Integrated Efficacy Analysis of Bulevirtide 10 mg Monotherapy in Patients With Chronic Hepatitis Delta

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Conclusions

- Long-term treatment with bulevirtide (BLV) 10 mg monotherapy was associated with higher rates of virologic, biochemical, and combined response, as well as greater declines in liver stiffness, compared with control at week 48
  - These rates improved or were maintained through week 96 with continued BLV treatment
- Reductions in alanine aminotransferase (ALT) levels and liver stiffness were observed at week 96, regardless of virologic response or ALT normalization status
- These findings support the efficacy of long-term BLV 10 mg treatment in people with hepatitis delta virus and compensated liver disease

Plain Language Summary

- Hepatitis delta virus is a serious liver infection that causes more liver damage than other hepatitis viruses
- Bulevirtide is a treatment for chronic hepatitis delta virus infection in adults with working livers
- This study evaluated the effectiveness of bulevirtide 10 mg over 96 weeks of treatment
- Overall, long-term treatment with bulevirtide was effective in most patients

References: 1. Alfaiate D, et al. *J Hepatol.* 2020;73(3):533-9. **2.** Rizzetto M, et al. *J Hepatol.* 2021;74(5):1200-11. **3.** Stockdale AJ, et al. *J Hepatol.* 2020;73(3):523-32. **4.** Da BL, et al. *Gastroenterol Rep.* 2019;7(4):231-45. **5.** Aseelah T, et al. *N Engl J Med.* 2023;389(1):58-70. **6.** Hepcludex (bulevirtide). European Medicines Agency. Gilead Sciences, Inc.; 2023. **7.** Hepcludex (bulevirtide acetate). Australian Register of Therapeutic Goods. Gilead Sciences, Inc.; 2024. **8.** Hepcludex. Product monograph. Gilead Sciences Canada, Inc.; 2025. **9.** Hepcludex. Full prescribing information. US Food and Drug Administration. Gilead Sciences, Inc.; 2026. **10.** Lampertico P, et al. *J Hepatol.* 2022;77(5):1422-30. **11.** Dietz-Fricke C, et al. *JHEP Rep.* 2023;5(4):100686. **12.** Wedemeyer H, et al. *J Hepatol.* 2024;81(4):621-9. **13.** Wedemeyer H, et al. *J Hepatol.* 2026;85(3):493-503.

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Introduction

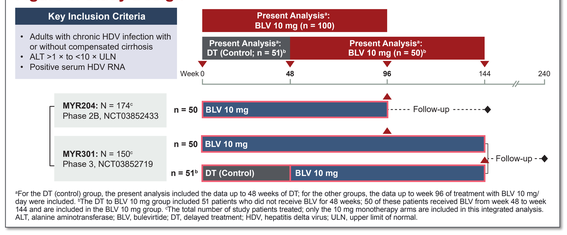
- Hepatitis delta virus (HDV) causes the most severe form of chronic viral hepatitis[1] and is estimated to affect approximately 12 million people worldwide[2-3]
- Infection with HDV is associated with more rapid progression to fibrosis and cirrhosis, earlier onset of hepatic complications, and a greater likelihood of liver transplantation compared with other forms of viral hepatitis[4-5]
- Bulevirtide (BLV), an entry inhibitor of HDV, is approved in the United States, the European Economic Area, and other regions for the treatment of chronic hepatitis delta in patients with compensated liver disease[6-9]
- Long-term BLV monotherapy has been demonstrated to be safe and well tolerated in clinical trials and real-world studies[10-13]

Objective

- To further evaluate the efficacy of BLV 10 mg monotherapy by assessing virologic parameters, alanine aminotransferase (ALT) normalization, and liver stiffness measurement (LSM) up to week 96 in an integrated analysis of the MYR301 and MYR204 studies

Methods

Figure 1. Study Design



[a]For the DT (control) group, the present analysis included the data up to 48 weeks of DT; for the other groups, the data up to week 96 of treatment with BLV 10 mg/day were included. [b]The DT 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. [c]The total number of study patients treated; only the 10 mg monotherapy arms are included in this integrated analysis.
ALT, alanine aminotransferase; BLV, bulevirtide; DT, delayed treatment; HDV, hepatitis delta virus; ULN, upper limit of normal.

- Data were included from 2 multicenter, open-label, randomized studies: the Phase 2 MYR204 study (NCT03852433) and the Phase 3 MYR301 study (NCT03852719; **Figure 1**)
- This integrated analysis included data from patients with HDV who received BLV 10 mg/day (approved as 8.5 mg delivered dose in the United States)[9] for 96 weeks or had 48 weeks of delayed treatment (control group; MYR301 only)
- Analyses included efficacy assessments of the following:
  - **Combined response (CR):** undetectable HDV RNA[a] or ≥2 $\log_{10}$ IU/mL decline from baseline and ALT normalization[b]
  - **Virologic response (VR):** undetectable HDV RNA[a] or ≥2 $\log_{10}$ IU/mL decline from baseline
  - **ALT normalization[b]**
  - **LSM change from baseline**
  - **ALT change from baseline**
  - **HDV RNA change from baseline**
  - **Undetectable HDV RNA[a]**
- Subgroup analyses by ALT normalization status and suboptimal VR at week 96 included patients with observed data at this time point
  - Partial VR (PR) was defined as ≥1 to <2 $\log_{10}$ IU/mL decline in HDV RNA from baseline, and nonresponse (NR) was defined as <1 $\log_{10}$ IU/mL decline from baseline
    - Patients with undetectable HDV RNA were not considered to have PR or NR
- HDV RNA levels were measured by reverse transcription–quantitative polymerase chain reaction using the RoboGene 2.0 (lower limit of quantitation [LLOQ], 50 IU/mL; limit of detection [LOD], 6 IU/mL)
- Liver stiffness was measured by transient elastography (FibroScan®)

[a]Undetectable HDV RNA was defined as <LLOQ (target not detected); LLOQ: 50 IU/mL, LOD: 6 IU/mL. [b]ALT upper limit of normal/normalization: defined at Russian sites as ≤31 U/L for females and ≤41 U/L for males and at all other sites as ≤34 U/L for females and ≤49 U/L for males.

Results

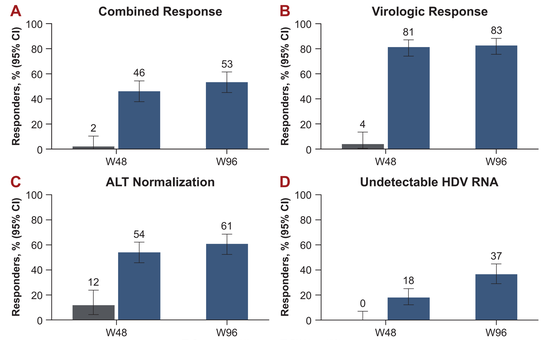
Table 1. Demographics and Baseline Characteristics

	BLV n = 150	Control n = 51
Age, years, mean (SD)	41 (8.2)	41 (7.5)
Male sex, n (%)	94 (63)	26 (51)
Race, n (%)		
White	126 (84)	40 (78)
Asian	21 (14)	11 (22)
Black	3 (2)	0
Cirrhosis present, n (%)	65 (43)	24 (47)
LSM, kPa, mean (SD)	14.5 (9.53)	15.3 (8.95)
HDV RNA, $\log_{10}$ IU/mL, mean (SD)	5.2 (1.40)	5.1 (1.36)
HDV genotype 1, n (%)	147 (98)	51 (100)
HBsAg, $\log_{10}$ IU/mL, mean (SD)	3.7 (0.61)	3.7 (0.47)
HBV DNA, $\log_{10}$ IU/mL, mean (SD)	1.2 (1.38)	0.9 (0.99)
ALT, U/L, mean (SD)	108 (84.8)	102 (61.9)
ALT category, n (%)		
>ULN to ≤1.5 × ULN	27 (18)	8 (16)
>1.5 × ULN	109 (73)	42 (82)
Concomitant HBV NA treatment,[a] n (%)	83 (55)	32 (63)
Prior IFN therapy, n (%)	79 (53)	29 (57)

[a]Concomitant NA treatment included concomitant medications with preferred names containing tenofovir, tenofovir alafenamide, tenofovir disoproxil fumarate, tenofovir disoproxil, entecavir, adefovir, lamivudine, telbivudine, or adefovir dipivoxil.
ALT, alanine aminotransferase; BLV, bulevirtide; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis delta virus; IFN, interferon; LSM, liver stiffness measurement; NA, nucleos(t)ide analogue; ULN, upper limit of normal.

- Overall, 150 patients receiving BLV and 51 control patients were included (**Table 1**)
- Nearly half the patients had cirrhosis at baseline; baseline demographics and disease characteristics were similar between treatment groups
- Most patients completed the week 96 visit (BLV, n = 143 [95%])

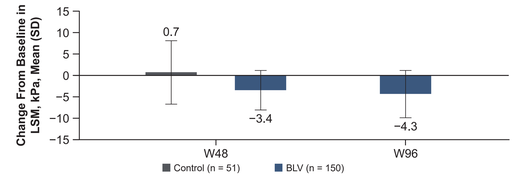
Figure 2. Proportion With (A) Combined Response, (B) Virologic Response, (C) ALT Normalization, and (D) Undetectable HDV RNA With BLV vs Control



For missing values, the missing-equals-failure approach was used. The 95% CIs were calculated based on the Clopper-Pearson exact method.
ALT, alanine aminotransferase; BLV, bulevirtide; HDV, hepatitis delta virus; W, week.

- Overall, rates of CR, VR, ALT normalization, and undetectable HDV RNA were higher than in the control group at week 48 and were increased or maintained through week 96 in patients treated with BLV (**Figure 2**)
- Patients receiving BLV had higher mean (SD) decreases in HDV RNA at week 48 compared with patients in the control group (−3.3 [1.36] vs −0.1 [1.05] $\log_{10}$ IU/mL), and these reductions persisted through week 96 (−3.8 [1.54] $\log_{10}$ IU/mL)

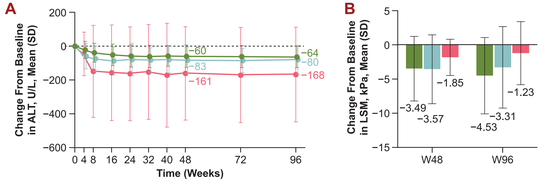
Figure 3. Mean Change From Baseline in LSM



Values are based on the number of patients with data available at each visit.
BLV, bulevirtide; LSM, liver stiffness measurement; W, week.

- The mean reduction from baseline in LSM was greater at week 48 in patients treated with BLV compared with the control group, with further reductions through week 96 in patients treated with BLV (**Figure 3**)

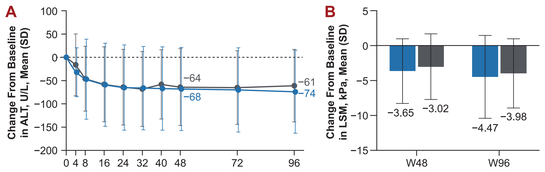
Figure 4. Mean Change From Baseline in (A) ALT Levels and (B) LSM With BLV by Virologic Response at Week 96



Values are based on the number of patients with data available at each visit. VR is defined as having undetectable HDV RNA and/or ≥2 log10 IU/mL decline from baseline; PR is defined as having ≥1 $\log_{10}$ IU/mL but <2 $\log_{10}$ IU/mL HDV RNA decline from baseline but not undetectable; NR is defined as having <1 $\log_{10}$ IU/mL HDV RNA decline from baseline but not undetectable. Mean (SD) baseline ALT levels for the VR, PR, and NR groups were 103 (66.6) U/L, 128 (75.6) U/L, and 216 (267.4) U/L, respectively. Mean (SD) baseline LSM values for the VR, PR, and NR groups were 14.6 (9.84) kPa, 14.3 (10.89) kPa, and 12.7 (2.08) kPa, respectively.
ALT, alanine aminotransferase; BLV, bulevirtide; HDV, hepatitis delta virus; LSM, liver stiffness measurement; NR, nonresponse; PR, partial response; VR, virologic response; W, week.

- Patients receiving BLV with and without VR at week 96 had improvements from baseline through week 96 in ALT levels and LSM (**Figure 4**)

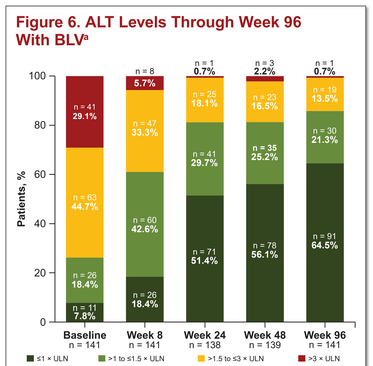
Figure 5. Mean Change From Baseline in (A) ALT Levels and (B) LSM With BLV by ALT Normalization Status at Week 96



Values are based on the number of patients with data available at each visit. Mean (SD) baseline ALT levels for the ALT normalization and no ALT normalization groups were 102 (88.3) U/L and 123 (80.9) U/L, respectively. Mean (SD) baseline LSM values for the ALT normalization and no ALT normalization groups were 13.8 (9.80) kPa and 15.7 (9.47) kPa, respectively.
ALT, alanine aminotransferase; BLV, bulevirtide; LSM, liver stiffness measurement; W, week.

- Patients without ALT normalization by week 96 had reductions in ALT levels and LSM similar to those patients with ALT normalization (**Figure 5**)

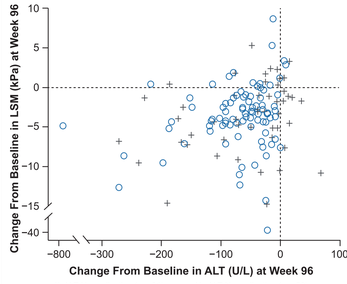
Figure 6. ALT Levels Through Week 96 With BLV[a]



Percentages are based on the patients with available values at each visit.
[a]Excludes 9 patients without available HDV RNA values at week 96.
ALT, alanine aminotransferase; BLV, bulevirtide; HDV, hepatitis delta virus; ULN, upper limit of normal.

- ALT improvement occurred as early as week 8 after treatment initiation and was maintained through week 96 (**Figure 6**)
- Of patients without ALT normalization at week 96, 30/50 (60%) had ALT ≤1.5 × the upper limit of normal (ULN), and only 1 patient had ALT >3 × ULN

Figure 7. Change From Baseline at Week 96 in LSM vs ALT Levels by Individual Patient and ALT Normalization Status at Week 96



Both the horizontal and vertical axes contain breaks to optimize data visualization.
ALT ULN/normalization: defined at Russian sites as ≤31 U/L for females and ≤41 U/L for males and at all other sites as ≤34 U/L for females and ≤49 U/L for males.
ALT, alanine aminotransferase; LSM, liver stiffness measurement; ULN, upper limit of normal.

- Most patients, including those who did not achieve ALT normalization, had improvements in ALT levels and LSM at week 96 (**Figure 7**)