



Clinical trial results:

A double blind, placebo-controlled study to assess the anti-viral effect, safety and tolerability of inhaled PC786 for the treatment of acute respiratory syncytial virus (RSV) infection in adult hematopoietic stem cell transplant recipients

Summary

EudraCT number	2018-001667-24
Trial protocol	GB
Global end of trial date	19 February 2019

Results information

Result version number	v1 (current)
This version publication date	17 May 2020
First version publication date	17 May 2020

Trial information

Trial identification

Sponsor protocol code	PC_RSV_004
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03715023
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pulmocide Ltd.
Sponsor organisation address	Pulmocide Ltd, 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	Interim
Date of interim/final analysis	27 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 February 2019
Global end of trial reached?	Yes
Global end of trial date	19 February 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the anti-viral effect of inhaled PC786 compared with placebo when added to standard of care (SoC) RSV treatment in haematopoietic stem cell transplant (HSCT) recipients with acute RSV infection
- To assess the safety and tolerability of 3 days of inhaled PC786 in HSCT subjects with acute RSV infection

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:

Subjects received SoC for treatment of RSV at the study site. All medications taken were recorded. Oral ribavirin was permitted at all times on the study. Intravenous ribavirin treatment as SoC may be administered if required, only if a subject was already enrolled in the study. Treatment with intravenous immunoglobulins was permitted throughout the study.

Evidence for comparator: -

Actual start date of recruitment	11 December 2018
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: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Six subjects met all of the eligibility criteria and were randomised to receive treatment at 3 sites in the UK between 11 Dec 2018 and 19 Feb 2019. One subject was withdrawn from the study without being dosed. Five subjects who received 3 doses of PC786 or placebo were therefore included in the safety population.

Pre-assignment

Screening details:

It was planned to recruit 30 subjects, with a minimum of 15 subjects to conduct an interim analysis after the winter 18/19 season. A total of six subjects were screened to take part in the study, of which, five subjects were randomised and completed the study.

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, Assessor

Blinding implementation details:

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.

Arms

Are arms mutually exclusive?	Yes
Arm title	PC786

Arm description:

Once daily doses of PC786 10mg administered by inhalation via a face mask for a total of 3 doses

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

Dosage and administration details:

Nebulised PC786 was administered by inhalation via a facemask at the study site at a dose of 10 mg once daily for three days. In addition to the study drug, subjects were treated according to the SoC at the study site.

Arm title	Placebo
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Arm description:

Once daily doses of placebo administered by inhalation via a face mask for a total of 3 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:

Nebulised placebo was administered by oral inhalation via a face mask once daily for 3 doses. In addition to the study drug, subjects were treated according to the SoC at the study site.

Number of subjects in period 1	PC786	Placebo
Started	2	3
Completed	2	3

Baseline characteristics

Reporting groups

Reporting group title	PC786
Reporting group description:	
Once daily doses of PC786 10mg administered by inhalation via a face mask for a total of 3 doses	
Reporting group title	Placebo
Reporting group description:	
Once daily doses of placebo administered by inhalation via a face mask for a total of 3 doses	

Reporting group values	PC786	Placebo	Total
Number of subjects	2	3	5
Age categorical			
PC786			
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)	2	3	5
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	41.5	57.3	
standard deviation	± 9.19	± 6.03	-
Gender categorical			
Units: Subjects			
Female	1	1	2
Male	1	2	3

End points

End points reporting groups

Reporting group title	PC786
Reporting group description: Once daily doses of PC786 10mg administered by inhalation via a face mask for a total of 3 doses	
Reporting group title	Placebo
Reporting group description: Once daily doses of placebo administered by inhalation via a face mask for a total of 3 doses	
Subject analysis set title	PC786
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pharmacokinetic Parameters for PC786	

Primary: Slope of RSV viral load

End point title	Slope of RSV viral load ^[1]
End point description: Slope of the RSV load over Days 1–3 measured in nasal secretions by reverse transcription quantitative polymerase chain reaction (RT-qPCR)	
End point type	Primary
End point timeframe: Baseline to day 3	

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: There are no treatment comparisons in this study due to the small sample size (N=5).

End point values	PC786	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Log10 PFUe/mL/day				
arithmetic mean (standard error)	-1.42 (± 0.193)	-0.73 (± 0.174)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Viral load to Day 7

End point title	Change in Viral load to Day 7
End point description: Change in RSV load from baseline to day 7 measured in nasal secretions by reverse transcription quantitative polymerase chain reaction (RT-qPCR)	
End point type	Secondary
End point timeframe: Days 1 to 7	

End point values	PC786	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Log 10 PFUe/mL				
arithmetic mean (standard error)	-4.27 ($\pm$ 0.58)	-2.70 ($\pm$ 0.625)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Viral Shedding

End point title	Duration of Viral Shedding
End point description:	
Duration of viral shedding	
End point type	Secondary
End point timeframe:	
Day 1 to day 28	

End point values	PC786	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: day				
arithmetic mean (standard error)	4.0 ($\pm$ 2)	19.67 ($\pm$ 8.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in viral load to day 4

End point title	Change in viral load to day 4
End point description:	
Change in RSV load from baseline (before first dose of PC786 or placebo) to Day 4	
End point type	Secondary
End point timeframe:	
Baseline to day 4 am	

End point values	PC786	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Log10 PFUe/mL				
arithmetic mean (standard error)	-4.27 ($\pm$ 0.58)	-2.18 ($\pm$ 0.523)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax

End point title	Cmax
End point description:	
Maximum plasma concentration	
End point type	Secondary
End point timeframe:	
Time 0h to day 28	

End point values	PC786			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: pg/mL				
number (not applicable)	3410			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax

End point title	Tmax
End point description:	
time to maximum concentration	
End point type	Secondary
End point timeframe:	
time 0h to day 28	

End point values	PC786			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: hour				
number (not applicable)	0.25			

Statistical analyses

No statistical analyses for this end point

Secondary: Lower Respiratory Tract Infection/Pneumonia and Oxygen Requirements and Ventilation

End point title	Lower Respiratory Tract Infection/Pneumonia and Oxygen Requirements and Ventilation
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End point description:

Development of LRTI or pneumonia (due to RSV or secondary [bacterial or fungal] infection), Oxygen Requirements and Invasive Ventilation

End point type	Secondary
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End point timeframe:

Baseline to Day 28

End point values	PC786	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Percent of Subjects				
Developed Pneumonia	0	100		
Increased oxygen saturation index	0	67		
Oxygen saturation values <97% on multiple days	0	100		
Required invasive ventilation	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Consent until completion of the subject's last study-related procedure (which may include contact for follow-up of safety).

Adverse event reporting additional description:

All clinically relevant changes (including laboratory safety testing), with the exception of expected signs and symptoms of RSV-related illness, observed during the study were recorded as an AE.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	PC786
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Reporting group description:

Once daily doses of PC786 10mg administered by inhalation via a face mask for a total of 3 doses

Reporting group title	Placebo
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Reporting group description:

Once daily doses of placebo administered by inhalation via a face mask for a total of 3 doses

Serious adverse events	PC786	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Neutropenic sepsis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Superinfection bacterial subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	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	2 / 2 (100.00%)	3 / 3 (100.00%)	
Investigations			
Blood magnesium decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood potassium decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Clostridium test positive			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Oxygen saturation decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Vascular disorders			
Vasodilatation			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	2	
General disorders and administration site conditions			

Peripheral swelling subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	
Ear and labyrinth disorders Excessive cerumen production subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 3 (66.67%) 2	
Vomiting subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	3 / 3 (100.00%) 3	
Cough subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	2 / 3 (66.67%) 2	
Productive cough subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	1 / 3 (33.33%) 1	
Sneezing subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	
Infections and infestations			

Febrile infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Pulmonary mycosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Poor recruitment during the 2018/19 RSV season meant that an interim analysis to adjust the sample size was not possible. The chances of completing enrolment in the study in the 2019/20 RSV season were low and the study was terminated prematurely.

Notes: