GILEAD | Medical Information

Hepcludex® (bulevirtide-gmod) Use in HIV Co-Infection

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 in people with HIV (PWH).

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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]

There is no information in the BLV US Prescribing Information regarding the use of BLV in PWH.

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.

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.

Clinical Data on BLV Use in PWH

In a phase 3 study (MYR301), participants with uncontrolled HIV were excluded; each of the BLV treatment groups had 1 PWH. Data were not presented for the PWH included in the study.[2,3]

In phase 2/2b clinical studies (MYR204, MYR203, and MYR202), PWH were excluded.[4-6]

Real-World Data on BLV Use in PWH

A retrospective, multicenter, real-world study (SAVE-D) evaluated the effectiveness and safety of BLV 2 mg monotherapy in patients with HDV and compensated cirrhosis.

Twenty-four PWH were included; effectiveness results in this patient group through Week 96 were similar to those in the group without HIV. Throughout the study, HIV RNA remained undetectable.[7]

A multicenter observational study was conducted among participants with HDV/HBV in the French Early Access Program to evaluate the efficacy and safety of ≥12 months of BLV 2 mg ± PEG-IFNα. PWH were eligible for inclusion (BLV 2 mg, n=14; BLV + PEG-IFNα, n=5); however, an analysis of data from PWH in this study was not conducted. Most participants achieved virologic response at Month 12, with a numerically higher rate of combined response (ie, undetectable HDV RNA or ≥2 $\log_{10}$ IU/mL decline in HDV RNA levels and ALT normalization) in the BLV 2 mg monotherapy group.[8,9]

A prospective, observational cohort study was conducted among the BuleDelta Cohort to evaluate the efficacy and safety of BLV ± PEG-IFN in participants with chronic HDV; 13 PWH were included, though no analysis of data from PWH in this study was conducted. At Week 48, 76% of participants achieved a virologic response, 50% achieved ALT normalization, and 33% achieved a combined response.[10]

A study that included participants from the French Early Access Program and BuleDelta Cohort was conducted to assess the efficacy and safety of 12 months of treatment with BLV 2 mg ± PEG-IFNα 2a in 38 PWH and with HBV/HDV. The median HDV RNA level decreased from 5.6 $\log_{10}$ IU/mL at baseline to 4.1 $\log_{10}$ IU/mL at Week 48, at which point the median CD4 count was 517 cells/mm^3.[11]

Clinical Data on BLV Use in PWH

In a phase 3 study (MYR301) participants with uncontrolled HIV were excluded; PWH with CD4 counts >500 cells/mL and an HIV RNA below the limit of detection for ≥12 months were permitted to enroll. Within the study, 2 participants with HIV were enrolled, with 1 in each of the BLV 2 mg and BLV 10 mg treatment groups. Data were not presented for the PWH included in the study.[2,3]

In phase 2/2b clinical studies (MYR204, MYR203, and MYR202), PWH were excluded.[4-6]

Real-World Data on BLV Use in PWH

Retrospective European Study (SAVE-D)

Study design and demographics

A retrospective, multicenter, real-world study in Europe evaluated the effectiveness and safety of BLV 2 mg as monotherapy in 244 patients with HDV and compensated cirrhosis. The primary endpoint was the proportion of patients who achieved virologic response, defined as an undetectable HDV RNA or a ≥2-log $_{10}$ IU/mL decrease in HDV RNA from baseline to Week 48.[7]

Baseline demographics in the overall patient population and among PWH are presented in Table 1. Twenty-four patients (10%) had HIV, and all had undetectable HIV RNA levels. The median (IQR) CD4 count and percentage were 338 (257–444) cells/mm^3 and 27% (22–35%), respectively. All PWH in the study were receiving effective ARV treatment, including the following regimens: BIC/FTC/TAF, n=11; RAL/FTC/TAF, n=5; RPV/FTC/TAF,

n=4; DRV + RAL + FTC/TDF, n=1; E/C/F/TAF, n=1; DTG/3TC, n=1; DOR/3TC/TDF, n=1. The PWH in the study were significantly older than the patients without HIV (*P*=0.02).[7,12]

Table 1. SAVE-D: Baseline Demographics and Disease Characteristics Overall and Among PWH[7,12]

Key Demographics and Characteristics	Overall: BLV 2 mg (n=244)	PWH: BLV 2 mg (n=24)
Age, median (IQR), years	49 (40–58)	56 (48–59)
Male, n (%)	148 (61)	17 (71)
CP score, A/B, n (%)	233 (95)[a]/11 (5)[b]	24 (100)/0
Liver stiffness, median (IQR), kPa	18.3 (13–26.3)	20.9 (13.3–26.3)
Esophageal varices, n (%)	91 (54)[c]	10 (42)[d]
Prior decompensation, n (%)	37 (15)[e]	Not reported
HDV genotype 1, n/N (%)	77/82 (94)	Not reported
HDV RNA, median (IQR), log_{10} IU/mL	5.4 (4.1–6.5)	5.3 (3.8–5.9)
Detectable HBV DNA,[f] n/N (%)	52 (21)	Not reported
HBsAg, median (IQR), log_{10} IU/mL	3.8 (3.4–4.1)	3.3 (2.4–3.9)
HBeAg negative, n (%)	227 (93)	20 (83)
Anti-HCV positive, n (%)	18 (7)[g]	Not reported
Current NUC use, n (%)	224 (92)	24 (100)
Previous IFN treatment, n (%)	142 (58)	13 (54)
HCC history, n (%)	18 (7)[h]	3 (13)
ALT level, median (IQR), IU/L	80 (55–130)	73 (51–141)

Abbreviation: CP=Child-Pugh; EGD=esophagogastroduodenoscopy.
[a]CP score of A6 in 59 patients (24%). [b]All had a CP score of B7.
[c]EGD results were available in 169 patients (69%), and 62 (37%) were receiving prophylaxis.
[d]EGD results were available in 16 patients. [e]Ascites, n=30 (12%); bleeding, n=7 (3%).
[f]Per local laboratory, median (IQR) HBV DNA was 1.4 (1–1.5) log IU/mL. [g]All had undetectable HCV RNA.
[h]Active HCC in 14 patients (6%).

Effectiveness results

Overall, 74% of patients had a virologic response by Week 120 (Table 2). Significant improvements from baseline to Week 96 in levels of AST, γ-glutamyltransferase, and albumin were observed during treatment with BLV (each, *P*<0.001). Liver stiffness measurements improved from a median (IQR) of 21.6 (19.9–23.1) kPa at baseline to 14.1 (11.7–16.5) kPa at Week 120. FIB-4 values improved from a median (IQR) of 5.5 (4.9–6) at baseline to 4.8 (3.4–5.6) at Week 120.[13]

Table 2. SAVE-D: Overall Virologic and Biochemical Response Results Through Week 120[13]

Parameter	Baseline (N=244)	Week 24 (n=230)	Week 48 (n=196)	Week 96 (n=129)	Week 120 (n=70)
HDV RNA decline from baseline, median (range), log IU/mL	N/A	1.8 (1–2.7)[a]	2.3 (1.2–3.6)[a]	2.6 (1.5–4.1)[a]	3 (1.6–4)[a]
ALT, median (range), U/L	80 (55–130)	39 (29–53)[a]	36 (27–53)[a]	33 (24–48)[a]	34 (24–49)[a]
Undetectable HDV RNA, %	0	17	27	40	41
Virologic response, %	0	52	64	71	74
Biochemical response,[b] %	8	53	58	63	59
Combined response,[c] %	0	33	43	51	49

[a]*P*<0.001 for change from baseline value.
[b]Defined as ALT normalization (ALT level <40 U/L).
[c]Defined as virologic response and biochemical response.

Effectiveness results through Week 96 for PWH were similar to those of patients without HIV (Table 3); HIV RNA remained undetectable during the study (Table 4).[7]

Table 3. SAVE-D: Effectiveness Results by HIV Status Through Week 96[12]

Parameter, %	Week 24		Week 48		Week 72		Week 96	
	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+
Virologic response	54	36	65	59	67	73	79	80
Biochemical response	54	45	59	65	58	69	56	100[a]
Combined response	35	18	45	41	47	45	52	80

[a]*P*=0.03 for comparison between HIV- and HIV+ patient groups.

Table 4. SAVE-D: Virologic and Biochemical Response Results in PWH Through Week 96[12]

Parameter	Baseline	Week 24	Week 48	Week 72	Week 96
HDV RNA, median (IQR), log_{10} IU/mL	5.3 (3.8–5.9)	3.5 (2.5–4.2)	1.9 (1.5–3.4)	1.8 (1.3–2)	1.5 (0.8–2.5)
ALT, median (IQR), U/L	73 (51–141)	43 (30–55)	30 (28–56)	34 (25–41)	37 (27–39)
Detectable HIV RNA, %	0	0	0	0	0
CD4 count, cells/mm^3	338	457	474	189	186
CD4 percentage	27	31	30	24	24

Safety results[13]

Safety results were reported for up to 120 weeks of BLV treatment (median [range]: 72 [24–120] weeks). A total of 12 patients (5%) discontinued BLV, and 9 patients were lost to follow-up. Reasons for BLV discontinuation consisted of virologic non-response (n=4), long-term undetectable HDV RNA levels (n=3), liver decompensation (n=2), non-compliance (n=2), and Grade 3 maculopapular rash with mild eosinophilia (n=1).

Mild, transient pruritus was reported in 11% of patients, and 3% of patients reported injection site reactions. Bile acid levels increased from a median (IQR) of 15 (9–32) mcmol/L at baseline to 35 (14–54) mcmol/L at Week 120 (*P*<0.001).

Through up to 120 weeks of treatment, 8 deaths (pneumonia, intestinal infarction, non-hepatic neoplasm, HCC progression, gastrointestinal bleeding, and acute-on-chronic liver failures) and 18 liver transplants (HCC, n=15; end-stage liver disease, n=3) occurred; the Week 120 death- and liver transplant-free survival rate was 88%. Eleven (4.5%) de novo HCC events occurred, resulting in a cumulative incidence (95% CI) of 6.1% (3–9%); 7 (2.9%) de novo decompensating events (ascites, n=4; variceal bleeding, n=3) occurred.

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

Study design and demographics

A multicenter, non-randomized, prospective and retrospective observational study evaluated the efficacy and safety of ≥12 months of treatment with BLV 2 mg SUBQ once daily monotherapy (12-month follow-up, n=77; 18-month follow-up, n=78) or BLV 2 mg SUBQ once daily with weekly PEG-IFNα (n=68) in participants with HDV/HBV. PWH were eligible for inclusion (BLV 2 mg, n=14; BLV + PEG-IFNα, n=5); however, an analysis of data from PWH in this study was not conducted.[8]

Eligible participants who underwent treatment within the cATU between September 2019 and September 2020 and had compensated cirrhosis, F3 or F2 fibrosis

(as evaluated by liver biopsy or Fibroscan), and ALT levels >2 × ULN for ≥6 months were included in the final analysis. Treatment regimen and on-treatment dose modifications were made according to the physician's choice.[8]

Table 5. cATU: Baseline Demographics and Disease Characteristics[9]

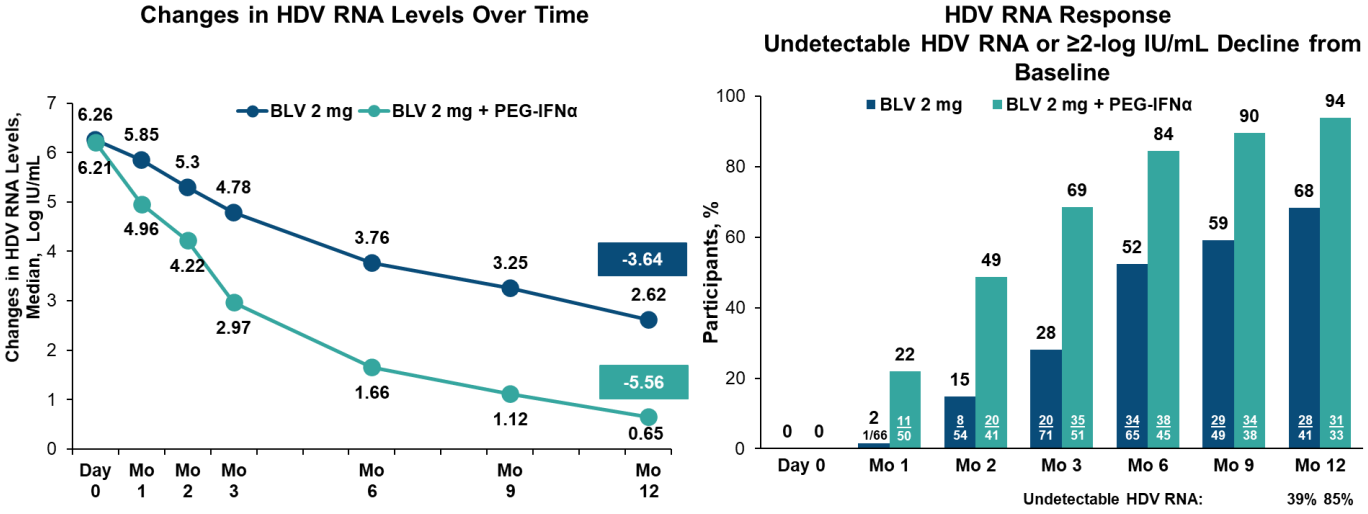
Key Demographics and Characteristics	BLV 2 mg (n=77)	BLV 2 mg + PEG-IFNα (n=68)
Age, mean ± SD, years	41.6±11.8	40.8±10.4
Male, n (%)	54 (70)	45 (66)
HIV co-infection, n (%)	14 (18.2)	7 (10.3)
Cirrhosis, n (%)	48 (62.3)	43 (63.2)
Liver stiffness, mean ± SD,[a] kPa	15.4±11	14.3±12.1
FIB-4 index,[a] mean ± SD	3.03±2.6	2.23±1.4
HDV RNA, median (IQR), log_{10} IU/mL	6.26 (1.3)	6.25 (1.5)
Undetectable HBV DNA, n/N (%)	49/72 (68.1)	40/61 (65.6)
HBeAg positive,[a] n (%)	9 (7.5)	5 (8.2)
Current NUC use, n (%)	64 (83.1)	49 (72.1)
ALT level, mean ± SD, IU/L	69.3±35.7	82.9±40.5

[a]Data were missing for 10 to 13 participants.

Efficacy

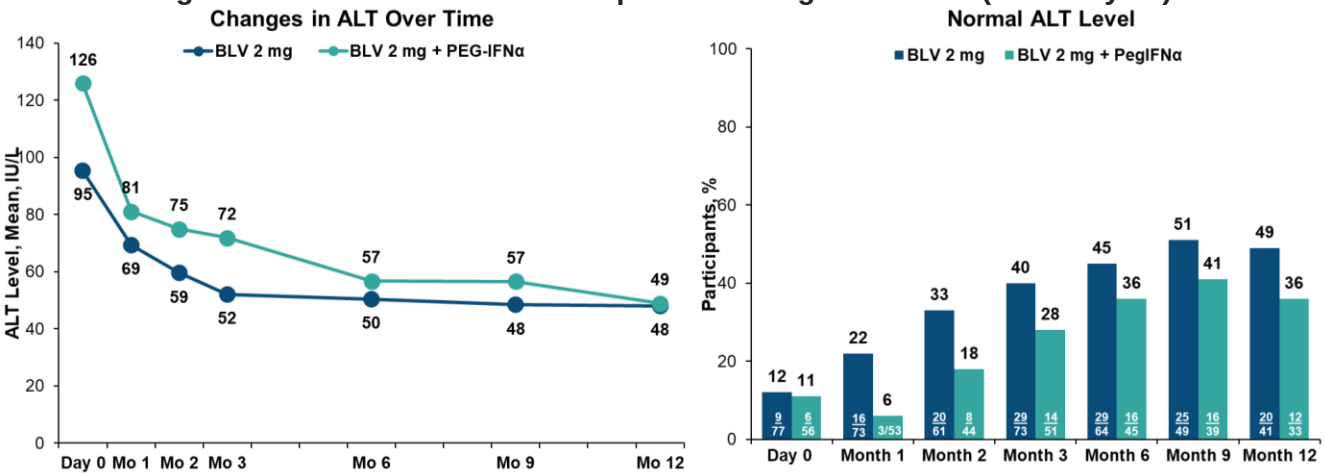
In the PP analysis (12 participants who discontinued PEG-IFNα were excluded from the PP analysis), HDV RNA levels decreased in both groups (Figure 1); however, the study was not adequately powered to compare outcomes by regimen. At Month 12, undetectable HDV RNA levels were observed in 39% of participants (16/41) who received BLV monotherapy and in 85% of participants (28/33) who received BLV + PEG-IFNα. Most participants achieved virologic response, defined as an undetectable HDV RNA level or a ≥2 log_{10} IU/mL decrease from baseline in HDV RNA (Figure 1).

Figure 1. cATU: Virologic Response Through Month 12 (PP Analysis)[9]



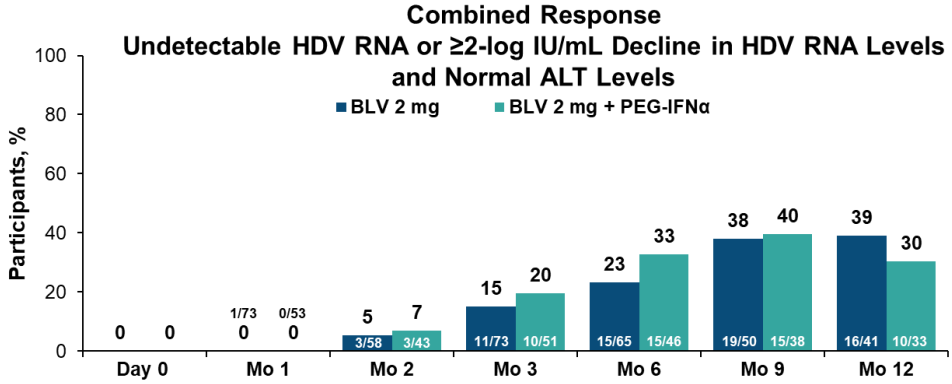
By Month 12, ALT levels decreased in both groups, and ALT normalization was achieved in 49% of participants (20/41) who received BLV 2 mg monotherapy and in 36% of participants (12/33) who received BLV + PEG-IFNα (Figure 2). The combined response rate through Month 12 is shown in Figure 3.

Figure 2. cATU: Biochemical Response Through Month 12 (PP Analysis)[9]



Note: ALT levels <40 IU/L were considered normal.

Figure 3. cATU: Combined Response Rates Through Month 12 (PP Analysis)[9]



Safety

At 12 months of follow-up, BLV treatment was well tolerated, and AEs led to few discontinuations in each group (Table 6). Bile acid elevations were asymptomatic and expected.

Table 6. cATU 12-Month Follow-Up: Safety Outcomes (ITT Analysis)[9]

Safety Outcomes, n (%)	BLV 2 mg (n=77)	BLV 2 mg + PEG-IFNα (n=68)
Any AE	29 (38)	43 (63)
Grade 3–4 AEs	7 (9)[a]	6 (9)[b]
Discontinuation due to an AE	2 (3)[c]	3 (4)[d]
Injection site reactions	2 (3)	2 (3)
Liver-related AEs	4 (5)[e]	2 (3)[f]
Elevated bile acid levels	76 (99)	68 (100)

[a]Included HCC (n=3), ascites, rectal cancer, fatigue, and ovarian hemorrhage.
[b]Included ascites, asthenia, ovarian cancer, neutropenia, fatigue, and variceal bleeding.
[c]Included ascites and rectal cancer.
[d]Included ascites, variceal bleeding, and fatigue.
[e]Included HCC and ascites.
[f]Included ascites and variceal bleeding.

Prospective Cohort Study in France (BuleDelta ANRS)[10]

Study design and demographics

An ongoing national, multicenter, observational cohort study evaluated the efficacy and safety of BLV as monotherapy or in combination with PEG-IFN in participants with chronic HDV. The ANRS BuleDelta study is an ongoing cohort study within the French BLV cATU program. A total of 180 participants were enrolled, and 115 participants had baseline and Week 24 outcome data (preliminary analysis). PWH were included in this study (n=13); however, no analysis of data from PWH in this study was conducted.

Table 7. BuleDelta ANRS Cohort: Baseline Demographics and Disease Characteristics[10]

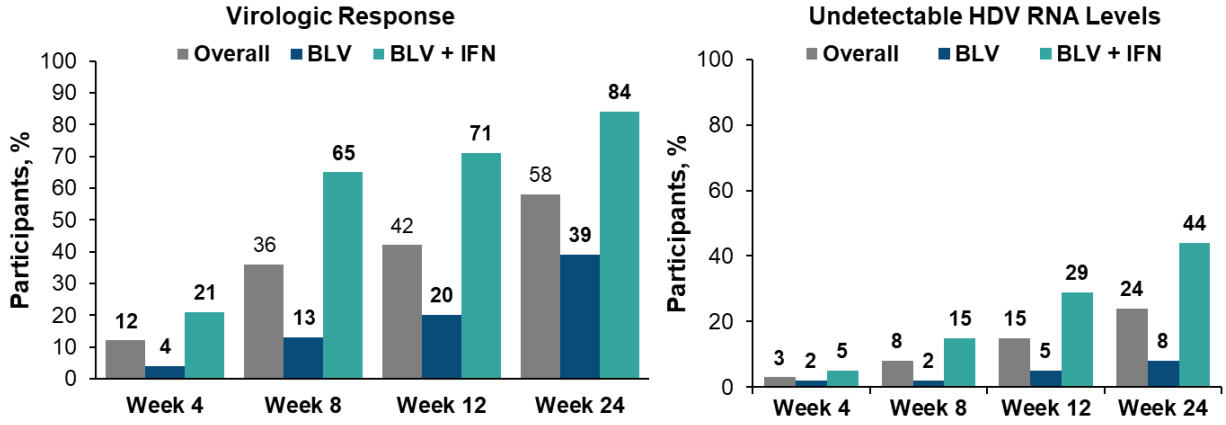
Key Demographics and Characteristics	Overall (N=115)	BLV (n=65)	BLV + PEG-IFN (n=50)
Age, mean ± SD, years	41.9±11	43±11	40.5±10.9
Male, n (%)	81 (70.4)	47 (72.3)	34 (68)
HIV co-infection, n/N (%)	13/98 (13.2)	9/55 (16.4)	4/43 (9.3)
Cirrhosis, n (%)	64 (55.7)	38 (58.5)	26 (52)
Fibroscan, mean ± SD (range), kPa	14.5±10.2 (4.2–59.8)	15.6±10.9 (5–59.8)	13.2±9.3 (4.2–48.8)
HDV RNA, mean ± SD, log_{10} IU/mL	6.3±1.3	6.3±1.3	6.4±1.3
Undetectable HBV DNA, n/N (%)	76/114 (66.7)	46/65 (70.8)	30/49 (61.2)
HBV DNA, mean ± SD, log_{10} IU/mL	2.4±1.5	2±0.8	2.8±1.9
HBsAg, mean ± SD, IU/mL	14,204±38,197	17,940±52,784	10,374±10,274
Current NUC use, n (%)	93 (80.9)	54 (83.1)	39 (78)
ALT level, mean ± SD, IU/L	116.4±86.3	107.4±78.8	127.9±94.6
Platelets, mean ± SD, G/L	143.7±57.5	139.7±58.2	149±56.7
Duration of BLV treatment, mean ± SD (range), months	17.9±6.5 (1.4–30.9)	17.6±6.4 (7.2–30.9)	18.2±6.6 (1.35–29.6)

Efficacy results

Efficacy results at Week 24

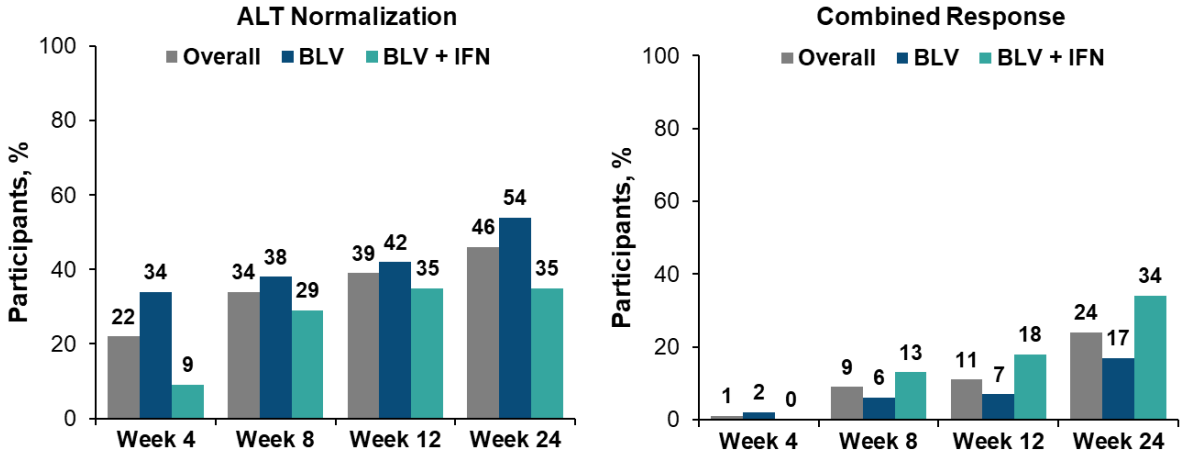
The proportions of participants who achieved virologic and biochemical responses through Week 24, overall and according to treatment regimen (BLV vs BLV + PEG-IFN), are summarized in Figure 4 and Figure 5. The virologic response rate was higher in participants who received BLV + PEG-IFN (84%) than in participants who received BLV without PEG-IFN (39%), whereas the ALT normalization rate was lower in participants who received the combination (35% vs 54%, respectively). In multivariate analyses, treatment with PEG-IFN between baseline and Week 12 was significantly associated with a virologic response (defined as undetectable HDV RNA levels or a ≥2 log IU/mL decrease from baseline in HDV RNA levels) at Week 24, with an odds ratio of 8.4 (95% CI: 3.39–20.79; *P*<0.0001).

Figure 4. BuleDelta ANRS Cohort: Rates of Virologic Response and Undetectable HDV RNA Levels Through Week 24[10]



Note: Virologic response was defined as undetectable HDV RNA levels or a ≥2 log IU/mL decrease from baseline in HDV RNA levels.

Figure 5. BuleDelta ANRS Cohort: Rates of ALT Normalization and Combined Response Through Week 24[10]

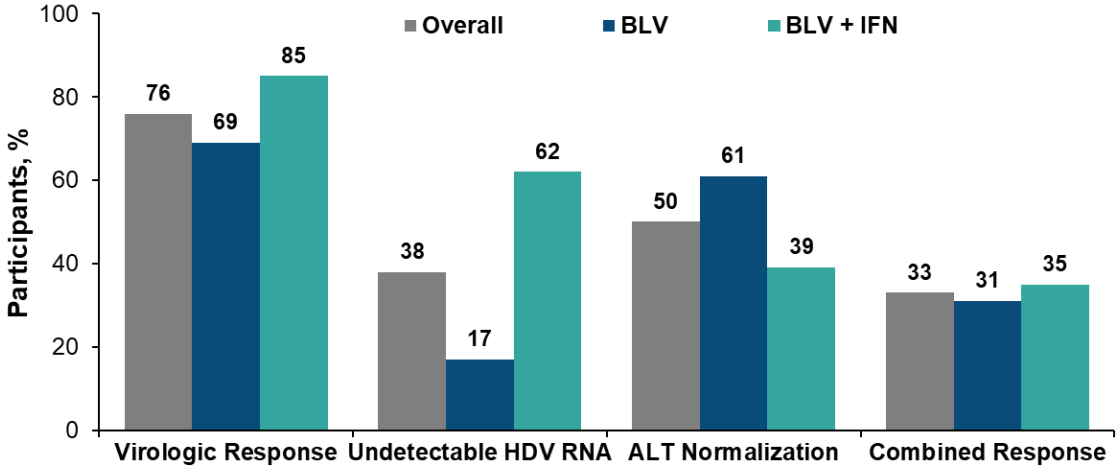


Note: Combined response was defined as a virologic response (undetectable HDV RNA levels or a ≥2 log IU/mL decrease from baseline in HDV RNA levels) with ALT normalization.

Efficacy results at Week 48

Efficacy data through Week 48 were available for 55 participants (BLV, n=29; BLV + PEG-IFN, n=26). Virologic and biochemical response rates at Week 48 are summarized in Figure 6. At Week 48, 76% of participants achieved a virologic response, 50% achieved ALT normalization, and 33% achieved a combined response (ie, virologic response with ALT normalization).

Figure 6. BuleDelta ANRS Cohort: Rates of Virologic and Biochemical Response at Week 48[10]



Note: Virologic response was defined as undetectable HDV RNA levels or a ≥2 log IU/mL decrease from baseline in HDV RNA levels.

Safety results

A summary of safety outcomes among the 128 participants with safety data through Week 24 is presented in Table 8. One death occurred in a participant with decompensated cirrhosis and HCC who had been treated for 2 years with BLV without PEG-IFN.

Table 8. BuleDelta ANRS Cohort: Safety Outcomes Through Week 24[10]

Safety Outcomes, n (%)	Overall (N=128)	BLV (n=68)	BLV + PEG-IFN (n=60)
Grade 3/4 AEs	53 (41)	19 (27)	34 (60)
SAEs	28 (22)	13 (18)	15 (26)
SAEs related to BLV	15 (12)	9 (13)	6 (11)
Increased bile acid SAEs[a]	13 (10)	9 (13)	4 (7)
Treatment discontinuation or interruption	13 (10)	5 (7)[b]	8 (13)[c]

[a]Bile acid levels >15 × ULN.
[b]Three participants reinitiated BLV.
[c]BLV discontinued, n=1; IFN discontinued, n=3; both BLV and IFN discontinued, n=4. Among the participants who discontinued both BLV and IFN, 3 reinitiated BLV, and 1 reinitiated IFN.

BLV ± PEG-IFNα 2a in PWH and HBV/HDV[11]

Study design and demographics

A study that included participants from the French Early Access Program and BuleDelta Cohort was conducted to assess the efficacy and safety of 12 months of treatment with BLV 2 mg ± PEG-IFNα 2a in PWH and HBV/HDV. The study included 38 participants who received either BLV 2 mg SUBQ once daily or BLV 2 mg SUBQ once daily + PEG-IFNα 2a once weekly. Baseline demographics are included in Table 9.

Table 9. Baseline Demographics and Disease Characteristics (de Ledinghen et al)[11]

Key Demographics and Characteristics		BLV ± PEG-IFNα 2a (N=38)
Age, mean, years		47.7
Male, %		73.7
Cirrhosis, %		68.4
HDV RNA, median, log_{10} IU/mL		5.6
HIV RNA, median, copies/mL		32
CD4, median, cells/mm^3		558
ARV regimen,[a] n (%)	Bitherapy[b] + integrase inhibitor alone	17 (47.2)
	Bitherapy[b] + non-nucleos(t)ide reverse transcriptase inhibitor alone	11 (30.6)
	Bitherapy[b] + antiprotease alone	3 (8.3)
	Bitherapy[b] + combination of two molecules	5 (13.8)
	ABC/DTG/3TC	2 (5.7)

Abbreviation: ABC=abacavir.
[a]Data available for 36 participants.
[b]Bitherapy included FTC/TAF (n=22; 61.1%) or FTC/TDF (n=12; 33.3%).

Efficacy

Of the 38 participants included in the study, 18 and 10 participants had detectable HIV RNA levels at baseline and Week 48/end of treatment, respectively. At Week 48/end of treatment, the median CD4 count was 517 cells/mm^3. The median HDV RNA level decreased over time with 5.6 log_{10} IU/mL at baseline, 4.5 log_{10} IU/mL at Week 12, 3.5 log_{10} IU/mL at Week 24, 3.5 log_{10} IU/mL at Week 36, and the median HDV RNA was 4.1 log_{10} IU/mL at Week 48. Changes in ALT and HDV RNA levels from baseline through Week 48 for participants receiving BLV and BLV + PEG-IFNα 2a are presented in Figure 7 and Figure 8, respectively.

Figure 7. Changes in HDV RNA and ALT Levels Through Week 48 in Participants Receiving BLV Monotherapy (PP Analysis; de Ledinghen et al)[11]

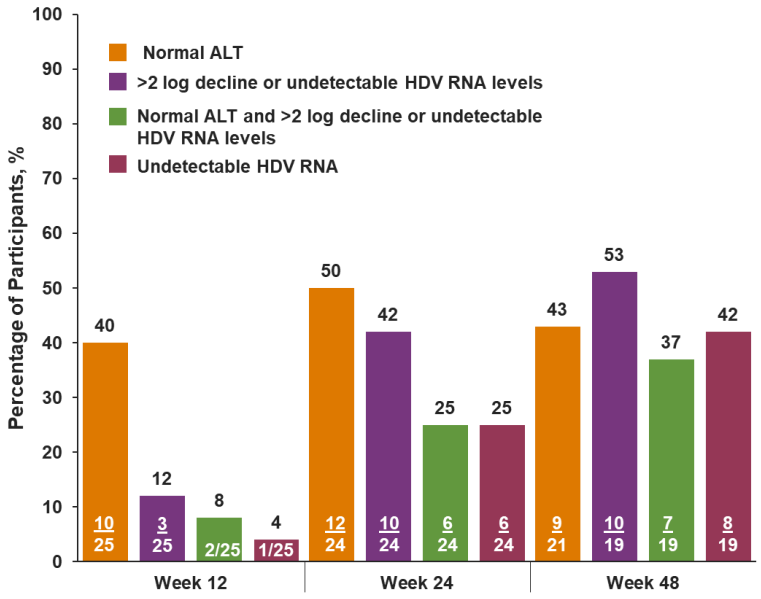
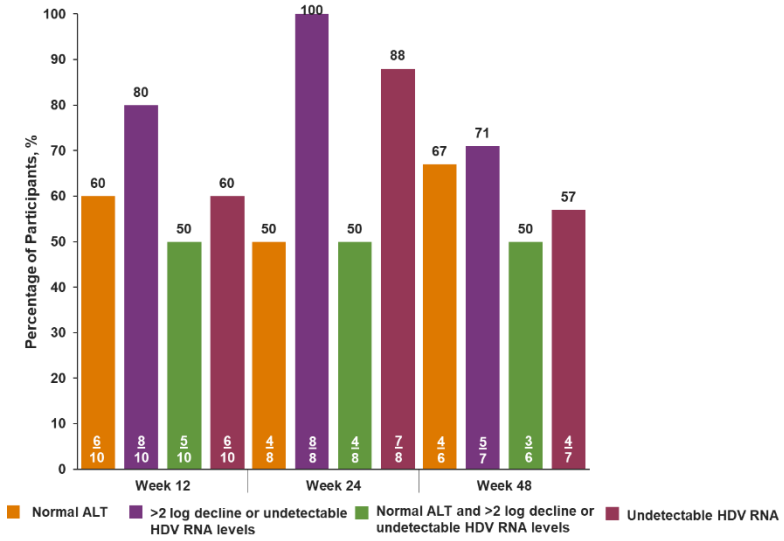


Figure 8. Changes in HDV RNA and ALT Levels Through Week 48 in Participants Receiving BLV + PEG-IFNα 2a (PP Analysis; de Ledinghen et al)[11]



Safety

Ten participants (26.3%) discontinued treatment at or before Week 48 for the following reasons: AEs, n=2 (n=1, variceal bleeding; n=1, thrombopenia); loss to follow-up or participant decision, n=4; and other reasons, n=4.

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Abbreviations

3TC=lamivudine
AE=adverse event
ANRS=l'Agence Nationale de Recherches sur le SIDA et les hépatites virales
ARV=antiretroviral
BIC=bictegravir
BLV=bulevirtide-gmod
cATU=Cohort Temporary Authorization for Use in France
CD=clusters of differentiation
DOR=doravirine
DRV=darunavir
DTG=dolutegravir
E/C/F/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
FIB-4=Fibrosis-4
FTC=emtricitabine
HBeAg=hepatitis B envelope antigen
HBsAg=hepatitis B surface antigen
HCC=hepatocellular carcinoma
IFN=interferon
NUC=nucleos(t)ide analogue
PEG=pegylated
PP=per protocol
PWH=people with HIV
RAL=raltegravir
RPV=rilpivirine
SAE=serious adverse event
SUBQ=subcutaneous(ly)
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
ULN=upper limit of normal

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:

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Adverse Event Reporting

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

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