# 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<br>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<br>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<br>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:<br>* Planned follow up period of 24 weeks including the following:<br>- 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.<br>- 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.<br>- 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.<br>- Patients who had not returned to normal results at the 24 week follow up timepoint were to be followed for an additional 24 weeks.<br>* 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:<br>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