Clinical trial results:
Open label, single-centre study to evaluate the efficacy of the bradykinin (BK) B2 receptor antagonist, Icatibant, in the relief of symptoms resulting from moderate to severe angioedema unresponsive to antihistamines

Summary

EudraCT number	2011-002339-24
Trial protocol	GB
Global end of trial date	03 May 2015

Results information

Result version number	v1 (current)
This version publication date	27 March 2019
First version publication date	27 March 2019
Summary attachment (see zip file)	Adverse Events (Adverse Events Log.xlsx) Con meds (Concomitant Medications Log.xlsx) End of study data (End of Study.xlsx) Demographics (ICAT screening Visit 1.xlsx) Medical history (Medical History.xlsx) Patient response data (Subject Diary results.xlsx)

Trial information

Trial identification

Sponsor protocol code	NA

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Barts Health NHS Trust
Sponsor organisation address	Whitechapel Road, London, United Kingdom, E1 1BB
Public contact	Chief Investigator, Dr Hilary Longhurst, +44 020324602825, hilary.longhurst@bartsandthelondon.nhs.uk
Scientific contact	Chief Investigator, Dr Hilary Longhurst, +44 020324602825, hilary.longhurst@bartsandthelondon.nhs.uk

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	28 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2015
Global end of trial reached?	Yes
Global end of trial date	03 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of the bradykinin (BK) B2 antagonist, Icatibant, in the relief of symptoms resulting from moderate to severe angioedema of the face, neck, arms, genitals, tongue, pharynx and larynx, where the diagnosis is of Idiopathic Angioedema - unresponsive to antihistamines.

Protection of trial subjects:

This trial will be overseen and reviewed by the Chief Investigator on an ongoing and regular basis, with the oversight of the sponsor (monitoring and auditing systems).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2012
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: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	9
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients where recruited from clinics run by the PI at Barts Health NHS Trust

Pre-assignment

Screening details:

All subjects attend a screening visit and those meeting all of the inclusion and none of the exclusion criteria were eligible for enrolment into the study

Period 1

Period 1 title	Treatment phase (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All patients
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	ICATABANT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

30mg SC

Number of subjects in period 1	All patients
Started	9
Completed	9

Baseline characteristics

End points

End points reporting groups

Reporting group title	All patients
Reporting group description: -	
Subject analysis set title	Primary objective
Subject analysis set type	Full analysis

Subject analysis set description:

Time to onset of symptom relief Number of episodes 14
Mean 4.3 hrs
Median 2.0 hrs
standard deviation 5.7 hrs
First quartile 1 hrs
Second quartile 5 hrs

Time to almost completed symtom relief Number of episodes 13
<20mm on VAS Mean 9.3 hrs
Median 8.0 hrs
standard deviation 8.2 hrs
First quartile 2.0 hrs
Third quartile 14.0 hrs
VAS at 4 hrs Number of episodes 12
Mean 37.3 mm
Median 24.0 mm
standard deviation 32.7 mm
First quartile 13.7 mm
Third quartile 53.3 mm

Primary: Time to onset of symptom relief

End point title	Time to onset of symptom relief[1]

End point description:

Skin Swelling : Mean 4.3hrs, Median =2hrs, SD=5.7, IQR=4.
Skin Pain : Mean 8.5hrs, Median =2hrs, SD=14.6, IQR=5.
Abdo Pain : Mean 4.3hrs, Median =1hrs, SD=6.6, IQR=4.625

End point type	Primary

End point timeframe:

01/10/12- 03/05/15

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	Primary objective			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: hrs				
arithmetic mean (standard deviation)	4.3 (± 5.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: VAS at 4hrs

End point title	VAS at 4hrs

End point description:

Skin Swelling VAS@4hrs, Mean 37.3, Median 24.0mm, SD=32.7mm IQR =39.6mm
Skin Pain VAS@4hrs, Mean 31.1, Median 26.0mm, SD= 29.87mm IQR =39.6mm
Abdo pain VAS@4hrs, Mean 37.3, Median 24.0mm, SD= 32.7mm IQR =45.7mm

End point type	Secondary

End point timeframe:

01/10/12-03/05/15

End point values	Primary objective			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: mm				
arithmetic mean (standard deviation)	37.3 (± 32.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to almost complete symtom relief

End point title	Time to almost complete symtom relief

End point description:

Skin Swelling Mean9.3hrs, Median 8.0hrs, SD=8.2hrs, IQR 8hrs
Skin Pain Mean 6.8hrs, Median 6.0hrs, SD=5.5hrs, IQR 10.25hrs
Abdo Pain Mean 5.8hrs, Median 2.0hrs, SD=8.4hrs, IQR 5.9hrs

End point type	Secondary

End point timeframe:

01/10/12-03/05/15

End point values	Primary objective			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: hrs				
arithmetic mean (standard deviation)	9.3 (± 8.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs were reported from 01/10/12 to 03/03/15	
Adverse event reporting additional description:	
NA	
Assessment type	Systematic

Dictionary used	
Dictionary name	AE description
Dictionary version	1

Reporting groups	
Reporting group title	All adverse events
Reporting group description: -	

Serious adverse events	All adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Immune system disorders			
Angioedema			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)		
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed occurrences (all) heartburn subjects affected / exposed occurrences (all) stomach cramps subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Hepatobiliary disorders Fatty liver subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		
Respiratory, thoracic and mediastinal disorders Respiratory tract infection subjects affected / exposed occurrences (all) Mouth ulceration subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Musculoskeletal and connective tissue disorders leg cramps subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Infections and infestations flu like symptoms subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		
Metabolism and nutrition disorders Injection site reaction			

subjects affected / exposed	7 / 9 (77.78%)		
occurrences (all)	15		
weight loss			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study failed to recruit its target of 20 , only 9 patients being recruited. Therefore interpretation of the data and reaching any firm conclusions regarding this study are limited.

Notes: