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Poster for you

High Rates of Adherence to Bulevirtide Monotherapy for Chronic Hepatitis Delta Through 96 Weeks: Results From an Interim Analysis of the Phase 3 Study MYR301

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Conclusions

- High adherence rates were observed through 96 weeks in patients with chronic hepatitis delta self-administering bulevirtide (BLV) via daily subcutaneous injections
- Treatment with BLV monotherapy through 96 weeks resulted in continued improvement in responses with maintained safety
- Virologic and biochemical responses were observed in most patients after 96 weeks of treatment with BLV monotherapy

Plain Language Summary

- Patients were treated with 2 mg or 10 mg of bulevirtide for 144 weeks and were then monitored for 96 weeks after the end of their treatment
- Adherence, the degree to which a person takes medications as prescribed, was determined using patient diary entries and drug accountability data
- Patients taking 2 mg or 10 mg of bulevirtide had mean rates of adherence of more than 95% at weeks 24 and 48; at 96 weeks, the mean rates of adherence were more than 98% and 94% for the patients taking the 2 mg dose and 10 mg dose, respectively
- Control of hepatitis delta virus and reduction of liver inflammation improved with continued bulevirtide treatment at either dose level through 96 weeks
- Bulevirtide was safe and well tolerated; no patients were required to stop taking bulevirtide or missed a dose because of any adverse events

Background

- Hepatitis delta virus (HDV) represents the most severe form of chronic viral hepatitis and is estimated to affect between 10 and 20 million individuals worldwide[1]
- Bulevirtide (BLV), a novel first-in-class entry inhibitor of HDV, is approved in the European Union at a dose of 2 mg/d for the treatment of chronic hepatitis delta with compensated liver disease[2]
- In the Phase 3 study MYR301, BLV 2 mg/d or 10 mg/d was shown to be safe and effective through 96 weeks[3] based on the combined endpoint of virologic response (undetectable or a ≥2 $\log_{10}$ IU/mL decline in HDV RNA from baseline)[4] and biochemical response (alanine aminotransferase [ALT] normalisation)

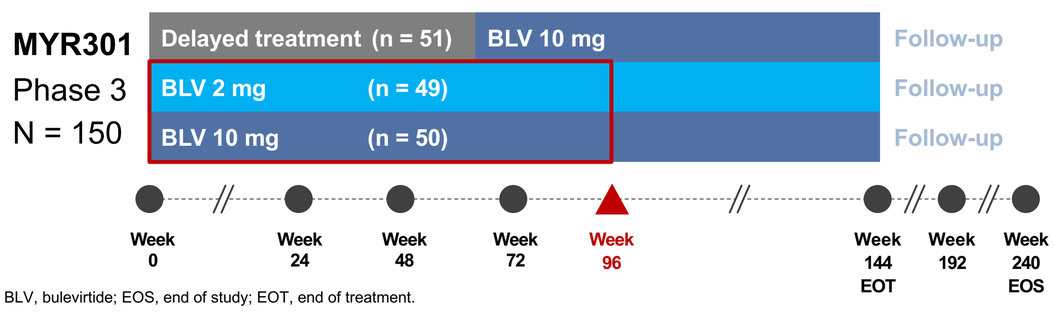
Objective

- This analysis describes patient adherence to, and efficacy and safety of, BLV monotherapy through 96 weeks in MYR301

Methods

- MYR301 (NCT03852719) is an open-label, randomised study evaluating 3 cohorts: a delayed-treatment arm not receiving anti-HDV therapy for 48 weeks followed by BLV 10 mg/d for 96 weeks and 2 arms receiving BLV 2 mg/d or BLV 10 mg/d to week (W) 144
- BLV 10 mg was self-administered as 2 subcutaneous (sc) injections of BLV 5 mg; BLV 2 mg was self-administered as 1 sc injection of BLV 2 mg
- In this analysis, data were included from all patients randomised to BLV 2 mg or BLV 10 mg up to W96

Figure 1 **MYR301 Study Schema**



BLV, bulevirtide; EOS, end of study; EOT, end of treatment.

- Treatment adherence was assessed at each visit using information collected from the following:
  - Patient diary
  - Study drug accountability (ie, the number of dispensed vials vs the number of returned vials [used and unused] of the study drug) collected at each visit
- Adherence to BLV was computed as the ratio of the cumulative dose of BLV administered to the planned total dose at a particular time point
- ALT upper limit of normal was 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
- HDV RNA levels were determined by RT-qPCR using the RoboGene HDV RNA Quantification Kit 2.0 (lower limit of quantitation, 50 IU/mL; limit of detection, 6 IU/mL)

Results

Table 1 **Demographics and Baseline Characteristics by BLV Study Group**

	BLV 2 mg (n = 49)	BLV 10 mg (n = 50)	Total (N = 99)
Male	30 (61)	30 (60)	60 (61)
Race			
White	41 (84)	43 (86)	84 (85)
Asian	8 (16)	6 (12)	14 (14)
Black or African American	0	1 (2)	1 (1)
Cirrhosis present, yes	23 (47)	24 (48)	47 (47)
HBeAg status, positive	4 (8)	7 (14)	11 (11)
Concomitant NA therapy, yes	32 (65)	27 (54)	59 (60)
Prior IFN therapy, yes	26 (53)	29 (58)	55 (56)
Genotype HDV-1[a]	49 (100)	48 (96)	97 (98)
LSM, kPa, mean (SD)	14.0 (8.2)	14.8 (9.3)	14.4 (8.7)
HDV RNA, $\log_{10}$ IU/mL, mean (SD)	5.1 (1.2)	5.0 (1.5)	5.0 (1.3)
ALT, U/L, mean (SD)	108 (63)	123 (81)	116 (72)

Data are presented as n (%) unless otherwise noted. [a]In the BLV 10 mg group, 1 patient had HDV genotype 5, and 1 patient was missing HDV genotype data. ALT, alanine aminotransferase; BLV, bulevirtide; HBeAg, hepatitis B e antigen; HDV, hepatitis delta virus; IFN, interferon; LSM, liver stiffness measurement; NA, nucleos(t)ide analogue.

- In the BLV 2 mg and 10 mg groups, 96% (47 of 49) and 94% (47 of 50) completed 96 weeks of treatment, respectively
- Reasons for study discontinuation included withdrawal of consent (2 each from BLV 2 mg and 10 mg groups [n = 4]) and physician decision (BLV 10 mg group [n = 1])

Results

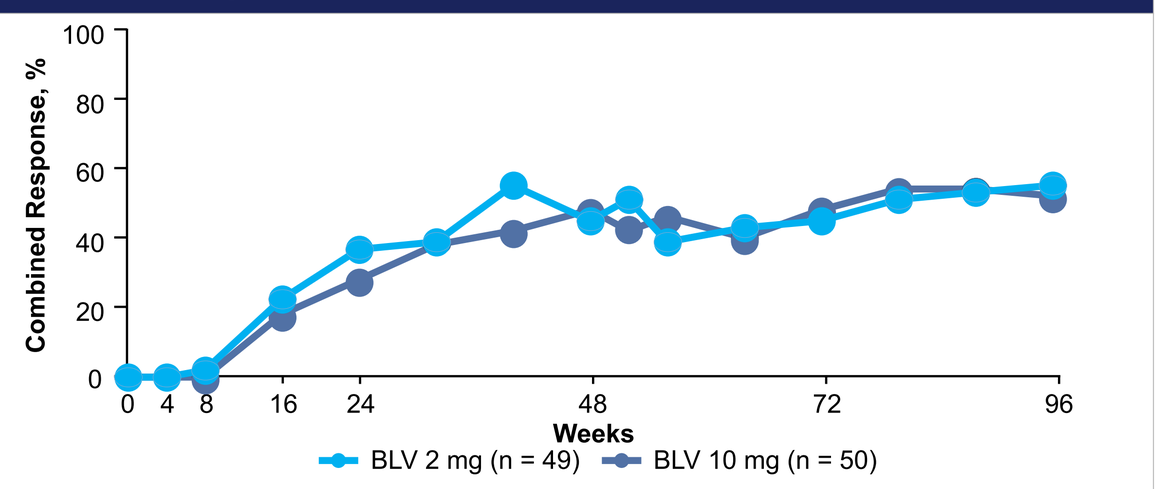
Table 2 **Adherence to BLV and Extent of Exposure**

	BLV 2 mg (n = 49)	BLV 10 mg (n = 50)
Week 24		
Total cumulative dose of BLV given, mg	335.6 (5.5)	1621.7 (236.4)
Number of missed BLV injections	0.4 (0.9)	1.0 (2.6)
Adherence to BLV, %	99.9 (1.6)[a]	96.5 (14.1)[b]
Week 48		
Total cumulative dose of BLV given, mg	669.0 (7.3)	3195.3 (618.5)
Number of missed BLV injections	0.9 (2.3)	5.0 (26.9)
Adherence to BLV, %	99.6 (1.1)[a]	95.1 (18.4)[b]
Week 96		
Total cumulative dose of BLV given, mg	1318.1 (117.8)	6357.5 (1420.7)
Number of missed BLV injections	4.4 (19.0)	6.1 (27.3)
Adherence to BLV, %	98.1 (8.8)[a]	94.6 (21.1)[b]

Values are expressed as mean (SD). [a]The BLV 2 mg group required only 1 injection of 2 mg. [b]The BLV 10 mg group required 2 injections of 5 mg. BLV, bulevirtide.

- Mean adherence rates exceeded 95% for the BLV 2 mg and 10 mg groups at W24 and W48 and were higher in the BLV 2 mg group
- At W96, mean adherence rates were 98.1% for the BLV 2 mg group and 94.6% for the BLV 10 mg group; the numbers of missed injections per patient were 4.4 in the 2 mg group and 6.1 in the 10 mg group
- Among patients who completed 96 weeks of the study (excluding 5 patients who discontinued prior to 96 weeks), mean adherence rates were 99.8% and 99.9% in the BLV 2 mg and BLV 10 mg groups, respectively

Figure 2 **Combined Response[a] Over Time**



[a]Combined response is defined as undetectable HDV RNA or a ≥2 $\log_{10}$ IU/mL decrease in HDV RNA from BL with ALT normalisation. This definition was not applicable at BL. ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; HDV, hepatitis delta virus.

- Combined response rates increased through 96 weeks for the BLV 2 mg and 10 mg groups

Table 3 **Key Efficacy and Safety Results at Weeks 48 and 96**

	BLV 2 mg (n = 49)		BLV 10 mg (n = 50)	
Study Week	**Week 48**	**Week 96**	**Week 48**	**Week 96**
Combined response, responder, n (%)	22 (45)	27 (55)	24 (48)	28 (56)
Virologic response,[a] responder, n (%)	36 (73)	37 (76)	38 (76)	41 (82)
Undetectable HDV RNA, responder, n (%)	6 (12)	10 (20)	10 (20)	18 (36)
ALT normalisation, responder, n (%)	25 (51)	31 (63)	28 (56)	32 (64)
Change in HDV RNA, $\log_{10}$ IU/mL,[b] least square mean (95% CI)	−2.6 (−3.0, −2.3)	−3.2 (−3.6, −2.8)	−3.0 (−3.4, −2.7)	−3.6 (−4.0, −3.2)
Change in LSM from BL, kPa, least square mean (95% CI)	−3.1 (−4.7, −1.5)	−4.0 (−5.6, −2.5)	−3.2 (−4.9, −1.4)	−4.7 (−6.3, −3.2)
AEs[c] at week 96 Number (%) of patients with:				
Any AE	41 (84)	47 (96)	44 (88)	48 (96)
Any Grade ≥3 AE	5 (10)	9 (18)	4 (8)	8 (16)
Any AE related to BLV	24 (49)	25 (51)	36 (72)	36 (72)
Injection-site reactions[d]	9 (18)	10 (20)	15 (30)	15 (30)
Any SAE[e]	2 (4)	2 (4)	1 (2)	4 (8)

[a]Undetectable HDV RNA levels or HDV RNA decreased ≥2 $\log_{10}$ IU/mL from BL. [b]Change in HDV RNA levels from baseline. [c]All AEs were treatment emergent over 96 weeks. [d]Grouped term including "injection-site" (reaction, erythema, pruritus, rash, swelling, haematoma, pain, bruising, dermatitis, and induration). [e]SAEs were defined as follows: BLV 2 mg—foot fracture, headache, hemiparesis, depression; BLV 10 mg—COVID-19 pneumonia, lumbar vertebral fracture. None of the SAEs were considered related to BLV. AE, adverse event; ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; HDV, hepatitis delta virus; LSM, liver stiffness measurement; SAE, serious adverse event.

- Treatment with BLV through 96 weeks was associated with improvements in virologic and biochemical responses in most patients, with response rates increasing over time
- BLV was safe and well tolerated; no serious adverse events were attributed to BLV or led to discontinuation
- Injection-site reactions were mild to moderate in severity and occurred more frequently in the BLV 10 mg group (2 injections daily) vs the BLV 2 mg group (1 injection daily)

References: **1.** Stockdale AJ, et al. *J Hepatol.* 2020;73:523-32. **2.** Hepcludex. European Medicines Agency SmPC. 2023. **3.** Wedemeyer H, et al. *Gut.* 2023;72:A103-4. **4.** Yurdaydin C, et al. *J Hepatol.* 2019;70:1008-15.

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