Clinical trial results:
Single-Dose Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of Apixaban in Pediatric Subjects at Risk for a Venous or Arterial Thrombotic Disorder

Summary

EudraCT number	2012-001581-15
Trial protocol	Outside EU/EEA
Global end of trial date	18 June 2019

Results information

Result version number	v1 (current)
This version publication date	31 May 2021
First version publication date	31 May 2021

Trial information

Trial identification

Sponsor protocol code	CV185-118

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001830-PIP10-80
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	06 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 June 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the PK of a single dose of apixaban in pediatric subjects

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	49
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	1
Infants and toddlers (28 days-23 months)	20
Children (2-11 years)	18
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

49 subjects were treated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Neonates up to 27 days old. Single dose of Apixaban 0.44 mg/m^2.

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

Dosage and administration details:

0.1 mg

Arm title	Group 2B

Arm description:

Infants 28 days to < 9 months. Single dose of Apixaban 1.08 mg/m^2.

Arm type	Experimental
Investigational medicinal product name	Apixaban Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

0.4 mg/mL dosed to 1.08 mg/m^2

Arm title	Group 2A

Arm description:

Young children 9 months to < 2 years. Single dose of Apixaban 1.08 mg/m^2 or 2.43 mg/m^2.

Arm type	Experimental
Investigational medicinal product name	Apixaban Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

0.4 mg/mL dosed to 1.08 mg/m^2 or 2.43 mg/m^2

Arm title	Group 3

Arm description:	
Young children 2 years to < 6 years. Single dose of Apixaban 1.17 mg/m^2.	
Arm type	Experimental
Investigational medicinal product name	Apixaban Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
0.4 mg/mL dosed to 1.17 mg/m^2	
Arm title	Group 4
Arm description:	
Children 6 years to < 12 years. Single dose of Apixaban 1.80 mg/m^2.	
Arm type	Experimental
Investigational medicinal product name	Apixaban Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
0.4 mg/mL dosed to 1.80 mg/m^2	
Arm title	Group 5
Arm description:	
Adolescents 12 years to < 18 years. Single dose of Apixaban 2.19 mg/m^2.	
Arm type	Experimental
Investigational medicinal product name	Apixaban Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
0.4 mg/mL dosed to 2.19 mg/m^2	

Number of subjects in period 1	Group 1	Group 2B	Group 2A
Started	1	11	9
Completed	1	11	9

Number of subjects in period 1	Group 3	Group 4	Group 5
Started	8	10	10
Completed	8	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Neonates up to 27 days old. Single dose of Apixaban 0.44 mg/m^2.	
Reporting group title	Group 2B
Reporting group description:	
Infants 28 days to < 9 months. Single dose of Apixaban 1.08 mg/m^2.	
Reporting group title	Group 2A
Reporting group description:	
Young children 9 months to < 2 years. Single dose of Apixaban 1.08 mg/m^2 or 2.43 mg/m^2.	
Reporting group title	Group 3
Reporting group description:	
Young children 2 years to < 6 years. Single dose of Apixaban 1.17 mg/m^2.	
Reporting group title	Group 4
Reporting group description:	
Children 6 years to < 12 years. Single dose of Apixaban 1.80 mg/m^2.	
Reporting group title	Group 5
Reporting group description:	
Adolescents 12 years to < 18 years. Single dose of Apixaban 2.19 mg/m^2.	

Reporting group values	Group 1	Group 2B	Group 2A
Number of subjects	1	11	9
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	1	0	0
Infants and toddlers (28 days-23 months)	0	11	9
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Age Continuous Units: years			
arithmetic mean	0.025	0.35	1.11
standard deviation	± 99999	± 0.18	± 0.35
Gender Categorical Units: Subjects			
Female	1	6	5
Male	0	5	4
Race Units: Subjects			
White	1	9	9
Black or African American	0	0	0
Other	0	2	0
Ethnicity Units: Subjects			

Hispanic/Latino	1	5	0
Not Hispanic/Latino	0	3	4
Not Reported	0	3	5

Reporting group values	Group 3	Group 4	Group 5
Number of subjects	8	10	10
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	8	10	0
Adolescents (12-17 years)	0	0	10
Age Continuous			
Units: years			
arithmetic mean	3.6	7.4	13.7
standard deviation	± 1.2	± 1.2	± 1.4
Gender Categorical			
Units: Subjects			
Female	4	6	6
Male	4	4	4
Race			
Units: Subjects			
White	8	8	7
Black or African American	0	2	3
Other	0	0	0
Ethnicity			
Units: Subjects			
Hispanic/Latino	1	3	0
Not Hispanic/Latino	2	5	6
Not Reported	5	2	4

Reporting group values	Total		
Number of subjects	49		
Age Categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	1		
Infants and toddlers (28 days-23 months)	20		
Children (2-11 years)	18		
Adolescents (12-17 years)	10		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		

Gender Categorical Units: Subjects			
Female	28		
Male	21		
Race Units: Subjects			
White	42		
Black or African American	5		
Other	2		
Ethnicity Units: Subjects			
Hispanic/Latino	10		
Not Hispanic/Latino	20		
Not Reported	19		

Subject analysis sets

Subject analysis set title	Group 2A - 2.43 mg/m^2
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects in the Group 2A (9 months to < 2 years) receiving study drug at a dose of 2.43 mg/m^2	
Subject analysis set title	Group 2A - 1.08 mg/m^2
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects in the Group 2A (9 months to < 2 years) receiving study drug at a dose of 1.08 mg/m^2	

Reporting group values	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Number of subjects	3	6	
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)	3	6	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Age Continuous Units: years arithmetic mean standard deviation	±	±	
Gender Categorical Units: Subjects			
Female			
Male			
Race Units: Subjects			
White			
Black or African American			
Other			

Ethnicity Units: Subjects			
Hispanic/Latino Not Hispanic/Latino Not Reported			

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
Neonates up to 27 days old. Single dose of Apixaban 0.44 mg/m^2.	
Reporting group title	Group 2B
Reporting group description:	
Infants 28 days to < 9 months. Single dose of Apixaban 1.08 mg/m^2.	
Reporting group title	Group 2A
Reporting group description:	
Young children 9 months to < 2 years. Single dose of Apixaban 1.08 mg/m^2 or 2.43 mg/m^2.	
Reporting group title	Group 3
Reporting group description:	
Young children 2 years to < 6 years. Single dose of Apixaban 1.17 mg/m^2.	
Reporting group title	Group 4
Reporting group description:	
Children 6 years to < 12 years. Single dose of Apixaban 1.80 mg/m^2.	
Reporting group title	Group 5
Reporting group description:	
Adolescents 12 years to < 18 years. Single dose of Apixaban 2.19 mg/m^2.	
Subject analysis set title	Group 2A - 2.43 mg/m^2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects in the Group 2A (9 months to < 2 years) receiving study drug at a dose of 2.43 mg/m^2	
Subject analysis set title	Group 2A - 1.08 mg/m^2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects in the Group 2A (9 months to < 2 years) receiving study drug at a dose of 1.08 mg/m^2	

Primary: Apparent Plasma Clearance (CL/F)

End point title	Apparent Plasma Clearance (CL/F)[1][2]
End point description:	
End point type	Primary
End point timeframe:	
Day 1, from pre-dose up to 26 hours following drug administration	

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 statistical analysis was performed for this endpoint.

[2] - 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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	8	9
Units: L/h				
geometric mean (geometric coefficient of variation)	0.0979 (± 99999)	0.347 (± 41.3)	1.62 (± 60.6)	2.69 (± 38.4)

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	6	
Units: L/h				
geometric mean (geometric coefficient of variation)	3.85 (± 66)	0.775 (± 98.8)	0.757 (± 55.4)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution of the Central Compartment (Vc/F)

End point title	Apparent Volume of Distribution of the Central Compartment (Vc/F)[3][4]

End point description:

End point type	Primary

End point timeframe:

Day 1, from pre-dose up to 26 hours following drug administration

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: No statistical analysis was performed for this endpoint.

[4] - 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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	8	9
Units: Liters (L)				
geometric mean (geometric coefficient of variation)	1.82 (± 99999)	2.69 (± 27.9)	8.97 (± 36.5)	15.4 (± 39.5)

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	6	

Units: Liters (L)				
geometric mean (geometric coefficient of variation)	23.6 (± 46.5)	4.71 (± 57.3)	4.55 (± 36.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Rate of absorption (Ka)

End point title	Rate of absorption (Ka)[5][6]

End point description:

End point type	Primary

End point timeframe:

Day 1, from pre-dose up to 26 hours following drug administration

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: No statistical analysis was performed for this endpoint.

[6] - 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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	8	9
Units: L/h				
geometric mean (geometric coefficient of variation)	0.545 (± 99999)	0.717 (± 135)	1.03 (± 50)	1.15 (± 54.9)

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	6	
Units: L/h				
geometric mean (geometric coefficient of variation)	1.14 (± 64.3)	1.31 (± 55)	1.36 (± 52.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Estimated Area Under the Plasma Concentration-Time Curve_AUC(INF)

End point title	Estimated Area Under the Plasma Concentration-Time Curve_AUC(INF)[7][8]

End point description:

End point type	Primary

End point timeframe:

Day 1, from pre-dose up to 26 hours following drug administration

Notes:

[7] - 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 statistical analysis was performed for this endpoint.

[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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	8	9
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	1120 (± 99999)	806 (± 31.1)	423 (± 67.7)	662 (± 21.7)

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	6	
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	815 (± 48.4)	1260 (± 68.7)	501 (± 43.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Estimated Plasma Concentration (Cmax)

End point title	Maximum Estimated Plasma Concentration (Cmax)[9][10]

End point description:

End point type	Primary

End point timeframe:

Day 1, from pre-dose up to 26 hours following drug administration

Notes:

[9] - 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 statistical analysis was performed for this endpoint.

[10] - 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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	8	9
Units: ng/mL				
geometric mean (geometric coefficient of variation)	45.9 (± 99999)	64 (± 59.5)	49.9 (± 54)	80 (± 28)

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	96.5 (± 29.6)	148 (± 35.1)	59.1 (± 37.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Estimated Time at which Maximum Plasma Concentration Occurs (Tmax)

End point title	Estimated Time at which Maximum Plasma Concentration Occurs (Tmax)[11][12]

End point description:

End point type	Primary

End point timeframe:

Day 1, from pre-dose up to 26 hours following drug administration

Notes:

[11] - 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 statistical analysis was performed for this endpoint.

[12] - 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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	8	9
Units: Hours				
median (full range (min-max))	4.54 (4.54 to 4.54)	2.32 (1.46 to 9.42)	1.91 (1.24 to 3.89)	1.71 (1.3 to 3.46)

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	

Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	6	
Units: Hours				
median (full range (min-max))	1.95 (1.32 to 6.39)	1.67 (1.15 to 2.61)	1.6 (1.16 to 2.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Experiencing Adverse Events

End point title	Number of Subjects Experiencing Adverse Events

End point description:

End point type	Secondary

End point timeframe:

From first dose to 5 days following first dose

End point values	Group 1	Group 2B	Group 2A	Group 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	9	8
Units: Subjects				
Adverse Events	0	4	3	2
Serious Adverse Events (SAEs)	0	0	0	0
Adverse Events leading to discontinuation	0	0	0	0

End point values	Group 4	Group 5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Subjects				
Adverse Events	3	3		
Serious Adverse Events (SAEs)	2	0		
Adverse Events leading to discontinuation	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Linear Slope of the Relationship Between Plasma Concentration and Anti-Xa Activity (SLP)

End point title	Linear Slope of the Relationship Between Plasma Concentration and Anti-Xa Activity (SLP)[13]

End point description:

End point type	Secondary

End point timeframe:

Day 1, from pre-dose up to 26 hours after drug administration

Notes:

[13] - 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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	9	8	10[14]
Units: IU/ng				
number (confidence interval 95%)	0.0211 (0.015 to 0.0272)	0.0158 (0.0143 to 0.0173)	0.0163 (0.0138 to 0.0188)	0.0153 (0.0146 to 0.016)

Notes:

[14] - The actual number of subjects analyzed is 11, including 1 subject analyzed under a different study

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10[15]	2	6	
Units: IU/ng				
number (confidence interval 95%)	0.0163 (0.0156 to 0.017)	0.0131 (0.011 to 0.0152)	0.0129 (0.0114 to 0.0145)	

Notes:

[15] - The actual number of subjects analyzed is 15, including 5 subjects analyzed under a different study

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Estimated Anti-Xa Activity (AXAmax)

End point title	Maximum Estimated Anti-Xa Activity (AXAmax)[16]

End point description:

End point type	Secondary

End point timeframe:

Day 1, from pre-dose up to 26 hours after drug administration

Notes:

[16] - 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: Results for Group 2A are being reported separately for subjects receiving 2.43 mg/m^2 or 1.08 mg/m^2 of study drug.

End point values	Group 1	Group 2B	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	11	8	9
Units: IU/mL				
geometric mean (geometric coefficient of variation)	0.0837 (± 99999)	0.456 (± 226)	0.464 (± 157)	0.303 (± 243)

End point values	Group 5	Group 2A - 2.43 mg/m^2	Group 2A - 1.08 mg/m^2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	6	
Units: IU/mL				
geometric mean (geometric coefficient of variation)	0.307 (± 293)	0.309 (± 427)	0.204 (± 216)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All AEs were collected from start of treatment up to 30 days of discontinuation of dosing	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	GROUP 1
Reporting group description:	
Neonates up to 27 days old. Single dose of Apixaban 0.44 mg/m^2.	
Reporting group title	GROUP 2A
Reporting group description:	
Young children 9 months to < 2 years. Single dose of Apixaban 1.08 mg/m^2 or 2.43 mg/m^2.	
Reporting group title	GROUP 2B
Reporting group description:	
Infants 28 days to < 9 months. Single dose of Apixaban 1.08 mg/m^2.	
Reporting group title	GROUP 3
Reporting group description:	
Young children 2 years to < 6 years. Single dose of Apixaban 1.17 mg/m^2.	
Reporting group title	GROUP 4
Reporting group description:	
Children 6 years to < 12 years. Single dose of Apixaban 1.80 mg/m^2.	
Reporting group title	GROUP 5
Reporting group description:	
Adolescents 12 years to < 18 years. Single dose of Apixaban 2.19 mg/m^2.	

Serious adverse events	GROUP 1	GROUP 2A	GROUP 2B
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			

subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GROUP 3	GROUP 4	GROUP 5
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 8 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	GROUP 1	GROUP 2A	GROUP 2B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	3 / 9 (33.33%)	4 / 11 (36.36%)
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Post procedural haemorrhage			

subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 1 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 1 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 1 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	GROUP 3	GROUP 4	GROUP 5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	3 / 10 (30.00%)	3 / 10 (30.00%)
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 8 (12.50%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Post procedural haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			

Non-cardiac chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Restlessness			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Product issues Device malfunction subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Infections and infestations Device related infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0

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