Clinical trial results:
A single-blind, placebo controlled, randomised study to evaluate antiviral activity and safety and pharmacokinetics of inhaled PC786 against respiratory syncytial virus (RSV) in healthy adult subjects in a virus challenge model

Summary

EudraCT number	2017-002563-18
Trial protocol	GB
Global end of trial date	09 May 2018

Results information

Result version number	v1 (current)
This version publication date	29 December 2019
First version publication date	29 December 2019

Trial information

Trial identification

Sponsor protocol code	PC_RSV_003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03382431
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pulmocide Ltd
Sponsor organisation address	52 Princes Gate, London, United Kingdom, SW7 2PG
Public contact	Director of Clinical Development, Pulmocide Ltd, +44 7766250133, Lindsey@pulmocide.com
Scientific contact	Director of Clinical Development, Pulmocide Ltd, +44 7766250133, Lindsey@pulmocide.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	30 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 May 2018
Global end of trial reached?	Yes
Global end of trial date	09 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the antiviral effect of inhaled PC786 compared to placebo in healthy adults who have received a clinical challenge strain of RSV (RSV-A Memphis 37b virus) inoculated via the intranasal route

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements. Known instances of non-conformance were documented and are not considered to have had an impact on the overall conclusions of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2017
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	United Kingdom: 56
Worldwide total number of subjects	56
EEA total number of subjects	56

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)	56
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Fifty six (56) healthy adult subjects were due to be inoculated with challenge virus and dosed with PC786/placebo to ensure that data for 40 evaluable subjects were obtained. A total of 56 healthy subjects were recruited to take part in the study at a single investigational site in the UK between 14 Nov 2017 and 28 Feb 2018.

Pre-assignment

Screening details:

A total of 163 subjects were screened to take part in the study; 107 subjects failed screening. Fifty six subjects were enrolled, inoculated with challenge virus and randomised to study treatment. All subjects completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PC786

Arm description:

Twice daily doses of PC786 5 mg for a total of 10 doses

Arm type	Experimental
Investigational medicinal product name	PC786 powder for reconstitution 30 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Twice daily doses of PC786 5 mg administered as an inhalation via a facemask for a total of 10 doses

Arm title	Placebo

Arm description:

Twice daily doses of placebo for a total of 10 doses

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Twice daily doses of placebo administered as an inhalation via a facemask

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: Due to a difference in appearance of the active and placebo treatments, the investigational product was prepared and dosed by independent staff team members who did not undertake any other study duties.

Number of subjects in period 1	PC786	Placebo
Started	28	28
Completed	28	28

Baseline characteristics

Reporting groups	
Reporting group title	PC786
Reporting group description:	
Twice daily doses of PC786 5 mg for a total of 10 doses	
Reporting group title	Placebo
Reporting group description:	
Twice daily doses of placebo for a total of 10 doses	

Reporting group values	PC786	Placebo	Total
Number of subjects	28	28	56
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	28	56
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	25.4	26.3	
standard deviation	± 5.63	± 5.89	-
Gender categorical Units: Subjects			
Female	10	9	19
Male	18	19	37

End points

End points reporting groups

Reporting group title	PC786
Reporting group description:	
Twice daily doses of PC786 5 mg for a total of 10 doses	
Reporting group title	Placebo
Reporting group description:	
Twice daily doses of placebo for a total of 10 doses	

Primary: Primary efficacy endpoint

End point title	Primary efficacy endpoint
End point description:	
The analysis of viral load AUC (time zero to Day 12) by nasal wash RT-qPCR for the ITT-IA analysis set described as all randomised subjects who received the challenge virus and at least one dose of study medication who had a positive quantitative PCR value >1.0 Log PFUe/mL immediately before dosing OR any subject who was qPCR negative before dosing and who subsequently had two or more qPCR positive results (>1.0 Log PFUe/mL) after the first dose dose of study medication.	
End point type	Primary
End point timeframe:	
From the last RT-qPCR measurement collected prior to the first dose of IMP until the last RT-qPCR measurement collected to to Day 12	

End point values	PC786	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: log10 PFUe x hr/mL				
least squares mean (standard deviation)	325.8 (± 199.19)	495.5 (± 199.22)		

Statistical analyses

Statistical analysis title	Descriptive statistics
Statistical analysis description:	
AUC descriptive statistics for derived RSV viral load parameters by treatment group (n, mean, SD, median (quartiles 1 and 3), minimum and maximum and comparison of treatment group means (mean, SE, 95% CI and p-value) were summarised.	
Comparison groups	PC786 v Placebo

Number of subjects included in analysis	34
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	= 0.0209
Method	t-test, 2-sided

Notes:

[1] - In this post-hoc analysis, an RSV viral load cut-off value of 1.0 Log10 PFUe/mL was used to define a new population, the Intent-to-Treat Infected Alternative (ITT-IA) population. This cut-off was designed to avoid the PCR detection of the inoculum itself in the absence of infection and improved the specificity of the assay to identify subjects truly infected with RSV.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Consent until final follow up visit	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	PC786
Reporting group description:	
Twice daily doses of PC786 5 mg for a total of 10 doses	
Reporting group title	Placebo
Reporting group description:	
Twice daily doses of placebo for a total of 10 doses	

Serious adverse events	PC786	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (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: 0 %

Non-serious adverse events	PC786	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 28 (42.86%)	14 / 28 (50.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 28 (14.29%)	4 / 28 (14.29%)	
occurrences (all)	4	4	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 28 (14.29%)	4 / 28 (14.29%)	
occurrences (all)	5	4	
Forced expiratory volume decreased			

subjects affected / exposed	2 / 28 (7.14%)	2 / 28 (7.14%)	
occurrences (all)	3	2	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 28 (3.57%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Forced vital capacity decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Nasal injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 28 (0.00%)	3 / 28 (10.71%)	
occurrences (all)	0	3	
Headache			
subjects affected / exposed	1 / 28 (3.57%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Application site rash			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Non-cardiac chest pain			

subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Photophobia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 28 (3.57%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
Cough			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Skin mass			

subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Costochondritis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 28 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported