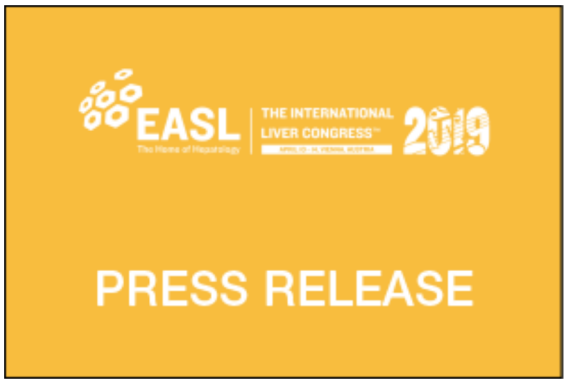
BULEVIRTIDE SHOWS PROMISE IN THE TREATMENT OF CHRONIC HEPATITIS B/D (HBV/HDV) COINFECTION

ILC 2019: First-in-class entry inhibitor bulevirtide (Myrcludex B) effective and well tolerated in combination with PEG-IFN-a in Phase 2b study involving individuals with chronic hepatitis B/D virus coinfection, producing high rates of viral suppression both on and off treatment with good tolerability



13 April 2019, Vienna, Austria

EASL (EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER)

A first-in-class treatment for chronic hepatitis B/D virus (HBV/HDV) coinfection has shown early promise, as the final results of a Phase 2b trial confirms high rates of viral suppression both on and off treatment, and good tolerability. When used in combination with peg-interferon-α 2a (PEG-IFN-α), above 50% of study participants who received bulevirtide (Myrcludex B) had undetectable HDV RNA after 48 weeks of treatment, which was sustained off-treatment in the majority of individuals. Undetectable levels of hepatitis B surface antigen (HBsAg) in some participants receiving the combination treatment also suggests a future role for bulevirtide in regimens targeted towards HBV cure.

HDV infection was first reported in humans in 1977, and is now thought to affect 15–20 million people in all age groups worldwide.[1] HDV infection can be an acute or chronic disease, but only occurs in people coinfected with HBV.[1] Chronic HDV infection is the most severe form of viral hepatitis infection and is often associated with the rapid development of cirrhosis and an increased risk of hepatocellular carcinoma.[1] Treatment options are currently very limited.[2]

Bulevirtide is a first-in-class agent that inhibits the entry of HDV into hepatocytes by blocking its binding to the sodium taurocholate cotransporting polypeptide (NTCP), thereby depriving HDV of key functions provided by HBV.[2,3] In the Phase 2b trial presented today at The International Liver Congress™ 2019 in Vienna, Austria, 60 patients with chronic HBV/HDV coinfection were randomized 1:1:1:1 into four

treatment groups: PEG-IFN-α 180 µg once weekly (qw) by subcutaneous (sc) injection (n=15), bulevirtide 2 mg once daily (qd) by sc injection + sc PEG-IFN-α qw (n=15), sc bulevirtide 5 mg qd + sc PEG-IFN-α qw (n=15) or sc bulevirtide 2 mg qd (n=15) – with all treatments administered for 48 weeks. The primary endpoint of the trial was undetectable serum HDV RNA at 72 weeks (i.e. 24 weeks after treatment completion).

As Professor Heiner Wedemeyer from the Essen University Hospital in Germany explained, over 48 weeks, PEG-IFN-α monotherapy resulted in a median HDV RNA log reduction of –1.30 and a normalization of alanine aminotransferase (ALT) levels in 4/15 patients (27%). The combination of bulevirtide and PEG-IFN-α resulted in a median HDV RNA log reduction of between –4.81 and –5.59 and a normalization of ALT levels in 11/30 patients (37%). Monotherapy with bulevirtide resulted in a median HDV RNA log reduction of –2.84 and a normalization of ALT levels in 10/15 patients (67%). HDV RNA was undetectable in 2/15 (13%) of patients who received PEG-IFN-α, 2/15 patients (13%) who received bulevirtide monotherapy, and 15/30 patients (50%) who received combination treatment.

At week 72, PEG-IFN-α monotherapy was associated with a median HDV RNA log reduction of –0.26 and a normalization of ALT levels in 1/15 patients (7%). The combination of bulevirtide and PEG-IFN-α was associated with a median HDV RNA log reduction of between –1.48 and –4.04 and a normalization of ALT levels in 12/30 patients (40%), while monotherapy with bulevirtide was associated with a median HDV RNA log reduction of –1.08 and a normalization of ALT levels in 3/15 patients (20%). HDV RNA was undetectable in 12/30 patients (40%), who received combination treatment. Remarkably, 4/15 patients (27%) treated with 2mg bulevirtide + PEG-IFN-α had undetectable HBsAg levels and 3/4 patients experienced HBsAg seroconversion.

Bulevirtide was well tolerated, with 155 drug-related adverse events (AEs) reported (mainly asymptomatic increase in total bile salts) by week 72. Most AEs (n=122) were mild in intensity and all resolved without sequelae. No serious bulevirtide-related AEs were reported.

'The results of this trial suggest that bulevirtide is a promising treatment for chronic HDV infection, and that the combination of bulevirtide and PEG-IFN-α has the potential to cure HBV/HDV coinfection in some patients,' said Prof. Wedemeyer.

###

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™ 2019 will take place from 10–14 April 2019 at the **Reed Messe Wien Congress and Exhibition Center, Vienna, Austria.**

About The European Association for the Study of the Liver (EASL)

Since its foundation in 1966, this not-for-profit organization 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, and 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: press2@easloffice.eu

- Telephone: +44 (0)1444 811099

Onsite location reference

Session title: General Session III and award ceremony II

Time, date and location of session: 10:00 – 12:00, 13/04/2019, Main Plenary

Presenter: Heiner Wedemeyer, Germany

Abstract: Final results of a multicenter, open-label phase 2 clinical trial (MYR203) to assess safety and efficacy of bulevirtide (Myrcludex B) in with PEG-interferon Alpha 2a in patients with chronic HBV/HDV co-infection (GS-13)

Author disclosures

Heiner Wedemeyer has received honoraria for consulting or speaking and/or research grants (last 5 years) from Abbott, AbbVie, BMS, Boehringer Ingelheim, Eiger, Gilead, JJ/Janssen-Cilag, Merck/Schering-Plough, Myr GmbH, Novartis, Roche, Roche Diagnostics, and Siemens

References

1. Koh C, et al. Pathogenesis of and new therapies for hepatitis D. 2019;156(2):461–76.e1.
2. Rizzetto M. Targeting hepatitis D. *Semin Liver Dis.* 2018;38(1):66–72.
3. Bogomolov P**x**, et al. Treatment of chronic hepatitis D with the entry inhibitor myrcludex B: First results of a phase Ib/IIa study. *J Hepatol.* 2016;65(3):490–8.

VIRAL HEPATITIS