Clinical trial results:
Ten03: A Phase III Open, Multicentre Study to Investigate the Safety and Efficacy of BPL's High Purity Factor X in the treatment of the Factor X Deficient Subjects Undergoing Surgery

Summary

EudraCT number	2009-015086-31
Trial protocol	GB ES
Global end of trial date	08 January 2014

Results information

Result version number	v1 (current)
This version publication date	18 July 2016
First version publication date	20 June 2014
Summary attachment (see zip file)	Final CSR Ten03 (final-clinical-summary-report-ten03.pdf)

Trial information

Trial identification

Sponsor protocol code	Ten03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01086852
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bio Products Laboratory Limited
Sponsor organisation address	Dagger Lane, Elstree, United Kingdom, WD6 3BX
Public contact	Miranda Norton, Bio Products Laboratory Ltd, 44 208 957 2661, miranda.norton@bpl.co.uk
Scientific contact	Miranda Norton, Bio Products Laboratory Ltd, 44 208 957 2661, miranda.norton@bpl.co.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000971-PIP01-10
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	08 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 January 2014
Global end of trial reached?	Yes
Global end of trial date	08 January 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety and efficacy of FACTOR X administered by bolus infusion to prevent bleeding and achieve haemostasis in factor X deficient subjects undergoing surgery.

Protection of trial subjects:

The following potential risks were monitored:

Infusion site reactions
Virology samples were taken at the prior to the first infusion and at the end of the study
factor X inhibitor samples were taken prior to the first infusion and throughout until the end of the study.
factor X levels were monitored at a local laboratory prior to and whilst during the treatment period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 June 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: 2
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	4
EEA total number of subjects	2

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)	4

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

4 subjects were screened and enrolled into the study, all 4 subjects completed the study.

Period 1

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

Arms

Arm title	ACTIVE TREATMENT

Arm description:

Raise plasma factor X to 70-90 IU/dL pre-surgery and maintain >50 IU/dL post-surgery until no longer at risk of bleeding due to surgery.

Arm type	Experimental
Investigational medicinal product name	FACTOR X
Investigational medicinal product code	
Other name	Human coagulation factor X
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Raise plasma factor X to 70-90 IU/dL pre-surgery and maintain >50 IU/dL post-surgery until no longer at risk of bleeding due to surgery.

Number of subjects in period 1	ACTIVE TREATMENT
Started	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial Period

Reporting group description: -

Reporting group values	Overall Trial Period	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
Adults (18-64 years)	4	4	
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	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	4	4	
Factor X severity			
Mild = plasma FX:C 5 to <20 IU/dL Moderate to severe = plasma FX:C <5 IU/dL			
Units: Subjects			
Mild	4	4	
Moderate - Severe	0	0	
Major or Minor Surgery			
Surgical procedures requiring day case or overnight stay, such as laparoscopic or arthroscopic procedures, will be defined as minor procedures. Procedures typically requiring full anaesthesia and involving opening of the major cavities, such as thoracic, abdominal, orthopaedic or open heart surgery, will be defined as major procedures. A Data Review Committee made the final decision with respect to assignment of severity (major or minor) of the surgeries.			
Units: Subjects			
Major	4	4	
Minor	0	0	

End points

End points reporting groups

Reporting group title	ACTIVE TREATMENT

Reporting group description:

Raise plasma factor X to 70-90 IU/dL pre-surgery and maintain >50 IU/dL post-surgery until no longer at risk of bleeding due to surgery.

Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population will be defined as all surgical procedures in which subjects were treated with at least one dose of FACTOR X and have undergone surgery.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population will be defined as all surgical procedures in which subjects receive at least part of one dose of study medication. For subjects who withdraw, safety data will be analysed up to the point of withdrawal, if the available data is adequate to allow a scientific analysis.

Primary: Blood loss during and after surgery

End point title	Blood loss during and after surgery[1]

End point description:

Blood loss will be assessed by the following:
Clinical estimation of volume of blood loss during surgery
Requirement for blood transfusion or infusion of autologous red cells during and after surgery
Number and duration of post-operative bleeding episodes
Measurements of haemoglobin pre-opeartively, post-operatively and at discharge.

End point type	Primary

End point timeframe:

Blood loss is measured during and after surgery, the overall assessment is made after the last dose of FACTOR X.

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: No formal statistical analysis was performed. This was a non-comparative study; efficacy endpoints related to bleeding during and after surgery,but no statistical hypothesis test was performed.

End point values	ACTIVE TREATMENT	ITT Population	Safety Population	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	4	4	
Units: Excellent/Good/Poor				
number (not applicable)				
Excellent	4	4	4	
Good	0	0	0	
Poor	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Consent to 28 days after the last dose of IMP	
Adverse event reporting additional description:	
All subjects receiving FACTOR X	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups	
Reporting group title	All subjects receiving FACTOR X

Reporting group description: -

Serious adverse events	All subjects receiving FACTOR X		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	All subjects receiving FACTOR X		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Post procedural discomfort	Additional description: Surgical wound site discomfort		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Contusion	Additional description: Right calf with bruising		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

Incision site complication	Additional description: 2 small vesicles around surgical site incision		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Vascular disorders			
Haematoma	Additional description: Right lower extremety haematoma, inner thigh		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia	Additional description: Fever		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Procedural pain	Additional description: Surgical Site Pain		
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	3		
Dyspepsia	Additional description: Indigestion		
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	Additional description: Sore throat		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Ecchymosis	Additional description: Ecchymosis on left thigh		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pruritus	Additional description: Pruritus on back		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Infections and infestations			
Herpes zoster	Additional description: Nerve Pain, Shingles		
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2012	Changes to the primary endpoints Changes to the secondary endpoints, as a consequence of changes to the primary endpoints Update to definitions of efficacy populations Addition of analysis to take into account effect of the severity of factor X deficiency on the efficacy of FACTOR X Update to the definition of major and minor surgery Clarification of treatment after the end of study Administrative changes
21 August 2012	Update to the surgeons' estimation of blood loss in line with updated primary efficacy analysis Administrative changes
03 January 2013	Revised study personnel to reflect new contract research organisation, INC Research. Revised the contact details for reporting SAEs to remove CROfessionals LLC. Details for contacting the sponsor to report SAEs were clarified
01 February 2013	Update to the dose calculation in line with pharmacokinetic data from study Ten01 (assumed incremental recovery of 2.0 IU/dL per IU/kg) Update to the half life in with pharmacokinetic data from study Ten01. Clarify that the FX level achieved should be checked before surgery. Update to arrangements for early discharge Administrative changes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported