Clinical trial results:
A PHASE 2, EXPLORATORY STUDY EVALUATING THE SAFETY AND ANTIVIRAL EFFICACY OF INARIGIVIR SOPROXIL IN NON-CIRRHOTIC, HEPATITIS B e ANTIGEN NEGATIVE SUBJECTS INFECTED WITH CHRONIC HEPATITIS B VIRUS AND RECEIVING OR STOPPING TREATMENT WITH A NUCLEOSIDE/NUCLEOTIDE INHIBITOR

Summary

EudraCT number	2019-000896-17
Trial protocol	GB
Global end of trial date	16 July 2020

Results information

Result version number	v1 (current)
This version publication date	08 November 2020
First version publication date	08 November 2020
Summary attachment (see zip file)	Adverse event listing (SBP-9200-HBV-206_70_Adverse Events Listing.pdf)

Trial information

Trial identification

Sponsor protocol code	SBP-9200-HBV-206

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Spring Bank Pharmaceuticals, Inc.
Sponsor organisation address	35 Parkwood Drive, Suite 210, Hopkinton, United States, MA 01748
Public contact	Don Mitchell, Spring Bank Pharmaceuticals, Inc., 1 508 689 9737, dmitchell@springbankpharm.com
Scientific contact	Don Mitchell, Spring Bank Pharmaceuticals, Inc., 1 508 689 9737, dmitchell@springbankpharm.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	16 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 July 2020
Global end of trial reached?	Yes
Global end of trial date	16 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the original protocol was to identify safety and antiviral efficacy of inarigivir in participants receiving nucleoside/nucleotide (NUC) analogue inhibitors and in subjects who discontinue NUCs.

The primary objective was amended in Standalone Protocol Amendment 1.1. dated 05 Mar 2020 to ensure adequate safety follow-up of subjects who received treatment under Protocol SBP-9200-HBV-206.

Protection of trial subjects:

The Investigator explained the benefits and risks of participation in the study to each subject or the subject's legally acceptable representative and obtained written informed consent prior to the subject entering the study and before initiation of any study-related procedure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2019
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	United Kingdom: 25
Country: Number of subjects enrolled	Canada: 39
Worldwide total number of subjects	64
EEA total number of subjects	25

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)	58
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was performed up to 28 days before Visit 2 to determine the eligibility of each subject.

Period 1

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

Arms

Arm title	Inarigivir

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Inarigivir soproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The initial dose of inarigivir administered was 400 mg daily with or without a Nucleoside/Nucleotide Inhibitor (NUC). Doses were administered as 2 inarigivir 200-mg tablets at least 1 hour before or after meals.

Number of subjects in period 1	Inarigivir
Started	64
Completed	58
Not completed	6
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Adverse event, non-fatal	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	64	64	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	58	58	
From 65-84 years	6	6	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	21	21	
Male	43	43	

End points

End points reporting groups

Reporting group title	Inarigivir

Reporting group description: -

Primary: Treatment emergent adverse events (TEAEs)

End point title	Treatment emergent adverse events (TEAEs)[1]

End point description:

End point type	Primary

End point timeframe:

From first dose to end of study

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were performed on this endpoint, as per protocol

End point values	Inarigivir			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: events	266			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From first dose to end of study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Inarigivir

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Only SAEs have been coded and reported within the EudraCT results database. A full listing of all adverse events (non-coded) is appended to the results dataset.

Serious adverse events	Inarigivir		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 64 (17.19%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Subarachnoid haemorrhage			

subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
abdominal pain upper			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			

subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cholecystitis acute			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute hepatitis B			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media chronic			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Inarigivir		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 64 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2020	Protocol standalone amendment 1.1 was implemented following the Urgent Safety Measure halt and implemented the following protocol changes: * Planned follow up period of 24 weeks including the following: - All patients to have weekly monitoring of liver function tests until results were normal or equal to baseline results for 4 consecutive weeks. Upon those 4 normal results, they were to return to the original schedule for the remainder of the 24 week follow up period. - If a patient was symptomatic or had elevated liver function tests, they were to have 2x weekly monitoring of liver function tests until there were normal results for 4 consecutive weeks. Upon those 4 normal results, they were to return to the original schedule for the remainder of the 24 week follow up period. - Patients with nausea, vomiting, abdominal pain or other symptoms of hepatic dysfunction who showed abnormal ALT/AST and an increase in INR or Bilirubin were to be considered for hospitalisation for biopsy and monitoring. All AEs or SAEs were to be followed until resolution. - Patients who had not returned to normal results at the 24 week follow up timepoint were to be followed for an additional 24 weeks. * Women of childbearing potential were to agree to use a highly effective method of contraception for 3 months after discontinuing study treatment, and men with female partners who were of childbearing potential were to agree that they or their partners would use a highly effective method of contraception for 3 months after discontinuing study treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 December 2019	Urgent Safety Measure: Due to multiple reports of Serious Adverse Events (SAEs) related to the Investigational Product (IP), as well as Adverse Events of Special Interest (AESIs), the study was halted. Patients have been reporting with elevations in alanine aminotransferase (ALT), Aspartate transaminase (AST), and Total Bilirubin amongst others, and reporting symptoms including, nausea, vomiting, abdominal pain, and anorexia.	-

Notes:

Limitations and caveats

None reported