Impressive SVR12 data for once-daily combination to treat HCV genotype 1 patients

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Results from three Phase III clinical trials (ION-1, ION-2 and ION-3) evaluating the investigational once-daily fixed-dose combination of the nucleotide analogue polymerase inhibitor sofosbuvir (SOF) 400mg and the NS5A inhibitor ledipasvir (LDV) 90mg, with and without ribavirin (RBV), for the treatment of genotype 1 chronic hepatitis C virus (HCV) infection have been presented at the International Liver Congress 2014.

"With cure rates well in excess of 90% with as little as eight weeks of treatment for some patients, these data represent a significant advance in the race to develop a new, all-oral treatment for Hepatitis C," said Professor Markus Peck-Radosavljevic, Secretary-General of the European Association for the Study of the Liver and Associate Professor of Medicine, University of Vienna, Austria.

"The results of the ION studies demonstrated highly satisfactory cure rates with a fixed dose combination of sofosbuvir/ledipasvir among patients with genotype 1 HCV infection without the use of either injectable interferon, which causes miserable flu-like symptoms, or ribavirin, an antiviral pill associated with a variety of troublesome side effects, including anaemia and rash," Professor Peck-Radosavljevic continued. "As a result of this marked improvement in tolerability, many more people are likely to seek treatment with this ribavirin-free regimen, which involves just one pill once a day."

Across the three ION studies, 1,952 patients with genotype 1 HCV infection were randomised to receive LDV/SOF with or without RBV for eight, 12 or 24 weeks of therapy. Of these, 1,512 patients were treatment-naïve, 440 were treatment experienced and 224 had compensated cirrhosis.

Of the 1,952 patients randomised in ION-1, ION-2 and ION-3, 1,886 patients (96.6%) achieved the primary efficacy endpoint of SVR12. Of the 66 patients (3.4%) who failed to achieve SVR12, 38 patients (1.9%) experienced virological failure: 36 due to relapse and two patients due to on-treatment breakthrough (with documented non-compliance). 28 patients (1.4%) were lost to follow-up.

Fewer adverse events were observed in the RBV-free, fixed-dose combination arms compared to the RBV-containing arms in all the ION studies. Adverse events observed in those taking LDV/SOF were generally mild and included fatigue and headache. In the RBV-containing arms of the ION studies, the most common adverse events were fatigue, headache, nausea and insomnia. Anaemia, which is a common side effect associated with RBV, was reported in 0.5% of patients in the LDV/SOF arms versus 9.2% of patients in the RBV-containing arms. Less than 1% of patients in the studies discontinued treatment due to treatment-emergent adverse events.

Genotype 1 is the most common, but hardest to treat, strain of the hepatitis C virus. Sofosbuvir belongs to a class of directly acting anti-viral (DAA) drugs known as nucleotide analogue polymerase inhibitors, which are designed to block an enzyme the hepatitis C virus needs to copy itself. Ledipasvir belongs to a promising new class of DAA drugs that work by blocking the NS5A protein, which the hepatitis C virus also needs to replicate.

ION STUDY SUMMARIES

ION-2 STUDY[1]

- The ION-2 study evaluated 440 treatment-experienced genotype 1 HCV patients, including 88 with compensated cirrhosis, who had failed past therapy with regimens containing Peg-IFN (including Peg-IFN plus a protease inhibitor)
- Patients received LDV/SOF with or without RBV for 12 or 24 weeks
- After 12 weeks of therapy, SVR-12 was 96.4% and 93.6% for SOF+LDV+RBV and SOF+LDV
- After 24 weeks of therapy, SVR-12 was 99.1% and 99.1% for SOF+LDV+RBV and SOF+LDV
- One patient experienced on-treatment virological failure
- No patients discontinued treatment due to an adverse event
- Nine patients (2%) had treatment-emergent SAEs
- Haemoglobin