Integrated Efficacy Analysis of Bulevirtide 10 mg From Studies MYR204 and MYR301 at Weeks 48 and 96 Across Subgroups

WED-593

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Viral Hepatitis B and D: New Therapies, Unapproved Therapies or Strategies

Conclusions

- Overall, treatment with bulevirtide (BLV) 10 mg demonstrated antiviral activity across subgroups with diverse demographics and disease characteristics
- Reductions in hepatitis delta virus (HDV) RNA were observed across baseline strata at both week 48 and week 96; patients with lower baseline HDV RNA were more likely to achieve undetectable levels, while clinically meaningful declines, which increased over time, were seen regardless of baseline level
- These findings support the use of BLV for treatment of patients with HDV and compensated liver disease

Plain Language Summary

- Hepatitis delta virus causes the most severe form of viral hepatitis
- Bulevirtide is a treatment for chronic hepatitis delta virus infection in adults with liver disease
- This study evaluated the efficacy of bulevirtide 10 mg across subgroups of patients with different demographic and disease characteristics
- Overall, long-term treatment with bulevirtide was effective and similar across different subgroups

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Introduction

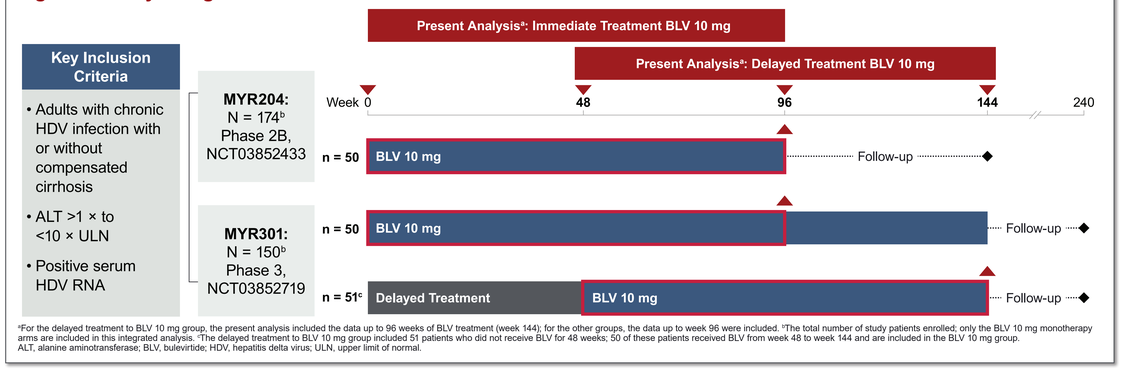
- Hepatitis delta virus (HDV) causes the most severe form of chronic viral hepatitis and is estimated to affect approximately 12 million people worldwide[1-3]
- HDV infection is associated with a more rapid progression to fibrosis and cirrhosis, earlier onset of hepatic complications, and a greater likelihood of liver transplantation compared with other forms of viral hepatitis[4,5]
- Bulevirtide (BLV), a first-in-class entry inhibitor of HDV, is approved in the United States, the European Economic Area, and several other countries for the treatment of patients with chronic hepatitis delta infection with compensated liver disease[6-8]
- Monotherapy with BLV 2 mg/day or 10 mg/day has been demonstrated to be effective and safe for up to 144 weeks of treatment[9-11]
- Additional data are needed to evaluate the efficacy of BLV 10 mg/day across diverse clinical and demographic patient subgroups

Objective

- To evaluate the efficacy of the BLV 10 mg dose across demographic and disease characteristic subgroups at weeks 48 and 96 in an integrated analysis of the MYR301 and MYR204 studies

Methods

Figure 1. Study Design



[a]For the delayed treatment to BLV 10 mg group, the present analysis included the data up to 96 weeks of BLV treatment (week 144); for the other groups, the data up to week 96 were included. [b]The total number of study patients enrolled; only the BLV 10 mg monotherapy arms are included in this integrated analysis. [c]The delayed treatment to BLV 10 mg group included 51 patients who did not receive BLV for 48 weeks; 50 of these patients received BLV from week 48 to week 144 and are included in the BLV 10 mg group.
ALT, alanine aminotransferase; BLV, bulevirtide; HDV, hepatitis delta virus; ULN, upper limit of normal.

- This integrated analysis included patients with HDV who received BLV 10 mg (approved as 8.5 mg delivered dose in the United States) once daily for up to 96 weeks in the MYR204 (Phase 2; NCT03852433) and MYR301 (Phase 3; NCT03852719) studies (**Figure 1**)
- Efficacy was measured by virologic response (undetectable HDV RNA[a] or ≥2 $\log_{10}$ IU/mL decline from baseline), biochemical response (alanine aminotransferase [ALT] normalisation[b]), combined response[c] (virologic response + biochemical response), and undetectable HDV RNA rates and liver stiffness change from baseline[d] at weeks 48 and 96
- Efficacy was measured across the following subgroups of patients:
  - Age (years; <45, ≥45), sex (male, female), race (White, other), cirrhosis (yes, no), concomitant hepatitis B virus treatment (yes, no), baseline ALT (≤1.5 × upper limit of normal [ULN], >1.5 × ULN), and baseline HDV RNA level (<median, ≥median)

[a]HDV RNA levels were determined by reverse transcription–quantitative polymerase chain reaction using RoboGene HDV RNA Quantification Kit 2.0. Undetectable HDV RNA was defined as less than the lower limit of quantitation (50 IU/mL) with target not detected. [b]ALT normalisation was defined as ≤31 U/L for females and ≤41 U/L for males (Russian sites) and ≤34 U/L for females and ≤49 U/L for males (all other sites). [c]For combined response, virologic response, undetectable HDV RNA, and ALT normalisation, the 95% CI was based on the Clopper-Pearson exact method, and the missing-equals-failure approach was used for missing values. [d]For liver stiffness change from baseline, the missing values remained missing.

Results

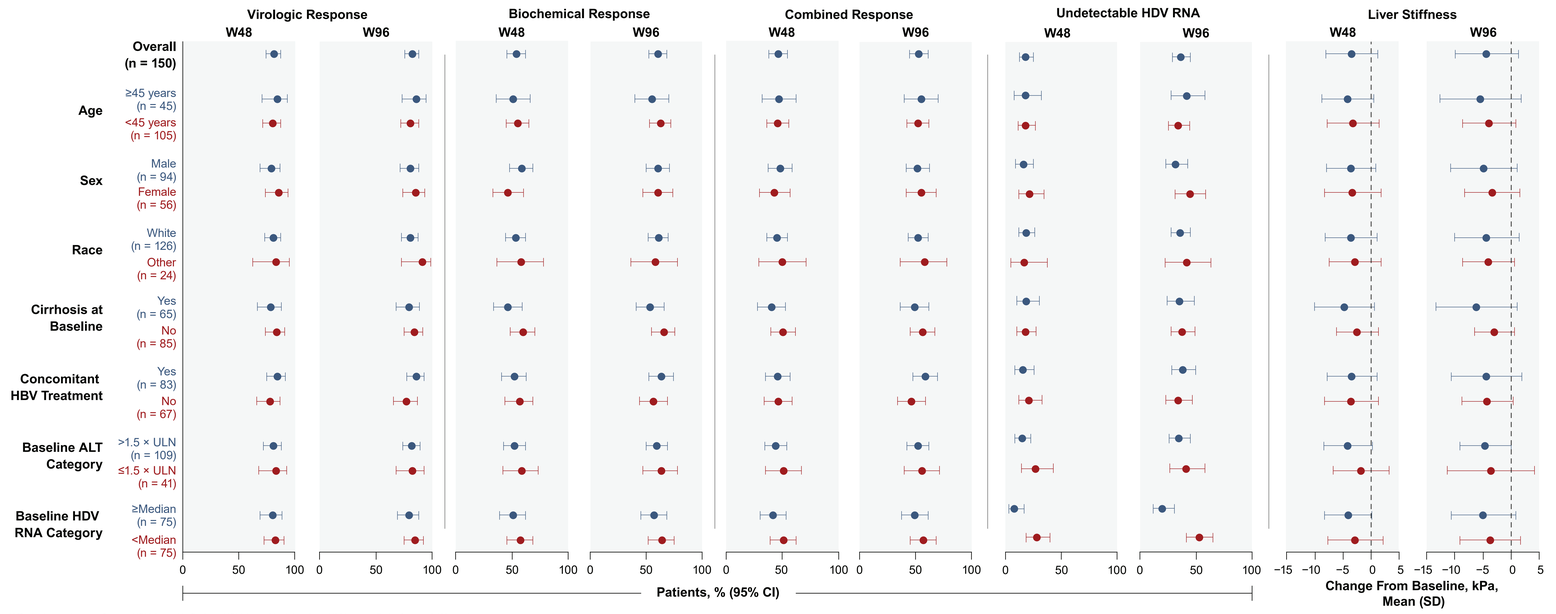
Table 1. Demographics and Disease Characteristics at Baseline

	Overall BLV 10 mg n = 150	Cirrhosis at Baseline	
		Yes (n = 65)	No (n = 85)
Age, years, mean (range)	41 (18–62)	42 (28–62)	41 (18–62)
Male sex, n (%)	94 (63)	42 (65)	52 (61)
Race, n (%)			
Asian	21 (14)	7 (11)	14 (16)
Black	3 (2)	1 (2)	2 (2)
White	126 (84)	57 (88)	69 (81)
BMI, kg/m², mean (SD)	25.5 (3.83)	25.0 (4.16)	25.9 (3.53)
BMI ≥30 kg/m², n (%)	18 (12)	8 (12)	10 (12)
Cirrhosis present, n (%)	65 (43)	65 (100)	NA
HDV genotype 1, n (%)	147 (98)	63 (97)	84 (99)
HDV RNA, log10 IU/mL, median (Q1, Q3)	5.50 (4.37, 6.21)	5.46 (4.15, 6.21)	5.56 (4.43, 6.19)
ALT, U/L, mean (SD)	108 (84.8)	103 (74.1)	111 (92.4)
ALT >1.5 × ULN, n (%)	109 (73)	46 (71)	63 (74)
HBsAg, log10 IU/mL, median (Q1, Q3)	3.81 (3.52, 4.00)	3.72 (3.40, 4.00)	3.89 (3.61, 4.06)
Concomitant HBV therapy, n (%)	83 (55)	43 (66)	40 (47)
Prior IFN therapy, n (%)	79 (53)	34 (52)	45 (53)
Liver stiffness, kPa, mean (SD)	14.5 (9.53)	20.3 (11.04)	10.1 (4.82)

ALT, alanine aminotransferase; BLV, bulevirtide; BMI, body mass index; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis delta virus; IFN, interferon; NA, not applicable; Q, quartile; ULN, upper limit of normal.

- Demographics and disease characteristics at baseline are shown in **Table 1**

Figure 2. Overview of Efficacy Results at Weeks 48 and 96 Overall and Across Subgroups



ALT, alanine aminotransferase; HBV, hepatitis B virus; HDV, hepatitis delta virus; ULN, upper limit of normal; W, week.

- Overall, treatment with BLV 10 mg monotherapy for up to 96 weeks maintained or improved the efficacy outcomes observed at week 48, and efficacy was consistent across subgroups (**Figure 2**)
- Undetectable HDV RNA rates (% of patients [95% CI]) were higher among patients with baseline viral loads less than median (53% [41%–65%] vs 20% [12%–31%]) at week 96