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Poster for you

Patient-Reported Outcomes Among Patients With Chronic Hepatitis Delta Treated With Bulevirtide 2 mg: Analysis of the Phase 3 MYR301 Trial at 96 Weeks

Maria Buti[1,2], Heiner Wedemeyer[3], Soo Aleman[4], Vladimir Chulanov[5], Viacheslav Morozov[6], Olga Sagalova[7], Tatyana Stepanova[8], Robert G Gish[9,10], Andrew Lloyd[11], Vithika Suri[12], Dmitry Manuilov[12], Grace M Chee[12], Audrey H Lau[12], Anu O Osinusi[12], John F Flaherty[12], Marvin Rock[12], Chong Kim[12], Shubhram Pandey[13], Barinder Singh[13], Pietro Lampertico[14,15]

[1]Liver Unit, Hospital Universitario Vall d'Hebron, Barcelona, Spain; [2]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBER-EHD) del Instituto Carlos III, Barcelona, Spain; [3]Clinic for Gastroenterology, Hepatology, Infectious Diseases and Endocrinology, Hannover Medical School, Hannover, Germany; [4]Department of Infectious Diseases, Karolinska Universitetssjukhuset, Karolinska Institutet, Stockholm, Sweden; [5]Department of Infectious Diseases, Sechenov University, Moscow, Russian Federation; [6]LLC Medical Company Hepatolog, Samara, Russian Federation; [7]South Ural State Medical University, Chelyabinsk, Russian Federation; [8]LLC Clinic of Modern Medicine, Moscow, Russian Federation; [9]Robert G. Gish Consultants, LLC, San Diego, CA, USA; [10]Hepatitis B Foundation, Doylestown, PA, USA; [11]Acaster Lloyd Consulting Ltd., London, UK; [12]Gilead Sciences, Inc., Foster City, CA, USA; [13]Pharmacoevidence Private Limited, Punjab, India; [14]Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [15]CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Conclusions

- Patients with chronic hepatitis delta virus infection treated with bulevirtide (BLV) 2 mg for 96 weeks (W) exhibited improvements across all domains of the Hepatitis Quality of Life Questionnaire (HQLQ)
- Large improvements (>15 points) were observed in 2 hepatitis-specific (HS) HQLQ domains, the HS limitations scale and HS health distress scale
- Improvements in all HQLQ domains were sustained or enhanced compared to 48W of treatment, demonstrating the long-term benefits of BLV 2 mg monotherapy

Plain Language Summary

- Chronic hepatitis delta infection can cause liver damage, liver cancer, and liver-related death
- In clinical trials, bulevirtide is safe, effective for viral load reduction, and well tolerated
- We report that treatment with bulevirtide significantly improved the quality of life in patients with chronic hepatitis delta virus infection, benefiting the lives of people living with chronic hepatitis delta

Introduction

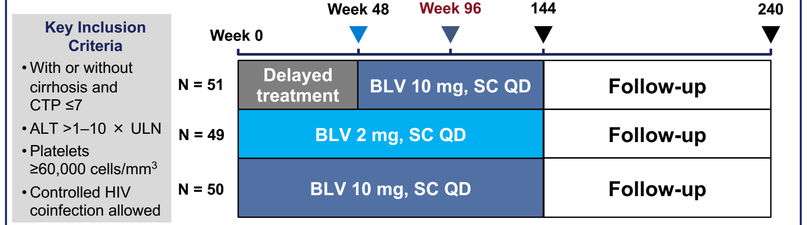
- Patients with chronic hepatitis delta (CHD) are at substantial risk of developing liver-related complications, including cirrhosis, hepatic decompensation, hepatocellular carcinoma, a need for liver transplant, and death[1,2]
- Compared to a control group of delayed treatment, bulevirtide (BLV) improved health-related quality of life among patients with CHD at both 24 and 48 weeks (W)[2,3]
- Patients with CHD have worse physical and psychologic scores on patient-reported outcome (PRO) questionnaires than do untreated patients with chronic hepatitis B virus monoinfection[4]

Objectives

- This study explored Hepatitis Quality of Life Questionnaire (HQLQ) outcomes in patients with CHD following 96W of treatment with BLV 2 mg in the ongoing MYR301 trial
  - This analysis focused specifically on the 2-mg group because BLV given at 2 mg once daily is the only approved treatment for patients with CHD in the European Union (EU)

Methods

Figure 1 **Full Study Design**



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

- MYR301 (NCT03852719) is a Phase 3, randomised, multicentre, open-label, parallel-group clinical trial in which 150 patients with CHD were enrolled
- Patients were randomised (1:1:1) to receive 1 of 3 treatments:
  - BLV 2 mg (n = 49) for 144W
  - BLV 10 mg (n = 50) for 144W
  - Delayed treatment (n = 51) for 48W followed by BLV 10 mg for 96W
- Patients completed the HQLQ, comprising the 36-Item Short Form Health Survey questionnaire and 4 hepatitis-specific (HS) health domain scores (15 supplemental items), independently at baseline (BL), 24W, 48W, and 96W
- Higher scores on the HQLQ (range 0–100) indicate better health-related quality of life
- The data were analysed using a mixed-model, repeated-measures method to estimate the least squares mean change from BL at different time points for the BLV 2-mg group, the dose approved for use in the EU

Table 1 **Baseline Demographic and Disease Characteristics**

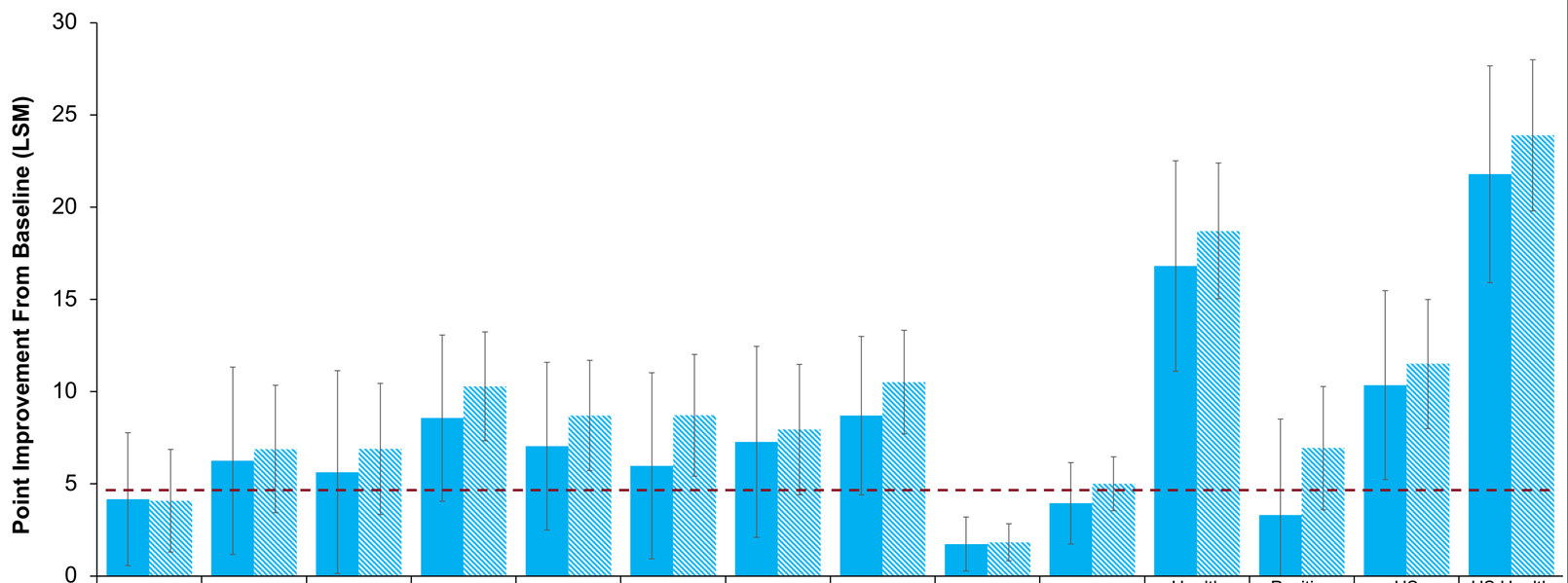
	Control[a] n = 51	BLV 2 mg n = 49
Age, years, mean (SD)	40.5 (7.5)	43.6 (9.0)
Male sex, n (%)	26 (51.0)	30 (61.2)
Race, n (%)		
White	40 (78.4)	41 (83.7)
Asian	11 (21.6)	8 (16.3)
Black or African descent	0	0
Cirrhosis, n (%)	24 (47.1)	23 (46.9)
Platelets, 10^9 cells/L, mean (SD)	158 (57)	153 (53)
Liver stiffness, kPa, mean (SD)	15.3 (9.0)	14.0 (8.2)
ALT, U/L, mean (SD)	102 (62)	108 (63)
HDV RNA, $\log_{10}$ IU/mL, mean (SD)	5.08 (1.36)	5.01 (1.32)[b]
HDV genotype, n (%)		
1	51 (100)	49 (100)
5	0	0
HBsAg, $\log_{10}$ IU/mL, mean (SD)	3.68 (0.47)	3.67 (0.51)[b]
HBV DNA, $\log_{10}$ IU/mL, mean (SD)	0.89 (0.99)	1.31 (1.30)[b]
HBeAg positive, n (%)	4 (7.8)	4 (8.2)
HBV genotype, n (%)		
A	0	1 (2)
D	10 (19.6)	14 (28.6)
E	0	0
Missing	24 (47.1)	16 (32.7)
Previous IFN therapy, n (%)	29 (56.9)	26 (53.1)
Concomitant HBV NA treatment, n (%)	32 (62.7)	31 (63.3)

[a]Delayed treatment. [b]Data missing from 1 patient.
ALT, alanine aminotransferase; BLV, bulevirtide; 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 and disease characteristics were similar at BL across groups
- Less than 10% of patients dropped out of the BLV 2-mg group by 96W

Results

Figure 2 **Improvement From Baseline to 48W and 96W in HQLQ Domain Scores Among Patients With CHD Treated With BLV 2 mg**

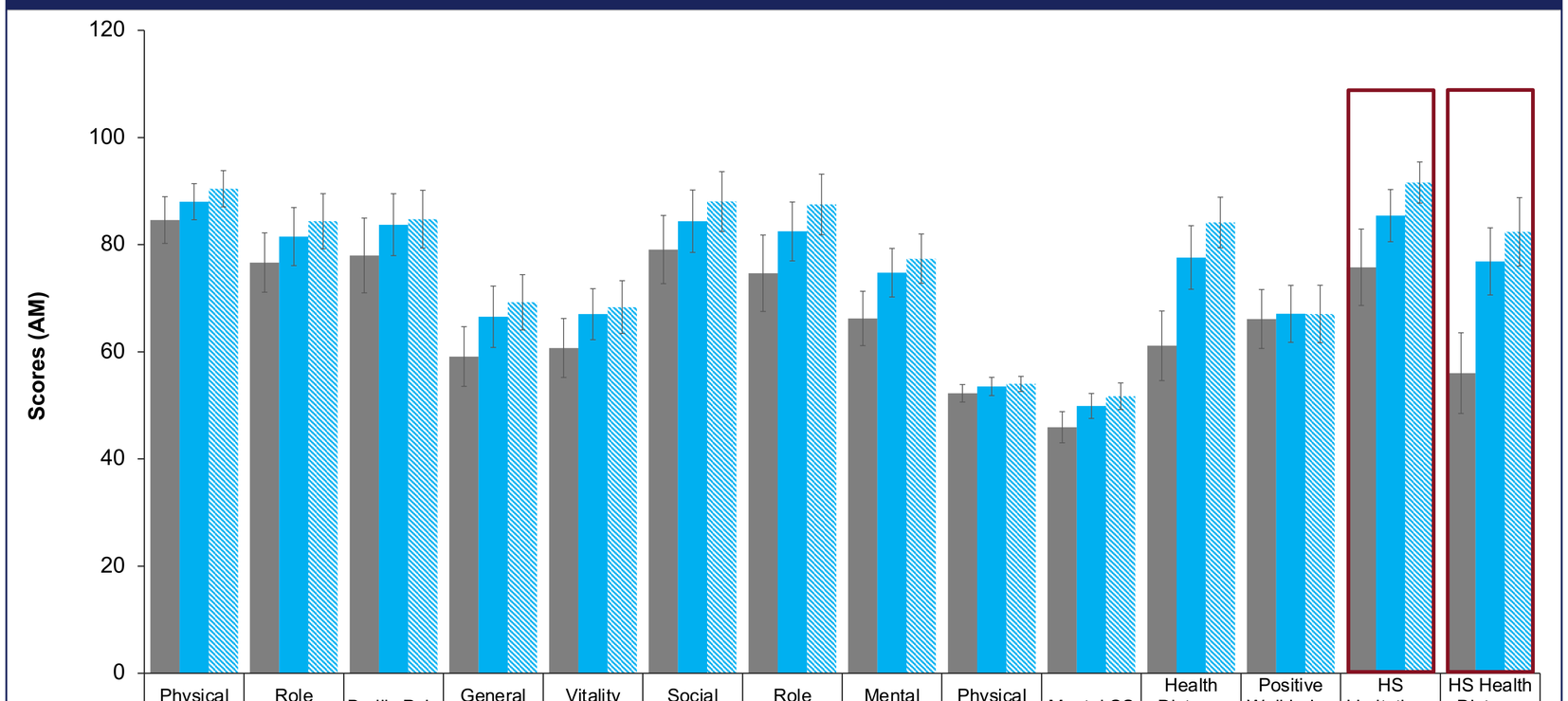


	Physical Functioning	Role Physical	Bodily Pain	General Health	Vitality Scale	Social Functioning	Role Emotional	Mental Health	Physical CS	Mental CS	Health Distress Scale	Positive Well-Being Scale	HS Limitations Scale	HS Health Distress Scale
48W n = 48	4,2	6,3	5,6	8,6	7,1[a]	6,0	7,3	8,7[a]	1,7	4,0	16,8	3,3	10,4	21,8
96W n = 46	4,1	6,9	6,9	10,3	8,7	8,7	8,0	10,5	1,8	5,0	18,7	6,9	11,5	23,9

The mixed model included treatment, region, presence of cirrhosis, visit, and treatment-by-visit interaction as fixed-effect factors and baseline score as the covariate. The dashed line denotes a change of ≥5 points, which may be considered clinically meaningful. All values were significantly improved from baseline (P <.05) except for the positive well-being scale at W48.
[a]n = 47.
BLV, bulevirtide; CHD, chronic hepatitis delta; CS, component summary; HQLQ, Hepatitis Quality of Life Questionnaire; HS, hepatitis-specific; LSM, least squares mean; W, week.

- The least squares mean score improvements from BL were ≥5 points at 96W in all domains except the physical functioning and physical component summary domains
- **Compared to their BL scores, patients who received BLV experienced statistically significant improvements in all HQLQ domains at 96W**

Figure 3 **Absolute HQLQ Domain Scores Among Patients With CHD Treated With BLV 2 mg**



	Physical Functioning	Role Physical	Bodily Pain	General Health	Vitality Scale	Social Functioning	Role Emotional	Mental Health	Physical CS	Mental CS	Health Distress Scale	Positive Well-being Scale	HS Limitations Scale	HS Health Distress Scale
BL n = 49	84,6	76,7	78,0	59,1	60,7	79,1	74,7	66,2	52,3	45,9	61,1	66,1	75,8	56,0
48W n = 48	88,0	81,5	83,7	66,5	67,0[a]	84,4	82,5	74,8[a]	53,5	49,9	77,6	67,1	85,4	76,9
96W n = 46	90,4	84,4	84,8	69,2	68,3	88,0	87,5	77,4	54,0	51,7	84,1	67,1	91,6	82,4

[a]n = 47.
The mixed model included treatment, region, presence of cirrhosis, visit, and treatment-by-visit interaction as fixed-effect factors and BL score as the covariate.
AM, arithmetic mean; BL, baseline; BLV, bulevirtide; CHD, chronic hepatitis delta; CS, component summary; HQLQ, Hepatitis Quality of Life Questionnaire; HS, hepatitis-specific; W, week.

- At 96W, substantial improvements (>15 points) from BL were observed in specific HS health domains: HS limitations (15.8 points) and HS health distress (26.4 points)
- HQLQ improvements from BL at 48W with BLV 2 mg were sustained or improved at 96W, emphasising its enduring efficacy as a monotherapy

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 control groups and prevent broad generalisation of these outcomes to all population groups
- Additionally, an inherent detraction of PRO questionnaires is the subjective nature of patients' responses, which may differ across race/ethnicity and geography/country
- Finally, due to ethical considerations, no control group was included beyond 48W

References: **1.** Lampertico P, et al. *J Hepatol*. 2022;77(5):1422-30. **2.** Buti M, et al. *J Hepatol*. 2022;77(Supp 1):S013. **3.** Buti M, et al. *J Hepatol*. Preproof. 2024. doi: https://doi.org/10.1016/j.jhep.2024.06.031. **4.** Buti M, et al. *J Hepatol*. 2021;3(3):100280.

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