Clinical trial results:
An open-label study to assess the safety, pharmacokinetics and pharmacodynamics of inhaled PC945 in adult Cystic Fibrosis (CF) patients with persistent pulmonary Aspergillus fumigatus infection.

Summary

EudraCT number	2018-000243-87
Trial protocol	GB
Global end of trial date	01 June 2020

Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021

Trial information

Trial identification

Sponsor protocol code	PC_ASP_003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03870841
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pulmocide Ltd
Sponsor organisation address	44 Southampton Buildings, London, United Kingdom, WC2A 1AP
Public contact	Dr Lance Berman, Pulmocide Ltd, +34 660 745 200 , Lance@pulmocide.com
Scientific contact	Dr Lance Berman, Pulmocide Ltd, +34 660 745 200 , Lance@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	15 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2020
Global end of trial reached?	Yes
Global end of trial date	01 June 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

• To investigate the safety and tolerability of once daily treatment with inhaled PC945 for 28 days in adult subjects with CF who have persistent pulmonary Aspergillus fumigatus infection
• To obtain estimates of derived systemic pharmacokinetic parameters of PC945 and the potential circulating metabolite(s), if detectable, following single and repeat doses of PC945

The study was terminated early as a result of the COVID-19 outbreak as the study was being conducted in a vulnerable patient group that was at very high risk of severe illness from COVID-19 and recruitment was halted by the hospitals involved in the study. As it was not possible to predict when recruitment could recommence, and it was unlikely that the trials could be completed without significant changes to the protocols, the Sponsor stopped the study on 01 June 2020.

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 PC945 in addition to their standard of care treatments

Evidence for comparator: -

Actual start date of recruitment	23 May 2019
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: 4
Worldwide total number of subjects	4
EEA total number of subjects	0

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)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eighteen subjects were to be enrolled to ensure that at least 10 subjects received PC945 and completed the study

Pre-assignment

Screening details:

Six subjects were entered into the study, two of whom failed screening. Four subjects were recruited, one of whom was an earlier screening failure who was re-screened and then successfully entered the study. One subject was discontinued when the study was halted temporarily; the study was then terminated early as a result of COVID-19.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open label study with no blinding implementation.

Arms

Arm title	PC945

Arm description:

Once daily doses of PC945 5 mg (emitted dose) once daily for 28 days

Arm type	Experimental
Investigational medicinal product name	PC945
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

5mg (emitted dose) once daily for 28 days administered as a suspension for inhalation via a nebuliser

Number of subjects in period 1	PC945
Started	4
Completed	3
Not completed	1
Trial halted temporarily	1

Baseline characteristics

Reporting groups	
Reporting group title	PC945
Reporting group description:	
Once daily doses of PC945 5 mg (emitted dose) once daily for 28 days	

Reporting group values	PC945	Total	
Number of subjects	4	4	
Age categorical 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)	4	4	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	28.5		
standard deviation	± 7.68	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	2	2	

End points

End points reporting groups

Reporting group title	PC945
Reporting group description:	
Once daily doses of PC945 5 mg (emitted dose) once daily for 28 days	

Primary: PC945 Cmax Day 1

End point title	PC945 Cmax Day 1[1]
End point description:	
Maximum PC945 plasma concentration observed from time 0 to 2 hours post dose; summary statistics provided.	
End point type	Primary
End point timeframe:	
Day 1	

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: Summary statistics provided - no formal analysis conducted.

End point values	PC945			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	0.219 (± 33.9)			

Statistical analyses

No statistical analyses for this end point

Primary: PC945 Cmax Day 14

End point title	PC945 Cmax Day 14[2]
End point description:	
Maximum PC945 plasma concentration from time 0 to 2 hour post dose; summary statistics provided.	
End point type	Primary
End point timeframe:	
Day 14	

Notes:

[2] - 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: Summary statistics provided - no formal analysis conducted.

End point values	PC945			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	0.791 (± 125)			

Statistical analyses

No statistical analyses for this end point

Primary: PC945 AUC 0-2h Day 1

End point title	PC945 AUC 0-2h Day 1[3]

End point description:

Area under the PC945 plasma concentration - time curve from 0 to 2 hour post dose; summary statistics provided.

End point type	Primary

End point timeframe:

Day 1

Notes:

[3] - 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: Summary statistics provided - no formal analysis conducted.

End point values	PC945			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	0.241 (± 5.3)			

Statistical analyses

No statistical analyses for this end point

Primary: PC945 AUC 0-2h Day 14

End point title	PC945 AUC 0-2h Day 14[4]

End point description:

Area under PC945 plasma concentration-time curve from 0 to 2 hour post dose; summary statistics provided.

End point type	Primary

End point timeframe:

Day 14

Notes:

[4] - 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: Summary statistics provided - no formal analysis conducted.

End point values	PC945			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	1.49 (± 125)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were to be reported from Visit 2 until completion of the subject's last study-related procedure.

Adverse event reporting additional description:

Prior to Visit 2, from the time of signing consent, only AEs considered to be related to study procedures will be recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	PC945

Reporting group description: -

Serious adverse events	PC945		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	PC945		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Investigations			
Cortisol decreased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	4		
Sputum increased			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
Rales			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Wheezing			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Dyspnoea exertional			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Haemoptysis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Increased viscosity of bronchial secretion			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pleuritic pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Sputum discoloured			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Psychiatric disorders			

Depressed mood subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Joint stiffness subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Infections and infestations Lower respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 2 / 4 (50.00%) 2		

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? Yes

Date	Interruption	Restart date
15 November 2019	The study had been placed on temporary hold due to a quality issue with the study drug (sweet odour/taste) that was attributed to the terminal sterilisation of the product via ionising radiation. There were no AEs owing to the quality issue. The quality issue had no impact on the active ingredient PC945 or product performance. The study was scheduled to be restarted using study drug manufactured via aseptic processing.	24 April 2020
01 June 2020	The PC_ASP_003 study was terminated early as a result of the COVID-19 outbreak as the study was being conducted in a vulnerable patient group that was at very high risk of severe illness from COVID-19 and recruitment was halted by the hospitals involved in the study. As it was not possible to predict when recruitment could recommence, and it was unlikely that the trials could be completed without significant changes to the protocols, the Sponsor stopped the study on 01 June 2020.	-

Notes:

Limitations and caveats

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

Due to the early termination and the limited number of subjects who completed the study no formal analysis are presented for secondary endpoints.

Notes: