Clinical trial results:
A phase IIa, randomised, double-blind, placebo-controlled study using outpatient setting to investigate the duration of effect and evaluate further safety of PrEP-001 given prophylactically in healthy subjects, subsequently challenged with human rhinovirus (HRV-16)

Summary

EudraCT number	2015-005492-25
Trial protocol	GB
Global end of trial date	07 October 2016

Results information

Result version number	v1 (current)
This version publication date	21 April 2018
First version publication date	21 April 2018

Trial information

Trial identification

Sponsor protocol code	PrEP-CS-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03338556
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PrEP Biopharm Limited
Sponsor organisation address	42 New Road, London, United Kingdom, E1 2AX
Public contact	Bruce Malcolm Chief Scientific Officer, PrEP Biopharm Limited, info@prepbiopharm.com
Scientific contact	Bruce Malcolm Chief Scientific Officer, PrEP Biopharm Limited, info@prepbiopharm.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	07 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 October 2016
Global end of trial reached?	Yes
Global end of trial date	07 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the prophylactic effect of repeated intranasal dosing of PrEP-001 in healthy subjects, subsequently challenged with HRV-16, on the changes in clinical symptoms when compared to placebo at two different dosing regimens

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy:

None

Evidence for comparator:

Placebo

Actual start date of recruitment	30 March 2016
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: 102
Worldwide total number of subjects	102
EEA total number of subjects	102

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)	102
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All subjects recruited in the United Kingdom were healthy males and/or females, 18 to 55 years of age, who met the eligibility criteria. First patient consented 30 March 2016. Last Patient Last Visit 7 October 2016.

Pre-assignment

Screening details:

Healthy males and/or females, 18 to 55 years, with no history of major medical conditions from the medical history, physical examination, and routine laboratory tests as determined by the Investigator at a screening evaluation.

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, Data analyst

Blinding implementation details:

Double blind

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A - PrEP-001

Arm description:

PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).

Arm type	Experimental
Investigational medicinal product name	PrEP-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

6.4 mg PrEP-001 nasal powder once daily

Arm title	Cohort A - Placebo

Arm description:

Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

6.4 mg matching placebo nasal powder once daily

Arm title	Cohort B- PrEP-001

Arm description:

PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).

Arm type	Experimental
Investigational medicinal product name	PrEP-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

6.4 mg PrEP-001 nasal powder once daily

Arm title	Cohort B - Placebo

Arm description:

Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

6.4 mg matching placebo nasal powder once daily

Number of subjects in period 1	Cohort A - PrEP-001	Cohort A - Placebo	Cohort B- PrEP-001
Started	25	27	24
Completed	25	27	24

Number of subjects in period 1	Cohort B - Placebo
Started	26
Completed	26

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A - PrEP-001
Reporting group description:	
PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort A - Placebo
Reporting group description:	
Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort B- PrEP-001
Reporting group description:	
PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort B - Placebo
Reporting group description:	
Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).	

Reporting group values	Cohort A - PrEP-001	Cohort A - Placebo	Cohort B- PrEP-001
Number of subjects	25	27	24
Age categorical			
Units: Subjects			
Adults (18-55 years)	25	27	24
Age continuous			
Units: years			
arithmetic mean	24.3	24.9	21.7
standard deviation	± 6.26	± 8.30	± 2.93
Gender categorical			
Units: Subjects			
Female	12	11	4
Male	13	16	20

Reporting group values	Cohort B - Placebo	Total	
Number of subjects	26	102	
Age categorical			
Units: Subjects			
Adults (18-55 years)	26	102	
Age continuous			
Units: years			
arithmetic mean	22.2		
standard deviation	± 3.58	-	
Gender categorical			
Units: Subjects			
Female	9	36	
Male	17	66	

End points

End points reporting groups

Reporting group title	Cohort A - PrEP-001
Reporting group description:	
PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort A - Placebo
Reporting group description:	
Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort B- PrEP-001
Reporting group description:	
PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort B - Placebo
Reporting group description:	
Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).	

Primary: Overall total symptom score, defined as the sum of the total symptom scores from Day 1 to Day 8, inclusive, using the 10-point symptom diary card

End point title	Overall total symptom score, defined as the sum of the total symptom scores from Day 1 to Day 8, inclusive, using the 10-point symptom diary card
End point description:	
End point type	Primary
End point timeframe:	
Day 1 to Day 8	

End point values	Cohort A - PrEP-001	Cohort A - Placebo	Cohort B- PrEP-001	Cohort B - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	23	21	24
Units: Overall total symptom score				
arithmetic mean (standard deviation)	22.5 (± 21.63)	34.2 (± 38.67)	36.2 (± 38.19)	33.5 (± 40.54)

Statistical analyses

Statistical analysis title	ITT analysis set
Comparison groups	Cohort B- PrEP-001 v Cohort B - Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.519
Method	t-test, 2-sided

Secondary: The area under the curve (AUC) of symptom scores, using symptoms from Day 1 to Day 8 from the 10-point symptom diary card, calculated separately for total symptoms, upper respiratory tract, lower respiratory tract and systemic viral symptoms

End point title	The area under the curve (AUC) of symptom scores, using symptoms from Day 1 to Day 8 from the 10-point symptom diary card, calculated separately for total symptoms, upper respiratory tract, lower respiratory tract and systemic viral symptoms
End point description: Using 10 item diary card	
End point type	Secondary
End point timeframe: Day 1 to Day 8	

End point values	Cohort A - PrEP-001	Cohort A - Placebo	Cohort B- PrEP-001	Cohort B - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	23	20	23
Units: AUC total symptom score				
arithmetic mean (standard deviation)	10668.8 (± 10359.03)	16543.3 (± 18742.21)	17782.2 (± 18533.03)	16385.7 (± 19936.53)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Reporting from consent to last patient last visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Cohort A - PrEP-001
Reporting group description:	
PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort A - Placebo
Reporting group description:	
Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 7 and Day - 6 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort B- PrEP-001
Reporting group description:	
PrEP-001 6400 µg/day, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).	
Reporting group title	Cohort B - Placebo
Reporting group description:	
Placebo matching PrEP-001, equally divided over both nostrils, on 2 consecutive days. Dosed Day - 4 and Day - 3 prior to intranasal challenge with HRV-16 (Day 0).	

Serious adverse events	Cohort A - PrEP-001	Cohort A - Placebo	Cohort B- PrEP-001
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 27 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Cohort B - Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Cohort A - PrEP-001	Cohort A - Placebo	Cohort B- PrEP-001
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 25 (76.00%)	16 / 27 (59.26%)	18 / 24 (75.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 27 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 25 (0.00%)	1 / 27 (3.70%)	2 / 24 (8.33%)
occurrences (all)	0	1	2
Blood fibrinogen increased			
subjects affected / exposed	3 / 25 (12.00%)	2 / 27 (7.41%)	0 / 24 (0.00%)
occurrences (all)	3	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 25 (0.00%)	2 / 27 (7.41%)	2 / 24 (8.33%)
occurrences (all)	0	2	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 25 (0.00%)	2 / 27 (7.41%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Blood bilirubin increased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 27 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Neutrophil count decreased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 27 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
injury, poisoning and procedural complications			
subjects affected / exposed	12 / 25 (48.00%)	10 / 27 (37.04%)	8 / 24 (33.33%)
occurrences (all)	20	15	12
Sun burn			
subjects affected / exposed	0 / 25 (0.00%)	1 / 27 (3.70%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			

subjects affected / exposed	0 / 25 (0.00%)	0 / 27 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	3
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 27 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 25 (12.00%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0

Non-serious adverse events	Cohort B - Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 26 (42.31%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Blood fibrinogen increased			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	4 / 26 (15.38%)		
occurrences (all)	4		
Lymphocyte count decreased			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		

Injury, poisoning and procedural complications			
injury, poisoning and procedural complications			
subjects affected / exposed	6 / 26 (23.08%)		
occurrences (all)	13		
Sun burn			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2016	Change of PI Change of Sponsor Representative Exclusion criteria added: o Subjects with a diagnosis of mild or moderate depressive episode(s) which occurred 2 or more years ago, with good evidence of preceding stressors and which resolved within approximately 3 months could be included in the Investigator's opinion – clarification of existing criteria o During screening, if subjects had a total cholesterol level > 6mmol/L they were excluded from the study- additional safety Minor administrative changes for clarity and aid clinical delivery
14 June 2016	Change of design for Cohort C from day -13/14 dosing to Day -7 dosing only Change in primary endpoint from the area under the curve (AUC) of total symptom score to overall symptom score Amendment and additional secondary endpoints added Minor administrative changes to improve clarity and aid clinical delivery.

Notes:

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.

The above study results support a daily dosing regime for PrEP-001.

Notes: