Clinically Significant Portal Hypertension May Improve in Some Patients With Chronic Hepatitis Delta After 48 Weeks of Bulevirtide Treatment: A Pooled Analysis of Phase 2/3 Clinical Trials

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MYR301, MYR204, and MYR203

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Conclusions

- Bulevirtide (BLV) treatment was associated with a numerically greater improvement in clinically significant portal hypertension (CSPH) classification by Week 48 compared with control, as assessed by both the Baveno-VII criteria and the ANTICIPATE model
- Patients receiving BLV were >2-fold more likely than the control group to improve from rule-in CSPH to gray zone/rule-out status by Baveno-VII criteria; findings are limited by the small sample sizes
- Treatment-associated improvements were observed in a subset of patients; improvements in CSPH category were not limited to patients with virologic response or alanine aminotransferase normalization
- Improvements in CSPH with BLV were observed at this early assessment at Week 48, and further studies are needed to provide insight into the long-term benefit of BLV on portal hypertension progression

Plain Language Summary

- Bulevirtide improves key markers of chronic hepatitis delta disease activity and may also reduce clinically significant portal hypertension
- Using noninvasive clinically significant portal hypertension assessment tools, this study found that bulevirtide may improve or slow the progression of clinically significant portal hypertension in some patients with chronic hepatitis delta, even when virus levels are not reduced and other liver tests are not normal

References: **1.** Vanderschueren E, et al. *Ann Gastroenterol*. 2025;38:380-91. **2.** Jachs M, et al. *J Hepatol*. 2024;81:248-57. **3.** Vutien P, et al. *Hepatology*. 2025;82:422-37. **4.** de Franchis R, et al. *J Hepatol*. 2022;76:959-74. **5.** Abraldes JG, et al. *Hepatology*. 2016;64:2173-84. **6.** HEPCLUDEX® (bulevirtide-gmod) for injection, for subcutaneous use [prescribing information]. Gilead Sciences, Inc.; 2026. **7.** European Medicines Agency. HEPCLUDEX 2 mg powder for solution for injection [summary of product characteristics]. Accessed July 21, 2026. https://www.ema.europa.eu/en/documents/product-information/hepcludex-epar-product-information_en.pdf. **8.** Therapeutic Goods Administration. Hepcludex (bulevirtide acetate). Accessed July 21, 2026. https://www.tga.gov.au/resources/auspmd/hepcludex-bulevirtide-acetate. **9.** HEPCLUDEX®. Product monograph. Gilead Sciences Canada, Inc.; 2025. **10.** Wedemeyer H, et al. *J Hepatol*. 2026;85:493-503. **11.** Asselah T, et al. *N Engl J Med*. 2024;391:133-43. **12.** Lampertico P, et al. *Liver Int*. 2025;45:e70008. **13.** Sandmann L, et al. *JHEP Rep*. 2025;8:101643.

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Introduction

- Patients with chronic hepatitis delta (CHD) often show rapid progression of fibrosis to advanced chronic liver disease and clinically significant portal hypertension (CSPH), which increases the risk of liver-related events[1,2]
- While hepatic venous pressure gradient (HVPG) measurements are the standard for CSPH diagnosis, models based on noninvasive tests for liver stiffness measurement (LSM) and platelet (PLT) count, such as Baveno-VII and ANTICIPATE, can be used to accurately reflect the risk of CSPH in patients with CHD[2-5]
- Bulevirtide (BLV), a first-in-class entry inhibitor, is approved in the United States, European Economic Area, and several other countries for the treatment of CHD with compensated liver disease[6-9]
  - In clinical trials, BLV demonstrated virologic responses (VRs), alanine aminotransferase (ALT) normalization, and improvement in LSM at Week 48 that further improved with continued long-term treatment[10-12]
  - In a real-world study, patients with portal hypertension who responded to BLV treatment had clinically meaningful decreases in HVPG[13]
- There are limited data on the prevalence of CSPH in patients with CHD and the effect of BLV treatment on its course using noninvasive models

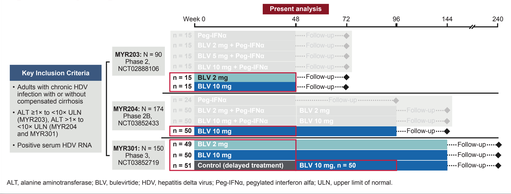
Objective

- This analysis evaluated CSPH prevalence and the early impact of BLV monotherapy (at 48 weeks) using noninvasive CSPH-based models in patients with CHD

Methods

- Data from patients with CHD treated with BLV 10 mg (8.5 mg/day delivered dose) or 2 mg monotherapy in the MYR301 (NCT03852719), MYR204 (NCT03852433), and MYR203 (NCT02888106) studies were pooled and analyzed (**Figure 1**)
  - Patients with detectable baseline hepatitis delta virus (HDV) RNA and with LSM and PLT values available at baseline and Week 48 were included
  - Outcomes were compared with patients from the control (delayed treatment) arm at 48 weeks in MYR301

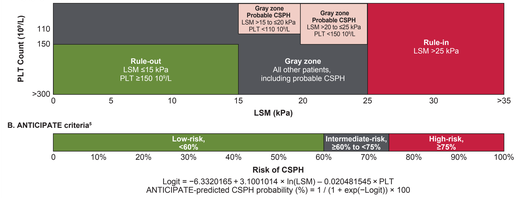
Figure 1. Study Design



ALT, alanine aminotransferase; BLV, bulevirtide; HDV, hepatitis delta virus; Peg-IFNα, pegylated interferon alfa; ULN, upper limit of normal.

- Efficacy outcomes assessed at Week 48 included the following:
  - VR, defined as a ≥2 $\log_{10}$ IU/mL decline from baseline in HDV RNA or undetectable HDV RNA
  - ALT normalization
  - Combined response (VR + ALT normalization)
- LSM and PLT data at baseline and Week 48 were used to assess CSPH risk using the Baveno-VII and ANTICIPATE models[2-5] (**Figure 2**)

Figure 2. CSPH Risk Models



Logit = −6.3320165 + 3.1001014 × ln(LSM) − 0.0204815 45 × PLT
ANTICIPATE-predicted CSPH probability (%) = 1 / (1 + exp(−Logit)) × 100

LSM units: kPa. PLT units: 10³/L. For the ANTICIPATE calculation, PLT counts >150 were set to 150.
CSPH, clinically significant portal hypertension; LSM, liver stiffness measurement; PLT, platelet.

Results

- Baseline characteristics were similar between BLV and control groups (**Table 1**)

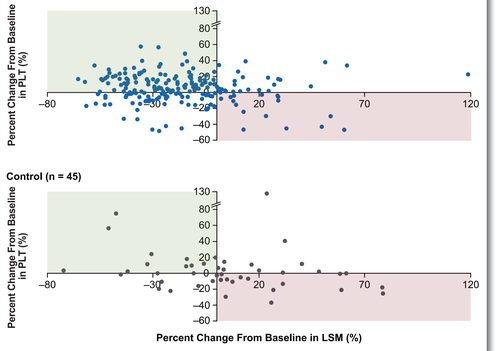
Table 1. Demographic and Baseline Disease Characteristics

	BLV (n = 206)	Control (n = 45)
Age, years, mean (SD)	41 (8.5)	41 (7.5)
Sex, male, n (%)	136 (66)	23 (51)
Race, n (%)		
Asian	25 (12)	11 (24)
Black or African American	3 (1)	0
White	178 (86)	34 (76)
Body mass index, kg/m², mean (SD)	25.1 (3.6)	25.4 (3.7)
Cirrhosis present, n (%)[a]	85 (41)	20 (44)
PLT, 10^9/L, mean (SD)	164 (51.9)	158 (52.0)
LSM, kPa, mean (SD)	14.3 (9.1)	14.5 (8.4)
ALT, U/L, mean (SD)	108 (78.4)	83 (53.4)
HDV RNA, $\log_{10}$ IU/mL, mean (SD)	5.3 (1.3)	4.9 (1.6)
HBsAg, $\log_{10}$ IU/mL, mean (SD)	3.7 (0.6)	3.7 (0.7)
Previous IFN therapy, n (%)	93 (45)	24 (53)
Concomitant HBV NA treatment, n (%)	120 (58)	27 (60)

[a]Cirrhosis status was missing for 14 patients in the BLV group.
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 analog; PLT, platelet.

- For patients receiving BLV, LSM improved more from baseline to Week 48 than for the control group (mean kPa change [SD], –3.1 [4.8] vs –0.02 [5.6]; mean percent change [SD], –17.2% [26.6] vs 4.3% [34.2]; **Figure 3**)
- Similar results were observed for PLT (mean 10^9/L change [SD], 7 [31] vs 0 [36]; mean percent change [SD], 4.7% [18.7] vs 3.9% [27.9])

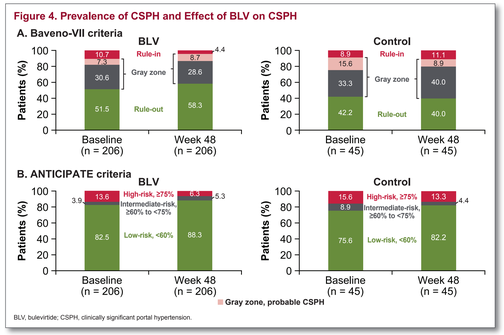
Figure 3. Percent Change From Baseline to Week 48 in PLT and LSM



BLV, bulevirtide; LSM, liver stiffness measurement; PLT, platelet.

- Baveno-VII: Rule-in CSPH prevalence at baseline was similar between groups (BLV, 10.7%; control, 8.9%; **Figure 4A**)
  - From baseline to Week 48, this proportion decreased in the BLV group (10.7% to 4.4%) but remained similar in the control group (8.9% to 11.1%)
- ANTICIPATE: High-risk CSPH (≥75%) prevalence at baseline was similar between groups (BLV, 13.6%; control, 15.6%; **Figure 4B**)
  - From baseline to Week 48, this proportion decreased in the BLV group (13.6% to 6.3%) but remained similar in the control group (15.6% to 13.3%)

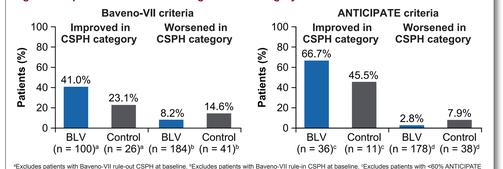
Figure 4. Prevalence of CSPH and Effect of BLV on CSPH



BLV, bulevirtide; CSPH, clinically significant portal hypertension.

- Compared with the control group, the BLV group had a higher proportion of patients improving and a lower proportion worsening in CSPH category by both Baveno-VII and ANTICIPATE criteria (**Figure 5**)

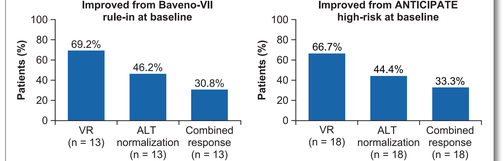
Figure 5. Improvement and Worsening in CSPH Category



[a]Excludes patients with Baveno-VII rule-out CSPH at baseline. [b]Excludes patients with Baveno-VII rule-in CSPH at baseline. [c]Excludes patients with <60% ANTICIPATE risk (low-risk) at baseline. [d]Excludes patients with ≥75% ANTICIPATE risk (high-risk) at baseline.
BLV, bulevirtide; CSPH, clinically significant portal hypertension.

- Among BLV-treated patients who improved from Baveno-VII rule-in criteria at baseline (n = 13), 69.2% achieved VR at Week 48, with combined response and ALT normalization observed in 30.8% to 46.2% (**Figure 6**); similar efficacy was observed in patients who improved from ANTICIPATE high-risk criteria (n = 18)

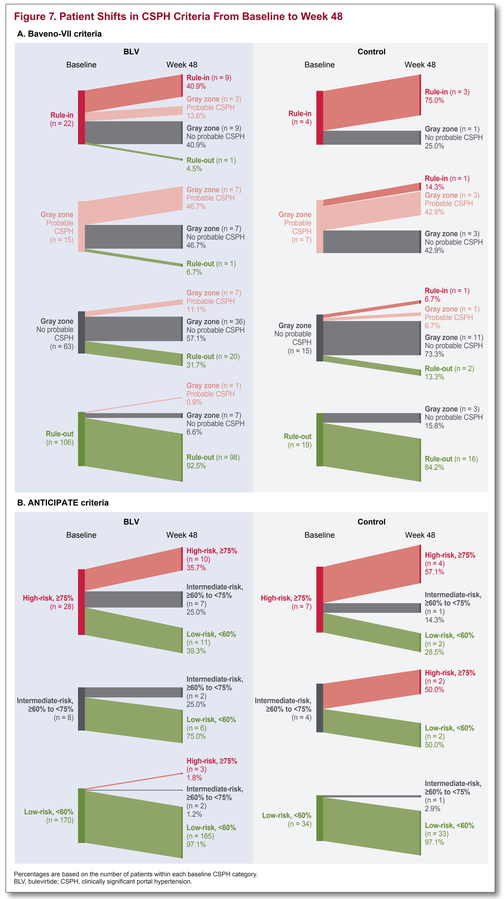
Figure 6. BLV Efficacy Responses in Patients Who Improved From Baseline Rule-In/High-Risk CSPH



ALT, alanine aminotransferase; BLV, bulevirtide; CSPH, clinically significant portal hypertension; VR, virologic response.

- Baveno-VII: BLV was associated with a greater numerical proportion improving from rule-in at baseline to gray zone/rule-out at Week 48 compared with control (59.1% vs 25.0%); rates of patients with gray zone probable CSPH status at baseline who were stable or improved at Week 48 were 100% vs 85.7% (**Figure 7A**)
- ANTICIPATE: BLV was associated with a greater numerical proportion improving from high-risk at baseline to intermediate-/low-risk compared with control (64.3% vs 42.9%); rates of patients with intermediate-risk status at baseline who were stable or improved at Week 48 were 100% vs 50.0% (**Figure 7B**)

Figure 7. Patient Shifts in CSPH Criteria From Baseline to Week 48



Percentages are based on the number of patients within each baseline CSPH category.
BLV, bulevirtide; CSPH, clinically significant portal hypertension.