# European Association for the Study of the Liver
## Berlin, Germany, 30 March–3 April

# Alisporivir may offer hope for patients with untreated hepatitis C

A potential new oral treatment for hepatitis C, alisporivir (DEB025), cured almost 50% more previously untreated patients with the most common form of hepatitis C when the drug was added to a standard treatment regimen.

The phase II data, presented at the European Association for the Study of the Liver (EASL)'s 46th Annual Congress, were described as 'fantastic' by EASL vice-secretary Professor Mark Thursz, professor of hepatology at Imperial College, London.

Presenting the study results in the opening ceremony, Professor Robert Flisiak from the Medical University of Bialystok, Poland, told the congress: 'This novel agent has the potential to be an important component of future hepatitis C treatment.'

The ESSENTIAL study involved 300 previously untreated patients infected with genotype 1 hepatitis C virus. Of those treated with alisporivir plus standard of care (pegylated-interferon alfa 2a/ribavirin), 76% achieved superior viral cure compared to 55% of patients on standard care alone ($P$=0.008) 24 weeks after stopping treatment.

The study's principal investigator Professor Stefan Zeuzem from Goethe University Hospital in Frankfurt said: 'Hepatitis C is difficult to treat and current therapies are effective only in about half of patients with the most prevalent genotype. These results are exciting because a large majority of patients achieved sustained viral response with alisporivir.'

Alisporivir is the first in a new class of drugs called cyclophilin inhibitors. Unlike other compounds in development that target the hepatitis C virus directly, alispirovir targets host proteins that the hepatitis C virus uses for replication. A phase IIb trial looking at the potential of the agent in hepatitis C virus patients with genotypes 2 and 3 is underway. The host proteins are needed for replication in all types of hepatitis C virus infection so there is potential for the agent to have broad activity. There are six variations of hepatitis C virus.

A pivotal international phase III study is now underway to evaluate the efficacy and safety of alisporivir combined with standard care in previously untreated hepatitis C virus G1 patients. The phase II study found that serious adverse events occurred in 6.9% of patients treated with alispirovir and standard care compared to 5.5% of patients treated with standard care alone.

Professor Flisiak reported a higher serum level of bilirubin (32.9% *vs* 1.4% in the alisporivir-treated group compared to standard care alone) but this was transient and reversible and associated with the initial loading dose. Final data from the phase III ESSENTIAL-2 are expected in March 2013.

**Rhonda Siddall**

# New clinical guidelines for management of hepatitis C infection

EASL has published the first clinical practice guidelines for the management of hepatitis C infection, providing expert recommendations on the standard of care for the diagnosis, treatment and monitoring of patients with chronic hepatitis C virus infection and associated complications. The guidelines, launched at the meeting, will be updated to include new treatment options as they are approved by the European Medicines Agency. They can be accessed at www.easl.eu/_clinical-practice-guideline

The guidelines' key recommendations include:

- Liver biopsy remains the reference method
- Non-invasive diagnostic methods such as transient elastrography and biomarkers should be used to identify patients with mild fibrosis or cirrhosis
- Goal of therapy is to eradicate hepatitis C virus infection
- Sustained virological response is the only endpoint of therapy
- Standard of care for chronic hepatitis C patients should be a combination of pegylated interferon and ribavirin.

The guidelines were published against a raft of new data confirming that a range of protease inhibitors will help treat patients who have previously failed therapy for chronic hepatitis C treatment.


Clinical Practice Guidelines

EASL Clinical Practice Guidelines: Management of hepatitis C virus infection

EASL vice-secretary Professor Mark Thursz, professor of hepatology at Imperial College, London, said: 'Retreatment with standard of care regimens has achieved only 10–20% sustained virological response rates but the new trial data shows sustained virological response rates of 40–80% when protease inhibitors are used, even in the presence of IL-28b genotype.'

Two protease inhibitors, boceprevir and telaprevir, are expected to launch this year. The final results of phase III trials (Bacon et al, 2011; Poordad et al, 2011), published in the *New England Journal of Medicine* and announced at EASL, showed that re-treatment of hepatitis C patients with the addition of either protease inhibitor to standard of care regimen significantly improved sustained virological response rates in treatment-failure patients.

**Rhonda Siddall**

Bacon BR, Gordon SC, Lawitz E et al for the HCV RESPOND-2 Investigators (2011) Boceprevir for Previously Treated Chronic HCV Genotype 1 Infection. *N Engl J Med* **364**: 1207–17

Poordad F, McCone J Jr, Bacon BR et al for the SPRINT-2 Investigators (2011) Boceprevir for Untreated Chronic HCV Genotype 1 Infection. *N Engl J Med* **364**: 1195–206