Clinical trial results:
A Multicenter, Open-label, Randomized Phase 3 Clinical Study to Assess Efficacy and Safety of Bulevirtide in Patients with Chronic Hepatitis Delta

Summary

EudraCT number	2019-001213-17
Trial protocol	SE DE IT
Global end of trial date	08 August 2024

Results information

Result version number	v1 (current)
This version publication date	21 August 2025
First version publication date	21 August 2025

Trial information

Trial identification

Sponsor protocol code	MYR301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Clinicaltrials.gov: NCT03852719

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of bulevirtide administered subcutaneously for 48 weeks at a dose of 2 mg or 10 mg once daily for treatment of chronic hepatitis delta in comparison to delayed treatment.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international
scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 14
Country: Number of subjects enrolled	Germany: 27
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Russian Federation: 85
Worldwide total number of subjects	150
EEA total number of subjects	65

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	150
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Germany, Italy, Russia, and Sweden.

Pre-assignment

Screening details:

183 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Delayed Treatment/Bulevirtide 10 mg/Day

Arm description:

After an observational period of 48 weeks, participants received bulevirtide 10 mg/day subcutaneous (SC) injection for 96 weeks and were followed for up to 96 weeks (Up to Week 240).

Arm type	Experimental
Investigational medicinal product name	Bulevirtide 10 mg
Investigational medicinal product code	
Other name	Myrcludex B, Hepcludex
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via SC injections.

Arm title	Bulevirtide 2 mg/day

Arm description:

Participants received bulevirtide 2 mg/day SC injection for 144 weeks and were followed for up to 96 weeks (Up to Week 240).

Arm type	Experimental
Investigational medicinal product name	Bulevirtide 2 mg
Investigational medicinal product code	
Other name	Myrcludex B, Hepcludex
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via SC injections.

Arm title	Bulevirtide 10 mg/Day

Arm description:

Participants received bulevirtide 10 mg/day SC injection for 144 weeks and were followed for up to 96 weeks (Up to Week 240).

Arm type	Experimental
Investigational medicinal product name	Bulevirtide 10 mg
Investigational medicinal product code	
Other name	Myrcludex B, Hepcludex
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
Administered via SC injections.

Number of subjects in period 1	Delayed Treatment/Bulevirtide 10 mg/Day	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day
Started	51	49	50
Completed	28	28	30
Not completed	23	21	20
Physician decision	5	4	1
Adverse Event	2	1	4
Death	1	-	-
Pregnancy	2	1	-
Withdrawal of consent	8	8	9
Progressive disease	1	4	1
Lost to follow-up	1	-	-
Reason not Specified	3	3	5

Baseline characteristics

Reporting groups	
Reporting group title	Delayed Treatment/Bulevirtide 10 mg/Day
Reporting group description:	
After an observational period of 48 weeks, participants received bulevirtide 10 mg/day subcutaneous (SC) injection for 96 weeks and were followed for up to 96 weeks (Up to Week 240).	
Reporting group title	Bulevirtide 2 mg/day
Reporting group description:	
Participants received bulevirtide 2 mg/day SC injection for 144 weeks and were followed for up to 96 weeks (Up to Week 240).	
Reporting group title	Bulevirtide 10 mg/Day
Reporting group description:	
Participants received bulevirtide 10 mg/day SC injection for 144 weeks and were followed for up to 96 weeks (Up to Week 240).	

Reporting group values	Delayed Treatment/Bulevirtide 10 mg/Day	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day
Number of subjects	51	49	50
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	51	49	50
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41	44	41
standard deviation	± 7.5	± 9.0	± 8.5
Gender categorical Units: Subjects			
Female	25	19	20
Male	26	30	30
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	11	8	6
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	40	41	43
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Liver stiffness			
Units: kPa			
arithmetic mean	15.3	14.0	14.8
standard deviation	± 8.95	± 8.19	± 9.26
Hepatitis Delta Virus (HDV) Ribonucleic Acid (RNA)			
Units: log10 IU/mL			
arithmetic mean	5.08	5.10	4.96
standard deviation	± 1.358	± 1.194	± 1.461

Reporting group values	Total		
Number of subjects	150		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	150		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	64		
Male	86		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	25		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	124		
More than one race	0		
Unknown or Not Reported	0		
Liver stiffness			
Units: kPa			
arithmetic mean			
standard deviation	-		
Hepatitis Delta Virus (HDV) Ribonucleic Acid (RNA)			
Units: log10 IU/mL			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Delayed Treatment/Bulevirtide 10 mg/Day

Reporting group description:

After an observational period of 48 weeks, participants received bulevirtide 10 mg/day subcutaneous (SC) injection for 96 weeks and were followed for up to 96 weeks (Up to Week 240).

Reporting group title	Bulevirtide 2 mg/day

Reporting group description:

Participants received bulevirtide 2 mg/day SC injection for 144 weeks and were followed for up to 96 weeks (Up to Week 240).

Reporting group title	Bulevirtide 10 mg/Day

Reporting group description:

Participants received bulevirtide 10 mg/day SC injection for 144 weeks and were followed for up to 96 weeks (Up to Week 240).

Subject analysis set title	Delayed Treatment
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Observation period of 48 weeks.

Subject analysis set title	Bulevirtide 2 mg/Day
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received bulevirtide 2 mg/day SC injection for 48 weeks which continued up to 144 weeks and were followed for 96 weeks (Up to Week 240).

Subject analysis set title	Bulevirtide 10 mg/Day
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received bulevirtide 10 mg/day SC injection for 48 weeks which continued up to 144 weeks and were followed for 96 weeks (Up to Week 240).

Subject analysis set title	Delayed Treatment/Bulevirtide 10 mg/Day
Subject analysis set type	Sub-group analysis

Subject analysis set description:

After an observational period of 48 weeks, participants received bulevirtide 10 mg/day SC injection for 96 weeks and were followed for up to 96 weeks (Up to Week 240).

Primary: Percentage of Participants With Combined Response at Week 48

End point title	Percentage of Participants With Combined Response at Week 48

End point description:

Combined response was defined as fulfilment of two conditions simultaneously: Undetectable (< lower limit of quantification (LLOQ, target not detected)) HDV RNA or decrease by ≥ 2 log10 IU/mL from baseline; and ALT normalization.
Analysis Population Description: The Full Analysis Set included participants randomized to delayed treatment arm or randomized to bulevirtide and received bulevirtide at least once after randomization. Participants were grouped according to randomized treatment. The arm titles and descriptions in this outcome measure are entered accordingly.

End point type	Primary

End point timeframe:

Week 48

End point values	Delayed Treatment	Bulevirtide 2 mg/Day	Bulevirtide 10 mg/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	51	49	50	
Units: percentage of participants				
number (confidence interval 95%)	2.0 (0.0 to 10.4)	44.9 (30.7 to 59.8)	48.0 (33.7 to 62.6)	

Statistical analyses

Statistical analysis title	Delayed Treatment V/s Bulevirtide 2 mg/Day
Comparison groups	Delayed Treatment v Bulevirtide 2 mg/Day
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [1]
Method	Fisher exact
Parameter estimate	Difference in percentages
Point estimate	42.9
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	27
upper limit	58.5

Notes:

[1] - Fisher's exact test was used for comparison of bulevirtide 2 mg versus Delayed Treatment using a significance level of 0.04 at Week 48.

Statistical analysis title	Delayed Treatment V/s Bulevirtide 10 mg/Day
Comparison groups	Delayed Treatment v Bulevirtide 10 mg/Day
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [2]
Method	Fisher exact
Parameter estimate	Difference in percentages
Point estimate	46
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	30.5
upper limit	61.4

Notes:

[2] - Fisher's exact test was used for comparison of bulevirtide 10 mg versus Delayed Treatment using a significance level of 0.04 at Week 48.

Secondary: Percentage of Participants With Undetectable HDV RNA at Week 48

End point title	Percentage of Participants With Undetectable HDV RNA at Week 48

End point description:

Undetectable HDV RNA at Week 48 means undetectable (< LLOQ, target not detected) HDV RNA at Week 48.
Analysis Population Description : Participants in the Full Analysis Set were analyzed. Participants were grouped according to randomized treatment. The arm titles and descriptions in this outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Week 48

End point values	Delayed Treatment	Bulevirtide 2 mg/Day	Bulevirtide 10 mg/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	51	49	50	
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 7.0)	12.2 (4.6 to 24.8)	20.0 (10.0 to 33.7)	

Statistical analyses

Statistical analysis title	Bulevirtide 2 mg/Day V/s Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/Day v Bulevirtide 10 mg/Day
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4139 [3]
Method	Fisher exact
Parameter estimate	Difference in percentages
Point estimate	7.8
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-8.5
upper limit	24.3

Notes:

[3] - Fisher's exact test was used for the comparison of bulevirtide 10 mg versus bulevirtide 2 mg using a significance level of 0.04 at Week 48.

Secondary: Percentage of Participants With Alanine Aminotransferase (ALT) Normalization at Week 48

End point title	Percentage of Participants With Alanine Aminotransferase (ALT) Normalization at Week 48

End point description:

ALT normalization was defined as an ALT value within the normal range, based on the central

laboratories [Russian sites: ≤ 31 U/L for females and ≤ 41 U/L for males; all other sites: ≤ 34 U/L for females and ≤ 49 U/L for males]).
Analysis Population Description : Participants in the Full Analysis Set were analyzed. Participants were grouped according to randomized treatment. The arm titles and descriptions in this outcome measure are entered accordingly.

End point type	Secondary
End point timeframe:	
Week 48	

End point values	Delayed Treatment	Bulevirtide 2 mg/Day	Bulevirtide 10 mg/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	51	49	50	
Units: percentage of participants				
number (confidence interval 95%)	11.8 (4.4 to 23.9)	51.0 (36.3 to 65.6)	56.0 (41.3 to 70.0)	

Statistical analyses

Statistical analysis title	Delayed Treatment V/s Bulevirtide 2 mg/Day
Comparison groups	Bulevirtide 2 mg/Day v Delayed Treatment
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [4]
Method	Fisher exact
Parameter estimate	Difference in percentages
Point estimate	39.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	20
upper limit	55.8

Notes:

[4] - Fisher's exact test was used for comparison of bulevirtide 2 mg versus Delayed treatment using a significance level of 0.05.

Statistical analysis title	Delayed Treatment V/s Bulevirtide 10 mg/Day
Comparison groups	Delayed Treatment v Bulevirtide 10 mg/Day
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [5]
Method	Fisher exact
Parameter estimate	Difference in percentages
Point estimate	44.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	25.8
upper limit	59.9

Notes:

[5] - Fisher's exact test was used for comparison of bulevirtide 10 mg versus Delayed treatment using a significance level of 0.05.

Secondary: Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 48

End point title	Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 48

End point description:

ANCOVA was used for analysis.
Analysis Population Description : Participants in the Full Analysis Set with available data were analyzed. Data is reported separately for changes from Baseline at Week 48 for the Delayed Treatment arm and for Delayed Treatment/Bulevirtide 10 mg/day arm after 48 weeks of BLV 10 mg treatment. Participants were grouped according to randomized treatment and study design. The arm titles and descriptions in the outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Baseline (Baseline for Delayed Treatment/Bulevirtide 10 mg/day is reset at Week 48), Week 48

End point values	Delayed Treatment	Bulevirtide 2 mg/Day	Bulevirtide 10 mg/Day	Delayed Treatment/Bulevirtide 10 mg/Day
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	46	48	42	48
Units: kPa				
least squares mean (confidence interval 95%)	0.87 (-0.79 to 2.53)	-3.06 (-4.67 to -1.45)	-3.16 (-4.88 to -1.43)	-3.36 (-4.60 to -2.12)

Statistical analyses

Statistical analysis title	Delayed Treatment V/s Bulevirtide 10 mg/Day
Comparison groups	Delayed Treatment v Bulevirtide 10 mg/Day
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-4.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.39
upper limit	-1.65

Notes:

[6] - Least squares (LS) means, standard errors (SE) and 95% CIs were from an analysis of covariance (ANCOVA) model for change from baseline at W48 in liver stiffness adjusted for treatment group, region, and presence of cirrhosis; with baseline liver stiffness as a covariate.

Statistical analysis title	Delayed Treatment V/s Bulevirtide 2 mg/Day
Comparison groups	Delayed Treatment v Bulevirtide 2 mg/Day
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.0009
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-3.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.23
upper limit	-1.63

Notes:

[7] - Least squares (LS) means, standard errors (SE) and 95% CIs were based on the mixed-effects model for repeated measurements (MMRM) model for change from baseline with treatment (BLV 2 mg, BLV 10 mg, and DT to BLV 10 mg group), region, presence of cirrhosis, visit and treatment by visit interaction as fixed effects, and baseline value as a covariate.

Secondary: Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 96

End point title	Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 96

End point description:

Mixed model for repeated measurements (MMRM) was used for analysis.
Analysis Population Description : Participants from Full Analysis Set with available data were analyzed. Participants were grouped according to randomized treatment and study design. The arm titles and descriptions in the outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Baseline (Baseline for Delayed Treatment/Bulevirtide 10 mg/day is reset at Week 48), Week 96

End point values	Bulevirtide 2 mg/Day	Bulevirtide 10 mg/Day	Delayed Treatment/Bulevirtide 10 mg/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	47	47	48	
Units: kPa				
least squares mean (confidence interval	-4.31 (-5.54 to	-4.88 (-6.11 to	-4.20 (-5.41 to	

95%)	-3.08)	-3.65)	-2.98)	

Statistical analyses

Statistical analysis title	Bulevirtide 2 mg/Day V/s Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/Day v Bulevirtide 10 mg/Day
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.5156
Method	MMRM
Parameter estimate	Difference in Least Square (LS) Mean
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	2.3

Notes:

[8] - Least squares (LS) means, standard errors (SE) and 95% CIs were based on the mixed-effects model for repeated measurements (MMRM) model for change from baseline with treatment (BLV 2 mg, BLV 10 mg, and DT to BLV 10 mg group), region, presence of cirrhosis, visit and treatment by visit interaction as fixed effects, and baseline value as a covariate.

Secondary: Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 144

End point title	Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 144[9]

End point description:

MMRM was used for analysis.
Analysis Population Description : Participants from Full Analysis Set with available data were analyzed. Participants were grouped according to randomized treatment and study design. The arm titles and descriptions in the outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Baseline, Week 144

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical comparison was planned or performed.

End point values	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	43		
Units: kPa				
least squares mean (confidence interval 95%)	-5.24 (-6.85 to -3.63)	-4.03 (-5.67 to -2.40)		

Statistical analyses

Statistical analysis title	Bulevirtide 2 mg/Day V/s Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/day v Bulevirtide 10 mg/Day
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.2977
Method	MMRM
Parameter estimate	Difference in Least Square (LS) Mean
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	1.08

Notes:

[10] - Least squares (LS) means, standard errors (SE) and 95% CIs were based on the mixed-effects model for repeated measurements (MMRM) model for change from baseline with treatment (BLV 2 mg, BLV 10 mg, and DT to BLV 10 mg group), region, presence of cirrhosis, visit and treatment by visit interaction as fixed effects, and baseline value as a covariate.

Secondary: Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 192

End point title	Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 192[11]

End point description:

Participants from Full Analysis Set with available data were analyzed. Participants were grouped according to randomized treatment and study design. The arm titles and descriptions in the outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Baseline (Baseline for DT to BLV 10 mg was reset at Week 48), Week 192

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical comparison was planned or performed.

End point values	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day	Delayed Treatment/Bulevirtide 10 mg/Day	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	35	34	35	
Units: kPa				
least squares mean (confidence interval 95%)	-3.74 (-5.28 to -2.20)	-3.70 (-5.27 to -2.14)	-1.91 (-3.49 to -0.34)	

Statistical analyses

Statistical analysis title	Bulevirtide 2 mg/Day V/s Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/day v Bulevirtide 10 mg/Day
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.9719 [13]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.23
upper limit	2.15

Notes:

[12] - Least squares (LS) means, standard errors (SE) and 95% CIs were based on the mixed-effects model for repeated measurements (MMRM) model for change from baseline with treatment (BLV 2 mg, BLV 10 mg, and DT to BLV 10 mg group), region, presence of cirrhosis, visit and treatment by visit interaction as fixed effects, and baseline value as a covariate.
[13] - P-value was based on the mixed-effects model for repeated measurements (MMRM) model.

Secondary: Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 240

End point title	Change From Baseline in Liver Stiffness, as Measured by Elastography at Week 240[14]

End point description:

MMRM was used for analysis.
Analysis Population Description : Participants from Full Analysis Set with available data were analyzed. Participants were grouped according to randomized treatment and study design. The arm titles and descriptions in the outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Baseline (Baseline for DT to BLV 10 mg was reset at Week 48), Week 240

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical comparison was planned or performed.

End point values	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day	Delayed Treatment/Bulevirtide 10 mg/Day	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28	29	28	
Units: kPa				
least squares mean (confidence interval 95%)	-1.20 (-3.71 to 1.31)	-3.31 (-5.78 to -0.84)	-3.59 (-6.14 to -1.04)	

Statistical analyses

Statistical analysis title	Bulevirtide 2 mg/Day V/s Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/day v Bulevirtide 10 mg/Day
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.2369 [16]
Method	MMRM
Parameter estimate	LS-Mean of Difference
Point estimate	2.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	5.63

Notes:

[15] - Least squares (LS) means, standard errors (SE), 95% CIs were based on the mixed-effects model for repeated measurements (MMRM) model for change from baseline
[16] - P-value was based on the mixed-effects model for repeated measurements (MMRM) model.

Secondary: Percentage of Participants With Undetectable HDV RNA 24 Weeks After Scheduled End of Treatment (Sustained Virological Response)

End point title	Percentage of Participants With Undetectable HDV RNA 24 Weeks After Scheduled End of Treatment (Sustained Virological Response)[17]

End point description:

Undetectable HDV RNA 24 Weeks after Scheduled End of Treatment means undetectable (< LLOQ, target not detected) HDV RNA at Week 168.
Analysis Population Description : Participants in the Full Analysis Set were analyzed. Participants were grouped according to randomized treatment and study design. The arm titles and descriptions in the outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Week 168

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical comparison was planned or performed.

End point values	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day	Delayed Treatment/Bulevirtide 10 mg/Day	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	49	50	50	
Units: percentage of participants				
number (confidence interval 95%)	18.4 (8.8 to 32.0)	26.0 (14.6 to 40.3)	18.0 (8.6 to 31.4)	

Statistical analyses

Statistical analysis title	Bulevirtide 2 mg/Day V/s Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/day v Bulevirtide 10 mg/Day
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4695 [18]
Method	Fisher exact
Parameter estimate	Response Rate Difference
Point estimate	7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	24.4

Notes:

[18] - P-value was based on Fisher's Exact Test.

Statistical analysis title	BLV 2 mg/Day V/s Delayed Treatment/BLV 10 mg/Day
Comparison groups	Bulevirtide 2 mg/day v Delayed Treatment/Bulevirtide 10 mg/Day
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1 [19]
Method	Fisher exact
Parameter estimate	Response Rate Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.3
upper limit	15.5

Notes:

[19] - P-value was based on Fisher's Exact Test.

Secondary: Percentage of Participants With Undetectable HDV RNA 48 Weeks After Scheduled End of Treatment (Sustained Virological Response)

End point title	Percentage of Participants With Undetectable HDV RNA 48

	Weeks After Scheduled End of Treatment (Sustained Virological Response)[20]

End point description:

Undetectable HDV RNA 48 Weeks after Scheduled End of Treatment means undetectable (< LLOQ, target not detected) HDV RNA at Week 192.
Analysis Population Description : Participants in the Full Analysis Set were analyzed. Participants were grouped according to randomized treatment and study design. The arm titles and descriptions in the outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Week 192

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical comparison was planned or performed.

End point values	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day	Delayed Treatment/Bulevirtide 10 mg/Day	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	49	50	50	
Units: percentage of participants				
number (confidence interval 95%)	16.3 (7.3 to 29.7)	24.0 (13.1 to 38.2)	16.0 (7.2 to 29.1)	

Statistical analyses

Statistical analysis title	Bulevirtide 2 mg/Day V/s Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/day v Bulevirtide 10 mg/Day
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4539 [21]
Method	Fisher exact
Parameter estimate	Response Rate Difference
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	24

Notes:

[21] - P-value was based on Fisher's Exact Test.

Statistical analysis title	BLV 2 mg/Day V/s DT/Bulevirtide 10 mg/Day
Comparison groups	Bulevirtide 2 mg/day v Delayed Treatment/Bulevirtide 10 mg/Day

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1 [22]
Method	Fisher exact
Parameter estimate	Response Rate Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.6
upper limit	15.5

Notes:

[22] - P-value was based on Fisher's Exact Test.

Secondary: Percentage of Participants Who Prematurely Discontinued Study Drug Due to an Adverse Event (AE) by Week 144

End point title	Percentage of Participants Who Prematurely Discontinued Study Drug Due to an Adverse Event (AE) by Week 144[23]

End point description:

An AE was defined as any untoward medical occurrence in a participant administered study drug and which did not necessarily have a causal relationship with the study drug. An AE could therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not related to the study drug.
Analysis Population Description : Participants in the SAS were analyzed. The SAS included all participants who were randomized into the study and took at least 1 dose of BLV study drug, or who were randomized to the delayed treatment group. Participants were grouped according to actual treatment received for time points Week 0 to 144. The arm titles and descriptions in this outcome measure are entered accordingly.

End point type	Secondary

End point timeframe:

Delayed Treatment/Bulevirtide 10 mg/day arm: Week 48 up to Week 144; Bulevirtide 2mg/day and 10 mg/day arms: First dose date up to Week 144

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical comparison was planned or performed.

End point values	Bulevirtide 2 mg/day	Bulevirtide 10 mg/Day	Delayed Treatment/Bulevirtide 10 mg/Day	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	49	50	50	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: Up to Week 240; Adverse Events: Week 0-48, Week 0-144, Week 48-144 and >Week 144 up to Week 240 per treatment description

Adverse event reporting additional description:

Participants grouped according to treatment received for time points Week (Wk) 0 to 48, 0 to 144, 48 to 144 and last treatment received after Wk144, up to Wk240. Arm titles and descriptions were entered accordingly. Actual treatment= randomized treatment, unless actual treatment was different than randomized treatment for entire treatment duration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Delayed Treatment (Baseline to Week 48)

Reporting group description:

Observation for 48 weeks.

Reporting group title	Bulevirtide 10 mg/Day (Baseline to Week 48)

Reporting group description:

Bulevirtide 10 mg/day SC injection for 48 weeks.

Reporting group title	Bulevirtide 2 mg/Day (Baseline to Week 144)

Reporting group description:

Participants received bulevirtide 2 mg/day SC injection for 144 weeks.

Reporting group title	DT/Bulevirtide 10 mg/Day (After EOT (>Week 144 up to Week 240)

Reporting group description:

After 96 weeks of treatment (Up to Week 144) with bulevirtide 10 mg/day SC injection, participants were followed for up to 96 weeks (Up to Week 240).

Reporting group title	Delayed Treatment/Bulevirtide 10 mg/Day (Week 48 to Week 144)

Reporting group description:

After an observational period of 48 weeks, participants received bulevirtide 10 mg/day SC injection for 96 weeks (Up to Week 144).

Reporting group title	Bulevirtide 2 mg/Day (After EOT (>Week 144 up to Week 240))

Reporting group description:

After 144 weeks of treatment with bulevirtide 2 mg/day, participants were followed for up to 96 weeks (up to Week 240).

Reporting group title	Bulevirtide 10 mg/Day (After EOT (>Week 144 up to Week 240))

Reporting group description:

After 144 weeks of treatment with bulevirtide 10 mg/day SC injection, participants were followed for up to 96 weeks (Up to Week 240).

Reporting group title	Bulevirtide 2 mg/Day (Baseline to Week 48)

Reporting group description:

Bulevirtide 2 mg/day SC injection for 48 weeks.

Reporting group title	Bulevirtide 10 mg/Day (Baseline to Week 144)

Reporting group description:

Participants received bulevirtide 10 mg/day SC injection for 144 weeks.

Serious adverse events	Delayed Treatment (Baseline to Week 48)	Bulevirtide 10 mg/Day (Baseline to Week 48)	Bulevirtide 2 mg/Day (Baseline to Week 144)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 51 (1.96%)	1 / 50 (2.00%)	3 / 49 (6.12%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase ~ increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phyllodes tumour			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foot fracture			

subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Varices oesophageal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic fibrosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			

subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatitis D			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic hepatitis B			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19 pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis E			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Yersinia infection			

subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DT/Bulevirtide 10 mg/Day (After EOT (>Week 144 up to Week 240)	Delayed Treatment/Bulevirtide 10 mg/Day (Week 48 to Week 144)	Bulevirtide 2 mg/Day (After EOT (>Week 144 up to Week 240))
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 49 (16.33%)	3 / 50 (6.00%)	7 / 46 (15.22%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0		0
Investigations			
Alanine aminotransferase ~ increased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Phyllodes tumour			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Foot fracture			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Varices oesophageal			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			

subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic fibrosis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Urinary retention			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatitis D			
subjects affected / exposed	2 / 49 (4.08%)	0 / 50 (0.00%)	4 / 46 (8.70%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic hepatitis B			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 49 (2.04%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	1 / 49 (2.04%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19 pneumonia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus pneumonia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis E			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Yersinia infection			

subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Bulevirtide 10 mg/Day (After EOT (>Week 144 up to Week 240))	Bulevirtide 2 mg/Day (Baseline to Week 48)	Bulevirtide 10 mg/Day (Baseline to Week 144)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 47 (14.89%)	2 / 49 (4.08%)	6 / 50 (12.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase ~ increased			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phyllodes tumour			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Foot fracture			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Varices oesophageal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			

subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic fibrosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Urinary retention			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatitis D			
subjects affected / exposed	4 / 47 (8.51%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic hepatitis B			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19 pneumonia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	2 / 50 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus pneumonia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis E			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Yersinia infection			

subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Delayed Treatment (Baseline to Week 48)	Bulevirtide 10 mg/Day (Baseline to Week 48)	Bulevirtide 2 mg/Day (Baseline to Week 144)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 51 (58.82%)	41 / 50 (82.00%)	44 / 49 (89.80%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)	3 / 50 (6.00%)	3 / 49 (6.12%)
occurrences (all)	0	3	3
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 50 (4.00%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Injection site erythema			
subjects affected / exposed	0 / 51 (0.00%)	5 / 50 (10.00%)	3 / 49 (6.12%)
occurrences (all)	0	5	13
Fatigue			
subjects affected / exposed	1 / 51 (1.96%)	7 / 50 (14.00%)	7 / 49 (14.29%)
occurrences (all)	1	18	12
Injection site reaction			
subjects affected / exposed	0 / 51 (0.00%)	5 / 50 (10.00%)	3 / 49 (6.12%)
occurrences (all)	0	7	3
Pyrexia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 50 (4.00%)	3 / 49 (6.12%)
occurrences (all)	0	2	3
Injection site pruritus			
subjects affected / exposed	0 / 51 (0.00%)	3 / 50 (6.00%)	2 / 49 (4.08%)
occurrences (all)	0	6	2
Injection site swelling			

subjects affected / exposed	0 / 51 (0.00%)	3 / 50 (6.00%)	1 / 49 (2.04%)
occurrences (all)	0	3	1
Oedema peripheral			
subjects affected / exposed	0 / 51 (0.00%)	2 / 50 (4.00%)	0 / 49 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 51 (1.96%)	3 / 50 (6.00%)	0 / 49 (0.00%)
occurrences (all)	1	8	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	3 / 49 (6.12%)
occurrences (all)	0	1	6
Transaminases increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 51 (1.96%)	1 / 50 (2.00%)	3 / 49 (6.12%)
occurrences (all)	1	1	8
Alpha-2 macroglobulin increased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	4 / 49 (8.16%)
occurrences (all)	1	0	4
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 51 (5.88%)	1 / 50 (2.00%)	2 / 49 (4.08%)
occurrences (all)	4	1	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 51 (1.96%)	2 / 50 (4.00%)	1 / 49 (2.04%)
occurrences (all)	1	4	1
Alanine aminotransferase increased			
subjects affected / exposed	4 / 51 (7.84%)	3 / 50 (6.00%)	5 / 49 (10.20%)
occurrences (all)	4	3	6
Amylase increased			

subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	3 / 49 (6.12%)
occurrences (all)	2	0	4
Activated partial thromboplastin time ~ prolonged			
subjects affected / exposed	2 / 51 (3.92%)	1 / 50 (2.00%)	0 / 49 (0.00%)
occurrences (all)	2	1	0
Hepatitis D RNA positive			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	2 / 49 (4.08%)
occurrences (all)	1	0	2
Bradycardia			
subjects affected / exposed	0 / 51 (0.00%)	3 / 50 (6.00%)	1 / 49 (2.04%)
occurrences (all)	0	3	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 51 (0.00%)	10 / 50 (20.00%)	10 / 49 (20.41%)
occurrences (all)	0	21	33
Dizziness			
subjects affected / exposed	0 / 51 (0.00%)	3 / 50 (6.00%)	2 / 49 (4.08%)
occurrences (all)	0	3	2
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	8 / 51 (15.69%)	5 / 50 (10.00%)	10 / 49 (20.41%)
occurrences (all)	10	6	14
Neutropenia			
subjects affected / exposed	3 / 51 (5.88%)	5 / 50 (10.00%)	8 / 49 (16.33%)
occurrences (all)	5	5	12
Leukopenia			
subjects affected / exposed	10 / 51 (19.61%)	5 / 50 (10.00%)	10 / 49 (20.41%)
occurrences (all)	12	6	23
Eosinophilia			

subjects affected / exposed	0 / 51 (0.00%)	5 / 50 (10.00%)	5 / 49 (10.20%)
occurrences (all)	0	5	5
Lymphopenia			
subjects affected / exposed	4 / 51 (7.84%)	4 / 50 (8.00%)	8 / 49 (16.33%)
occurrences (all)	8	5	22
Anaemia			
subjects affected / exposed	3 / 51 (5.88%)	2 / 50 (4.00%)	5 / 49 (10.20%)
occurrences (all)	4	2	5
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 51 (1.96%)	5 / 50 (10.00%)	2 / 49 (4.08%)
occurrences (all)	1	13	2
Nausea			
subjects affected / exposed	2 / 51 (3.92%)	4 / 50 (8.00%)	3 / 49 (6.12%)
occurrences (all)	2	6	9
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)	2 / 50 (4.00%)	0 / 49 (0.00%)
occurrences (all)	0	9	0
Abdominal pain			
subjects affected / exposed	1 / 51 (1.96%)	4 / 50 (8.00%)	2 / 49 (4.08%)
occurrences (all)	1	9	3
Gastritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic fibrosis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Hyperbilirubinaemia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 50 (4.00%)	4 / 49 (8.16%)
occurrences (all)	0	2	6
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 51 (0.00%)	7 / 50 (14.00%)	6 / 49 (12.24%)
occurrences (all)	0	10	7
Alopecia			

subjects affected / exposed	0 / 51 (0.00%)	2 / 50 (4.00%)	3 / 49 (6.12%)
occurrences (all)	0	2	3
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	2 / 51 (3.92%)	1 / 50 (2.00%)	4 / 49 (8.16%)
occurrences (all)	3	1	10
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	3
Osteopenia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	3
Myalgia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 50 (4.00%)	1 / 49 (2.04%)
occurrences (all)	0	3	1
Muscle spasms			
subjects affected / exposed	0 / 51 (0.00%)	3 / 50 (6.00%)	1 / 49 (2.04%)
occurrences (all)	0	3	4
Arthralgia			
subjects affected / exposed	0 / 51 (0.00%)	4 / 50 (8.00%)	6 / 49 (12.24%)
occurrences (all)	0	4	7
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 51 (3.92%)	0 / 50 (0.00%)	5 / 49 (10.20%)
occurrences (all)	2	0	9
Covid-19			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	5 / 49 (10.20%)
occurrences (all)	1	0	6
Urinary tract infection			
subjects affected / exposed	1 / 51 (1.96%)	2 / 50 (4.00%)	2 / 49 (4.08%)
occurrences (all)	3	2	5
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	13 / 51 (25.49%)	7 / 50 (14.00%)	22 / 49 (44.90%)
occurrences (all)	13	7	31

Non-serious adverse events	DT/Bulevirtide 10 mg/Day (After EOT (>Week 144 up to Week 240)	Delayed Treatment/Bulevirtide 10 mg/Day (Week 48 to Week 144)	Bulevirtide 2 mg/Day (After EOT (>Week 144 up to Week 240))
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 49 (69.39%)	41 / 50 (82.00%)	31 / 46 (67.39%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 49 (2.04%)	2 / 50 (4.00%)	0 / 46 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 49 (8.16%)	1 / 50 (2.00%)	3 / 46 (6.52%)
occurrences (all)	4	1	3
Injection site erythema			
subjects affected / exposed	0 / 49 (0.00%)	2 / 50 (4.00%)	0 / 46 (0.00%)
occurrences (all)	0	6	0
Fatigue			
subjects affected / exposed	4 / 49 (8.16%)	3 / 50 (6.00%)	0 / 46 (0.00%)
occurrences (all)	4	3	0
Injection site reaction			
subjects affected / exposed	0 / 49 (0.00%)	3 / 50 (6.00%)	0 / 46 (0.00%)
occurrences (all)	0	4	0
Pyrexia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	1 / 46 (2.17%)
occurrences (all)	0	1	1
Injection site pruritus			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	0	3	0
Injection site swelling			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Sleep disorder			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	2 / 46 (4.35%)
occurrences (all)	1	0	2
Transaminases increased			
subjects affected / exposed	2 / 49 (4.08%)	0 / 50 (0.00%)	2 / 46 (4.35%)
occurrences (all)	2	0	2
Bilirubin conjugated increased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	4 / 46 (8.70%)
occurrences (all)	1	0	4
Lipase increased			
subjects affected / exposed	0 / 49 (0.00%)	2 / 50 (4.00%)	1 / 46 (2.17%)
occurrences (all)	0	2	1
Alpha-2 macroglobulin increased			
subjects affected / exposed	6 / 49 (12.24%)	2 / 50 (4.00%)	2 / 46 (4.35%)
occurrences (all)	6	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 49 (30.61%)	1 / 50 (2.00%)	17 / 46 (36.96%)
occurrences (all)	21	2	18
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 49 (6.12%)	2 / 50 (4.00%)	8 / 46 (17.39%)
occurrences (all)	4	3	8
Alanine aminotransferase increased			
subjects affected / exposed	18 / 49 (36.73%)	0 / 50 (0.00%)	19 / 46 (41.30%)
occurrences (all)	23	0	21
Amylase increased			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Activated partial thromboplastin time ~ prolonged			
subjects affected / exposed	1 / 49 (2.04%)	2 / 50 (4.00%)	2 / 46 (4.35%)
occurrences (all)	2	2	2
Hepatitis D RNA positive			

subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	3 / 46 (6.52%)
occurrences (all)	1	0	3
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 49 (0.00%)	4 / 50 (8.00%)	1 / 46 (2.17%)
occurrences (all)	0	6	2
Bradycardia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 49 (2.04%)	7 / 50 (14.00%)	0 / 46 (0.00%)
occurrences (all)	1	12	0
Dizziness			
subjects affected / exposed	1 / 49 (2.04%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	7 / 49 (14.29%)	7 / 50 (14.00%)	6 / 46 (13.04%)
occurrences (all)	9	10	6
Neutropenia			
subjects affected / exposed	3 / 49 (6.12%)	3 / 50 (6.00%)	3 / 46 (6.52%)
occurrences (all)	3	6	4
Leukopenia			
subjects affected / exposed	5 / 49 (10.20%)	7 / 50 (14.00%)	2 / 46 (4.35%)
occurrences (all)	6	9	2
Eosinophilia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	7 / 49 (14.29%)	5 / 50 (10.00%)	3 / 46 (6.52%)
occurrences (all)	10	9	3
Anaemia			

subjects affected / exposed	5 / 49 (10.20%)	3 / 50 (6.00%)	1 / 46 (2.17%)
occurrences (all)	5	5	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 49 (0.00%)	2 / 50 (4.00%)	0 / 46 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	1 / 49 (2.04%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 49 (0.00%)	2 / 50 (4.00%)	0 / 46 (0.00%)
occurrences (all)	0	2	0
Gastritis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic fibrosis			
subjects affected / exposed	3 / 49 (6.12%)	2 / 50 (4.00%)	5 / 46 (10.87%)
occurrences (all)	3	2	5
Hyperbilirubinaemia			
subjects affected / exposed	1 / 49 (2.04%)	3 / 50 (6.00%)	1 / 46 (2.17%)
occurrences (all)	2	5	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences (all)	1	0	1
Alopecia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 49 (0.00%)	2 / 50 (4.00%)	0 / 46 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue			

disorders			
Neck pain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 49 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 50 (2.00%)	2 / 46 (4.35%)
occurrences (all)	1	2	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 49 (0.00%)	3 / 50 (6.00%)	2 / 46 (4.35%)
occurrences (all)	0	3	2
Covid-19			
subjects affected / exposed	2 / 49 (4.08%)	5 / 50 (10.00%)	1 / 46 (2.17%)
occurrences (all)	3	5	1
Urinary tract infection			
subjects affected / exposed	1 / 49 (2.04%)	2 / 50 (4.00%)	1 / 46 (2.17%)
occurrences (all)	1	4	1
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	7 / 49 (14.29%)	14 / 50 (28.00%)	6 / 46 (13.04%)
occurrences (all)	7	16	6

Non-serious adverse events	Bulevirtide 10 mg/Day (After EOT (>Week 144 up to Week 240))	Bulevirtide 2 mg/Day (Baseline to Week 48)	Bulevirtide 10 mg/Day (Baseline to Week 144)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 47 (70.21%)	35 / 49 (71.43%)	46 / 50 (92.00%)
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	4 / 50 (8.00%)
occurrences (all)	0	1	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 47 (8.51%)	1 / 49 (2.04%)	2 / 50 (4.00%)
occurrences (all)	4	1	3
Injection site erythema			
subjects affected / exposed	0 / 47 (0.00%)	2 / 49 (4.08%)	5 / 50 (10.00%)
occurrences (all)	0	2	5
Fatigue			
subjects affected / exposed	5 / 47 (10.64%)	5 / 49 (10.20%)	9 / 50 (18.00%)
occurrences (all)	6	8	22
Injection site reaction			
subjects affected / exposed	0 / 47 (0.00%)	3 / 49 (6.12%)	6 / 50 (12.00%)
occurrences (all)	0	3	8
Pyrexia			
subjects affected / exposed	2 / 47 (4.26%)	1 / 49 (2.04%)	4 / 50 (8.00%)
occurrences (all)	2	1	6
Injection site pruritus			
subjects affected / exposed	0 / 47 (0.00%)	2 / 49 (4.08%)	3 / 50 (6.00%)
occurrences (all)	0	2	6
Injection site swelling			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	3 / 50 (6.00%)
occurrences (all)	0	1	3
Oedema peripheral			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	1	0	3
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	2 / 47 (4.26%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	2	0	8
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 47 (2.13%)	2 / 49 (4.08%)	1 / 50 (2.00%)
occurrences (all)	1	3	2

Transaminases increased			
subjects affected / exposed	7 / 47 (14.89%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences (all)	7	0	1
Bilirubin conjugated increased			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	2 / 47 (4.26%)	2 / 49 (4.08%)	1 / 50 (2.00%)
occurrences (all)	2	3	5
Alpha-2 macroglobulin increased			
subjects affected / exposed	3 / 47 (6.38%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	3	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 47 (23.40%)	1 / 49 (2.04%)	1 / 50 (2.00%)
occurrences (all)	11	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 47 (8.51%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	5	0	6
Alanine aminotransferase increased			
subjects affected / exposed	11 / 47 (23.40%)	2 / 49 (4.08%)	4 / 50 (8.00%)
occurrences (all)	11	2	4
Amylase increased			
subjects affected / exposed	1 / 47 (2.13%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences (all)	1	1	0
Activated partial thromboplastin time ~ prolonged			
subjects affected / exposed	3 / 47 (6.38%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences (all)	3	0	1
Hepatitis D RNA positive			
subjects affected / exposed	4 / 47 (8.51%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences (all)	4	0	0
Weight decreased			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Sinus bradycardia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	2	0	4
Bradycardia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 47 (2.13%)	9 / 49 (18.37%)	12 / 50 (24.00%)
occurrences (all)	1	25	49
Dizziness			
subjects affected / exposed	0 / 47 (0.00%)	2 / 49 (4.08%)	4 / 50 (8.00%)
occurrences (all)	0	2	4
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	5 / 47 (10.64%)	5 / 49 (10.20%)	8 / 50 (16.00%)
occurrences (all)	6	6	17
Neutropenia			
subjects affected / exposed	4 / 47 (8.51%)	2 / 49 (4.08%)	10 / 50 (20.00%)
occurrences (all)	5	3	17
Leukopenia			
subjects affected / exposed	4 / 47 (8.51%)	7 / 49 (14.29%)	9 / 50 (18.00%)
occurrences (all)	5	9	20
Eosinophilia			
subjects affected / exposed	0 / 47 (0.00%)	5 / 49 (10.20%)	5 / 50 (10.00%)
occurrences (all)	0	5	5
Lymphopenia			
subjects affected / exposed	4 / 47 (8.51%)	4 / 49 (8.16%)	6 / 50 (12.00%)
occurrences (all)	5	5	16
Anaemia			
subjects affected / exposed	1 / 47 (2.13%)	3 / 49 (6.12%)	3 / 50 (6.00%)
occurrences (all)	1	3	7
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	5 / 50 (10.00%)
occurrences (all)	1	0	13
Nausea			

subjects affected / exposed	0 / 47 (0.00%)	3 / 49 (6.12%)	6 / 50 (12.00%)
occurrences (all)	0	9	9
Diarrhoea			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	1	0	10
Abdominal pain			
subjects affected / exposed	1 / 47 (2.13%)	1 / 49 (2.04%)	4 / 50 (8.00%)
occurrences (all)	1	1	11
Gastritis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	1	0	3
Hepatobiliary disorders			
Hepatic fibrosis			
subjects affected / exposed	4 / 47 (8.51%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences (all)	4	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 47 (0.00%)	2 / 49 (4.08%)	2 / 50 (4.00%)
occurrences (all)	0	2	5
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 47 (6.38%)	6 / 49 (12.24%)	8 / 50 (16.00%)
occurrences (all)	3	7	11
Alopecia			
subjects affected / exposed	0 / 47 (0.00%)	2 / 49 (4.08%)	3 / 50 (6.00%)
occurrences (all)	0	2	3
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 47 (0.00%)	3 / 49 (6.12%)	3 / 50 (6.00%)
occurrences (all)	0	4	4
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Osteopenia			
subjects affected / exposed	0 / 47 (0.00%)	2 / 49 (4.08%)	0 / 50 (0.00%)
occurrences (all)	0	2	0

Myalgia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	0	4
Muscle spasms			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	0	3
Arthralgia			
subjects affected / exposed	1 / 47 (2.13%)	3 / 49 (6.12%)	8 / 50 (16.00%)
occurrences (all)	1	4	8
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 47 (2.13%)	4 / 49 (8.16%)	2 / 50 (4.00%)
occurrences (all)	1	7	2
Covid-19			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	8 / 50 (16.00%)
occurrences (all)	0	1	9
Urinary tract infection			
subjects affected / exposed	2 / 47 (4.26%)	1 / 49 (2.04%)	6 / 50 (12.00%)
occurrences (all)	3	1	8
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	7 / 47 (14.89%)	7 / 49 (14.29%)	19 / 50 (38.00%)
occurrences (all)	8	7	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2019	Protocol Amendment 1 Summary: Administrative: Sponsor address updated; EudraCT number added. Abbreviations: Added for EQ-5O, FSS, HQLQ™, Local Reactions assessment, Treatment Compliance, and Quality of Life questionnaires. Synopsis: Tenofovir provision clarified: Sponsor provides if unavailable via routine medical care. Patient Rationale: Aligned with updated Exclusion Criteria. Eligibility: Plasma HOV RNA can now confirm patient eligibility. Exclusion Criteria Updates: Child-Pugh hepatic insufficiency >7 (uncomplicated esophageal varices allowed; exclude current/history of bleeding/ligation within 2 yrs). HCV/uncontrolled HIV coinfection: HCV Ab+ OK if HCV RNA negative. HIV+ OK if CD4 >500/mL & HIV RNA undetectable >12 mos. Uncontrolled arterial hypertension within 3 months pre-study (SBP >150 or DBP >100 mmHg despite treatment) allowed post-Study Medical Monitor confirmation. Current/previous (within last 2 yrs) decompensated liver disease (incl. coagulopathy, hepatic encephalopathy, esophageal varices hemorrhage). History of regular systemic glucocorticosteroid use (inhalative allowed). Participation in other investigational drug studies within 30 days pre-randomization. Prior bulevirtide receipt (incl. clinical trials). New/Revised Sections: Treatment Compliance section added. Prohibited treatments: Confirmed inhalative glucocorticosteroids allowed. Physical Examination: Added assessment of local injection site reactions (per Table 1; record in eCRF; AE if clinically significant). New section on Local bulevirtide injection site reactions. Pregnancy Reporting: Male subjects' pregnant partners require Information Sheet & ICF for pregnancy outcome data collection.

17 March 2021	New abbreviation is added (INR), ·'Lower Limit of Detection" is changed to "Limit of Detection" The list o f countries is corrected - Sweden was added It is added that tenofovir in tablets wi ll be provided by Sponsor and in patients in whom tenofovir is contraindicated, entecavir (tablets) will be provided. Primary Efficacy Endpoint: It is corrected that Undetectable HOV RNA is <LoD Exploratory endpoints: "Clinical events (decompensation, liver related death)" is changed to "Liver related clinical events (cirrhosis development; development or worsening jaundice, coagulopathy, ascites, hepatic encephalopathy; bleeding from esophageal varices; Hepatocellular carcinoma development; liver transplantation; liver related hospitalization: amount of hospitalizations and duration of each period of hospitalization; liver related death) at all postbaseline assessments" Other variables: "HBeAg and HBeAg antibodies status at all postbaseline assessments (for patients with positive HBeAg at SCR)" is added. Primary Efficacy Endpoint: It is corrected that Undetectable HOV RNA is <LoD Exploratory endpoints: "Clinical events (decompensation, liver related death) is changed to "Liver related clinical events (cirrhosis development; development or worsening jaundice, coagulopathy, ascites, hepatic encephalopathy; bleeding from esophageal varices; Hepatocellular carcinoma development; liver transplantation; liver related hospitalization: amount of hospitalizations and duration of each period of hospitalization; liver related death) at all postbaseline assessments" Other variables: "HBeAg and HBeAg antibodies status at all postbaseline assessments (for patients with positive HBeAg at SCR)" is added. The list of countries is corrected - Sweden was added The following is added: "The study will be considered to have started when the first patient has provided signed informed consent, and will be considered to have finished after the last patient has completed the last follow-up
16 September 2021	The major update(s) to the protocol and related rationale are as follows: An additional Phase 2 treatment arm was added that includes zimberelimab to allow the assessment of the efficacy and safety of magrolimab in combination with pembrolizumab +platinum + 5-FU (Cohort 1 Arm A) versus pembrolizumab + platinum + 5-FU (Cohort 1 Arm B) versus zimberelimab + platinum + 5-FU (Cohort 1 Arm C). Arm C was added to provide a comparison of zimberelimab with pembrolizumab in combination with magrolimab and chemotherapeutics in the treatment of head and neck squamous cell carcinoma (HNSCC).
25 April 2022	The primary reasons for this amendment are to: (1) update the regulatory and clinical development status of bulevirtide, (2) give instructions for operational changes in sample collection, and (3) specify changes to the statistical analyses.
19 October 2022	The primary reason for this amendment is to update the definition of viral breakthrough and nonresponders used for virologic resistance analysis and clarify the criteria for selection of the samples that will be tested for resistance.
25 January 2023	A Week 180 visit was added with additional assessments to allow a more standardized approach for study investigators to monitor and manage posttreatment hepatitis exacerbation. Updated the definition of hepatitis delta virus (HDV) ribonucleic acid (RNA) undetectable" to "< lower limit of quantification (LLOQ), target not detected." To identify and monitor participants at risk of developing a hepatitis flare, specific procedures were added for the management of posttreatment exacerbation of hepatitis, ie, if laboratory results indicated alanine aminotransferase (ALT) elevations. An optional third liver biopsy was added to the list of assessments. The timing of an exploratory analysis was changed from Week 168 to Week 192. Clarified details of adverse event (AE)/serious AE reporting procedures period and liver-related clinical events. Addition of Appendix 2 (Monitoring Study Participants for Posttreatment ALT Elevation: Flowchart) and Appendix 3 (Unscheduled Visit for Management of posttreatment ALT Elevations). Definition of Per Protocol Analysis Set was updated Updated the word 'Subject' to 'Participants' and other style-related changes included where possible.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported