Impact of Bulevirtide Treatment on Patient-Reported Outcomes Among Patients With Hepatitis Delta in Europe

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Viral Hepatitis B and D: Current Therapies

FRI-605

Conclusions

- Patients with chronic hepatitis delta virus (HDV) infection who received bulevirtide (BLV) therapy reported better disease-specific health-related quality of life (HRQoL) outcomes than treatment-naïve patients
  - Patients treated with BLV had significantly higher odds of overall improvement in disease severity compared with treatment-naïve patients
- Generic and symptom-specific HRQoL measures showed no significant differences between BLV-treated and treatment-naïve patients
- Disease-specific HRQoL measures should be administered to determine the health burden caused by HDV infection, as generic and symptom-specific measures may not be sufficiently sensitive

Plain Language Summary

- Chronic hepatitis delta is a liver disease caused by infection with the hepatitis delta virus that results in negative effects on health-related quality of life
- A previous clinical study showed that patients who received the antiviral drug bulevirtide reported improvements in their health-related quality of life
- In a real-world setting, patients with hepatitis delta virus infection who were treated with bulevirtide reported significant improvements in health-related quality of life compared with patients who did not receive bulevirtide, as assessed by questionnaires that measured impacts specific to liver disease
- Patients treated with bulevirtide were more likely to experience physician-reported improvement in disease severity compared with patients who had not received bulevirtide

References: **1.** Miao Z, et al. *J Infect Dis*. 2020;221(10):1677-87. **2.** Buti M, et al. *JHEP Rep*. 2021;3(3):100280. **3.** Hepcludex (bulevirtide). European Medicines Agency. Gilead Sciences, Inc.; 2023. **4.** Hepcludex (bulevirtide acetate). Australian Register of Therapeutic Goods. Gilead Sciences, Inc.; 2024. **5.** Hepcludex. Product monograph. Gilead Sciences Canada, Inc.; 2025. **6.** Dietz-Fricke C, et al. *JHEP Rep*. 2023;5(4):100686. **7.** Wedemeyer H, et al. *J Hepatol*. 2024;81(4):621-9. **8.** Wedemeyer H, et al. Presentation at the European Association for the Study of the Liver; May 7–10, 2025; Amsterdam, the Netherlands. Presentation LBO-004. **9.** Buti M, et al. *J Hepatol*. 2025;82(1):28-36. **10.** Anderson P, et al. *Curr Med Res Opin*. 2008;24(11):3063-72. **11.** Anderson P, et al. *Curr Med Res Opin*. 2023;39(12):1707-15. **12.** Babineaux SM, et al. *BMJ Open*. 2016;6(8):e010352. **13.** Higgins V, et al. *Diabetes Metab Syndr Obes*. 2016;9:371-80.

Acknowledgements: This study was sponsored by Gilead Sciences, Inc. Medical writing and editorial support were provided by Stephanie Biedka, PhD, of Red Nucleus, and funded by Gilead Sciences, Inc. The analysis described here used data from the Adelphi Real World Disease Specific Programme™, which is a wholly owned Adelphi Real World product.

Disclosures: Conflict of interest disclosures may be viewed using the QR code at the top right.

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Introduction

- Infection with hepatitis delta virus (HDV), a defective RNA virus that requires the presence of hepatitis B virus for propagation, leads to the most severe form of viral hepatitis[1]
- Chronic HDV infection is associated with less favourable clinical outcomes and worse health-related quality of life (HRQoL) compared with chronic hepatitis B alone[1,2]
- 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[3-5]
- BLV has been shown to be safe and effective in both clinical trial and real-world settings[6-8]
- When used as a monotherapy, BLV improved HRQoL outcomes among patients with HDV in a randomised controlled trial[9]
- Evidence on the effect of BLV on HRQoL in a real-world setting is limited

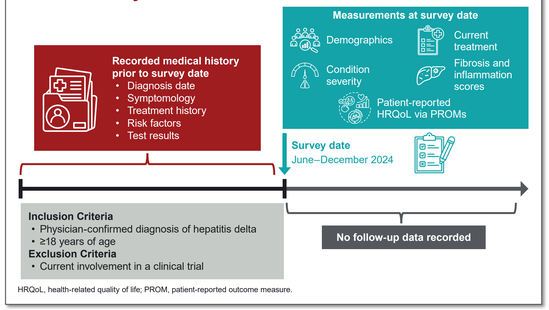
Objective

- To describe the HRQoL outcomes of patients with HDV infection in a real-world setting who received BLV or were treatment naïve

Methods

- Data were drawn from the Adelphi Real World Hepatitis Disease Specific Programme, a cross-sectional survey with retrospective data collection of physicians and their patients with HDV infection from June 2024 to December 2024 in France, Germany, Italy, Spain, and the UK[10-13] (**Figure 1**)
- Physicians (primary care, infectious disease specialists, and hepatologists) provided data on up to 4 consecutively consulting patients with HDV infection seen during routine care, including 2 patients who were prescribed BLV and 2 regardless of treatment status
  - Patients in the BLV group were prescribed BLV at the survey date or as their most recent treatment
  - Treatment-naïve patients were not prescribed treatment at the survey date or were prescribed treatment other than BLV (ie, entecavir, tenofovir, lamivudine, adefovir, telbivudine, peginterferon, or interferon)
- At the time of consultation, patients were invited to complete a voluntary patient self-completion survey, which included the following patient-reported outcome measures (PROMs):
  - Hepatitis B Quality of Life (HBQoL) questionnaire, a disease-specific measure of quality of life
  - EuroQol 5-Dimension visual analogue scale (EQ-5D VAS) and EQ-5D 5-Level (EQ-5D-5L), generic measures of quality of life
  - Work Productivity and Activity Impairment (WPAI) questionnaire, a generic measure of quality of life
  - Fatigue Severity Scale (FSS), a symptom-specific measure of quality of life
- Descriptive analyses focused on physician-reported patient demographics and the impact on HRQoL via PROMs
  - Missing data were not included when calculating percentages, and missing values were not imputed
- The effect of BLV was assessed using Mann-Whitney U tests, t-tests, unadjusted ordinal logistic regression, and inverse probability weighted regression adjustment (IPWRA)
  - Covariates for IPWRA included gender, birth or previous/current residence in a high-risk hepatitis B region, time since hepatitis B diagnosis, and severity of symptoms at diagnosis

Figure 1. Cross-Sectional Analysis of Linked Physician and Patient Survey Data



HRQoL, health-related quality of life; PROM, patient-reported outcome measure.

Results

Table 1. Patients and Physicians per Country

Country, n (%)	Patients n = 553	Physicians n = 164
France	120 (22)	36 (22)
Germany	135 (24)	40 (24)
Italy	144 (26)	41 (25)
Spain	71 (13)	32 (20)
UK	83 (15)	15 (9)

- Overall, 164 physicians reported data on 553 patients (**Table 1**)

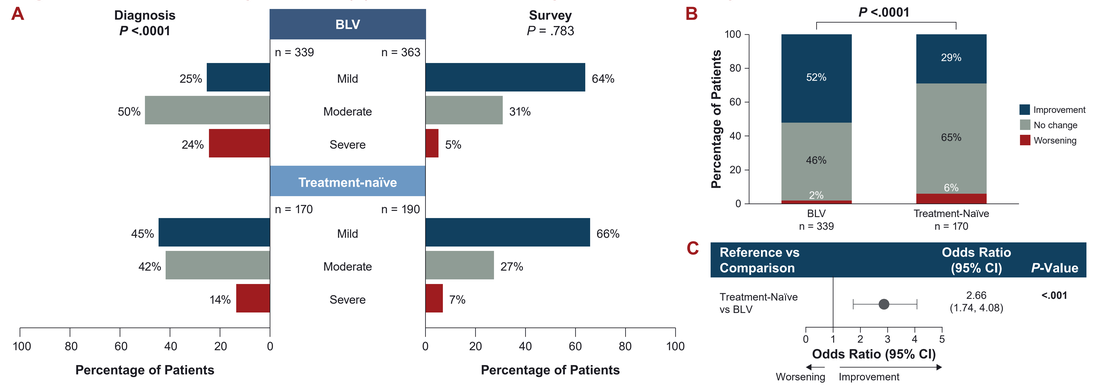
Table 2. Physician-Reported Patient Demographics

Patient Characteristics	BLV n = 363	Treatment-Naïve n = 190
Age, y, median (Q1, Q3)	41 (33, 51)	45 (36, 56)
Sex, n (%)	**n = 362**	**n = 186**
Female	105 (29)	64 (34)
Male	257 (71)	122 (66)
Race,[a] n (%)	**n = 262**	**n = 171**
White	191 (73)	118 (69)
Black African or Caribbean	28 (11)	26 (15)
Other[b]	43 (16)	27 (16)
Most recent ALT measurement	**n = 250**	**n = 133**
ALT, U/L, median (Q1, Q3)	60 (37, 126)	49 (33, 83)
Metavir liver inflammation score, n (%)	**n = 228**	**n = 78**
A1 (minimal activity)	87 (38)	33 (42)
A2 (moderate activity)	107 (47)	35 (45)
A3 (severe activity)	34 (15)	10 (13)
Liver fibrosis score, n (%)	**n = 336**	**n = 157**
F0 (absence of fibrosis)	45 (13)	32 (20)
F1 (portal fibrosis with no septa)	80 (24)	37 (24)
F2 (portal fibrosis with infrequent septa)	124 (37)	40 (25)
F3 (numerous septa but no cirrhosis)	48 (14)	23 (15)
F4 (compensated or decompensated cirrhosis)	39 (12)	25 (16)

[a]Respondents could select multiple race categories; physician-reported patient race was not collected in France. [b]Other includes East or Southeast Asian, South Asian (Indian subcontinent), Middle Eastern or North African, and other.
ALT, alanine aminotransferase; BLV, bulevirtide; Q, quartile; y, year.

- Of the 553 patients, 363 (66%) received BLV and 190 (34%) were treatment naïve (**Table 2**)
- Most patients were White (71%) and male (69%)

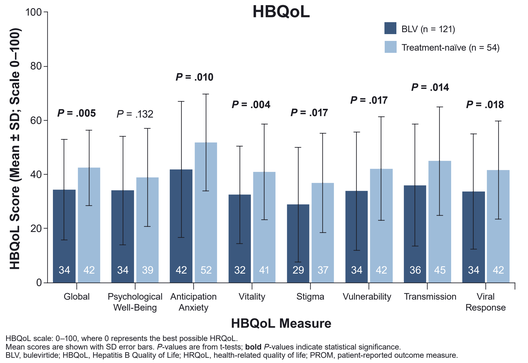
Figure 2. (A) Physician-Reported Disease Severity at Diagnosis and Survey Dates, (B) Change in Disease Severity From the Diagnosis Date to the Survey Date, and (C) Effect of BLV Therapy on Disease Severity



Disease severity considered patient fibrosis and cirrhosis status and was reported as mild, moderate, or severe.
The *P*-values are from Mann-Whitney U tests (**Figure 2A** and **Figure 2B**) and ordinal logistic regression (**Figure 2C**); **bold** *P*-values indicate statistical significance. In **Figure 2A**, the *P*-values assess the difference in disease severity between patients receiving BLV and treatment-naïve patients at the diagnosis date and at the survey date.
BLV, bulevirtide.

- A significant difference in disease severity at diagnosis was observed between patients receiving BLV and treatment-naïve patients (**Figure 2A**)
- There was a significant difference in the change in disease severity from diagnosis to the survey date between the groups by both Mann-Whitney U test (**Figure 2B**) and IPWRA when comparing improvement vs no improvement (average treatment effect [95% CI], 0.30 [0.16, 0.45]; *P* <.0001), with BLV treatment corresponding to a 30-percentage-point increase in the probability of improvement
- Patients receiving BLV had 2.66-fold (95% CI, 1.74, 4.08; *P* <.001) higher odds of being classified in a less severe disease category compared with treatment-naïve patients (**Figure 2C**)

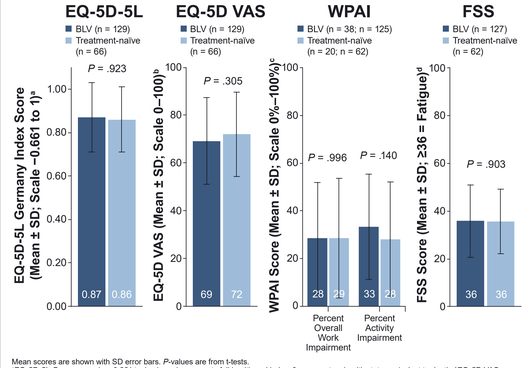
Figure 3. Disease-Specific PROMs



HBQoL scale: 0–100, where 0 represents the best possible HRQoL.
Mean scores are shown with SD error bars. *P*-values are from t-tests; **bold** *P*-values indicate statistical significance.
BLV, bulevirtide; HBQoL, Hepatitis B Quality of Life; HRQoL, health-related quality of life; PROM, patient-reported outcome measure.

- Patients who received BLV therapy reported significantly improved HBQoL scores across most HBQoL dimensions compared with treatment-naïve patients (**Figure 3**)
  - HBQoL Global scores were significantly improved among treated patients by both t-test (*P* = .005) and IPWRA (average treatment effect [95% CI], −9.74 [−15.28, −4.20]; *P* <.001) analyses

Figure 4. Generic and Symptom-Specific PROMs



Mean scores are shown with SD error bars. *P*-values are from t-tests.
[a]EQ-5D-5L Germany scale: −0.661 to 1, where 1 represents full health and below 0 represents a health state equivalent to death. [b]EQ-5D VAS scale: 0–100, where 100 represents the best possible HRQoL. [c]WPAI scale: 0%–100%, where 100% indicates severe impairment. [d]FSS scores ≥36 indicate fatigue.
BLV, bulevirtide; EQ-5D-5L, EuroQol 5-Dimension 5-Level; EQ-5D VAS, EuroQol 5-Dimension visual analogue scale; FSS, Fatigue Severity Scale; HRQoL, health related quality of life; PROM, patient-reported outcome measure; WPAI, Work Productivity and Activity Impairment.

- There were no significant differences observed between BLV-treated and treatment-naïve patients in generic and symptom-specific PROMs (**Figure 4**)

Limitations

- Underlying disease burden may vary between patients prescribed BLV and those who are treatment naïve
- The duration of BLV therapy may vary among patients prescribed BLV
- Physicians retrospectively captured patient information, introducing the potential for recall bias
- All physicians and patients were recruited from 5 European countries, and only patients who were actively consulting with their physicians were included; as such, results may not be generalisable to all patients with chronic hepatitis delta
- Data on BLV use in Spain were not collected due to a lack of reimbursement at the time of data collection