Clinical trial results:
A Phase 2a, Multi-center, Double-blind, Placebo-controlled Study Evaluating ABI-H0731 + Entecavir vs Entecavir Alone for the Treatment of Viremic, HBeAg-positive Patients with Chronic Hepatitis B

Summary

EudraCT number	2018-002042-36
Trial protocol	GB
Global end of trial date	21 June 2019

Results information

Result version number	v1 (current)
This version publication date	06 January 2021
First version publication date	06 January 2021

Trial information

Trial identification

Sponsor protocol code	ABI-H0731-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03577171
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Assembly Biosciences
Sponsor organisation address	11711 North Meridian Street, Suite 310, Carmel, Indiana, United States, 46032
Public contact	Linda Baher, Sr. Director, Clinical Operations, Assembly Biosciences, 1 415-521-3808, clinicaltrials@assemblybio.com
Scientific contact	Linda Baher, Sr. Director, Clinical Operations, Assembly Biosciences, 1 415-521-3808, clinicaltrials@assemblybio.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	21 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 June 2019
Global end of trial reached?	Yes
Global end of trial date	21 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine if ABI-H0731 given in combination with a standard of care (SOC) entecavir (ETV) is safe and effective in participants with chronic hepatitis B infection (cHBV).

Protection of trial subjects:

This study will be conducted in compliance with IRB/IEC and International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines; Title 21 Part 56 of the US Code of Federal Regulations (CFR) relating to IRBs/IECs and GCP as described in the US FDA CFR (21 CFR § 50, 56, 312; applicable ICH guidelines regarding clinical safety data management (E2A, E2B(R3)); European Community directives 2001/20, 2001/83, 2003/94 and 2005/28 as enacted into local law, and with ICH guidelines regarding scientific integrity (E4, E8, E9, and E10). In addition, this study will adhere to all local regulatory requirements, and requirements for data protection.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	United States: 14
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	25
EEA total number of subjects	2

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 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	24
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 13 sites worldwide (8 sites in the US, 1 site in Hong Kong, 2 sites in Canada, 1 site in the United Kingdom, and 1 site in New Zealand).

Pre-assignment

Screening details:

There was a screening period of up to 45 days.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	ABI-H0731 + SOC ETV

Arm description:

Participants with chronic hepatitis B infection (cHBV) who are currently not being treated will receive ABI-H0731 along with standard of care (SOC) entecavir (ETV) tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to continue open-label ABI-H0731 for up to an additional year if necessary.

Arm type	Experimental
Investigational medicinal product name	ABI-H0731
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive 300mg QD of ABI-H0731 tablets orally.

Investigational medicinal product name	Entecavir (ETV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive standard of care (SOC) ETV (0.5 mg QD) orally as per approved package insert.

Arm title	Placebo + SOC ETV

Arm description:

Participants with cHBV who are currently not being treated will receive matching placebo along with SOC ETV tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to start treatment on open-label ABI-H0731 for up to a year if necessary.

Arm type	Active comparator
Investigational medicinal product name	Entecavir (ETV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Participants will receive SOC ETV (0.5 mg QD) orally as per approved package insert.	
Investigational medicinal product name	Placebo Oral Tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive matching QD placebo tablets orally.

Number of subjects in period 1	ABI-H0731 + SOC ETV	Placebo + SOC ETV
Started	13	12
Completed	13	12

Baseline characteristics

Reporting groups	
Reporting group title	ABI-H0731 + SOC ETV
Reporting group description:	
Participants with chronic hepatitis B infection (cHBV) who are currently not being treated will receive ABI-H0731 along with standard of care (SOC) entecavir (ETV) tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to continue open-label ABI-H0731 for up to an additional year if necessary.	
Reporting group title	Placebo + SOC ETV
Reporting group description:	
Participants with cHBV who are currently not being treated will receive matching placebo along with SOC ETV tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to start treatment on open-label ABI-H0731 for up to a year if necessary.	

Reporting group values	ABI-H0731 + SOC ETV	Placebo + SOC ETV	Total
Number of subjects	13	12	25
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	35.7	34.1	
standard deviation	± 14.13	± 11.39	-
Gender categorical			
Units: Subjects			
Female	10	7	17
Male	3	5	8
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	13	12	25
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	13	11	24
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	0	0	0
More than one race	0	0	0

End points

End points reporting groups

Reporting group title	ABI-H0731 + SOC ETV

Reporting group description:

Participants with chronic hepatitis B infection (cHBV) who are currently not being treated will receive ABI-H0731 along with standard of care (SOC) entecavir (ETV) tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to continue open-label ABI-H0731 for up to an additional year if necessary.

Reporting group title	Placebo + SOC ETV

Reporting group description:

Participants with cHBV who are currently not being treated will receive matching placebo along with SOC ETV tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to start treatment on open-label ABI-H0731 for up to a year if necessary.

Primary: Change in Mean log10 HBV DNA From Baseline (Day 1) to Week 12 or Week 24 on ABI H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point title	Change in Mean log10 HBV DNA From Baseline (Day 1) to Week 12 or Week 24 on ABI H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point description:

Hepatitis B virus (HBV) DNA was measured using COBAS TaqMan Version 2.0. The lower limit of quantitation (LLOQ) was 20 IU/mL and the limit of detection (LOD) was 10 IU/mL.

End point type	Primary

End point timeframe:

Baseline, Week 12, and Week 24

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Log10 International Units (IU)				
arithmetic mean (standard deviation)				
Baseline	7.91 (± 0.890)	8.03 (± 0.999)		
Change from Baseline at Week 12	-4.45 (± 1.027)	-3.30 (± 1.182)		
Change from Baseline at Week 24	-5.33 (± 1.594)	-4.20 (± 0.976)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Statistical Analysis 1 for Change in Mean log10 HBV DNA From Baseline (Day 1) to Week 12 or Week 24 on ABI H0731 + SOC ETV as Compared to Placebo + SOC ETV.

Least Squares (LS) Mean Difference ABI-H0731 + SOC ETV minus Placebo + SOC ETV at Week 12.

Comparison groups	ABI-H0731 + SOC ETV v Placebo + SOC ETV

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0077
Method	Repeated measures analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.154
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.986
upper limit	-0.322

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Statistical Analysis 2 for Change in Mean log10 HBV DNA From Baseline (Day 1) to Week 12 or Week 24 on ABI H0731 + SOC ETV as Compared to Placebo + SOC ETV.

Least Squares Mean Difference ABI-H0731 + SOC ETV minus Placebo + SOC ETV at Week 24.

Comparison groups	Placebo + SOC ETV v ABI-H0731 + SOC ETV
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0084
Method	Repeated measures analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.141
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.973
upper limit	-0.309

Secondary: Number of Participants One or More Adverse Events

End point title	Number of Participants One or More Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Up to Follow-up (maximum up to Week 36)

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Participants	7	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Premature Study Discontinuation

End point title	Number of Participants With Premature Study Discontinuation

End point description:

End point type	Secondary

End point timeframe:

Up to Follow-up (maximum up to Week 36)

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With One or More Abnormal Safety Laboratory Result

End point title	Number of Participants With One or More Abnormal Safety Laboratory Result

End point description:

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Participants	8	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With a Clinically-significant Electrocardiogram Abnormality

End point title	Number of Participants With a Clinically-significant Electrocardiogram Abnormality

End point description:

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Alanine Aminotransferase (ALT) at Baseline Who Have Normal ALT at Week 24 on ABI-H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point title	Number of Participants With Abnormal Alanine Aminotransferase (ALT) at Baseline Who Have Normal ALT at Week 24 on ABI-H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[1]	4[2]		
Units: Participants	4	2		

Notes:

[1] - Participants in the ITT population with abnormal ALT at Baseline.

[2] - Participants in the ITT population with abnormal ALT at Baseline.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With a Decline in Viral DNA to Below Limit of Quantitation on ABI-H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point title	Number of Participants With a Decline in Viral DNA to Below Limit of Quantitation on ABI-H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point description:

HBV DNA was measured using COBAS TaqMan Version 2.0. The LLOQ was 20 IU/mL and the LOD was 10 IU/mL. The number of participants with HBV DNA below the limit of quantitation (<20 IU/mL) and target detected (≥10 IU/mL) was assessed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 12, 16, 20, and 24

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Participants				
Baseline	0	0		
Week 2	0	0		
Week 4	0	0		
Week 8	1	0		
Week 12	1	0		
Week 16	2	0		
Week 20	1	1		
Week 24	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Viral Suppression, Defined as HBV DNA <20 IU/mL, on ABI-H0731 + ETV as Compared to Placebo + ETV

End point title	Median Time to Viral Suppression, Defined as HBV DNA <20 IU/mL, on ABI-H0731 + ETV as Compared to Placebo + ETV

End point description:

Median time to viral suppression will be calculated and evaluated between participants on ABI-H0731 + ETV as compared to placebo + ETV.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 12, 16, 20, and 24

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: Hours				
median (full range (min-max))	(to)	(to)		

Notes:

[3] - Analysis of this outcome measure was not performed because of insufficient data.

[4] - Analysis of this outcome measure was not performed because of insufficient data.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Emergence of Resistant HBV Variants on ABI-H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point title	Number of Participants With Emergence of Resistant HBV Variants on ABI-H0731 + SOC ETV as Compared to Placebo + SOC ETV

End point description:

Emergence of a resistant HBV variant was defined as an increase of ≥1 log10 IU/mL from the nadir in HBV DNA.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Participants				
Emergence of resistant HBV variants	1	1		
No emergence of resistant HBV variants	12	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Levels of ABI-H0731 on ABI-H0731 + SOC ETV Therapy

End point title	Trough Levels of ABI-H0731 on ABI-H0731 + SOC ETV

End point description:

End point type	Secondary

End point timeframe:

Before dosing at Baseline (Day 1), Weeks 2, 4, 12, and 24

Notes:

[5] - 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: Analysis was only planned for the ABI-H0731 arm.

End point values	ABI-H0731 + SOC ETV			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Day 1)	0 (± 0)			
Week 2	1480 (± 458)			
Week 4	1290 (± 434)			
Week 12	1270 (± 413)			
Week 24	1470 (± 547)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Levels of ETV on ABI-H0731 + ETV Therapy as Compared With Placebo + ETV Therapy

End point title	Trough Levels of ETV on ABI-H0731 + ETV Therapy as Compared With Placebo + ETV Therapy

End point description:

End point type	Secondary

End point timeframe:

Before dosing at Baseline (Day 1), Weeks 2, 4, 12, and 24

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Day 1)	0.00325 (± 0.0113)	0 (± 0)		
Week 2	0.432 (± 0.126)	0.497 (± 0.473)		

Week 4	0.419 (± 0.119)	0.618 (± 0.736)		
Week 12	0.378 (± 0.149)	0.666 (± 0.766)		
Week 24	0.411 (± 0.143)	0.408 (± 0.131)		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough to Peak Ratios of ABI-H0731 on ABI-H0731 + ETV Therapy

End point title	Trough to Peak Ratios of ABI-H0731 on ABI-H0731 + ETV Therapy[6]

End point description:

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 12, and 24

Notes:

[6] - 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: Analysis was only planned for the ABI-H0731 arm.

End point values	ABI-H0731 + SOC ETV			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Ratio				
arithmetic mean (standard deviation)	()			

Notes:

[7] - Trough to peak ratios were not calculated due to an insufficient # of optional peak exposure samples

Statistical analyses

No statistical analyses for this end point

Secondary: Trough to Peak Ratios of ETV on ABI-H0731 + ETV Therapy as Compared With Placebo + ETV Therapy

End point title	Trough to Peak Ratios of ETV on ABI-H0731 + ETV Therapy as Compared With Placebo + ETV Therapy

End point description:

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 12, 24, and 28

End point values	ABI-H0731 + SOC ETV	Placebo + SOC ETV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Ratio				
arithmetic mean (standard deviation)	()	()		

Notes:

[8] - Trough to peak ratios were not calculated due to an insufficient # of optional peak exposure samples

[9] - Trough to peak ratios were not calculated due to an insufficient # of optional peak exposure samples

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Week 36	
Adverse event reporting additional description: Safety population.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	ABI-H0731 + SOC ETV
Reporting group description: Participants with chronic hepatitis B infection (cHBV) who are currently not being treated will receive ABI-H0731 along with standard of care (SOC) entecavir (ETV) tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to continue open-label ABI-H0731 for up to an additional year if necessary.	
Reporting group title	Placebo + SOC ETV
Reporting group description: Participants with cHBV who are currently not being treated will receive matching placebo along with SOC ETV tablets orally for 24 weeks. Eligible participants may enter a separate extension study after Week 24 to start treatment on open-label ABI-H0731 for up to a year if necessary.	

Serious adverse events	ABI-H0731 + SOC ETV	Placebo + SOC ETV	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	ABI-H0731 + SOC ETV	Placebo + SOC ETV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 13 (53.85%)	5 / 12 (41.67%)	
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Electrocardiogram T wave abnormal			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain lower			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Abdominal pain upper			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Epistaxis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Skin irritation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Psychiatric disorders			
Stress			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
Folliculitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Viral infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2018	Protocol Amendment 1 - Summary of Changes: - Clarified inclusion criteria - Revised the prohibited concomitant therapy section - Revised Subjects with Alanine Aminotransferase Elevations section - Corrections and revisions to the Schedule of Assessments - Administrative changes
30 July 2018	Protocol Version 2.1 (UK) - Summary of Changes: - Revised Subjects with Alanine Aminotransferase Elevations section - Revised Schedule of Assessments - Clarified Blinding section - Added Section 6.3.3.1: Unblinding for Emergency Situations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported