Clinical trial results:
A Phase II, Repeated Dose, Double-Blinded, Randomised, Controlled Study to Examine the Prophylactic Efficacy, Safety and Tolerability of PrEP-001 in Healthy Subjects Subsequently Challenged with Influenza A/Perth/16/2009(H3N2) Virus

Summary

EudraCT number	2015-002895-26
Trial protocol	GB
Global end of trial date	14 March 2016

Results information

Result version number	v1 (current)
This version publication date	15 March 2018
First version publication date	15 March 2018

Trial information

Trial identification

Sponsor protocol code	PrEP-CS-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	hVIVO Services Limited
Sponsor organisation address	QMB Innovation Centre, 42 New Road, London, United Kingdom, E1 2AX
Public contact	Regulatory Affairs, hVIVO Services Limited, regsubmissions@hvivo.com
Scientific contact	Regulatory Affairs, hVIVO Services Limited, regsubmissions@hvivo.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	20 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 March 2016
Global end of trial reached?	Yes
Global end of trial date	14 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the prophylactic effect of repeated intranasal dosing of PrEP-001 in healthy subjects subsequently challenged with Influenza A/Perth/16/2009 (H3N2) Virus on the incidence of laboratory-confirmed Influenza illness when compared to placebo.

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: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2015
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: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	66
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were healthy males and/or females, 18 to 55 years of age, who met the eligibility criteria outlined in the Protocol.

Pre-assignment period milestones

Number of subjects started	66
Number of subjects completed	66

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, Carer, Assessor

Blinding implementation details:

Cohort A: Cohort A was open label. No randomisation was applied. All Subjects received virus inoculum only on Day 0.
Cohort B: PrEP-001 and placebo treatment arms were double blinded and randomised 1:1.

Arms

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

Arm description:

PrEP-001

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

Dosage and administration details:

6400 µg micrograms per day (4 x 800µg per nostril), equally divided over both nostrils (powder).

Arm title	Cohort B: Placebo

Arm description:

Placebo to PrEP-001

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

Dosage and administration details:

Other than active ingredient it is identical to PrEP-001.

Arm title	Cohort A: Sentinel group

Arm description:	
Challenge Virus Only. No IMP.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Cohort B: PrEP-001	Cohort B: Placebo	Cohort A: Sentinel group
Started	27	28	11
Completed	25	27	11
Not completed	2	1	0
Abnormal lab finding	1	1	-
Physician decision	1	-	-

Baseline characteristics

End points

End points reporting groups	
Reporting group title	Cohort B: PrEP-001
Reporting group description: PrEP-001	
Reporting group title	Cohort B: Placebo
Reporting group description: Placebo to PrEP-001	
Reporting group title	Cohort A: Sentinel group
Reporting group description: Challenge Virus Only. No IMP.	

Primary: Area under the curve (AUC) of total symptom score Day 1	
End point title	Area under the curve (AUC) of total symptom score Day 1
End point description:	
End point type	Primary
End point timeframe: The primary endpoint was the area under the curve (AUC) of total symptom score Day 1 (post viral challenge) to Day 8 (quarantine discharge).	

End point values	Cohort B: PrEP-001	Cohort B: Placebo	Cohort A: Sentinel group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	27	11	
Units: mins*score				
arithmetic mean (standard deviation)	4502.6 (± 6144.84)	9859.6 (± 12215.84)	17956.5 (± 23780.83)	

Statistical analyses

Statistical analysis title	Descriptive statistics
Statistical analysis description: Continuous variables was summarised using number of observations, mean, standard deviation, median, lower quartile, upper quartile, minimum and maximum values. Categorical variables was summarised using proportions (counts and percentages).	
Comparison groups	Cohort B: Placebo v Cohort B: PrEP-001
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.05 [2]
Method	No formal method.

Notes:

[1] - Descriptive statistics

[2] - No formal statistics was performed, the p-value that is included in the above box is irrelevant

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Collected from informed consent until final follow up visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Overall safety population

Reporting group description: -

Serious adverse events	Overall safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 66 (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	Overall safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 66 (72.73%)		
Investigations			
Alanine aminotransferase increased	Additional description: For occurrences all number 14 is the minimum value.		
subjects affected / exposed	14 / 66 (21.21%)		
occurrences (all)	14		
Aspartate aminotransferase increased	Additional description: For occurrences all number 11 is the minimum value		
subjects affected / exposed	11 / 66 (16.67%)		
occurrences (all)	11		
Blood cholesterol increased	Additional description: For occurrences all number 8 is the minimum value		
subjects affected / exposed	8 / 66 (12.12%)		
occurrences (all)	8		
Activated partial thromboplastin time prolonged	Additional description: For occurrences all number 6 is the minimum value		

subjects affected / exposed	6 / 66 (9.09%)		
occurrences (all)	6		
Low density lipoprotein increased	Additional description: For occurrences all number 5 is the minimum value		
subjects affected / exposed	5 / 66 (7.58%)		
occurrences (all)	5		
C-reactive protein increased	Additional description: For occurrences all number 4 is the minimum value		
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	4		
Lipase increased	Additional description: For occurrences all number 4 is the minimum value		
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	4		
Blood fibrinogen increased	Additional description: For occurrences all number 3 is the minimum value		
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		
Blood triglycerides increased	Additional description: For occurrences all number 3 is the minimum value		
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		
Neutrophil count decreased	Additional description: For occurrences all number 3 is the minimum value		
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		
White blood cell count increased	Additional description: For occurrences all number 2 is the minimum value		
subjects affected / exposed	2 / 66 (3.03%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Procedural haemorrhage	Additional description: For occurrences all number 17 is the minimum value		
subjects affected / exposed	17 / 66 (25.76%)		
occurrences (all)	17		
Skin abrasion	Additional description: For occurrences all number 2 is the minimum value		
subjects affected / exposed	2 / 66 (3.03%)		
occurrences (all)	2		
Nervous system disorders			
Headache	Additional description: For occurrences all number 5 is the minimum value		
subjects affected / exposed	5 / 66 (7.58%)		
occurrences (all)	5		
General disorders and administration site conditions			

Pyrexia	Additional description: For occurrences all number 2 is the minimum value. The adverse event of pyrexia for one of these two subjects was reviewed post database lock and determined to be a symptom rather than an AE (the database was not changed).		
subjects affected / exposed	2 / 66 (3.03%)		
occurrences (all)	2		
Infections and infestations			
Viral upper respiratory tract infection	Additional description: For occurrences all number 3 is the minimum value		
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		

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

None reported