these patients, the variants were selected out by treatment.

Professor Heiner Wedemeyer, EASL's Secretary General, said: "While the regulatory approval of these new treatments is a highly anticipated milestone in HCV therapy, these studies show that care must be taken in the prescription and use of the new compounds. What we want to avoid is a rapid spread of HCV resistance within the patient population, which could drastically lower the effectiveness of the new drugs."

The current standard of care for chronic HCV is the combination of pegylated interferon-alfa and ribavirin, but only 40-54% of patients infected with HCV genotype 1 achieve a sustained virological response (SVR).[7,8] Novel antiviral therapeutics are much sought after to treat

patients who don't respond to the current standard of care. As such, a large number of new drugs for HCV are at various stages of preclinical and clinical development.[9]

However, as each new copy of the HCV genome exhibits on average one nucleotide change per replication cycle, HCV's replication machinery allows the virus to quickly come up with mutations that render it resistant to antiviral drugs. This is a major concern for successful anti-HCV therapy.[10]

NS3 protease inhibitors block the function of the HCV NS3 protease, an enzyme essential for HCV's replication. NS5A replication complex inhibitors block the function of HCV nonstructural protein 5A, a multifunctional protein essential for HCV replication.[10]

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Provided by European Association for the Study of the Liver

Citation: Data suggest liver experts should take care when prescribing novel antiviral HCV drugs

(2011, April 2) retrieved 2 May 2024 from https://medicalxpress.com/news/2011-04-liver-experts-antiviral-hcv-drugs.html

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