



Clinical trial results:

A Phase 2, Single-Center, Double-Blind, Placebo-Controlled, Study of PUL-042 Inhalation Solution in Rhinovirus-induced Symptoms in Current Smokers with Gold Stage 0 Chronic Obstructive Pulmonary Disease (COPD).

Summary

EudraCT number	2018-002806-30
Trial protocol	GB
Global end of trial date	16 December 2020

Results information

Result version number	v1 (current)
This version publication date	21 April 2022
First version publication date	21 April 2022
Summary attachment (see zip file)	Summary Report (PUL-042-402) (Summary Final Report PUL-042-402.pdf)

Trial information

Trial identification

Sponsor protocol code	PUL-042-402
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03794557
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pulmotect, Inc.
Sponsor organisation address	3900 Essex Lane, Suite 575, Houston, United States, TX 77027
Public contact	Brenton Scott, PhD, Pulmotect, Inc., 1 713579-9226, bscott@pulmotect.com
Scientific contact	Brenton Scott, PhD, Pulmotect, Inc., 1 713579-9226, bscott@pulmotect.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	14 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 December 2020
Global end of trial reached?	Yes
Global end of trial date	16 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effects of PUL-042 Inhalation Solution on peak lower respiratory symptom score in GOLD stage 0 COPD subjects with an experimentally introduced rhinovirus infection with laboratory human rhinovirus strain HRV A16. All subjects will be negative for serum neutralizing antibody to HRV A16 at screening prior to viral inoculation.

Protection of trial subjects:

An external Data Safety Monitoring Board (DSMB) was used to evaluate safety of the study. There were three voting members. None of the voting members had any affiliation with Pulmotect, Inc.

The DSMB reviewed study data on an ongoing basis as specified in the DSMB charter.

The first cohort tested consisted of 2 subjects (1 active and 1 placebo) and was a sentinel group. The second cohort (2 active and 2 placebo) was not dosed until both subjects in the sentinel group had completed treatment through Day 21 and the Principal Investigator and the Medical Monitor agreed that dosing of the second cohort could proceed.

The second cohort of 4 subjects (2 active and 2 placebo) was followed until all subjects completed Day 21. At that point, the DSMB reviewed the data from the first 6 subjects (3 active and 3 placebo) and was asked to make a recommendation to continue with the study, prior to any further subjects being dosed.

The Principal Investigator or Medical Monitor could independently terminate the study at any time.

Background therapy:

Current smokers with >10 pyh;

Subject had risk of COPD defined by GOLD Staging Criteria level 0 where the subjects' post-bronchodilator FEV1/FVC ratio >0.70 and FEV1 is >80% normal predicted;

Evidence for comparator:

Not applicable - comparator was standard of care for the disease plus placebo.

Actual start date of recruitment	19 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 24
Worldwide total number of subjects	24
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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled from 1 site, in 1 country: ICRRU, St Mary's Hospital, London, United Kingdom.

Screening of patients lasted from November 2018 to November 2020. The first patient was randomised on 21 January 2019, with the last patient being randomised in to the study 3 November 2020

Pre-assignment

Screening details:

In total 143 subjects were screened, 24 of which passed screening (16.8%). Potential subjects failed screening for a number of different reasons. There was not a trend in screening failure.

Period 1

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

Blinding implementation details:

The pharmacy personnel at the clinical site were responsible for the preparation of the appropriate concentration of PUL-042. Members of the site team, responsible for administration and clinical assessment, were blinded.

In addition, an unblinded monitor was employed to carry out the pharmacy visits and drug reconciliation, ensuring that the blinding of the monitor reviewing the clinical data was maintained.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

Patients treated with active treatment

Arm type	Experimental
Investigational medicinal product name	PUL-042
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

20.3 µg Pam2 : 29.8 µg ODN administered 24 hours prior to inoculation with HRV A16 followed by a second dose of PUL-042 (20.3 µg Pam2 : 29.8 µg ODN) administered 48 hours post inoculation with HRV A16

Arm title	Placebo
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Arm description:

Patients treated with placebo treatment 24 hours prior to inoculation with HRV A16 followed by a second dose of placebo treatment administered 48 hours post inoculation with HRV A16

Arm type	Placebo
Investigational medicinal product name	Placebo to match PUL-042
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Placebo of equal volume to match PUL-042

Number of subjects in period 1^[1]	Active	Placebo
Started	11	11
Completed	9	10
Not completed	2	1
Consent withdrawn by subject	1	-
Physician decision	1	-
Adverse event, non-fatal	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 24 subjects passed screening. One subject was lost to follow up prior to randomisation. Another subject was withdrawn due to an investigator's decision regarding an abnormal chest X-ray prior to dosing on Study Day -1. So, 23 were subsequently randomised, 22 of whom became the safety population.

Baseline characteristics

Reporting groups

Reporting group title	Active
Reporting group description:	
Patients treated with active treatment	
Reporting group title	Placebo
Reporting group description:	
Patients treated with placebo treatment 24 hours prior to inoculation with HRV A16 followed by a second dose of placebo treatment administered 48 hours post inoculation with HRV A16	

Reporting group values	Active	Placebo	Total
Number of subjects	11	11	22
Age categorical			
Patient Age was collected at patient enrollment			
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)	11	11	22
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Patient gender was collected at patient enrollment			
Units: Subjects			
Female	4	4	8
Male	7	7	14

End points

End points reporting groups

Reporting group title	Active
Reporting group description:	
Patients treated with active treatment	
Reporting group title	Placebo
Reporting group description:	
Patients treated with placebo treatment 24 hours prior to inoculation with HRV A16 followed by a second dose of placebo treatment administered 48 hours post inoculation with HRV A16	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety population	

Primary: Effects of PUL-042 Inhalation Solution on peak lower respiratory symptom score

End point title	Effects of PUL-042 Inhalation Solution on peak lower respiratory symptom score
End point description:	
LRSS was measured repeatedly during each dosing day, by means of patients completing a questionnaire	
End point type	Primary
End point timeframe:	
Pre-treatment to Day 14	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: LRSS				
arithmetic mean (standard deviation)	5.11 (\pm 0.78)	5.00 (\pm 2.92)		

Statistical analyses

Statistical analysis title	Primary Statistical Analysis
Statistical analysis description:	
All statistical analysis was performed according to the Statistical Analysis Plan. Statistical analysis for the primary endpoints on the infected and evaluable population involved the use of analysis of co-variance (ANCOVA) to identify differences between placebo and PUL-042 treated subjects for all primary symptom score endpoints. The symptom scores were analysed firstly as actual values; additionally, data was analysed as adjusted from baseline which involved subtracting the baseline scores.	
Comparison groups	Placebo v Active

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	≤ 0.05 ^[2]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - The ANCOVA analysis for the primary and secondary endpoints was shown as model estimates, reporting P-values for any treatment effect for significant differences between PUL-042 and placebo, and also for any baseline effect; whereby the baseline score was analysed as a co-variate, thus improving the efficiency of the analysis by reducing the variability (minimum variance unbiased estimator).

[2] - A significant P-value for the baseline effect indicated that the ANCOVA had significantly reduced the experimental error variance for the baseline co-variate.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were recorded at each clinic visit from signing of the Informed Consent Form until completion of the End of Study visit (Day 42)

Adverse event reporting additional description:

At every patient visit, patients were asked non-leading questions to determine the occurrence of AEs. In addition, all AEs reported spontaneously during the course of the clinical study were recorded.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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Reporting groups

Reporting group title	Active
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Reporting group description:

Patients receiving active treatment

Reporting group title	Placebo
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Reporting group description:

Patients receiving placebo treatment (placebo).

Serious adverse events	Active	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (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	Active	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	10 / 11 (90.91%)	
Investigations			
Forced expiratory volume decreased			
subjects affected / exposed	6 / 11 (54.55%)	4 / 11 (36.36%)	
occurrences (all)	7	5	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 11 (27.27%)	3 / 11 (27.27%)	
occurrences (all)	4	4	

Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 11 (18.18%)	3 / 11 (27.27%)	
occurrences (all)	2	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2018	<p>The purpose of the submission was to provide an updated protocol for study PUL-042-402 (new protocol version 4; 7 November 2018).</p> <p>The clinical protocol was amended in version 4: the descriptions of the clinical blood tests being conducted, as these were variously referred to as Haematology and biochemistry, clinical laboratory (LFTs, haematology, Chemistry), or serum chemistry, in protocol PUL-042-402; Version 3, dated 25th October, 2018. The sponsor now referred to blood analytes (Na+, glucose etc.) as serum chemistry, identified liver function tests, serum CRP and haematology tests independently.</p> <p>This did not change the overall number of blood tests; just a more accurate reflection of what tests were to be performed and when. Other changes were editorial and non-substantial in nature.</p>
01 July 2019	<p>The purpose of the amendment was to provide PUL-042-402 (protocol version 5; 28th June, 2019).</p> <p>The active protocol provided for collection of vital signs at 15 minutes and 30 minutes post-dose on D-1 and D2 as represented in Table 2 'Schedule of Events'. This was not reflected in the corresponding wording in Section 7 of the main body of the protocol (specifically Sections 7.11.3 and 7.14.1). The Sponsor modified these paragraphs in Section 7, such that they corresponded with the 'Schedule of Events' appropriately. In addition, the Sponsor added Lower Respiratory Symptom Score (LRSS) diary completion at 15 minutes as well as at 30 minutes post-dose on D-1 and D2 to provide symptom information in tandem with vital signs. The DSMB was comfortable with this addition.</p> <p>The sponsor is also taking this opportunity to make some additional corrections/revisions to the protocol. These changes were editorial and non-substantial in nature.</p>
28 October 2019	<p>The purpose of the amendment was to provide PUL-042-402 protocol version 6; 22nd October, 2019.</p> <p>The changes included and increase of the Number of Subjects such that twenty four subjects would be enrolled. Twelve subjects would be randomised to each arm, to allow for additional potential unevaluable patients. In addition, the Study Drug Administration was updated to permit the use of a CE-marked facemask (PARI Adult Mask Soft or the PARI SMARTMASK) as an alternative to study drug administration by inhalation by mouth, both via a Pari Sprint nebulizer.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 March 2020	1st wave of the COVID19 pandemic of 2020	03 August 2020

Notes:

Limitations and caveats

None reported