Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Phase II Study to Evaluate the Efficacy and Safety of SPX-101 Inhalation Solution in Subjects with Cystic Fibrosis (HOPE-1 STUDY: HYDRATION FOR OPTIMAL PULMONARY EFFECTIVENESS)

Summary

EudraCT number	2016-005230-30
Trial protocol	GB PT IT
Global end of trial date	24 June 2019

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	SPX-101-CF-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03229252
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Spyryx Biosciences, Inc.
Sponsor organisation address	801-10 Capitola Drive, Durham, United States, 27713
Public contact	Dr. Rob Tarran, Spyryx Biosciences, Inc., +1 9199667052, contact@spyryxbio.com
Scientific contact	Dr. Rob Tarran, Spyryx Biosciences, Inc., +1 9199667052, contact@spyryxbio.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	02 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2019
Global end of trial reached?	Yes
Global end of trial date	24 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of SPX-101 in subjects with CF

Protection of trial subjects:

None needed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
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	Portugal: 8
Country: Number of subjects enrolled	United Kingdom: 36
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Canada: 16
Worldwide total number of subjects	91
EEA total number of subjects	75

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)	91
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruiting began in October, 2017 and ended in June, 2019. The trial was run in Canada, United Kingdom, France, Italy and Portugal.

Pre-assignment

Screening details:

Subjects were screened at Visit 1 and then entered a variable-length screening period of 3 to 28 days, to time the randomization so that the first dose of the study drug would coincide, if applicable, to the start of an inhaled antibiotic cycle.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SPX-101 Low Dose

Arm description:

Inhalation solution twice daily for 28-days. SPX-101 inhalation solution.

Arm type	Experimental
Investigational medicinal product name	SPX-101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Inhalation solution twice daily for 28-days

Arm title	SPX-101 High Dose

Arm description:

Inhalation solution twice daily for 28-days. SPX-101 inhalation solution.

Arm type	Experimental
Investigational medicinal product name	SPX-101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Inhalation solution twice daily for 28-days

Arm title	Placebo

Arm description:

Placebo inhalation solution twice daily for 28-days. Normal saline inhalation solution.

Arm type	Placebo

Investigational medicinal product name	Normal Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Normal saline inhalation solution

Number of subjects in period 1	SPX-101 Low Dose	SPX-101 High Dose	Placebo
Started	15	45	31
Completed	15	39	29
Not completed	0	6	2
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	6	1

Baseline characteristics

Reporting groups	
Reporting group title	SPX-101 Low Dose
Reporting group description:	
Inhalation solution twice daily for 28-days. SPX-101 inhalation solution.	
Reporting group title	SPX-101 High Dose
Reporting group description:	
Inhalation solution twice daily for 28-days. SPX-101 inhalation solution.	
Reporting group title	Placebo
Reporting group description:	
Placebo inhalation solution twice daily for 28-days. Normal saline inhalation solution.	

Reporting group values	SPX-101 Low Dose	SPX-101 High Dose	Placebo
Number of subjects	15	45	31
Age categorical Units: Subjects			
Adults (18-64 years)	15	45	31
Age continuous Units: years			
arithmetic mean	33.7	31.9	30.8
standard deviation	± 8.62	± 8.49	± 7.82
Gender categorical Units: Subjects			
Female	4	22	11
Male	11	23	20

Reporting group values	Total		
Number of subjects	91		
Age categorical Units: Subjects			
Adults (18-64 years)	91		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	37		
Male	54		

End points

End points reporting groups

Reporting group title	SPX-101 Low Dose
Reporting group description:	
Inhalation solution twice daily for 28-days. SPX-101 inhalation solution.	
Reporting group title	SPX-101 High Dose
Reporting group description:	
Inhalation solution twice daily for 28-days. SPX-101 inhalation solution.	
Reporting group title	Placebo
Reporting group description:	
Placebo inhalation solution twice daily for 28-days. Normal saline inhalation solution.	

Primary: Change in percent predicted FEV1

End point title	Change in percent predicted FEV1
End point description:	

End point type	Primary
End point timeframe:	
From baseline to day 28	

End point values	SPX-101 Low Dose	SPX-101 High Dose	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	45	31	
Units: Change in baseline in ppFEV1				
arithmetic mean (standard deviation)	0.800 (± 6.5049)	0.890 (± 6.7061)	1.633 (± 6.3302)	

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

The comparison between each treatment group and placebo will be evaluated by using an analysis of covariance (ANCOVA) model, which will include treatment as the factor, and the stratification factor as a covariate (i.e., baseline lung function categories [ppFEV1 40.0% to 55.0% or 55.1% to 80.0% for Cohort 1] and the concomitant use of hypertonic saline for Cohort 2). Also included in the ANCOVA model for Cohort 2 is baseline ppFEV1. Descriptive statistics will include the number of observations,

Comparison groups	SPX-101 Low Dose v SPX-101 High Dose v Placebo

Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.1
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: screening to day 30	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	SPX-101 Low Dose
Reporting group description: -	
Reporting group title	SPX-101 High Dose
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	SPX-101 Low Dose	SPX-101 High Dose	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	3 / 45 (6.67%)	1 / 31 (3.23%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 45 (2.22%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal Obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 45 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough and Dyspnea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 45 (2.22%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Infective Pulmonary Exacerbation of Cystic Fibrosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 45 (2.22%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
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	SPX-101 Low Dose	SPX-101 High Dose	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 15 (66.67%)	29 / 45 (64.44%)	20 / 31 (64.52%)
Investigations			
Forced expiratory volume decreased			
subjects affected / exposed	0 / 15 (0.00%)	4 / 45 (8.89%)	0 / 31 (0.00%)
occurrences (all)	0	4	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 45 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	0 / 15 (0.00%)	4 / 45 (8.89%)	1 / 31 (3.23%)
occurrences (all)	0	4	1
Migraine			
subjects affected / exposed	1 / 15 (6.67%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	2 / 15 (13.33%)	2 / 45 (4.44%)	2 / 31 (6.45%)
occurrences (all)	2	3	2
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)	0 / 45 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	1 / 15 (6.67%)	2 / 45 (4.44%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	2 / 45 (4.44%)	1 / 31 (3.23%)
occurrences (all)	1	2	1
Frequent bowel movements			
subjects affected / exposed	1 / 15 (6.67%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Tongue coated			
subjects affected / exposed	1 / 15 (6.67%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 15 (0.00%)	5 / 45 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	5	0
Cough			
subjects affected / exposed	4 / 15 (26.67%)	6 / 45 (13.33%)	6 / 31 (19.35%)
occurrences (all)	4	6	6
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	4 / 45 (8.89%)	1 / 31 (3.23%)
occurrences (all)	0	4	1
Epistaxis			
subjects affected / exposed	1 / 15 (6.67%)	2 / 45 (4.44%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Increased viscosity of bronchial secretion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Infective exacerbation of cystic fibrosis			
subjects affected / exposed	1 / 15 (6.67%)	3 / 45 (6.67%)	4 / 31 (12.90%)
occurrences (all)	1	3	4
Lower respiratory tract congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 45 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Nasal congestion			

subjects affected / exposed	3 / 15 (20.00%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	3	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	3 / 45 (6.67%)	2 / 31 (6.45%)
occurrences (all)	0	3	2
Sputum discoloured			
subjects affected / exposed	1 / 15 (6.67%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Sputum increased			
subjects affected / exposed	3 / 15 (20.00%)	4 / 45 (8.89%)	2 / 31 (6.45%)
occurrences (all)	3	4	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 15 (13.33%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Wheezing			
subjects affected / exposed	1 / 15 (6.67%)	4 / 45 (8.89%)	0 / 31 (0.00%)
occurrences (all)	2	7	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 45 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2017	Added procedures for emergency unblinding to protocol
14 May 2018	Removal of PK blood draw and update to randomization ratios

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported