ILC 2017: First large randomised placebo-controlled trial of fibrate therapy in patients with primary biliary cholangitis shows treatment is well tolerated

Study demonstrates that bezafibrate plus ursodeoxycholic acid (UDCA) is associated with an improvement of symptoms, liver function tests and surrogate markers of the disease

April 22, 2017, Amsterdam, The Netherlands: The results of the BEZURSO study, presented today, found that bezafibrate in combination with UDCA normalised prognostic markers of liver disease in patients with primary biliary cholangitis (PBC) with an inadequate response to UDCA. The study, presented at The International Liver Congress™ 2017 in Amsterdam, The Netherlands, showed that the bezafibrate and UDCA combination therapy was well tolerated, normalised prognostic biochemical parameters, improved fatigue and itching, and prevented progression of liver stiffness and ELF score, which are predictors of liver failure and mortality.1,2

PBC is a chronic autoimmune disease that can damage and eventually destroy bile ducts.3 It is an inflammatory condition which can lead to cirrhosis, liver failure and cancer.3 PBC affects mostly middle-aged women and may progress silently for years; over time, symptoms such as fatigue and itching (pruritus) emerge, often resulting in poor quality of life for patients.3 PBC is a disease that cannot be cured: there is no therapy that can stop its progression. A large proportion of patients respond to the administration of UDCA, which can significantly improve liver function tests, and slow the destruction of bile ducts as well as disease progression.4,5 However, more than 30% of patients do not respond adequately to UDCA treatment, and thus remain at high risk of disease progression which may require a liver transplant, as well as reduced survival rates.5 Additional treatments for these patients are urgently needed.4,5

“This study is the first large randomised trial of fibrates in patients with PBC who had responded inadequately to UDCA,” said Dr Christophe Corpechot, head of the Reference Center for Inflammatory Biliary Diseases, Paris, France, and lead author of the study. “The study provides evidence supporting the use of a combination of fibrates and UDCA in this population, with normalisation of liver function tests, improved symptoms and prevention of liver disease progression.”

The BEZURSO study (Bezafibrate in Combination with Ursodeoxycholic Acid in Primary Biliary Cirrhosis) was a randomised, double-blind, placebo-controlled trial of bezafibrate for the treatment of PBC in 100 patients with an incomplete response to UDCA.7 Patients with an inadequate biochemical response to UDCA, as defined by the Paris-2 criteria, were randomised to two years of either bezafibrate 400 mg/day or placebo, in combination with UDCA 13–15 mg/kg/day. Normalisation of liver function tests was the primary endpoint.
The primary endpoint was reached in 15 (30%) patients in the bezafibrate group compared with no patients in the placebo group (p<0.0001). Alkaline phosphatase normalisation occurred in 67% of patients in the bezafibrate group compared with 0% in the placebo group. Fatigue and itching were significantly reduced in the bezafibrate group, as well as surrogate markers of liver fibrosis (liver stiffness and ELF score). The rates of serious adverse events were similar in both groups. The rates of end-stage liver complications did not differ between the treatment groups (4% in both groups).

“This study could have an important impact on clinical practice, as it shows that patients with PBC who do not respond adequately to current treatment with UDCA, could obtain a notable benefit with additional bezafibrate therapy, a drug which is already used for the treatment of hypercholesterolaemia,” said Prof Marco Marzioni, Professor of Gastroenterology, Università Politecnica delle Marche – “Ospedali Riuniti” University Hospital of Ancona, Italy and EASL Governing Board Member.

Liver function tests
Liver function tests are a group of blood tests that provide information about the state of someone’s liver. These tests include normal serum levels of total bilirubin (a substance found in bile that is produced when the liver breaks down old red blood cells), alkaline phosphatase (an enzyme mostly made in the liver; abnormal levels indicate liver disease), transaminases (enzymes that are useful markers of liver injury), albumin (a protein made by the liver; decreased levels are observed in chronic liver disease) and prothrombin time at month 24 (measures how long it takes blood to clot; prothrombin is made by the liver and low levels indicates liver disease).

About The International Liver Congress™
This annual congress is the biggest event in the EASL calendar, attracting scientific and medical experts from around the world to learn about the latest in liver research. Attending specialists present, share, debate and conclude on the latest science and research in hepatology, working to enhance the treatment and management of liver disease in clinical practice. This year, the congress is expected to attract approximately 10,000 delegates from all corners of the globe. The International Liver Congress™ 2017 will take place from April 19 – 23, at the RAI Amsterdam, Amsterdam, The Netherlands.

About The European Association for the Study of the Liver (EASL) (www.easl.eu)
Since its foundation in 1966, this not-for-profit organisation has grown to over 4,000 members from all over the world, including many of the leading hepatologists in Europe and beyond. EASL is the leading liver association in Europe, having evolved into a major European Association with international influence, with an impressive track record in promoting research in liver disease, supporting wider education and promoting changes in European liver policy.

Contact
For more information, please contact the ILC Press Office at:
- Email: ILCpressoffice@ruderfinn.co.uk
- Telephone: +44 (0)7841 009 252
Onsite location reference
Session title: Late breaker session
Time, date and location of session: 16:00 – 18:00, Saturday 22 April, Hall 5
Presenter: Christophe Corpechot, France
Abstract: A 2-year multicenter, double-blind, randomized, placebo-controlled study of bezafibrate for the treatment of primary biliary cholangitis in patients with inadequate biochemical response to ursodeoxycholic acid therapy (BEZURSO) (LBO-01), 16:00 – 16:15

Author disclosures
Intercept Pharma, GlaxoSmithKline, AbbVie.

References