Clinical trial results:
A phase 2b, multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-selection study of S-600918 in patients with refractory chronic cough

Summary

EudraCT number	2019-002283-27
Trial protocol	GB CZ PL
Global end of trial date	28 December 2020

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	1812VA323

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04110054
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shionogi B.V.
Sponsor organisation address	Kingsfordweg 151, Amsterdam, Netherlands, 1043 GR
Public contact	Regulatory Affairs, Shionogi B.V., +44 2030534200, shionogiclintrials-admin@shionogi.co.jp
Scientific contact	Regulatory Affairs, Shionogi B.V., +44 2030534200, shionogiclintrials-admin@shionogi.co.jp

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	28 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 December 2020
Global end of trial reached?	Yes
Global end of trial date	28 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the optimal dose of S-600918 in patients with refractory chronic cough by evaluating the change from baseline in 24-hour cough frequency (coughs per hour) with S-600918 compared with placebo

Protection of trial subjects:

The study was conducted in accordance with the protocol approved by the IRB/IEC, all applicable regulatory requirements (including patient privacy requirements), current ICH GCP, and the ethical principles outlined in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2020
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	Poland: 49
Country: Number of subjects enrolled	United Kingdom: 38
Country: Number of subjects enrolled	Czechia: 29
Country: Number of subjects enrolled	United States: 150
Country: Number of subjects enrolled	Japan: 91
Country: Number of subjects enrolled	Ukraine: 49
Worldwide total number of subjects	406
EEA total number of subjects	78

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)	285
From 65 to 84 years	121
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were screened prior to enrollment

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Active 50mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	S-600918
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50mg, 150mg or 300mg, once daily for 4 weeks

Arm title	Active 150mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	S-600918
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50mg, 150mg or 300mg, once daily for 4 weeks

Arm title	Active 300mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	S-600918
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50mg, 150mg or 300mg, once daily for 4 weeks

Arm title	Placebo

Arm description: -

Arm type	Placebo

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
once daily for 4 weeks

Number of subjects in period 1	Active 50mg	Active 150mg	Active 300mg
Started	101	103	100
Completed	100	99	92
Not completed	1	4	8
Consent withdrawn by subject	-	3	2
Adverse event, non-fatal	1	1	4
Covid-19	-	-	2

Number of subjects in period 1	Placebo
Started	102
Completed	99
Not completed	3
Consent withdrawn by subject	-
Adverse event, non-fatal	3
Covid-19	-

Baseline characteristics

Reporting groups	
Reporting group title	Active 50mg
Reporting group description: -	
Reporting group title	Active 150mg
Reporting group description: -	
Reporting group title	Active 300mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Active 50mg	Active 150mg	Active 300mg
Number of subjects	101	103	100
Age categorical Units: Subjects			
Adults (18-64 years)	63	70	74
From 65-84 years	38	33	26
Gender categorical Units: Subjects			
Female	79	76	68
Male	22	27	32

Reporting group values	Placebo	Total	
Number of subjects	102	406	
Age categorical Units: Subjects			
Adults (18-64 years)	78	285	
From 65-84 years	24	121	
Gender categorical Units: Subjects			
Female	77	300	
Male	25	106	

End points

End points reporting groups

Reporting group title	Active 50mg
Reporting group description: -	
Reporting group title	Active 150mg
Reporting group description: -	
Reporting group title	Active 300mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Percent Change in Hourly Cough Counts in 24 Hours

End point title	Percent Change in Hourly Cough Counts in 24 Hours[1]
End point description:	
End point type	Primary
End point timeframe:	
Following 4 weeks of treatment	

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 have been uploaded

End point values	Active 50mg	Active 150mg	Active 300mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	102	96	99
Units: percent change in hourly cough count				
geometric mean (confidence interval 95%)	-55.16 (-55.16 to -55.16)	-61.08 (-61.08 to -61.08)	-65.32 (-65.32 to -65.32)	-60.38 (-60.38 to -60.38)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
4 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	Active - 50mg
Reporting group description: -	
Reporting group title	Active - 150 mg
Reporting group description: -	
Reporting group title	Active - 300mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Active - 50mg	Active - 150 mg	Active - 300mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	0 / 100 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 102 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Active - 50mg	Active - 150 mg	Active - 300mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 101 (4.95%)	15 / 103 (14.56%)	34 / 100 (34.00%)
Nervous system disorders			

Dysgeusia			
subjects affected / exposed	2 / 101 (1.98%)	12 / 103 (11.65%)	27 / 100 (27.00%)
occurrences (all)	2	12	27
Headache			
subjects affected / exposed	3 / 101 (2.97%)	2 / 103 (1.94%)	1 / 100 (1.00%)
occurrences (all)	3	2	1
Hypogeusia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	6 / 100 (6.00%)
occurrences (all)	0	1	6

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 102 (9.80%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	7		
Hypogeusia			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 September 2020	Inclusion of COVID-19 measures. Amendment was not considered substantial in all countries

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported