

**Clinical trial results:****A Phase III Open, Multicentre Study to Investigate the Pharmacokinetics, Safety and Efficacy of BPL's High Purity Factor X in the Treatment of Severe and Moderate Factor X Deficiency****Summary**

EudraCT number	2009-011145-18
Trial protocol	GB ES DE
Global end of trial date	30 October 2013

Results information

Result version number	v2 (current)
This version publication date	17 July 2016
First version publication date	17 July 2014
Version creation reason	<ul style="list-style-type: none">• New data added to full data set• Correction of full data set List of non-serious AE's - some SAEs have been listed in here in error, as they are reported in the SAE section they will be removed from here. Spain is listed as ongoing, this is not correct so will be changed to completed. Change of public contact to Head of Medical Affairs.
Summary attachment (see zip file)	Final CSR Ten01 (final-clinical-summary-report-ten01.pdf)

Trial information**Trial identification**

Sponsor protocol code	TEN01
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00930176
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bio Products Laboratory Limited
Sponsor organisation address	Dagger Lane, Elstree, United Kingdom,
Public contact	Head of Medical Affairs, Bio Products Laboratory Limited, +44 0208957 2200, medinfo@bpl.co.uk
Scientific contact	Head of Medical Affairs, Bio Products Laboratory Limited, +44 0208957 2200, medinfo@bpl.co.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 October 2013
Global end of trial reached?	Yes
Global end of trial date	30 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the pharmacokinetics of Factor X after a single dose of 25 IU/kg in subjects with severe or moderate FX deficiency

Protection of trial subjects:

The number of blood samples collected for the PK profile is the minimum recommended by the regulatory authorities and the International Society for Thrombosis and Haemostasis (ISTH)

Background therapy: -

Evidence for comparator:

Not applicable

Actual start date of recruitment	05 May 2010
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	Turkey: 6
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	16
EEA total number of subjects	8

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	6
Adults (18-64 years)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

17 subjects were screened for the study. One subject was ineligible; 16 subjects were enrolled to the study.

Period 1

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

Arms

Arm title	Active treatment
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Arm description:

FACTOR X 25 IU/kg to treat a bleed

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:

25 IU/kg to treat a bleed and for any preventative use.

Raise plasma FX 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	16
Completed	15
Not completed	1
Adverse event, serious fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
Reporting group description: -	

Reporting group values	Overall Trial	Total	
Number of subjects	16	16	
Age categorical			
Age at screening for the study			
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)	6	6	
Adults (18-64 years)	10	10	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Age at study entry			
Units: years			
arithmetic mean	27.1		
full range (min-max)	12 to 58	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	6	6	
FXD severity			
Severe = plasma FX:C <1 IU/dL			
Moderate = plasma FX:C 1-<5 IU/dL			
Units: Subjects			
Severe	14	14	
Moderate	2	2	

End points

End points reporting groups

Reporting group title	Active treatment
Reporting group description: FACTOR X 25 IU/kg to treat a bleed	

Primary: FX:C Incremental recovery

End point title	FX:C Incremental recovery ^[1]
End point description: Combined incremental recovery (peak increment within the first hour post-dose) for 31 PK assessments.	
End point type	Primary
End point timeframe: At Baseline and Repeat PK Assessment	

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: This was not a statistically powered study

End point values	Active treatment			
Subject group type	Reporting group			
Number of subjects analysed	16 ^[2]			
Units: IU/dL per IU/kg				
geometric mean (geometric coefficient of variation)	2.07 (\pm 21.01)			

Notes:

[2] - Value given is the mean of 31 results: 16 for Baseline Visit + 15 for Repeat PK assessment

Statistical analyses

No statistical analyses for this end point

Primary: FX:C Half-life

End point title	FX:C Half-life ^[3]
End point description: Half-life of FX:C after bolus dose of 25 IU/kg	
End point type	Primary
End point timeframe: Baseline Visit and Repeat PK Assessment	

Notes:

[3] - 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: This was not a statistically powered study

End point values	Active treatment			
Subject group type	Reporting group			
Number of subjects analysed	16 ^[4]			
Units: hours				
geometric mean (geometric coefficient of variation)	29.36 (± 22.89)			

Notes:

[4] - Value is the mean of 31 results: 16 for Baseline Visit + 15 for Repeat PK assessment

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Consent to 30 days post-last dose of IMP

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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Reporting groups

Reporting group title	Active treatment
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Reporting group description:

All subjects receiving FACTOR X

Serious adverse events	Active treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 16 (37.50%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Dysmenorrhoea			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Menorrhagia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nosocomial infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer helicobacter			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Active treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Infusion site erythema			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Infusion site pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Non-cardiac chest pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Pyrexia			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Swelling</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ulcer</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vessel puncture site haematoma</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 16 (6.25%)</p> <p>2</p> <p>1 / 16 (6.25%)</p> <p>1</p> <p>2 / 16 (12.50%)</p> <p>2</p> <p>1 / 16 (6.25%)</p> <p>1</p>		
<p>Immune system disorders</p> <p>Urticaria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 16 (6.25%)</p> <p>2</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal congestion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tachypnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p>		
<p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 16 (6.25%)</p> <p>1</p>		
<p>Injury, poisoning and procedural complications</p>			

Contusion subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2		
Fall subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Head injury subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Joint injury subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Thermal burn subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Headache subjects affected / exposed occurrences (all)	8 / 16 (50.00%) 14		
Migraine subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 4		
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Constipation			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Gingivitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	6		
Odynophagia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Toothache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Dermatitis allergic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	14		
Back pain			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	10		
Groin pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Joint stiffness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Neck pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	4		
Osteoarthritis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in extremity			

subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	8		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Fungal infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	7 / 16 (43.75%)		
occurrences (all)	11		
Oral infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Osteomyelitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	9		
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 July 2010	First bleeding episode to be treated under the supervision of a physician. Addition of definition of treatment failure. Update in definition of efficacy criteria. Clarification of the assessments of bleeds to be used in the efficacy evaluation. Addition of success criteria. Addition of the definition of excessive blood loss in surgery. Update in efficacy assessment criteria for menorrhagic bleeds. Change to the washout period before PK assessments. Amendments to selected PK parameters & analyses.
03 November 2010	Addition of blood sample collections for thrombogenicity marker assays. Change to infusion rate. Change to instructions regarding assessments of bleeds if subject was sleeping at the defined timepoint. Clarification on the efficacy assessment of FACTOR X in treating a bleed if the investigator's and subject's assessments differed.
08 April 2011	Addition of table listing number of bleeds required to meet the criteria for treatment success. Addition of PK parameter AUC(0-t) Change of CRO. Change in name and status of Sponsor.
15 October 2012	Change to primary and secondary efficacy endpoints for the surgery component of the protocol. Change to study procedures for subjects undergoing surgery, as a consequence of changes to the primary and secondary endpoints. Update to definitions of efficacy populations. Update to definitions of major and minor surgeries. Updates to data analysis for consistency with updated efficacy endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported