Patient-Reported Outcomes Measuring an Individual's Overall Self-Rated Health After Long-Term Treatment With Bulevirtide 2 mg for Chronic Hepatitis Delta in the Phase 3 MYR301 Trial

WED-029

MYR301

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Conclusions

- Patients with chronic hepatitis delta (CHD) treated with bulevirtide (BLV) 2 mg reported improvements in their perceived health state at 144 weeks of treatment compared with baseline
- These improvements were greater than the perceived health state reported at 48 and 96 weeks of treatment, thereby demonstrating the long-term benefits of BLV monotherapy

Plain Language Summary

- Bulevirtide is a safe and effective treatment for chronic hepatitis delta that lowers the amount of virus in the blood and reduces liver disease–related activity
- In this study, patients' perceived health state was improved at 144 weeks of bulevirtide 2 mg treatment compared with their perceived health state before treatment, or at 48 or 96 weeks of treatment
- The improvements in patients' perceived health state at 144 weeks of bulevirtide 2 mg treatment occurred regardless of whether the patients had cirrhosis

References: **1.** Lampertico P, et al. *J Hepatol.* 2022;77(5):1422-30. **2.** Degasperi E, et al. *J Hepatol.* Accepted manuscript. 2025. doi:10.1016/j.jhep.2024.12.044. **3.** Hepcludex. Summary of product characteristics. European Medicines Agency. Gilead Sciences, Inc.; 2023. **4.** Wedemeyer H, et al. *N Engl J Med.* 2023;389(1):22-32. **5.** Hepcludex (bulevirtide acetate). Australian Register of Therapeutic Goods. Gilead Sciences, Inc.; 2024. **6.** Buti M, et al. *J Hepatol.* 2022;77(Supp 1):S013. **7.** EuroQol Research Foundation. EQ-5D-3L User Guide. 2018.

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INTRODUCTION

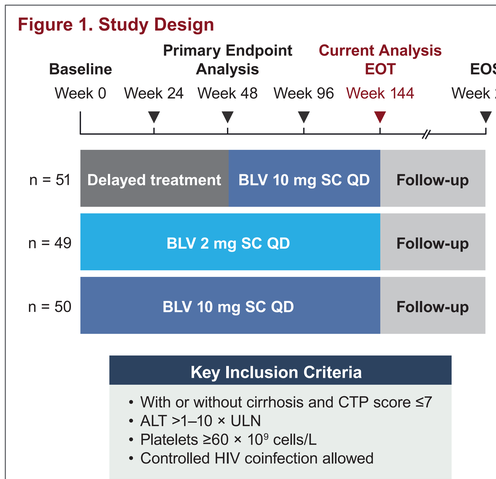
- CHD is the most severe form of viral hepatitis, affecting nearly 12 to 20 million people worldwide[1,2]
- BLV is a first-in-class entry inhibitor approved in the European Union (EU) and several non-EU countries for the treatment of CHD[3-5]
- Patients with CHD who received 48 weeks of BLV 2 mg monotherapy reported greater improvements in their perceived health state compared with patients who received no treatment[6]

OBJECTIVE

- This patient-reported outcome (PRO) study was an exploratory analysis of EQ-5D visual analogue scale (VAS) outcomes at 144 weeks (end of treatment) of BLV 2 mg dosing among patients with CHD

METHODS

Figure 1. Study Design



ALT, alanine aminotransferase; BLV, bulevirtide; CTP, Child-Turcotte-Pugh; EOS, end of study; EOT, end of treatment; QD, once daily; SC, subcutaneous; ULN, upper limit of normal.

- MYR301 (NCT03852719) was a Phase 3, randomised, multicentre, open-label, parallel-group clinical trial in which 150 patients with CHD were enrolled (**Figure 1**)
- Patients were randomised (1:1:1) to receive 1 of 3 treatments:
  - BLV 2 mg (n = 49) for 144 weeks
  - BLV 10 mg (n = 50) for 144 weeks
  - Delayed treatment (DT; n = 51) for 48 weeks followed by BLV 10 mg for 96 weeks
- Patients completed the EQ-5D VAS assessment on their own at key time points, including baseline, 24 weeks, 48 weeks, 96 weeks, and 144 weeks
- The EQ-5D VAS records patients' self-rated perceived health on a scale from 0 to 100, reflecting "the worst health you can imagine" (0) to "the best health you can imagine" (100)[7]
- Mean (95% CI) EQ-5D VAS scores and least squares mean (LSM) changes from baseline were calculated using a mixed-effects model for repeated measures
- Changes from baseline where the 95% CI included 0 were considered not statistically significant
- Subgroup analyses of patients by cirrhosis status at baseline were conducted

RESULTS

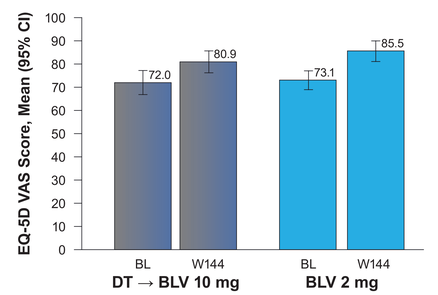
Table 1. Baseline Characteristics

Baseline Variables	DT → BLV 10 mg n = 51	BLV 2 mg n = 49	BLV 10 mg n = 50
Age, years, mean (SD)	41 (7.5)	44 (9.0)	41 (8.5)
Sex, male, n (%)	26 (51.0)	30 (61.2)	30 (60.0)
Race, n (%)			
White	40 (78.4)	41 (83.7)	43 (86.0)
Asian	11 (21.6)	8 (16.3)	6 (12.0)
Black or African descent	0	0	1 (2.0)
Cirrhosis, n (%)	24 (47.1)	23 (46.9)	24 (48.0)
Platelets, 10^9/L, mean (SD)	158 (57.0)	153 (52.5)	160 (53.1)
Liver stiffness, kPa, mean (SD)	15 (9.0)	14 (8.2)	15 (9.3)
ALT, U/L, mean (SD)	102 (61.9)	108 (62.5)	123 (80.6)
HDV RNA, $\log_{10}$ IU/mL, mean (SD)	5.1 (1.36)	5.1 (1.19)	5.0 (1.46)
HDV genotype, n (%)			
1	51 (100)	49 (100)	48 (96.0)[a]
5	0	0	1 (2.0)
HBsAg, $\log_{10}$ IU/mL, mean (SD)	3.7 (0.47)	3.7 (0.52)[b]	3.6 (0.59)[c]
HBV DNA, $\log_{10}$ IU/mL, mean (SD)	0.9 (0.99)	1.3 (1.29)[a]	1.1 (1.26)[b]
HBeAg positive, n (%)	4 (7.8)	4 (8.2)	7 (14.0)
HBV genotype, n (%)			
A	4 (7.8)	2 (4.1)	3 (6.0)
D	39 (76.5)	44 (89.8)	43 (86.0)
E	0	0	1 (2.0)
Missing	8 (15.7)	3 (6.1)	3 (6.0)
Previous IFN therapy, n (%)	29 (56.9)	26 (53.1)	29 (58.0)
Concomitant HBV NA treatment, n (%)	32 (62.7)	32 (65.3)	27 (54.0)

[a]Data missing from 1 patient. [b]Data missing from 2 patients. [c]Data missing from 3 patients.
ALT, alanine aminotransferase; BLV, bulevirtide; DT, delayed treatment; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis delta virus; IFN, interferon; NA, nucleos(t)ide analogue.

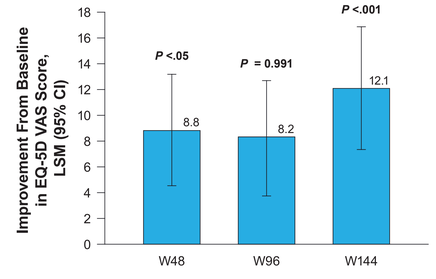
- Demographic characteristics (**Table 1**) and EQ-5D VAS scores (range, 72.0–73.9) were similar between treatment groups at baseline
- Twelve patients dropped out of the study by week 144, with no discontinuations due to study treatment; 7 patients had dropped out by week 96, and 5 patients had dropped out by week 48

Figure 2. EQ-5D VAS Score at Baseline and Week 144



Data values above the bars represent the arithmetic mean.
BL, baseline; BLV, bulevirtide; DT, delayed treatment; VAS, visual analogue scale; W, week.

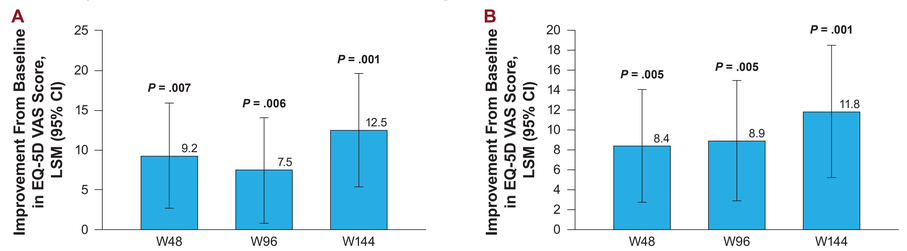
Figure 3. EQ-5D VAS Score Improvements From Baseline to 48, 96, and 144 Weeks in Patients With CHD Treated With BLV 2 mg



LSM was calculated from a mixed-effects model for repeated measures. Data values above the bars represent the LSM.
BLV, bulevirtide; CHD, chronic hepatitis delta; LSM, least squares mean; VAS, visual analogue scale; W, week.

- For patients who received BLV 2 mg (n = 44 at week 144), the mean (95% CI) EQ-5D VAS score at week 144 was 85.5 (81.14–89.91; **Figure 2**)
- The LSM (95% CI) score improvement from baseline to week 144 was 12.1 (7.32–16.87) and was considered statistically significant (**Figure 3**)
- The LSM improvement in EQ-5D VAS score from baseline reported at week 144 of BLV 2 mg treatment was greater than the LSM improvements from baseline to week 48 and week 96 (**Figure 3**)

Figure 4. EQ-5D VAS Score Change From Baseline to Weeks 48, 96, and 144 in Patients With CHD A) With or B) Without Cirrhosis Treated With BLV 2 mg



LSM was calculated from a mixed-effects model for repeated measures. Data values above the bars represent the LSM.
BLV, bulevirtide; CHD, chronic hepatitis delta; LSM, least squares mean; VAS, visual analogue scale; W, week.

- Among patients with cirrhosis, the LSM (95% CI) improvement in EQ-5D VAS score from baseline to week 144 (12.5 [5.32–19.61]; n = 21) was significant and greater than the LSM improvements from baseline to week 48 and week 96 (**Figure 4A**)
- Similarly, for patients without cirrhosis, the LSM (95% CI) improvement in EQ-5D VAS score from baseline to week 144 (11.8 [5.20–18.39]; n = 23) was significant and greater than corresponding scores at week 48 and week 96 (**Figure 4B**)
- The ≥7-point improvements from baseline EQ-5D VAS scores among patients with CHD treated with BLV 2 mg may be considered clinically meaningful
  - A rapid review of 54 studies employing the EQ-5D VAS for various disease conditions found clinically meaningful changes occurred at ≥7 to ≥10 points (data not shown)

LIMITATIONS

- Limitations of this PRO analysis and interpretations include the open-label trial design, relatively small sample size, low population diversity, and exploratory nature of the analysis
- These limitations may reduce the sensitivity of the questionnaires to detect differences in PROs between the treatment and DT groups during the first 48 weeks of the study, and prevent broad generalisation of these outcomes to all population groups
- An inherent detraction of PRO questionnaires is the subjective nature of patients' responses, which may differ across race/ethnicity and geography/country
- Due to ethical considerations, no control group was included beyond 48 weeks

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