GILEAD | Medical Information

Hepcludex® (bulevirtide-gmod) Poor Response to Treatment

This document is in response to your request for information regarding the use of Hepcludex® (bulevirtide-gmod [BLV]) for the treatment of chronic HDV infection and data on poor response to treatment.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hdv/hepcludex/hepcludex_pi.

Summary

Product Labeling[1]

Severe acute exacerbations of HDV and HBV may occur after BLV is discontinued, especially in patients with cirrhosis, who may be at increased risk of more severe flares or progression to hepatic decompensation. Monitor hepatic function closely with both clinical and laboratory follow-up, including monitoring HBV DNA and HDV RNA viral load, for ≥6 months in patients who discontinue BLV. Resumption of antiviral therapy may be warranted.

BLV is indicated for the treatment of chronic HDV infection in adults without cirrhosis or with compensated cirrhosis.

This indication is approved under accelerated approval based on a decrease in HDV RNA and ALT normalization. An improvement in disease-related clinical outcomes has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

The recommended dosage in adults is BLV 8.5 mg once daily administered by SUBQ injection.

BLV should be continued as long as it is associated with a response to treatment. The optimal treatment duration is unknown.

The efficacy of BLV once daily in the treatment of adults with chronic HDV infection without cirrhosis or with compensated cirrhosis is based on data through Week 144 from a multicenter, randomized, open-label, parallel-arm phase 3 trial, Trial MYR301 (NCT03852719), in which 100 participants received BLV 8.5 mg once daily. The MYR301 protocol specified the BLV dose as 10 mg; however, a dose recovery study later showed that the delivered dose was 8.5 mg.

Further supportive data from an additional 50 adult participants with chronic HDV infection without cirrhosis or with compensated cirrhosis receiving BLV 8.5 mg SUBQ once daily for 96 weeks is available from a randomized, open-label, exploratory phase 2b trial,

Trial MYR204 (NCT03852433). At Week 96, 48% and 22% of participants achieved combined response and undetectable HDV RNA, respectively. At 24 weeks posttreatment, response rates were 26% and 12%, respectively.

Clinical Data on BLV in Participants With Poor Early Virologic Response

A subanalysis of participants in the MYR301 study evaluated whether continued BLV 2 mg or 10 mg treatment up to Week 96 would lead to improved virologic response rates in participants who did not achieve virologic response at Week 24. Of the 14 participants with a nonresponse and the 22 participants with a partial response at Week 24, 43% (n=6) and 82% (n=18), respectively, achieved virologic response at Week 96 with continued BLV treatment.[2]

A subanalysis of participants in the MYR204 study who had a suboptimal response to BLV + PEG-IFNα treatment or had virologic relapse or rebound during the posttreatment follow-up period showed that there was no association between virologic response and amino acid substitutions in NTCP, HBV preS1, or HDAg.[3]

In a subanalysis of participants from the MYR204 and MYR301 studies with chronic HDV who received BLV 2 mg or 10 mg for 96 weeks and had early suboptimal virologic response at Week 24, 7/15 participants with a nonresponse and 25/34 with a partial response achieved a virologic response at Week 96 with continued BLV treatment.[4]

Real-World Data on BLV in Patients With Poor Early Virologic Response

Three studies conducted among patients in the French Early Access Program assessed the efficacy of BLV ± PEG-IFNα with early suboptimal virologic response:

- One study assessed the efficacy of BLV 2 mg once daily ± PEG-IFNα-2a once weekly in patients with poor early virologic response. A total of 56% of patients with an HDV RNA decrease of <1 $\log_{10}$ IU/mL from baseline through Month 3 had an HDV RNA decline >2 $\log_{10}$ IU/mL at Month 12.[5]
- Another study evaluated the efficacy of adding PEG-IFNα to BLV 2 mg or switching from BLV 2 mg to 10 mg ± PEG-IFNα in patients with suboptimal response. In the BLV 2 mg + PEG-IFNα group, 5/6 patients (83.3%) at Month 6 and 6/7 patients (85.7%) at Month 12 achieved a virologic response. In the BLV 10 mg ± PEG-IFNα group, 1/9 (11%) and 2/10 patients (20%) achieved a virologic response after 3 and 6 months, respectively.[6]
- Another study evaluated efficacy and safety outcomes of ≥3 months of BLV 10 mg ± PEG-IFNα-2a administered to 15 patients who responded poorly to ≥3 months of BLV 2 mg. No significant virologic change was observed.[7]

Clinical Data on BLV in Participants With Poor Early Virologic Response

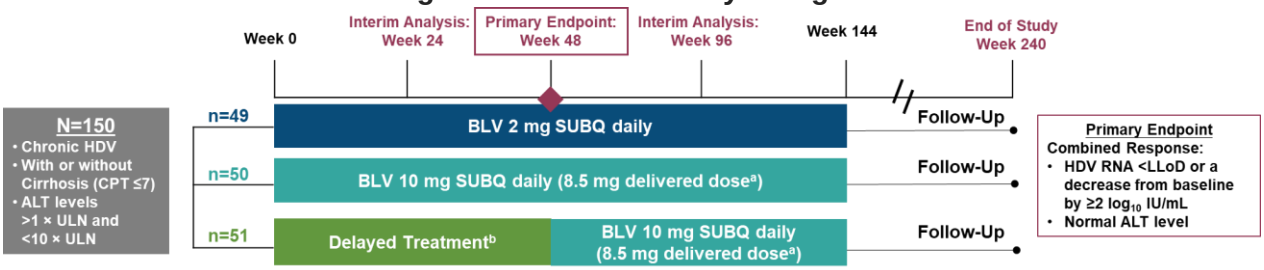
MYR301 Study

Study design and demographics

MYR301 was an open-label, multicenter, randomized, phase 3 study that evaluated the safety and efficacy of BLV in participants with chronic HDV (N=150). The study assessed the safety and efficacy of BLV 2 mg or 10 mg over 144 weeks, compared with delayed

treatment for the first 48 weeks, followed by 96 weeks of BLV 10 mg (Figure 1).[2] The primary endpoint was the combined response of undetectable (<LLoD) HDV RNA or a decrease of ≥2 log_{10} IU/mL from baseline and ALT normalization at Week 48.[8]

Figure 1. MYR301: Study Design[2,9]



Abbreviations: CPT=Child-Pugh-Turcotte; ULN=upper limit of normal.
[a]The MYR301 protocol specified the dose as 10 mg per vial; the delivered dose was 8.5 mg.
[b]Participants in the delayed treatment arm did not receive BLV treatment through Week 48.

Table 1. MYR301: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		BLV 2 mg (n=49)	BLV 10 mg (n=50)	Delayed Treatment (n=51)
Age, mean (SD), years		44 (9)	41 (8.5)	41 (7.5)
Male, n (%)		30 (61)	30 (60)	26 (51)
Race, n (%)	White	41 (84)	43 (86)	40 (78)
	Asian	8 (16)	6 (12)	11 (22)
	Black or African American	0	1 (2)	0
Cirrhosis, n (%)		23 (47)	24 (48)	24 (47)
ALT level, median (Q1, Q3), U/L		90 (65, 136)	108 (63, 161)	80 (57, 116)
HDV RNA, mean (SD), log_{10} IU/mL		5.1 (1.19)	5 (1.46)	5.1 (1.36)
GT, n (%)[a]	HDV-1	49 (100)	48 (96)	51 (100)
	HDV-5	0	1 (2)	0
HBeAg-, n (%)		45 (92)	43 (86)	47 (92)
Prior IFN therapy, n (%)		26 (53)	29 (58)	29 (57)
Concomitant NUC therapy, n (%)		32 (65)	27 (54)	32 (63)

[a]Data missing for 1 participant in the BLV 10 mg group.

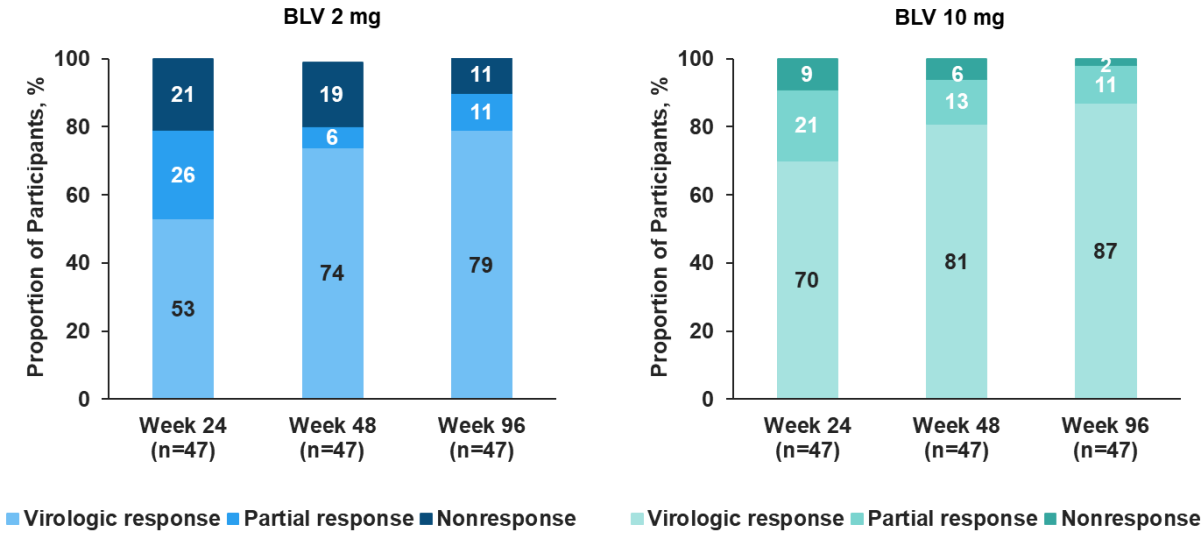
Subanalysis of participants without a virologic response at Week 24

A subanalysis was conducted among participants in the MYR301 study to determine whether continued BLV 2 mg or 10 mg treatment up to Week 96 would lead to improved virologic and biochemical response rates in participants who had a suboptimal virologic response, which included virologic nonresponse and partial response at Week 24. A virologic nonresponse was defined as having an HDV RNA decline of <1 log IU/mL from baseline, and a virologic partial response was defined as an HDV RNA decline of ≥1 and <2 log IU/mL from baseline. Participants who were randomly assigned to immediate treatment with BLV 2 mg or 10 mg and completed 96 weeks of treatment (n=94) were included in the subanalysis.[2]

The proportion of participants in each treatment group with a partial response or nonresponse decreased over time (Figure 2).[9] Of the 14 participants (BLV 2 mg, n=10; BLV 10 mg, n=4) with a nonresponse and 22 participants (BLV 2 mg, n=12; BLV 10 mg, n=10) with a partial response at Week 24, 43% (n=6) and 82% (n=18), respectively, achieved a virologic response at Week 96 with continued BLV treatment. With regard to

overall suboptimal response, similar responses were observed for both doses: 64% of participants (14/22) with a suboptimal response at Week 24 while receiving BLV 2 mg achieved a virologic response at Week 96, compared with 71% (10/14) of those receiving BLV 10 mg. A total of 5/14 nonresponders and 1/22 partial responders at Week 24 had a nonresponse at Week 96.[2]

Figure 2. MYR301: Proportion of Participants With Nonresponse, Partial Response, or Virologic Response From Week 24 to Week 96[9]



By Week 96, participants in both treatment groups with a nonresponse or partial response at Week 24 had decreases in HDV RNA and ALT levels; numerically higher decreases were seen among those who had a partial response than among those who had a nonresponse (Table 2). A total of 77% of participants (17/22) with a partial response and 29% (4/14) of those with a nonresponse achieved ALT normalization at Week 96. Among the 5 participants who had a nonresponse at Week 24 and through Week 96, 4 had >50% decreases in ALT levels from baseline, including 1 participant who had ALT levels within normal limits.[2]

Table 2. MYR301: Changes in ALT and HDV RNA Levels Through Week 96 Among Participants With a Partial Response or Nonresponse at Week 24[9]

	Time Point	Virologic Response Groups at Week 24	
		Nonresponse (n=14)	Partial Response (n=22)
ALT, median (Q1, Q3), U/L	Baseline	117 (57, 146)	78 (59, 125)
	Week 24	57 (46, 94)	36 (28, 44)
	Week 48	59 (36, 75)	31 (27, 43)
	Week 96	54 (32, 76)	28 (21, 40)
	Change from baseline at Week 96	-44 (-79, 7)	-49 (-97, -13)
HDV RNA, mean (SD), log_{10} IU/mL	Baseline	4.4 (2)	5.3 (1.3)
	Week 24	3.8 (1.8)	3.7 (1.4)
	Week 48	3.6 (2.1)	2.6 (1.5)
	Week 96	2.8 (2.1)	1.9 (1.3)
	Change from baseline at Week 96	-1.6 (1.7)	-3.4 (1.3)

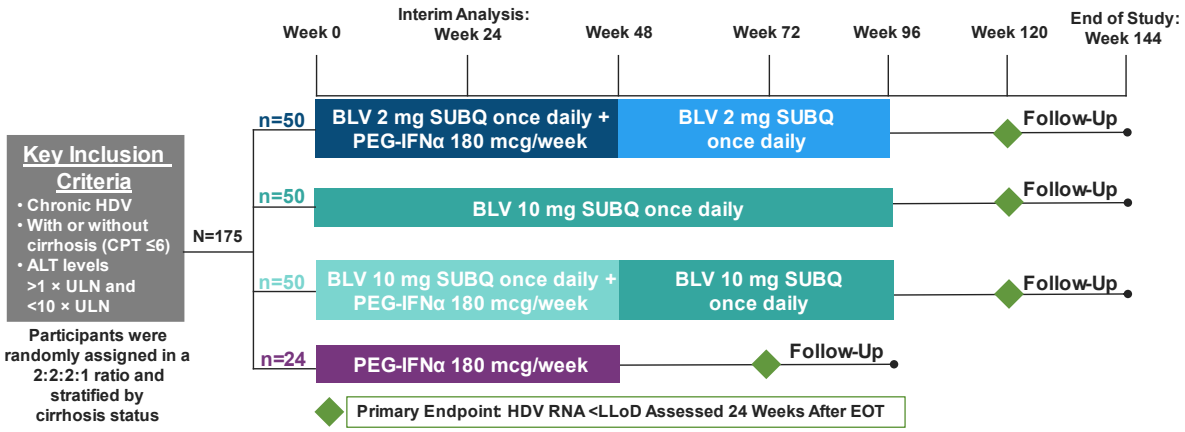
No safety data were reported for this subanalysis.

MYR204: Virologic Analysis of Participants With Suboptimal Response

Study design

MYR204 assessed the efficacy and safety of BLV ± PEG-IFNα treatment for chronic HDV for 96 weeks followed by 48 weeks of off-treatment follow-up (Figure 3). A virologic analysis of participants who received BLV-containing regimens and had a suboptimal response to treatment (N=150) was performed and included an assessment of HBV/HDV GT, NTCP sequencing, deep sequencing of HBV preS1, and deep sequencing of the HDV HDAg gene. Participants were included in the on-treatment RAP if they fell into one of the following categories of suboptimal response to treatment: nonresponse (HDV RNA decline <1 $\log_{10}$ IU/mL from baseline through EOT), virologic breakthrough (2 consecutive HDV RNA values ≥LLoQ if HDV RNA <LLoQ was previously achieved at ≥2 consecutive assessments or a confirmed increase in HDV RNA ≥1 $\log_{10}$ IU/mL from nadir, if the nadir was previously ≥1 $\log_{10}$ IU/mL below baseline levels at 2 consecutive assessments), virologic blip at EOT (met criteria for virologic blip for only 1 visit at EOT), or persistent viremia (HDV RNA >100 IU/mL through EOT). The off-treatment RAP included participants with virologic relapse (undetectable HDV RNA at EOT and detectable levels at follow-up Week 48) or virologic rebound (detectable HDV RNA at EOT and ≥2 $\log_{10}$ IU/mL increase in HDV RNA from EOT to follow-up Week 48).[3]

Figure 3. MYR204: Study Design[3,10]



Results[3]

Overall, 36/150 participants (24%) were included in the RAP at EOT: BLV 10 mg, n=18; BLV 2 mg + PEG-IFNα, n=13; and BLV 10 mg + PEG-IFNα, n=5. Most of these participants (n/N=25/36; 69%) experienced a virologic breakthrough, and 1 participant had a nonresponse to treatment. Suboptimal on-treatment response or posttreatment virologic relapse or rebound were not associated with amino acid substitutions in HBV preS1, HDAg, or NTCP, and there was no evidence of resistance to BLV in participants who had a suboptimal response to treatment.

In the off-treatment RAP, 49/150 participants (33%) experienced virologic relapse or rebound at follow-up Week 48: BLV 10 mg, n=22; BLV 10 mg + PEG-IFNα, n=15; and BLV 2 mg + PEG-IFNα, n=12. During the follow-up period, amino acid development and loss in HDAg was reported in 8 and 9 cases, respectively; none of the substitutions occurred in >1 participant, and all remained sensitive to BLV in vitro.

MYR204 and MYR301 Studies: Subanalysis at Week 96[4]

Study designs and demographics

A subanalysis of participants with chronic HDV from the MYR204 and MYR301 studies who received BLV 2 mg or 10 mg for 96 weeks and had an early suboptimal virologic response at Week 24 was conducted to evaluate whether continued BLV monotherapy led to improvement in virologic and biochemical responses. At Week 24, 49/141 participants (35%) were identified as having a suboptimal virologic response; 15 participants (11%) had a nonresponse (HDV RNA decrease <1 $\log_{10}$ IU/mL from baseline), and 34 participants (24%) had a partial response (HDV RNA decrease ≥1 and <2 $\log_{10}$ IU/mL from baseline).

Table 3. MYR204 and MYR301: Baseline Demographics and Disease Characteristics of Nonresponders and Partial Responders[4]

Key Demographics and Characteristics		Nonresponse (n=15)	Partial Response (n=34)
Age, mean (SD), years		44 (12)	41 (7)
Male, n (%)		11 (73)	21 (62)
Race, n (%)	White	8 (53)	33 (97)
	Asian	7 (47)	1 (3)
Cirrhosis, n (%)		4 (27)	13 (38)
Liver stiffness, mean (SD), kPa		11.8 (7.1)	13 (6.6)
ALT, median (Q1, Q3), U/L		101 (52, 146)	93 (60, 125)
HDV RNA, mean (SD), $\log_{10}$ IU/mL		4.4 (1.9)	5.3 (1.3)
HDV GT 1, n (%)		15 (100)	34 (100)
HBeAg+, n (%)		0	5 (15)
Previous IFN therapy, n (%)		8 (53)	19 (56)
Concomitant NUC therapy, n (%)		9 (60)	18 (53)

Abbreviation: Q=quartile.

Efficacy

The proportions of participants with a nonresponse or partial response in each treatment group decreased with continued treatment. A total of 7/15 participants with a nonresponse and 25/34 with a partial response at Week 24 achieved a virologic response (HDV RNA decrease ≥2 $\log_{10}$ IU/mL from baseline or undetectable HDV RNA) at Week 96 with continued BLV treatment. A total of 8 participants with a nonresponse and 9 participants with a partial response at Week 24 did not achieve a virologic response at Week 96.

Virologic responses at Weeks 48 and 96 in patients with a suboptimal response at Week 24 are presented by BLV dose in Table 4.

Table 4. MYR204 and MYR301: Virologic Responses at Weeks 48 and 96 by Treatment Group Among Patients with a Suboptimal Response at Week 24[4]

Response Category, n		Virologic Response Groups at Week 24			
		BLV 2 mg (n=47)		BLV 10 mg (n=94)	
		Nonresponse (n=10)	Partial Response (n=12)	Nonresponse (n=5)	Partial Response (n=22)
Week 48	Nonresponder	8	1	3	4
	Partial responder	1	0	0	6
	Virologic responder	1	11	2	12
Week 96	Nonresponder	4	1	1	3
	Partial responder	3	0	0	5
	Virologic responder	3	11	4	14

Note: A virologic responder was defined as having undetectable RNA levels or an HDV RNA decline of ≥2 $\log_{10}$ IU/mL from baseline.

Through Week 96, improvements from baseline in ALT and HDV RNA levels were observed among most participants with a partial response or nonresponse in both treatment groups (Table 5).

Table 5. MYR204 and MYR301: Change in ALT and HDV RNA Levels From Baseline to Week 96 by Treatment Group at Week 24[4]

	Virologic Response Groups at Week 24					
	BLV 2 mg (n=47)			BLV 10 mg (n=94)		
	Nonresponse (n=10)	Partial Response (n=12)	Virologic Response (n=25)	Nonresponse (n=5)	Partial Response (n=22)	Virologic Response (n=67)
HDV RNA, mean, $\log_{10}$ IU/mL	-1.8	-3	-3.8	-1.9	-2.7	-3.9
ALT, median, U/L	-44	-55	-43	+7	-65	-61

No safety data were reported for this subanalysis.

Real-World Data on BLV in Patients With Poor Early Virologic Response

French Early Access Program (cATU): BLV 2 mg ± PEG-IFNα[5]

Study design and demographics

A real-world cohort study was conducted between September 2019 and September 2020 to assess the efficacy of BLV 2 mg once daily ± PEG-IFNα-2a once weekly in treating HDV in patients with poor early virologic response. Eligible patients had F2 fibrosis with persistent ALT levels >2 × the upper limit of normal for ≥6 months, compensated cirrhosis, or F3 fibrosis. Virologic response was evaluated at Month 12 according to the virologic response at Month 3 and at Month 18 according to the virologic response at Month 6. A total of 103 patients were included in the study (Table 6).

Table 6. cATU: Baseline Demographics and Characteristics[5]

Key Demographics and Characteristics	BLV 2 mg (n=57)	BLV 2 mg + PEG-IFN (n=46)
Age, mean, years	42.1	41.5
Male, n (%)	42 (73.7)	30 (65.2)
Country of birth, Europe/Africa, n	44 / 13	26 / 19
BMI, mean, kg/m^2	26.2	26
Cirrhosis, n (%)	21 (36.8)	27 (58.7)
Liver stiffness, mean, kPa	15.9	13
ALT level, mean, IU/L	95.3	126.3
HDV RNA level, median, log_{10} IU/mL	6.15	6.2
Undetectable HBV DNA, n (%)	37 (67.3)	28 (65.1)
HBeAg+, n (%)	7 (12.7)	4 (9.8)
Current NUC use, n (%)	47 (82.4)	38 (82.6)
HIV co-infection, n (%)	8 (14)	3 (6.5)

Results

At Month 12, 36% of patients (19/53) receiving BLV and 78% of patients (35/45) receiving BLV + PEG-IFN had undetectable HDV RNA. At Month 18, 32% of patients (11/34) receiving BLV and 60% of patients (12/20) receiving BLV + PEG-IFN had undetectable HDV.

Changes in HDV RNA levels among patients with poor response at Months 3 and 6 in the BLV monotherapy cohort and in the BLV + PEG-IFN cohort are presented in Figure 4 and Figure 5, respectively.

Figure 4. cATU: Changes in HDV RNA Levels Among Patients Receiving BLV Monotherapy Through Month 18[5]

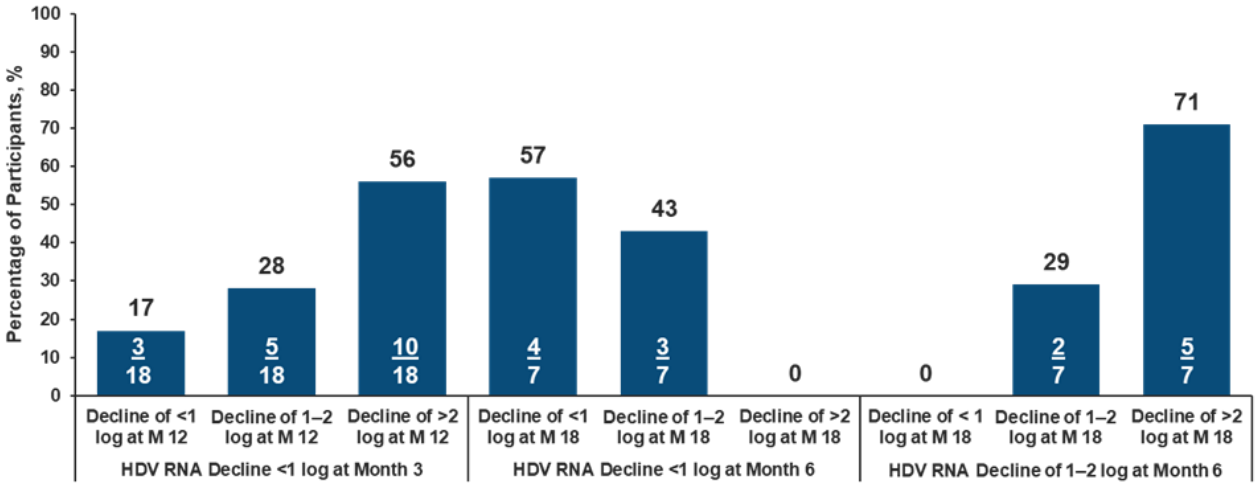
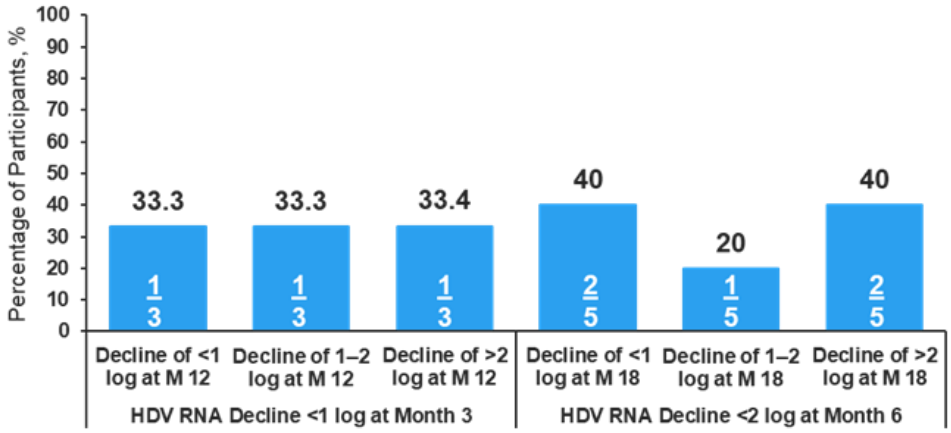


Figure 5. cATU: Changes in HDV RNA Levels Among Patients Receiving BLV + PEG-IFN Through Month 18[5]



French Early Access Program: Adding PEG-IFNα to BLV 2 mg vs Switching to BLV 10 mg[6]

Study design and demographics

A real-world, retrospective study evaluated the effectiveness of adding concomitant PEG-IFNα to BLV 2 mg (n=8) or switching from BLV 2 mg ± PEG-IFNα to BLV 10 mg ± PEG-IFNα (n=12) as HDV treatment in patients with suboptimal response (HDV RNA decline <2 $\log_{10}$ IU/mL from baseline) after 3 months of BLV treatment in the French Early Access Program. Adult patients were consecutively enrolled from September 2019 to September 2020, had compensated cirrhosis or chronic HDV with at least moderate fibrosis (>F2), and had elevated ALT levels. The primary endpoint was virological response (undetectable HDV RNA or decline >2 $\log_{10}$ IU/mL) after at least 3 months of the new treatment regimen.

The baseline demographics of patients who added PEG-IFNα to BLV 2 mg were the following: male, n/N=5/8; age, 19 to 60 years; LSM, 5 to 26.4 kPa; and cirrhosis, n/N=6/8. Patients who switched to BLV 10 mg ± PEG-IFNα had the following baseline demographics: male, n/N=10/12; age, 19 to 73 years; LSM, 8.1 to 28.8 kPa; and cirrhosis, n/N=9/12.

Results

Of the 6 patients who received BLV 2 mg + PEG-IFNα, 5 (83.3%) achieved a virologic response after 6 months of treatment. After 12 months, 6 patients (85.7%) achieved a virologic response, 5 of whom (71.4%) had undetectable HDV RNA; the remaining patient had an HDV RNA decline between 1 and 2 $\log_{10}$ IU/mL. At Month 12, 4 patients (57.1%) achieved normal ALT levels.

Of the patients who switched to BLV 10 mg ± PEG-IFNα, 1/9 (11%) and 2/10 patients (20%) achieved a virologic response after 3 and 6 months, respectively; no patients achieved undetectable HDV RNA. At Month 12, 1/5 patients (20%) achieved normal ALT levels.

ALT levels and mean changes in HDV RNA from time of treatment change to Month 6 are reported in Table 7.

Table 7. Mean HDV RNA Levels and ALT Levels by Treatment Group (de Ledinghen et al)[6]

		BLV 2 mg + PEG-IFNα (n=8)	BLV 10 mg ± PEG-IFNα (n=12)
HDV RNA, mean (SD), log_{10} IU/mL	At treatment change	5.85 (0.91)	6.03 (1.35)
	Month 3	4.54 (1.08)	5.58 (1.53)
	Month 6	2.36 (2.2)	4.67 (1.99)
ALT, range, IU/L	At treatment change	27–189	34–127
	Month 3	28–126	31–85
	Month 6	15–116	26–91

Safety data were not reported for this study.

French Early Access Program: Increased BLV Dosage[7]

Study design and demographics

A real-world, multicenter study was conducted to assess the efficacy and safety of daily BLV 10 mg ± PEG-IFNα-2a for ≥3 months as HBV/HDV treatment in patients who did not respond to ≥3 months of BLV 2 mg once daily as monotherapy or in addition to PEG-IFNα-2a once weekly in the French Early Access Program. Eligible patients also had compensated cirrhosis, severe fibrosis, or moderate fibrosis with elevated ALT levels. A total of 15 patients with chronic HBV/HDV infections were included in the study and had the following demographics: male, 66.7%; mean age, 43 years; cirrhosis, 66.7%; and a median HDV RNA of 6.52 log_{10} IU/mL at the time of inclusion and while receiving BLV 2 mg.

Results

Thirteen patients received BLV 10 mg monotherapy, and 2 patients received BLV 10 mg + PEG-IFNα-2a. The median HDV RNA and ALT levels at baseline in the BLV 10 mg group were 6.08 log_{10} IU/mL and 63.5 IU/L, respectively, and 2 patients had ALT levels <40 IU/L. One patient without cirrhosis who had long-term undetectable HDV RNA levels had a viral load of 5.15 log_{10} IU/mL when he initiated BLV 2 mg and a viral load of 3.43 log_{10} IU/mL when he started BLV 10 mg. When the BLV 10 mg dosage became unavailable, 2 patients switched back to BLV 2 mg with no observed subsequent change in viral load. After ≥6 months of BLV 10 mg ± PEG-IFNα-2a, no significant virological change was observed. The efficacy of BLV 10 mg through Months 9 or 12 is presented in Table 8.

Table 8. Effectiveness of BLV 10 mg in Patients Who Responded Poorly to BLV 2 mg (de Ledinghen et al)[7]

n (%)	Month 3	Month 6	Months 9 or 12
ALT <40 IU/L	3/10 (30)	3/8 (37.5)	3/9 (33.3)
Undetectable HDV RNA or a 2 log_{10} IU/mL decrease from baseline	2/11 (18.2)	2/8 (25)	1/11 (9.1)
Undetectable HDV RNA	1/11 (9.1)	2/8 (25)	0/11 (0)

No side effects were reported.

References

1. Enclosed. Gilead Sciences Inc. HEPCLUDEX® (bulevirtide) injection, for subcutaneous use. US Prescribing Information. Foster City, CA.
2. Wedemeyer H, Aleman S, Brunetto M, et al. Bulevirtide monotherapy in patients with chronic HDV: Efficacy and safety results through week 96 from a phase III randomized trial. *J Hepatol.* 2024;81:621–629.
3. Liu Y, Chang S, Xu S, et al. No amino acid substitution in HBV PreS1, HDAg, or NTCP associated with suboptimal response to bulevirtide in combination with pegylated interferon alfa-2a treatment in participants with chronic hepatitis delta: results from MYR204 a phase 2b study [Abstract SAT-371]. *Journal of Hepatology.* 2024;80(S1):S737-S738.
4. Lampertico P, Wedemeyer H, Brunetto MR, et al. Results From an Integrated Analysis at Week 96: Continued Treatment of Early Virologic Non-responders or Partial Responders With Bulevirtide Monotherapy for Chronic Hepatitis Delta Leads to Improvement in Virologic and Biochemical Responses. [Poster Presentation #63]. Paper presented at: AASLD - The Liver Meeting; November 10-14, 2023; Boston, MA.
5. De Ledinghen V, Bardou-Jacquet E, Metivier S, et al. HDV RNA decline less than 1 log after 6 months of BLV 2 mg monotherapy could define poor-response and lead to therapeutic decision. Data from real-life cohort. [Abstract] Paper presented at: European Association for the Study of the Liver (EASL); June 21-24, 2023; Vienna, Austria.
6. De-Lédinghen V, Hilleret M, Métivier S, et al. Is it useful to add PEG-IFNα in suboptimal responder patients to Bulevirtide 2 mg? Results from the French multicenter early access program. [Poster]. Paper presented at: AASLD - The Liver Meeting; November 10-14, 2023; Boston, MA.
7. De Ledinghen V, Minello A, Ganne-Carrie N, et al. Administration of BLV 10 mg in poor responder patients to 2 mg has no significant virologic effect after at least 6 months of treatment. [Poster SAT-184]. Paper presented at: European Association for the Study of the Liver (EASL); June 21-24, 2023; Vienna, Austria.
8. Wedemeyer H, Aleman S, Brunetto MR, et al. A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. *N Engl J Med.* 2023;389(1):22-32.
9. Wedemeyer H, Aleman S, Brunetto M, et al. Bulevirtide monotherapy in patients with chronic HDV: Efficacy and safety results through week 96 from a phase III randomized trial. [Supplementary]. *J Hepatol.* 2024;81:621–629.
10. Asselah T, Chulanov V, Lampertico P, et al. Bulevirtide Combined with Pegylated Interferon for Chronic Hepatitis D. *N Engl J Med.* 2024;391(2):133-143.

Abbreviations

BLV=bulevirtide-gmod
cATU=Cohort Autorisation Temporaire d'Utilisation
EOT=end of treatment
GT=genotype
HBeAg=hepatitis B envelope antigen
HDAg=hepatitis D antigen
IFN=interferon
LLoD=lower limit of detection
LLoQ=lower limit of quantification
LSM=liver stiffness measurement
NTCP=sodium taurocholate cotransporting polypeptide
NUC=nucleos(t)ide analogue
PEG-IFN/α=pegylated interferon/α
preS1=presurface protein 1
RAP=resistance analysis population
SUBQ=subcutaneous(ly)

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Hepcludex US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hdv/hepcludex/hepcludex_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact gilead.privacy@gilead.com.