



Clinical trial results:

An Open-label, Multi-centre Post-marketing Study to Assess the Efficacy and Safety of Voncento® in Subjects with Von Willebrand Disease

Summary

EudraCT number	2013-003305-25
Trial protocol	GB DE AT IE PL GR
Global end of trial date	15 February 2018

Results information

Result version number	v1 (current)
This version publication date	29 August 2018
First version publication date	29 August 2018

Trial information

Trial identification

Sponsor protocol code	CSLCT-BIO-12-83
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02552576
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring GmbH
Sponsor organisation address	Emil-von-Behring-Str.76, Marburg, Germany, 35041
Public contact	Clinical Study Manager, CSL Behring GmbH , clinicaltrials@cslbehring.com
Scientific contact	Clinical Study Manager, CSL Behring GmbH , clinicaltrials@cslbehring.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 March 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to collect long-term data on the haemostatic efficacy of Voncento in subjects with VWD who require a VWF product to control an NSB event or as prophylaxis therapy.

Protection of trial subjects:

This study was carried out in accordance with the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) principles of Good Clinical Practice, the Declaration of Helsinki, and with standard operating procedures for clinical research and development at CSL Behring and at the Contract Research Organization involved. The design of the study was discussed and agreed with the Pharmacovigilance Risk Assessment Committee (PRAC), the CHMP, and the Blood Products Working Party (BPWP). The study was planned to comply with the requirements of the EMA CHMP Guideline on the Clinical Investigation of Human Plasma Derived VWF Products (CPMP/BPWG/220/02), specifically in relation to the directives regarding post-marketing studies.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 October 2015
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	Poland: 11
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Greece: 1
Worldwide total number of subjects	26
EEA total number of subjects	26

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	0

months)	
Children (2-11 years)	4
Adolescents (12-17 years)	0
Adults (18-64 years)	20
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted at 10 to 15 sites in the United Kingdom, Germany, Greece, and Poland

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Voncento (on-demand)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Voncento
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Voncento was administered as bolus IV infusion with a rate not to exceed 6 mL/min. For on-demand treatment, for both adult and paediatric subjects, usually 40 to 80 IU/kg of Voncento corresponding to 20 to 40 IU FVIII:C/kg of body weight were recommended to achieve haemostasis. An initial dose of 80 IU/kg Voncento was to be required, especially in patients with Type 3 VWD.

Arm title	Voncento (prophylaxis)
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Voncento
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Voncento was administered as bolus IV infusion with a rate not to exceed 6 mL/min. For long-term prophylaxis in subjects 12 years and older, 25 to 40 IU of Voncento per kg body weight was to be considered at a frequency of 1 to 3 times per week; in subjects under 12 years, a prophylactic dose range of 40 to 80 IU Voncento/kg body weight was administered 1 to 3 times a week.

Number of subjects in period 1^[1]	Voncento (on-demand)	Voncento (prophylaxis)
Started	11	14
Completed	11	10
Not completed	0	4
Consent withdrawn by subject	-	2
Pregnancy	-	1
Lost to follow-up	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Analysis was done on the Safety Population which comprised all subjects who received at least 1 dose of Voncento. Twenty-six (26) subjects were enrolled in the study, but 1 subject that did not meet inclusion criteria was enrolled by mistake and was terminated by the sponsor before receiving any study drug, therefore n=25.

Baseline characteristics

Reporting groups

Reporting group title

Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	25	25	
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)	4	4	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	19	19	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	35.8		
standard deviation	± 19.13	-	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	13	13	

End points

End points reporting groups

Reporting group title	Voncento (on-demand)
Reporting group description: -	
Reporting group title	Voncento (prophylaxis)
Reporting group description: -	
Subject analysis set title	Safety Population (SP)
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety population comprised all subjects who received at least 1 dose of Voncento.	
Subject analysis set title	Efficacy Population (EP)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Efficacy population: The Efficacy population included all subjects of the safety population who had at least 1 post-baseline haemostatic efficacy assessment ("excellent", "good", "moderate", or "none") of Voncento for a non-surgical bleeding (NSB) event or a surgical procedure, or had at least 1 post-baseline assessment ("excellent", "good", "moderate", or "none") for a prophylaxis treatment.	

Primary: Investigator's Assessment of Haemostatic Efficacy on Non Surgical Bleeding (NSB) Events (EP)

End point title	Investigator's Assessment of Haemostatic Efficacy on Non Surgical Bleeding (NSB) Events (EP) ^[1]
End point description: Efficacy Grading Scale: Excellent = Haemostasis achieved / cessation of bleeding. Good = Slight oozing / partial but adequate control of bleeding; did not require additional product for unplanned treatment. Moderate = Moderate bleeding / moderate control of bleeding; required additional product for unplanned treatment. None = Severe uncontrolled bleeding.	
End point type	Primary
End point timeframe: Up to 12 months	
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: Only descriptive statistics were used	

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: Number of NSB events				
number (not applicable)				
Excellent	22	59		
Good	36	5		
Moderate	11	8		
None	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Subjects' Assessment of Haemostatic Efficacy per Bleeding Day on NSB events (EP)

End point title	Subjects' Assessment of Haemostatic Efficacy per Bleeding Day on NSB events (EP) ^[2]
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End point description:

Efficacy Grading Scale:

Excellent = Haemostasis achieved / cessation of bleeding.

Good = Slight oozing / partial but adequate control of bleeding; did not require additional product for unplanned treatment.

Moderate = Moderate bleeding / moderate control of bleeding; required additional product for unplanned treatment.

None = Severe uncontrolled bleeding.

End point type	Primary
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End point timeframe:

Up to 12 months

Notes:

[2] - 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: Only descriptive statistics were used

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: Number of NSB events				
number (not applicable)				
Excellent	14	52		
Good	77	45		
Moderate	49	14		
None	0	106		

Statistical analyses

No statistical analyses for this end point

Primary: Number of NSB events per 3-month interval (EP)

End point title	Number of NSB events per 3-month interval (EP) ^[3]
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End point description:

End point type	Primary
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End point timeframe:

Up to 12 months

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: Only descriptive statistics were used

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: Number of NSB events				
number (not applicable)				
Month 1-3	17	21		
Month 4-6	13	19		
Month 7-9	18	28		
Month 10-12	34	10		

Statistical analyses

No statistical analyses for this end point

Primary: Total Annual Bleeding Rate for Treated NSB Events(EP)

End point title	Total Annual Bleeding Rate for Treated NSB Events(EP) ^[4]
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End point description:

End point type	Primary
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End point timeframe:

Up to 12 months

Notes:

[4] - 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: Only descriptive statistics were used

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: bleeds per year per subject				
arithmetic mean (standard deviation)	6.2 (± 7.65)	6.2 (± 6.80)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of infusions per NSB event (EP)

End point title	Number of infusions per NSB event (EP) ^[5]
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End point description:

End point type	Primary
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End point timeframe:

Up to 12 months

Notes:

[5] - 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: Only descriptive statistics were used

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: infusions per event				
arithmetic mean (standard deviation)	2.4 (± 2.85)	2.5 (± 4.37)		

Statistical analyses

No statistical analyses for this end point

Primary: Total dose of Voncento per NSB event (EP)

End point title	Total dose of Voncento per NSB event (EP) ^[6]
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End point description:

End point type	Primary
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End point timeframe:

Up to 12 months

Notes:

[6] - 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: Only descriptive statistics were used

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: IU VWF:RCo/kg				
arithmetic mean (standard deviation)	147.6 (± 171.83)	167.2 (± 161.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator's Assessment of Hemostatic Efficacy on Prophylaxis Treatment (EP)

End point title	Investigator's Assessment of Hemostatic Efficacy on Prophylaxis Treatment (EP) ^[7]
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End point description:

Efficacy Grading Scale:

Excellent = Haemostasis achieved / cessation of bleeding.

Good = Slight oozing / partial but adequate control of bleeding; did not require additional product for unplanned treatment.

Moderate = Moderate bleeding / moderate control of bleeding; required additional product for unplanned

treatment.

None = Severe uncontrolled bleeding.

End point type	Secondary
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End point timeframe:

Up to 12 months

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data only collected on the Prophylaxis arm not the On-demand arm

End point values	Voncento (prophylaxis)			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number of events				
number (not applicable)				
Excellent	12			
Good	2			
Moderate	1			
None	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Subject's Assessment of Hemostatic Efficacy on Prophylaxis Treatment (EP)

End point title	Subject's Assessment of Hemostatic Efficacy on Prophylaxis Treatment (EP) ^[8]
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End point description:

Efficacy Grading Scale:

Excellent = Haemostasis achieved / cessation of bleeding.

Good = Slight oozing / partial but adequate control of bleeding; did not require additional product for unplanned treatment.

Moderate = Moderate bleeding / moderate control of bleeding; required additional product for unplanned treatment.

None = Severe uncontrolled bleeding.

End point type	Secondary
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End point timeframe:

Up to 12 months

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data only collected on the Prophylaxis arm not the On-demand arm

End point values	Voncento (prophylaxis)			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number of events				
number (not applicable)				
Excellent	11			
Good	4			

Moderate	1			
None	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator's Assessment of Hemostatic Efficacy for Surgery (EP)

End point title	Investigator's Assessment of Hemostatic Efficacy for Surgery (EP)
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End point description:

Efficacy Grading Scale:

Excellent = Haemostasis achieved / cessation of bleeding.

Good = Slight oozing / partial but adequate control of bleeding; did not require additional product for unplanned treatment.

Moderate = Moderate bleeding / moderate control of bleeding; required additional product for unplanned treatment.

None = Severe uncontrolled bleeding.

End point type	Secondary
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End point timeframe:

Up to 12 months

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: Number of surgical events				
number (not applicable)				
Excellent	4	3		
Good	5	0		
Moderate	0	0		
None	0	0		
Missing	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator's Assessment of Blood Loss for Surgery (EP)

End point title	Investigator's Assessment of Blood Loss for Surgery (EP)
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End point description:

The blood loss was judged to be "less", "equivalent", or "more" compared with the expected blood loss from a subject without a bleeding disorder undergoing the same procedure.

End point type	Secondary
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End point timeframe:

Up to 12 months

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: Number of surgical events				
number (not applicable)				
Less	1	1		
Equivalent	8	2		
More	0	0		
Missing	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of infusions required to treat a surgical bleeding event (EP)

End point title	Number of infusions required to treat a surgical bleeding event (EP)
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End point description:

End point type	Secondary
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End point timeframe:

Up to 12 months

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Number of infusions				
arithmetic mean (standard deviation)	15.8 (± 9.6)	3.3 (± 2.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose per infusion of Voncento required to treat a surgical bleeding event (EP)

End point title	Dose per infusion of Voncento required to treat a surgical bleeding event (EP)
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End point description:

End point type	Secondary
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End point timeframe:

Up to 12 months

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: IU VWF:RCo/kg				
arithmetic mean (standard deviation)	58.48 (± 37.670)	104.53 (± 87.105)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Inhibitors (SP)

End point title	Summary of Inhibitors (SP)
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End point description:

End point type	Secondary
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End point timeframe:

Up to 12 months

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: BU/mL				
number (not applicable)				
von Willebrand Inhibitor	0	0		
Factor VIII Inhibitor	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment Emergent Adverse Events (TEAEs)
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End point description:

End point type	Secondary
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End point timeframe:

Up to 12 months

End point values	Voncento (on-demand)	Voncento (prophylaxis)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: Number of subjects				
number (not applicable)				
TEAEs	7	12		
Serious TEAEs	1	1		
TEAEs of special interest	0	2		
Treatment-related TEAEs	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 months per subject

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Voncento (on-demand)
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Reporting group description: -

Reporting group title	Voncento (prophylaxis)
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Reporting group description: -

Serious adverse events	Voncento (on-demand)	Voncento (prophylaxis)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Voncento (on-demand)	Voncento (prophylaxis)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	12 / 14 (85.71%)	

Vascular disorders Haematoma subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0	1 / 14 (7.14%) 1 1 / 14 (7.14%) 6 1 / 14 (7.14%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 14 (7.14%) 1	
Psychiatric disorders Compulsive lip biting subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 1 / 11 (9.09%) 1	1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0	
Investigations Blood iron decreased subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	

Face injury subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Seizure subjects affected / exposed occurrences (all) Tongue biting subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0	2 / 14 (14.29%) 11 0 / 14 (0.00%) 0 1 / 14 (7.14%) 11 1 / 14 (7.14%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Iron deficiency anaemia subjects affected / exposed occurrences (all) Microcytosis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1	1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0	
Eye disorders Dry eye subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	
Gastrointestinal disorders Diarrhoea			

subjects affected / exposed	0 / 11 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Faeces discoloured			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	13	
Pain in extremity			

subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	
occurrences (all)	1	2	
Arthritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Osteitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	2 / 14 (14.29%)	
occurrences (all)	1	7	
Acute sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Post procedural infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

Urinary tract infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	
Metabolism and nutrition disorders Iron deficiency subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 14 (7.14%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2015	<ul style="list-style-type: none">• Prophylaxis treatment was added as treatment option in the study• The removal of the age restriction for participating subjects• Overall study duration was expected to be 2.5 years instead of 4

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported