Conclusions

- Long-term treatment with BLV monotherapy over 144 weeks remained safe and effective.
- Improvements in virologic and biochemical responses and liver stiffness, as well as low occurrence of liver-related outcomes, are supportive of the potential clinical benefits of long-term BLV monotherapy.

Plain Language Summary

- Patients with chronic hepatitis delta who received bulevirtide for 144 weeks achieved substantial reductions in their hepatitis delta virus RNA levels and had either improved or maintained key markers of liver health and function.

Introduction

- Hepatitis delta virus (HDV) infection affects between 10 and 20 million people worldwide and causes the most severe form of chronic viral hepatitis.
- Bulevirtide (BLV) is a first-in-class entry inhibitor approved in the EU, Great Britain, Switzerland, and the Russian Federation for the treatment of chronic hepatitis delta (CHD) and is recommended by the European Association for the Study of the Liver (EASL) guidelines for the treatment of CHD in patients with compensated liver disease.
- Previously published results demonstrated that BLV 2 mg or 10 mg monotherapy for 96 weeks led to HDV RNA reductions and alanine aminotransferase (ALT) improvements, and is generally safe.

Objective

- The objective of this interim analysis was to evaluate the long-term efficacy and safety of BLV 2 mg or 10 mg monotherapy through 144 weeks of therapy.

Methods

- MYR301 Study Design
  - The multi-center, open-label, randomized Phase 3 Study MYR301 (NCT03085271) was conducted at 16 sites across 4 countries (Germany, Italy, Russian Federation, and Sweden).
  - Primary endpoint: the proportion of patients achieving a combined response (undetectable HDV RNA or ≥2 log decline from baseline [BL] and ALT normalization) at week (W) 48.
  - HDV RNA was manually extracted and viral load was quantified using RoboGene 2.0.

- Treatment arms:
  - Arm A: BLV 2 mg; n = 50
  - Arm B: BLV 10 mg; n = 51
  - Arm C: 88% (44/50); withdrew consent, 5; physician decision, 1

Results

- Baseline Demographics and Disease Characteristics
  - See Table 1.

- Platelet Count, Liver Chemistries, and Other Efficacy Markers Over Time
  - See Table 2.

- Key Efficacy Over Time (by BLV Duration)
  - See Figure 1.

- Combined responses, ALT normalization, and virologic response rates increased through W96 and were maintained through W144; the response rates were similar between the BLV 2 mg and 10 mg arms.

- Rates of undetectable HDV RNA continually increased over 144 weeks for both the BLV 2 mg and 10 mg arms; rates were numerically higher for the BLV 10 mg arm.

- Among patients who achieved undetectable HDV RNA at any post-BL time points, those in the BLV 10 mg arm did so faster than in the BLV 2 mg arm.

- The mean (SD) number of weeks after starting BLV treatment to first reaching undetectable HDV RNA, as follows:
  - BLV 2 mg: 77 (45)
  - BLV 10 mg: 69 (41)

- Patient retention remained high through 144 weeks with no discontinuations related to study treatment; study completion rates are below:
  - Arm A: 89% (45/50); pregnancy, 1; death (plasma cell myeloma unrelated to BLV), 1
  - Arm B: 92% (45/50); withdraw consent, 3; pregnancy, 1
  - Arm C: 89% (44/50); withdraw consent, 3; physician decision, 1

- There were no drug discontinuations, serious AEs, or deaths attributed to BLV monotherapy and no reports of HDV reactivation (regardless of concomitant nucleos(t)ide analogue therapy) through 144 weeks of treatment.

- The safety profile was similar between the BLV 2 mg and 10 mg arms, except for injection-site reactions, which were more frequent in the BLV 10 mg arm (likely due to 2 daily BLV injections vs 1 daily injection with BLV 2 mg).

- Dose-dependent elevations in bilirubin and sodium remained asymptomatic and were not associated with any clinical sequelae throughout 144 weeks of treatment.