



Clinical trial results:

A double-blind, randomised, placebo-controlled, crossover study to assess the efficacy of XEN D0501, a TRPV1 antagonist, in reducing the frequency of cough in patients with chronic idiopathic cough

Summary

EudraCT number	2014-000306-36
Trial protocol	GB
Global end of trial date	15 June 2015

Results information

Result version number	v1 (current)
This version publication date	09 July 2016
First version publication date	09 July 2016

Trial information

Trial identification

Sponsor protocol code	XEN-D0501-CL-04
-----------------------	-----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02233699
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Xention Ltd
Sponsor organisation address	Unit 5, Quern House, Hinton Way, Great Shelford, United Kingdom, CB22 5LD
Public contact	Chief Medical Officer, Xention Limited, + 44 1223493900, info@xention.com
Scientific contact	Chief Medical Officer, Xention Limited, + 44 1223493900, info@xention.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 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2015
Global end of trial reached?	Yes
Global end of trial date	15 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effectiveness of XEN-D0501 over placebo in reducing objective daytime cough frequency.

Protection of trial subjects:

No specific measures required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2014
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	11
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening within 23 days prior to the first dose of study drug.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	XEN-D0501

Arm description: -

Arm type	Experimental
Investigational medicinal product name	XEN-D0501
Investigational medicinal product code	XEN-D0501
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

4 mg tablet formulation twice daily

Arm title	Placebo
------------------	---------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

4mg tablet formulation twice daily

Number of subjects in period 1	XEN-D0501	Placebo
Started	19	19
Completed	19	19

Baseline characteristics

Reporting groups

Reporting group title	XEN-D0501
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	XEN-D0501	Placebo	Total
Number of subjects	19	19	20
Age categorical			
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)	10	11	11
From 65-84 years	9	8	9
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	14	15	15
Male	5	4	5

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The FAS consisted of all patients who were randomized into the study and received at least 1 dose of study drug and for whom baseline and end-of-treatment objective daytime cough frequency data were available for at least 1 treatment.

Reporting group values	FAS		
Number of subjects	19		
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)	11		

From 65-84 years	8		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	15		
Male	4		

End points

End points reporting groups

Reporting group title	XEN-D0501
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The FAS consisted of all patients who were randomized into the study and received at least 1 dose of study drug and for whom baseline and end-of-treatment objective daytime cough frequency data were available for at least 1 treatment.	

Primary: Change from baseline at the end of each Treatment Period in objective daytime cough frequency.

End point title	Change from baseline at the end of each Treatment Period in objective daytime cough frequency.
End point description:	
End point type	Primary
End point timeframe:	
After 14 days treatment.	

End point values	XEN-D0501	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: Coughs/hour				
arithmetic mean (standard deviation)	6.72 (\pm 16.89)	0.37 (\pm 13.74)		

Statistical analyses

Statistical analysis title	Mixed effects linear model
Statistical analysis description:	
A mixed effects linear model was used with baseline and treatment period as fixed effects and patient as a random effect. The objective daytime cough frequency was log-transformed prior to analysis. The difference in the objective daytime cough frequency between active to placebo and 95% confidence interval were estimated. A significance value testing a hypothesis of a ratio of one (no difference between treatments) is presented.	
Comparison groups	XEN-D0501 v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4151
Method	Mixed models analysis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From subject signing off the informed consent form to subject's last visit

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	17.0
--------------------	------

Reporting groups

Reporting group title	XEN-D0501
-----------------------	-----------

Reporting group description: -

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Serious adverse events	XEN-D0501	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (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: 0.05 %

Non-serious adverse events	XEN-D0501	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 19 (94.74%)	9 / 19 (47.37%)	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Hot flush			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Peripheral coldness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Feeling of body temperature change subjects affected / exposed occurrences (all)	6 / 19 (31.58%) 6	0 / 19 (0.00%) 0	
Feeling hot subjects affected / exposed occurrences (all)	3 / 19 (15.79%) 3	0 / 19 (0.00%) 0	
Chest discomfort subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 1	0 / 19 (0.00%) 0	
Fatigue subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Feeling cold subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Temperature intolerance subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	2 / 19 (10.53%) 3	
Epistaxis subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	0 / 19 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	2 / 19 (10.53%) 2	
Sputum retention subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Throat tightness subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Psychiatric disorders			

Sleep disorder subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Investigations Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Body temperature fluctuation subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Cold agglutinins positive subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
International normalised ratio increased subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	
Platelet count increased subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Prothrombin time prolonged subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Injury, poisoning and procedural complications Muscle strain subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Thermal burn subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	0 / 19 (0.00%) 0	
Cardiac disorders Palpitations			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	9 / 19 (47.37%)	1 / 19 (5.26%)	
occurrences (all)	9	2	
Thermohypoaesthesia			
subjects affected / exposed	8 / 19 (42.11%)	0 / 19 (0.00%)	
occurrences (all)	12	0	
Headache			
subjects affected / exposed	3 / 19 (15.79%)	1 / 19 (5.26%)	
occurrences (all)	4	2	
Burning sensation			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Dizziness			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Hypoaesthesia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Sensory disturbance			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Ear pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Vertigo			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	0 / 19 (0.00%) 0	
Eye disorders Visual impairment subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	2 / 19 (10.53%) 2	
Paraesthesia oral subjects affected / exposed occurrences (all)	3 / 19 (15.79%) 4	0 / 19 (0.00%) 0	
Lip dry subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	0 / 19 (0.00%) 0	
Oral discomfort subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	0 / 19 (0.00%) 0	
Oral mucosal exfoliation subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	0 / 19 (0.00%) 0	
Oral pain subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	0 / 19 (0.00%) 0	
Chapped lips subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Dyspepsia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Hypoaesthesia oral subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Lip blister			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Lip swelling subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Mouth ulceration subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	3 / 19 (15.79%) 3	0 / 19 (0.00%) 0	
Blister subjects affected / exposed occurrences (all)	3 / 19 (15.79%) 2	0 / 19 (0.00%) 0	
Night sweats subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 19 (5.26%) 1	
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2014	<ul style="list-style-type: none">• Correction of exclusion criterion 19• Correction of the visit numbers in inclusion criteria 4 and 5• Revision of the study endpoints to clarify that the primary endpoint was the change from baseline at the end of each treatment period in objective daytime cough frequency of XEN-D0501 compared to placebo. Secondary endpoints were revised to clarify that the change from baseline at the end of each treatment period was assessed for the capsaicin cough response (Emax), objective 24-hour cough frequency and Leicester cough questionnaire. The difference between XEN-D0501 and placebo at the end of each treatment period was assessed for the hourly change in cough frequency and for the global rating of change scale and that the change from baseline over each treatment period was assessed for cough severity and urge to cough (VAS)• Revision of the statistical methodology used for the analysis of the secondary endpoints due to the revision of secondary endpoints.
04 March 2015	<ul style="list-style-type: none">• Clarification of the definition of "normal" chest radiography throughout the protocol.
12 May 2015	<ul style="list-style-type: none">• Revision of text to reduce the number of planned patients from 25 to 20 and the number of completed patients from 20 to at least 16.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported