Clinical trial results:
A double blind, randomised, placebo-controlled, crossover study assessing the use of XEN D0103 in patients with paroxysmal atrial fibrillation and implanted pacemakers allowing continuous beat-to-beat monitoring of drug efficacy

Summary

EudraCT number	2013-004456-38
Trial protocol	GB
Global end of trial date	14 May 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-D0103-CL-05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	14 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 May 2015
Global end of trial reached?	Yes
Global end of trial date	14 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the reduction in AF burden (time spent in AF as a proportion of the analysis period) by XEN-D0103 (50 mg BID) compared to placebo in patients with paroxysmal AF.

Protection of trial subjects:

No specific measures required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 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: 21
Worldwide total number of subjects	21
EEA total number of subjects	21

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)	1
From 65 to 84 years	19
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening procedures 42 to 14 days before 1st dose of study drug (XEN-D103/Placebo).

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Group 1

Arm description:

Subjects received 2 capsules Xen-D103 50 mg daily for 28 days

Arm type	Experimental
Investigational medicinal product name	XEN-D103
Investigational medicinal product code	XEN-D103
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received XEN-D103 50mg 2 capsules daily for 28 days.

Arm title	Group 2

Arm description:

Subjects received Placebo 2 capsules daily for 28 days

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

Dosage and administration details:

Subjects received 2 capsules placebo daily for 28 days

Number of subjects in period 1	Group 1	Group 2
Started	21	21
Completed	21	21

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period

Reporting group description: -

Reporting group values	Overall Period	Total	
Number of subjects	21	21	
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)	1	1	
From 65-84 years	19	19	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	8	8	
Male	13	13	

End points

End points reporting groups	
Reporting group title	Group 1
Reporting group description:	
Subjects received 2 capsules Xen-D103 50 mg daily for 28 days	
Reporting group title	Group 2
Reporting group description:	
Subjects received Placebo 2 capsules daily for 28 days	

Primary: Time spent in AF as a proportion of the analysis period	
End point title	Time spent in AF as a proportion of the analysis period
End point description:	
End point type	Primary
End point timeframe:	
Baseline to 56 days	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: percent				
arithmetic mean (standard deviation)	19.5 (± 25.7)	17.2 (± 20.6)		

Statistical analyses

Statistical analysis title	Generalised Mixed Model
Statistical analysis description:	
Generalised Mixed Model of Log Transformed AF burden with treatment and period as fixed effects and patient as a random effect intercept term.	
Comparison groups	Group 1 v Group 2
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.77
Method	Mixed models analysis
Parameter estimate	ratio of adjusted geometric Means
Point estimate	1.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.98
upper limit	1.05

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the time of informed consent through the to the last visit.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0
Reporting groups	
Reporting group title	Group 1
Reporting group description: -	
Reporting group title	Group 2
Reporting group description: -	

Serious adverse events	Group 1	Group 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (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: 0.05 %

Non-serious adverse events	Group 1	Group 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)	10 / 11 (90.91%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	3 / 11 (27.27%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Vomiting			

subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Lower respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

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