Clinical trial results:
An open-label, pilot study to assess safety, tolerability, pharmacokinetics and effects of inhaled PC945 in the pre-emptive treatment of Aspergillus fumigatus colonisation in lung transplant recipients

Summary

EudraCT number	2018-000240-26
Trial protocol	GB
Global end of trial date	01 June 2020

Results information

Result version number	v1 (current)
This version publication date	30 July 2021
First version publication date	30 July 2021

Trial information

Trial identification

Sponsor protocol code	PC_ASP_002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03905447
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 660745200, Lance@pulmocide.com
Scientific contact	Dr Lance Berman, Pulmocide Ltd, +34 660745200, 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	13 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 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 assess the safety and tolerability of PC945 in lung transplant recipients with A. fumigatus colonisation
• To ascertain 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 were able to receive standard of care post-transplant antifungal prophylaxis, which could include nebulised amphotericin B and/or a systemic antifungal.

Evidence for comparator: -

Actual start date of recruitment	05 September 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: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

It was anticipated that approximately 30 lung transplant recipients would be included in the Surveillance Phase and undergo SoC bronchoscopies in order to identify 10 subjects colonised with A. fumigatus for inclusion in the Pre-Emptive Treatment Phase with PC945.

Pre-assignment

Screening details:

Pre transplant consent was signed by 21 subjects. Two of these patients entered the 12 week post transplant surveillance phase before the study was put on temporary hold 15 November 2019. No subjects entered the treatment phase.

Pre-assignment period milestones

Number of subjects started	2
Number of subjects completed	2

Period 1

Period 1 title	Surveillance Phase (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 thus no blinding was implemented.

Arms

Arm title	Surveillance Period

Arm description:

A 12 week surveillance period commenced post transplant. Eligible subjects found to be colonised with A. fumigatus during the 12-week surveillance period were to enter the Pre-emptive PC945 Treatment Phase.
Subjects who were A. fumigatus-positive but with clinical, bronchoscopic or radiological features of respiratory fungal disease, or those infected with fungi other than A. fumigatus, were to receive SoC antifungal treatment.
Subjects without fungal infections participated in the Surveillance Phase only and did not receive PC945.

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:

PC945 5mg emitted dose, to be administered once daily for 28 days, in subjects found to be colonised with A. fumigatus during the 12-week surveillance period.
Subjects without fungal infections participated in the Surveillance Phase only and did not receive investigational product.

Number of subjects in period 1	Surveillance Period
Started	2
Completed	2

Baseline characteristics

Reporting groups	
Reporting group title	Surveillance Phase
Reporting group description:	
Surveillance Phase	

Reporting group values	Surveillance Phase	Total	
Number of subjects	2	2	
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)	2	2	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	2	2	
Male	0	0	

Subject analysis sets	
Subject analysis set title	Surveillance Phase
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients in the surveillance phase only - no treatment	

Reporting group values	Surveillance Phase		
Number of subjects	2		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	2		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	2		
Male	0		

End points

End points reporting groups

Reporting group title	Surveillance Period

Reporting group description:

A 12 week surveillance period commenced post transplant. Eligible subjects found to be colonised with A. fumigatus during the 12-week surveillance period were to enter the Pre-emptive PC945 Treatment Phase.
Subjects who were A. fumigatus-positive but with clinical, bronchoscopic or radiological features of respiratory fungal disease, or those infected with fungi other than A. fumigatus, were to receive SoC antifungal treatment.
Subjects without fungal infections participated in the Surveillance Phase only and did not receive PC945.

Subject analysis set title	Surveillance Phase
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients in the surveillance phase only - no treatment

Primary: Safety of PC945

End point title	Safety of PC945[1]

End point description:

End point type	Primary

End point timeframe:

Adverse events will be reported from 48 hours post-transplant until completion of the subject's last study-related procedure.

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 data to report. No adverse events nor safety issues were reported during the surveillance phase.

End point values	Surveillance Phase			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: number of adverse events	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Adverse events were to be reported from 48 hours post-transplant until completion of the subject's last study-related procedure.	
Adverse event reporting additional description:	
No adverse events were reported.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No subjects received study treatment and no adverse events were reported during the study. Two subjects were included in a 12 week surveillance phase before the study was terminated and no adverse events were reported by these subjects.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2018	Amendment 1 was written to define post-menopausal status and to increase the number of pregnancy tests performed in subjects taking IP. The number of days that female subjects must use an acceptable effective form of contraception after the final dose of PC945 was increased from 30 days to 55 days to account for the long half-life of PC945. Assessment of subjects' vital signs were to include temperature recordings. In addition, it was clarified that recognised complications of the lung transplant procedure were not to be recorded as adverse events unless the investigator considered these to be related to the study medication (PC945) or an antifungal prescribed as standard of care.
29 August 2019	Amendment 3 included: The criteria for being able to provide Extended PC945 treatment were too stringent (i.e., evidence of Aspergillus fumigatus was required in the Week 6 bronchoscopy for patients to qualify for extended treatment and if these were negative, there was no flexibility to continue treatment). There could be other patients that require >4 weeks of treatment. As cultures may be suppressed by the PC945 in the samples, it was considered to be prudent to also allow continued treatment in those patients that concerned investigators, on clinical grounds (e.g., with clinical or bronchoscopic features of disease). Other changes included : The bronchosorption synthetic absorption matrix (BSAM) sampling for collection of mucosal lining fluid for pharmacokinetic (PK) analysis was removed. Measurement of Aspergillus immunoglobulin (Ig)G, Aspergillus IgE and Total IgE were added. Bacterial microbiome assessments were included. The first in human study data were removed as they were included in the updated Investigator's Brochure.

Notes:

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.	09 April 2020

01 June 2020	The PC_ASP_002 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 of the study due to the COVID19 pandemic and given that no subjects received PC945 pre-emptive treatment there are no study data to be analysed or reported.

Notes: