Clinical trial results:
Single-dose pilot study of oral rivaroxaban in pediatric subjects with venous thromboembolism

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2009-017313-30
Trial protocol	AT DE IT IE FR
Global end of trial date	07 July 2015

Results information

Result version number	v1
This version publication date	03 July 2016
First version publication date	03 July 2016

Trial information

Trial identification

Sponsor protocol code	BAY59-7939/12892

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01145859
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer HealthCare AG
Sponsor organisation address	Kaiser Wilhelm Allee, D51368, Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com
Scientific contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000430-PIP01-08
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 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to investigate pharmacokinetics and pharmacodynamics of single oral doses of rivaroxaban in pediatric subjects in order to obtain weight adjusted doses with equivalent exposure compared to 10 milligram (mg) and 20 mg doses in adults.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 2010
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	Australia: 4
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	United States: 14
Worldwide total number of subjects	59
EEA total number of subjects	20

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)	9
Children (2-11 years)	41
Adolescents (12-17 years)	9
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 18 centers in 7 countries worldwide between 11 November 2010 (first subject first visit) and 7 July 2015 (last subject last visit).

Pre-assignment

Screening details:

Out of 72 enrolled subjects, 59 subjects were randomized and 13 subjects were excluded due to screening failures.

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	Age 12-18 Years: Tablet-Low Dose

Arm description:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kilogram (kg) received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

Arm title	Age 12-18 Years: Tablet-High Dose

Arm description:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

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from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

Arm title	Age 6-12 Years: Tablet-Low Dose

Arm description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

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Dosage and administration details:

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Arm title	Age 6-12 Years: Suspension-Low Dose

Arm description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 5 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 5 mg.

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Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

Arm title	Age 6-12 Years: Suspension-High Dose

Arm description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 10 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 10 mg.

Arm title	Age 2-6 Years: Suspension-Low Dose

Arm description:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Arm title	Age 2-6 Years: Suspension-High Dose

Arm description:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in

adults) ranging from 5 to 10 mg.

Arm title	Age 6 months-2 years: Suspension-Low Dose

Arm description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

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Arm description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
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Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Number of subjects in period 1	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose
Started	4	5	4
Completed	4	5	4

Number of subjects in period 1	Age 6-12 Years: Suspension-Low Dose	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose
Started	11	4	5
Completed	11	4	5

Number of subjects in period 1	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose	Age 6 months-2 years: Suspension-Low Dose
Started	11	5	6
Completed	11	5	6

Number of subjects in period 1	Age 6 months-2 years: Suspension-High Dose
Started	4
Completed	4

Reporting groups

Reporting group title	Age 12-18 Years: Tablet-Low Dose

Reporting group description:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kilogram (kg) received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

Reporting group title	Age 12-18 Years: Tablet-High Dose

Reporting group description:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

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Reporting group title	Age 2-6 Years: Suspension-Low Dose

Reporting group description:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

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Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

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Reporting group description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body

weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Reporting group title	Age 6 months-2 years: Suspension-High Dose

Reporting group description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Reporting group values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose
Number of subjects	4	5	4
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	16	14.8	10
standard deviation	± 1.4	± 1.9	± 0.8
Gender Categorical			
Units: Subjects			
Female	1	4	1
Male	3	1	3

Reporting group values	Age 6-12 Years: Suspension-Low Dose	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose
Number of subjects	11	4	5
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	7.5	8.5	9.2
standard deviation	± 1.5	± 1.9	± 1.8
Gender Categorical			
Units: Subjects			
Female	6	2	0
Male	5	2	5

Reporting group values	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose	Age 6 months-2 years: Suspension-Low Dose
Number of subjects	11	5	6
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	3.4	3.6	0.5
standard deviation	± 1.2	± 1.5	± 0.5

Gender Categorical Units: Subjects			
Female	5	3	3
Male	6	2	3

Reporting group values	Age 6 months-2 years: Suspension-High Dose	Total	
Number of subjects	4	59	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	0.5		
standard deviation	± 0.6	-	
Gender Categorical Units: Subjects			
Female	1	26	
Male	3	33	

End points

End points reporting groups

Reporting group title	Age 12-18 Years: Tablet-Low Dose

Reporting group description:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kilogram (kg) received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

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Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

Reporting group title	Age 6-12 Years: Tablet-Low Dose

Reporting group description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

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Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 5 mg.

Reporting group title	Age 6-12 Years: Tablet-High Dose

Reporting group description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

Reporting group title	Age 6-12 Years: Suspension-High Dose

Reporting group description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 10 mg.

Reporting group title	Age 2-6 Years: Suspension-Low Dose

Reporting group description:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Reporting group title	Age 2-6 Years: Suspension-High Dose

Reporting group description:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Reporting group title	Age 6 months-2 years: Suspension-Low Dose

Reporting group description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body

weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Reporting group title	Age 6 months-2 years: Suspension-High Dose

Reporting group description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

SAF (n=59) included all subjects who received at least one dose of study drug.

Subject analysis set title	Per protocol set (PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

PPS (n=59) included all subjects who received at least one dose of study drug with no relevant protocol deviations affecting pharmacokinetics or pharmacodynamics

Primary: Model Independent Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity (AUC) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity (AUC) of Rivaroxaban in Plasma[1][2]

End point description:

Area under the concentration versus time curve from zero to infinity after single dose. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 hours (h) (pre-dose) to 24 h post-dose

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: Inferential statistical analysis was planned for the overall data and not as per the reporting groups.
[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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[3]	5[4]	4[5]	11[6]
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	1340 (± 37.7)	1660 (± 39)	866 (± 36)	719 (± 42.4)

Notes:

[3] - PPS

[4] - PPS

[5] - PPS

[6] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[7]	5[8]		
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	1650 (± 38.9)	1060 (± 48)		

Notes:

[7] - PPS

[8] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Model Derived Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity (AUC) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity (AUC) of Rivaroxaban in Plasma[9]

End point description:

Area under the concentration versus time curve from zero to infinity after single dose. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

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: Inferential statistical analysis was planned for the overall data and not as per the reporting groups.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[10]	5[11]	4[12]	11[13]
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	1320 (± 13.1)	1760 (± 20.7)	902 (± 31.2)	720 (± 24.1)

Notes:

[10] - PPS

[11] - PPS

[12] - PPS

[13] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[14]	5[15]	11[16]	5[17]
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	1540 (± 52)	1070 (± 37.5)	674 (± 25.5)	755 (± 39)

Notes:

[14] - PPS

[15] - PPS

[16] - PPS

[17] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[18]	4[19]		
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	503 (± 20.6)	672 (± 29.4)		

Notes:

[18] - PPS

[19] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Model Independent Pharmacokinetic: Area Under the Concentration From Time Zero to the Last Data Point (AUC[0-tlast]) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Area Under the Concentration From Time Zero to the Last Data Point (AUC[0-tlast]) of Rivaroxaban in Plasma[20][21]

End point description:

Area under the concentration versus time curve from zero to tlast after single (first) dose. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[20] - 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 were done, inferential statistics were not planned.

[21] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[22]	5[23]	4[24]	11[25]
Units: microgram*hour per liter				
geometric mean (geometric coefficient of variation)	1260 (± 39.7)	1530 (± 40.4)	839 (± 35.6)	689 (± 42.8)

Notes:

[22] - PPS

[23] - PPS

[24] - PPS

[25] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[26]	5[27]		
Units: microgram*hour per liter				
geometric mean (geometric coefficient of variation)	1510 (± 35.8)	988 (± 44.3)		

Notes:

[26] - PPS

[27] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Model Independent Pharmacokinetic: Maximum Observed Drug Concentration (Cmax) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Maximum Observed Drug Concentration (Cmax) of Rivaroxaban in Plasma[28][29]

End point description:

Maximum observed drug concentration, directly taken from analytical data. Geometric meanand percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[28] - 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 were done, inferential statistics were not planned.

[29] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[30]	5[31]	4[32]	11[33]
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	161 (± 45.6)	206 (± 41.3)	115 (± 72.6)	89.2 (± 59.3)

Notes:

[30] - PPS

[31] - PPS

[32] - PPS

[33] - PPS

End point values	Age 6-12 Years: Tablet-	Age 6-12 Years:		

	High Dose	Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[34]	5[35]		
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	244 (± 21.1)	113 (± 42.9)		

Notes:

[34] - PPS

[35] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Model Derived Pharmacokinetic: Maximum Observed Drug Concentration (Cmax) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Maximum Observed Drug Concentration (Cmax) of Rivaroxaban in Plasma[36]

End point description:

Maximum observed drug concentration, directly taken from analytical data. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[36] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[37]	5[38]	4[39]	11[40]
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	129 (± 11.4)	180 (± 12)	118 (± 11)	82.5 (± 37.4)

Notes:

[37] - PPS

[38] - PPS

[39] - PPS

[40] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[41]	5[42]	11[43]	5[44]
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	172 (± 25.9)	85.1 (± 15.7)	84.2 (± 36)	60.1 (± 33.4)

Notes:

[41] - PPS

[42] - PPS

[43] - PPS

[44] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[45]	4[46]		
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	94.9 (± 28.3)	143 (± 14.7)		

Notes:

[45] - PPS

[46] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Model Derived Pharmacokinetic: Clearance (CL) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Clearance (CL) of Rivaroxaban in Plasma[47]

End point description:

Systemic Clearance (CL) is a quantitative measure of the rate at which a drug substance is removed from the body. The total systemic clearance after intravenous dose was estimated by dividing the total administered dose by the plasma Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity]). Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[47] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[48]	5[49]	4[50]	11[51]
Units: liter per hour				
geometric mean (geometric coefficient of variation)	7.58 (± 13.1)	6.96 (± 22.8)	6.79 (± 25.4)	5.78 (± 21)

Notes:

[48] - PPS

[49] - PPS

[50] - PPS

[51] - PPS

End point values	Age 6-12 Years: Tablet-	Age 6-12 Years:	Age 2-6 Years: Suspension-	Age 2-6 Years: Suspension-

	High Dose	Suspension-High Dose	Low Dose	High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[52]	5[53]	11[54]	5[55]
Units: liter per hour				
geometric mean (geometric coefficient of variation)	4.79 (± 16.1)	5.87 (± 29.4)	4.13 (± 26.3)	4.61 (± 30.5)

Notes:

[52] - PPS

[53] - PPS

[54] - PPS

[55] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[56]	4[57]		
Units: liter per hour				
geometric mean (geometric coefficient of variation)	3.96 (± 17.6)	3.95 (± 13.8)		

Notes:

[56] - PPS

[57] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Model Derived Pharmacokinetic: Volume of Distribution at Steady State (Vss) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Volume of Distribution at Steady State (Vss) of Rivaroxaban in Plasma[58]

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. Steady state volume of distribution (Vss) is the apparent volume of distribution at steady-state which is estimated by (D/AUC[0-infinity])*(AUMC[0-infinity])/AUC[0-infinity]) where D is the dose of study drug, AUMC(0-infinity) is the area under the first moment curve extrapolated to infinity and AUC(0-infinity) is the area under the plasma concentration-time curve from time zero to infinite time. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[58] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[59]	5[60]	4[61]	11[62]
Units: liter				

geometric mean (geometric coefficient of variation)	63 (± 8.77)	55.2 (± 13.2)	42.6 (± 11.3)	35.1 (± 9.62)

Notes:

[59] - PPS

[60] - PPS

[61] - PPS

[62] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[63]	5[64]	11[65]	5[66]
Units: liter				
geometric mean (geometric coefficient of variation)	40.1 (± 21.3)	38.8 (± 13.9)	25.2 (± 14.3)	25 (± 9.94)

Notes:

[63] - PPS

[64] - PPS

[65] - PPS

[66] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[67]	4[68]		
Units: liter				
geometric mean (geometric coefficient of variation)	20 (± 6.29)	20.5 (± 8.29)		

Notes:

[67] - PPS

[68] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Model Derived Pharmacokinetic: Absorption Rate Constant (Ka) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Absorption Rate Constant (Ka) of Rivaroxaban in Plasma[69]

End point description:

The rate at which a drug enters the body after administration is called the absorption rate, and is represented by the symbol ka. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[69] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[70]	5[71]	4[72]	11[73]
Units: 1/hour				
geometric mean (geometric coefficient of variation)	0.711 (± 7.32)	0.686 (± 12.3)	0.727 (± 20.3)	0.465 (± 79.1)

Notes:

[70] - PPS

[71] - PPS

[72] - PPS

[73] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[74]	5[75]	11[76]	5[77]
Units: 1/hour				
geometric mean (geometric coefficient of variation)	0.794 (± 12.7)	0.232 (± 20.7)	0.408 (± 66.2)	0.166 (± 53.8)

Notes:

[74] - PPS

[75] - PPS

[76] - PPS

[77] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[78]	4[79]		
Units: 1/hour				
geometric mean (geometric coefficient of variation)	0.545 (± 51)	0.72 (± 3.5)		

Notes:

[78] - PPS

[79] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Relative Change from Baseline in Prothrombin Time (PT)

End point title	Relative Change from Baseline in Prothrombin Time (PT)[80]

End point description:

Prothrombin time (PT) is a global clotting test assessing the extrinsic pathway of the blood coagulation cascade. The test is sensitive for deficiencies of Factors II, V, VII, and X, with sensitivity being best for Factors V, VII, and X and less pronounced for Factor II. The initial read-out is in seconds. Mean and standard deviation (SD) were reported. In the below table, "n" signifies subjects who were evaluable for the specified parameter for each arm, respectively. '99999' in the posting indicates that data were not calculated as no subjects were analysed for the specified time point.

End point type	Primary

End point timeframe:

0 h (Pre-dose) to 24 h post-dose

Notes:

[80] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[81]	5[82]	4[83]	11[84]
Units: seconds				
arithmetic mean (standard deviation)				
PT-baseline (n=4, 5, 4, 11, 4, 5, 11, 5, 5, 4)	18.03 (± 1.72)	16.02 (± 3.16)	17.88 (± 2.05)	15.83 (± 2.78)
PT-Change at 30 min (n=4,5,4,11,4,5,0,0,0,0)	1.26 (± 0.24)	1.12 (± 0.11)	1.11 (± 0.25)	1.27 (± 0.22)
PT-Change at 1h 30min (n=0,0,0,0,0,0,11,5,5,4)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
PT-Change at 2h (n=3,4,4,10,4,5,0,0,0,0)	1.84 (± 0.21)	1.62 (± 0.2)	1.49 (± 0.18)	1.32 (± 0.19)
PT- Change at 4h (n=4, 4, 0, 0, 0, 0, 0, 0, 0, 0)	1.56 (± 0.21)	1.77 (± 0.46)	99999 (± 99999)	99999 (± 99999)
PT-Change at 8h (n=3,5,4,11,4,5,10,5,0,0)	1.37 (± 0.12)	1.3 (± 0.19)	1.16 (± 0.1)	1.14 (± 0.13)
PT-Change at 20h (n=3,5,4,11,4,5,10,5,5,4)	1.13 (± 0.07)	1.02 (± 0.06)	1.05 (± 0.05)	1.05 (± 0.05)

Notes:

[81] - PPS

[82] - PPS

[83] - PPS

[84] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[85]	5[86]	11[87]	5[88]
Units: seconds				
arithmetic mean (standard deviation)				
PT-baseline (n=4, 5, 4, 11, 4, 5, 11, 5, 5, 4)	13.2 (± 0.59)	13.74 (± 0.27)	13.93 (± 2.19)	14.22 (± 1.67)
PT-Change at 30 min (n=4,5,4,11,4,5,0,0,0,0)	1.22 (± 0.24)	1.1 (± 0.04)	99999 (± 99999)	99999 (± 99999)
PT-Change at 1h 30min (n=0,0,0,0,0,0,11,5,5,4)	99999 (± 99999)	99999 (± 99999)	1.23 (± 0.13)	1.14 (± 0.13)
PT-Change at 2h (n=3,4,4,10,4,5,0,0,0,0)	1.59 (± 0.39)	1.2 (± 0.08)	99999 (± 99999)	99999 (± 99999)
PT- Change at 4h (n=4, 4, 0, 0, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
PT-Change at 8h (n=3,5,4,11,4,5,10,5,0,0)	1.25 (± 0.2)	1.17 (± 0.2)	1.1 (± 0.07)	1.07 (± 0.04)
PT-Change at 20h (n=3,5,4,11,4,5,10,5,5,4)	1.03 (± 0.03)	1.02 (± 0.07)	1.05 (± 0.03)	1 (± 0.05)

Notes:

[85] - PPS

[86] - PPS

[87] - PPS

[88] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[89]	4[90]		
Units: seconds				
arithmetic mean (standard deviation)				
PT-baseline (n=4, 5, 4, 11, 4, 5, 11, 5, 5, 4)	15.18 (± 2.69)	16.98 (± 2.94)		
PT-Change at 30 min (n=4,5,4,11,4,5,0,0,0,0)	99999 (± 99999)	99999 (± 99999)		
PT-Change at 1h 30min (n=0,0,0,0,0,0,11,5,5,4)	1.36 (± 0.24)	1.36 (± 0.17)		
PT-Change at 2h (n=3,4,4,10,4,5,0,0,0,0)	99999 (± 99999)	99999 (± 99999)		
PT- Change at 4h (n=4, 4, 0, 0, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)		
PT-Change at 8h (n=3,5,4,11,4,5,10,5,0,0)	99999 (± 99999)	99999 (± 99999)		
PT-Change at 20h (n=3,5,4,11,4,5,10,5,5,4)	1.02 (± 0.06)	0.99 (± 0.05)		

Notes:

[89] - PPS

[90] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Relative Change from Baseline in Adjusted Partial Thromboplastin Time (aPTT)

End point title	Relative Change from Baseline in Adjusted Partial Thromboplastin Time (aPTT)[91]

End point description:

The aPTT is a screening test for the intrinsic pathway and is sensitive for deficiencies of Factors I, II, V, VIII, IX, X, XI and XII. Higher values than the baseline indicate anticoagulant effects. In the below table, "n" signifies subjects who were evaluable for the specified parameter for each arm, respectively. '99999' in the posting indicates that data were not calculated as no subjects were analysed for the specified time point.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[91] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[92]	5[93]	4[94]	11[95]
Units: seconds				
arithmetic mean (standard deviation)				
aPTT-baseline (n=4,5,4,11,4,5,11,5,5,4)	42.975 (± 9.689)	35.16 (± 7.832)	47.25 (± 11.709)	37.373 (± 8.173)
aPTT-Change at 30 min (n=4,5,4,11,4,5,0,0,0,0)	1.148 (± 0.16)	1.009 (± 0.064)	1.055 (± 0.276)	1.255 (± 0.23)
aPTT-Change at 1h30min (n=0,0,0,0,0,0,11,5,5,4)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
aPTT-Change at 2h (n=3,4,4,10,4,5,0,0,0,0)	1.586 (± 0.17)	1.366 (± 0.096)	1.333 (± 0.174)	1.315 (± 0.117)
aPTT-Change at 4h (n=4,4,0,0,0,0,0,0,0,0)	1.448 (± 0.184)	1.432 (± 0.193)	99999 (± 99999)	99999 (± 99999)
aPTT-Change at 8h (n=3,5,4,11,4,5,10,5,0,0)	1.334 (± 0.042)	1.21 (± 0.127)	1.116 (± 0.143)	1.19 (± 0.159)
aPTT-Change at 20h (n=3,5,4,11,4,5,10,5,5,4)	1.117 (± 0.122)	1.01 (± 0.074)	1.043 (± 0.124)	1.05 (± 0.087)

Notes:

[92] - PPS

[93] - PPS

[94] - PPS

[95] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[96]	5[97]	11[98]	5[99]
Units: seconds				
arithmetic mean (standard deviation)				
aPTT-baseline (n=4,5,4,11,4,5,11,5,5,4)	32 (± 1.407)	28.96 (± 2.266)	32.764 (± 6.469)	31.86 (± 5.018)
aPTT-Change at 30 min (n=4,5,4,11,4,5,0,0,0,0)	1.18 (± 0.187)	1.057 (± 0.104)	99999 (± 99999)	99999 (± 99999)
aPTT-Change at 1h30min (n=0,0,0,0,0,0,11,5,5,4)	99999 (± 99999)	99999 (± 99999)	1.554 (± 1.129)	1.13 (± 0.206)
aPTT-Change at 2h (n=3,4,4,10,4,5,0,0,0,0)	1.433 (± 0.25)	1.159 (± 0.115)	99999 (± 99999)	99999 (± 99999)
aPTT-Change at 4h (n=4,4,0,0,0,0,0,0,0,0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
aPTT-Change at 8h (n=3,5,4,11,4,5,10,5,0,0)	1.247 (± 0.154)	1.216 (± 0.153)	1.123 (± 0.055)	1.113 (± 0.106)
aPTT-Change at 20h (n=3,5,4,11,4,5,10,5,5,4)	1.035 (± 0.03)	1.056 (± 0.076)	0.98 (± 0.117)	0.989 (± 0.092)

Notes:

[96] - PPS

[97] - PPS

[98] - PPS

[99] - PPS

End point values	Age 6 months-2 years: Suspension-	Age 6 months-2 years: Suspension-		

	Low Dose	High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[100]	4[101]		
Units: seconds				
arithmetic mean (standard deviation)				
aPTT-baseline (n=4,5,4,11,4,5,11,5,5,4)	37.64 (± 13.924)	42.425 (± 8.742)		
aPTT-Change at 30 min (n=4,5,4,11,4,5,0,0,0,0)	99999 (± 99999)	99999 (± 99999)		
aPTT-Change at 1h30min (n=0,0,0,0,0,0,11,5,5,4)	1.248 (± 0.303)	1.244 (± 0.18)		
aPTT-Change at 2h (n=3,4,4,10,4,5,0,0,0,0)	99999 (± 99999)	99999 (± 99999)		
aPTT-Change at 4h (n=4,4,0,0,0,0,0,0,0,0)	99999 (± 99999)	99999 (± 99999)		
aPTT-Change at 8h (n=3,5,4,11,4,5,10,5,0,0)	99999 (± 99999)	99999 (± 99999)		
aPTT-Change at 20h (n=3,5,4,11,4,5,10,5,5,4)	0.986 (± 0.087)	0.909 (± 0.12)		

Notes:

[100] - PPS

[101] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change from Baseline in Anti-factor Xa activity (anti-Xa)

End point title	Absolute Change from Baseline in Anti-factor Xa activity (anti-Xa)[102]

End point description:

This is a method for measuring the inhibition of Factor Xa activity determined by an ex vivo using a photometric method. Higher Values than the baseline indicate a more pronounced inhibition. "n" signifies subjects who were evaluable for the specified parameter for each arm, respectively. '99999' in the posting indicates that data were not calculated.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[102] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[103]	5[104]	4[105]	11[106]
Units: microgram per liter (mcg/L)				
arithmetic mean (standard deviation)				
Baseline(n=4, 5, 4, 11, 4, 5, 11, 5, 6, 4)	0 (± 0)	0 (± 0)	17.12 (± 34.24)	0 (± 0)
Change at 30 min(n=3, 2, 4, 8, 2, 3, 0, 0, 0, 0)	99.454 (± 34.7872)	84.8155 (± 87.7725)	46.4458 (± 53.8409)	67.9855 (± 43.3122)
Change at 1h30min(n=0, 0, 0, 0, 0, 0, 10, 3, 4, 2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Change at 2 h(n=2, 5, 3, 10, 4, 3, 0, 0, 0, 0)	155.07 (± 17.211)	175.3064 (± 73.6695)	92.15 (± 111.9477)	74.2293 (± 53.298)
Change at 4 h(n=3, 4, 0, 0, 0, 0, 0, 0, 0, 0)	91.756 (± 42.8758)	234.0675 (± 80.8278)	99999 (± 99999)	99999 (± 99999)
Change at 8 h(n=4, 5, 3, 10, 4, 4, 9, 3, 0, 0)	53.6625 (± 29.0532)	76.8676 (± 46.0017)	10.9533 (± 43.6964)	31.0553 (± 15.2461)
Change at 20 h(n=0, 1, 1, 0, 2, 1, 0, 1, 0, 0)	99999 (± 99999)	16.236 (± 99999)	-35.621 (± 99999)	99999 (± 99999)

Notes:

[103] - PPS

[104] - PPS

[105] - PPS

[106] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[107]	5[108]	11[109]	5[110]
Units: microgram per liter (mcg/L)				
arithmetic mean (standard deviation)				
Baseline(n=4, 5, 4, 11, 4, 5, 11, 5, 6, 4)	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Change at 30 min(n=3, 2, 4, 8, 2, 3, 0, 0, 0, 0)	156.995 (± 26.5519)	24.4307 (± 5.9235)	99999 (± 99999)	99999 (± 99999)
Change at 1h30min(n=0, 0, 0, 0, 0, 0, 10, 3, 4, 2)	99999 (± 99999)	99999 (± 99999)	77.1636 (± 54.3735)	56.924 (± 42.6556)
Change at 2 h(n=2, 5, 3, 10, 4, 3, 0, 0, 0, 0)	132.8078 (± 86.8632)	62.0813 (± 21.3843)	99999 (± 99999)	99999 (± 99999)
Change at 4 h(n=3, 4, 0, 0, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at 8 h(n=4, 5, 3, 10, 4, 4, 9, 3, 0, 0)	52.8778 (± 31.0733)	74.3968 (± 75.865)	30.6717 (± 13.9351)	25.0467 (± 7.6683)
Change at 20 h(n=0, 1, 1, 0, 2, 1, 0, 1, 0, 0)	24.5795 (± 4.7284)	15.446 (± 99999)	99999 (± 99999)	23.28 (± 99999)

Notes:

[107] - PPS

[108] - PPS

[109] - PPS

[110] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[111]	4[112]		
Units: microgram per liter (mcg/L)				
arithmetic mean (standard deviation)				
Baseline(n=4, 5, 4, 11, 4, 5, 11, 5, 6, 4)	0 (± 0)	0 (± 0)		
Change at 30 min(n=3, 2, 4, 8, 2, 3, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)		
Change at 1h30min(n=0, 0, 0, 0, 0, 0, 10, 3, 4, 2)	106.3098 (± 78.7218)	144.66 (± 63.4558)		
Change at 2 h(n=2, 5, 3, 10, 4, 3, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)		

Change at 4 h(n=3, 4, 0, 0, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)		
Change at 8 h(n=4, 5, 3, 10, 4, 4, 9, 3, 0, 0)	99999 (± 99999)	99999 (± 99999)		
Change at 20 h(n=0, 1, 1, 0, 2, 1, 0, 1, 0, 0)	99999 (± 99999)	99999 (± 99999)		

Notes:

[111] - PPS

[112] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Baseline Adjusted Maximum Effect (Emax) and Effect at Expected Time of Minimum Drug Concentration in Plasma (Etrough) of PT and aPTT

End point title	Baseline Adjusted Maximum Effect (Emax) and Effect at Expected Time of Minimum Drug Concentration in Plasma (Etrough) of PT and aPTT[113]

End point description:

Prothrombin time (PT) is a global clotting test assessing the extrinsic pathway of the blood coagulation cascade. The test is sensitive for deficiencies of Factors II, V, VII, and X, with sensitivity being best for Factors V, VII, and X and less pronounced for Factor II. The initial read-out is in seconds. Higher values than the baseline indicate anticoagulant effects. Baseline adjusted maximum Effect (Emax) on PT was measured as maximum PT (measured in seconds) minus PT (measured in seconds) at baseline. Emax on aPTT was measured as the ratio of maximum aPTT (measured in seconds) divided by aPTT (measured in seconds) at baseline.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[113] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[114]	5[115]	4[116]	11[117]
Units: seconds				
arithmetic mean (standard deviation)				
baseline adjusted Emax - PT	13.2 (± 4.45)	11.5 (± 7.73)	8.93 (± 3.83)	5.7 (± 3.8)
baseline adjusted Etrough - aPTT	4.6 (± 4.97)	0.02 (± 2.92)	1.08 (± 4.64)	1.99 (± 3.65)

Notes:

[114] - PPS

[115] - PPS

[116] - PPS

[117] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[118]	5[119]	11[120]	5[121]
Units: seconds				

arithmetic mean (standard deviation)				
baseline adjusted Emax - PT	8.73 (± 4.74)	3.96 (± 1.97)	3.49 (± 2.05)	2.16 (± 1.31)
baseline adjusted Etrough - aPTT	1.1 (± 0.949)	1.74 (± 2.49)	0.69 (± 3.68)	-0.24 (± 3.02)

Notes:

[118] - PPS

[119] - PPS

[120] - PPS

[121] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[122]	4[123]		
Units: seconds				
arithmetic mean (standard deviation)				
baseline adjusted Emax - PT	5.44 (± 3.82)	6.13 (± 2.99)		
baseline adjusted Etrough - aPTT	0.44 (± 3.36)	-4.48 (± 6.12)		

Notes:

[122] - PPS

[123] - PPS

Statistical analyses

No statistical analyses for this end point

Primary: Baseline Adjusted Emax and Etrough of anti -Xa

End point title	Baseline Adjusted Emax and Etrough of anti -Xa[124]

End point description:

This is a method for measuring the inhibition of Factor Xa activity determined by an ex vivo using a photometric method. Higher Values than the baseline indicate a more pronounced inhibition. Emax on anti-Factor Xa activity was measured as the ratio of maximum anti-Factor Xa activity (measured in U/L) divided by anti-Factor Xa activity (measured in U/L) at baseline. '99999' in the posting indicates that data were not calculated.

End point type	Primary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[124] - 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 were done, inferential statistics were not planned.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[125]	0[126]	0[127]	0[128]
Units: microgram per liter (mcg/L)				

Notes:

[125] - Data were not available to report as it was presented graphically, as per planned analysis

[126] - Data were not available to report as it was presented graphically, as per planned analysis

[127] - Data were not available to report as it was presented graphically, as per planned analysis

[128] - Data were not available to report as it was presented graphically, as per planned analysis

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[129]	0[130]	0[131]	0[132]
Units: microgram per liter (mcg/L)				

Notes:

[129] - Data were not available to report as it was presented graphically, as per planned analysis

[130] - Data were not available to report as it was presented graphically, as per planned analysis

[131] - Data were not available to report as it was presented graphically, as per planned analysis

[132] - Data were not available to report as it was presented graphically, as per planned analysis

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[133]	0[134]		
Units: microgram per liter (mcg/L)				

Notes:

[133] - Data were not available to report as it was presented graphically, as per planned analysis

[134] - Data were not available to report as it was presented graphically, as per planned analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged in-patient hospitalization; lifethreatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent adverse events were defined as adverse events/serious adverse events that started or worsened after the study drug treatment.

End point type	Secondary

End point timeframe:

From the start of study treatment up to 11 days

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[135]	5[136]	4[137]	11[138]
Units: subjects				
TEAEs	2	1	1	4
TESAEs	1	0	0	0

Notes:

[135] - SAF

[136] - SAF

[137] - SAF

[138] - SAF

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[139]	5[140]	11[141]	5[142]
Units: subjects				
TEAEs	3	0	2	1
TESAEs	0	0	0	0

Notes:

[139] - SAF

[140] - SAF

[141] - SAF

[142] - SAF

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[143]	4[144]		
Units: subjects				
TEAEs	2	0		
TESAEs	0	0		

Notes:

[143] - SAF

[144] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Model Independent Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity Divided by Dose (AUC/D) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity Divided by Dose (AUC/D) of Rivaroxaban in Plasma[145]

End point description:

Area under the concentration versus time curve from zero to infinity after single (first) dose divided by dose. AUC/D of Rivaroxaban was reported. Geometric mean and percentagegeometric coefficient of

variation (%CV) were reported. In the below categories of the table, "n" signifies the number of subjects evaluable for the corresponding analyte.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[145] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[146]	5[147]	4[148]	11[149]
Units: hours per liter (h/L)				
geometric mean (geometric coefficient of variation)	0.134 (± 37.7)	0.0878 (± 40)	0.141 (± 26.8)	0.173 (± 39.6)

Notes:

[146] - PPS

[147] - PPS

[148] - PPS

[149] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[150]	5[151]		
Units: hours per liter (h/L)				
geometric mean (geometric coefficient of variation)	0.145 (± 18.9)	0.11 (± 46.7)		

Notes:

[150] - PPS

[151] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Derived Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity Divided by Dose (AUC/D) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Area Under the Concentration Versus Time Curve From Zero to Infinity Divided by Dose (AUC/D) of Rivaroxaban in Plasma

End point description:

Area under the concentration versus time curve from zero to infinity after single (first) dose divided by dose. AUC/D of Rivaroxaban was reported. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[152]	5[153]	4[154]	11[155]
Units: hours per liter (h/L)				
geometric mean (geometric coefficient of variation)	0.132 (± 13.1)	0.0931 (± 22.8)	0.147 (± 25.4)	0.173 (± 21)

Notes:

[152] - PPS

[153] - PPS

[154] - PPS

[155] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[156]	5[157]	11[158]	5[159]
Units: hours per liter (h/L)				
geometric mean (geometric coefficient of variation)	0.135 (± 16.1)	0.11 (± 29.4)	0.242 (± 26.3)	0.14 (± 30.5)

Notes:

[156] - PPS

[157] - PPS

[158] - PPS

[159] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[160]	4[161]		
Units: hours per liter (h/L)				
geometric mean (geometric coefficient of variation)	0.253 (± 17.6)	0.164 (± 13.8)		

Notes:

[160] - PPS

[161] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Independent Pharmacokinetic: Area Under the Concentration divided by dose (mg) per kg body weight (AUCnorm) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Area Under the Concentration divided by dose (mg) per kg body weight (AUCnorm) of Rivaroxaban in Plasma[162]

End point description:

Area under the concentration versus time from zero to infinity after single (first) dose, divided by dose per kilogram body weight. Geometric and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[162] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[163]	5[164]	4[165]	11[166]
Units: kilogram*hour per liter (kg*h/L)				
geometric mean (geometric coefficient of variation)	9.12 (± 37.3)	5.02 (± 37.9)	5.63 (± 32.9)	5.11 (± 41.7)

Notes:

[163] - PPS

[164] - PPS

[165] - PPS

[166] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[167]	5[168]		
Units: kilogram*hour per liter (kg*h/L)				
geometric mean (geometric coefficient of variation)	6.37 (± 60.1)	3.8 (± 39.4)		

Notes:

[167] - PPS

[168] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Derived Pharmacokinetic: Area Under the Concentration divided by dose (mg) per kg body weight (AUCnorm) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Area Under the Concentration divided by dose (mg) per kg body weight (AUCnorm) of Rivaroxaban in Plasma

End point description:

Area under the concentration versus time from zero to infinity after single (first) dose, divided by dose per kilogram body weight. Geometric and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[169]	5[170]	4[171]	11[172]
Units: kilogram*hour per liter (kg*h/L)				
geometric mean (geometric coefficient of variation)	8.99 (± 15.1)	5.32 (± 20.5)	5.87 (± 21.3)	5.11 (± 22.7)

Notes:

[169] - PPS

[170] - PPS

[171] - PPS

[172] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[173]	5[174]	11[175]	5[176]
Units: kilogram*hour per liter (kg*h/L)				
geometric mean (geometric coefficient of variation)	4.89 (± 31.5)	3.82 (± 27)	3.81 (± 31.3)	2.2 (± 51)

Notes:

[173] - PPS

[174] - PPS

[175] - PPS

[176] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[177]	4[178]		
Units: kilogram*hour per liter (kg*h/L)				
geometric mean (geometric coefficient of variation)	2.22 (± 16.9)	1.54 (± 26.4)		

Notes:

[177] - PPS

[178] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Independent Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose (Cmax/D) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose (Cmax/D) of Rivaroxaban in Plasma[179]

End point description:

Maximum observed drug concentration, directly taken from analytical data, divided by dose. Cmax/D of Rivaroxaban wasreported. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[179] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[180]	5[181]	4[182]	11[183]
Units: 1/liter				
geometric mean (geometric coefficient of variation)	0.0161 (± 45.7)	0.0109 (± 45.8)	0.0188 (± 59.9)	0.0214 (± 58.5)

Notes:

[180] - PPS

[181] - PPS

[182] - PPS

[183] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[184]	5[185]		
Units: 1/liter				
geometric mean (geometric coefficient of variation)	0.0214 (± 35.9)	0.0117 (± 58)		

Notes:

[184] - PPS

[185] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Derived Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose (Cmax/D) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose (Cmax/D) of Rivaroxaban in Plasma

End point description:

Maximum observed drug concentration, directly taken from analytical data, divided by dose. Cmax/D of Rivaroxaban was reported. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[186]	5[187]	4[188]	11[189]
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	0.0129 (± 11.4)	0.00952 (± 18.7)	0.0193 (± 15.7)	0.0198 (± 40.7)

Notes:

[186] - PPS

[187] - PPS

[188] - PPS

[189] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[190]	5[191]	11[192]	5[193]
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	0.0151 (± 27.1)	0.0088 (± 23.8)	0.0303 (± 42)	0.0112 (± 24.5)

Notes:

[190] - PPS

[191] - PPS

[192] - PPS

[193] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[194]	4[195]		
Units: microgram per liter				
geometric mean (geometric coefficient of variation)	0.0476 (± 40.3)	0.035 (± 15.8)		

Notes:

[194] - PPS

[195] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Independent Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose per Kilogram Body Weight (Cmax,norm) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose per Kilogram Body Weight (Cmax,norm) of Rivaroxaban in Plasma[196]

End point description:

Maximum observed drug concentration, directly taken from analytical data, divided by dose per kilogram body weight. Geometric and percentage geometric coefficient of variation (%CV) were reported. 0 h (pre-dose) to 24 h post-dose

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[196] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[197]	5[198]	4[199]	11[200]
Units: kilogram per liter (kg/L)				
geometric mean (geometric coefficient of variation)	1.09 (± 43.5)	0.623 (± 38.2)	0.747 (± 74.4)	0.633 (± 57.6)

Notes:

[197] - PPS

[198] - PPS

[199] - PPS

[200] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[201]	5[202]		
Units: kilogram per liter (kg/L)				
geometric mean (geometric coefficient of variation)	0.942 (± 51.2)	0.405 (± 41.1)		

Notes:

[201] - PPS

[202] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Derived Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose per Kilogram Body Weight (Cmax,norm) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Maximum Observed Drug Concentration Divided by Dose per Kilogram Body Weight (Cmax,norm) of Rivaroxaban in Plasma

End point description:

Maximum observed drug concentration, directly taken from analytical data, divided by dose per kilogram body weight. Geometric and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[203]	5[204]	4[205]	11[206]
Units: kilogram per liter (kg/L)				
geometric mean (geometric coefficient of variation)	0.876 (± 3.52)	0.544 (± 8.09)	0.77 (± 4.66)	0.586 (± 35.8)

Notes:

[203] - PPS

[204] - PPS

[205] - PPS

[206] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[207]	5[208]	11[209]	5[210]
Units: kilogram per liter (kg/L)				
geometric mean (geometric coefficient of variation)	0.546 (± 7.49)	0.305 (± 7.53)	0.476 (± 31.5)	0.175 (± 20.7)

Notes:

[207] - PPS

[208] - PPS

[209] - PPS

[210] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[211]	4[212]		
Units: kilogram per liter (kg/L)				
geometric mean (geometric coefficient of variation)	0.418 (± 29.9)	0.329 (± 12)		

Notes:

[211] - PPS

[212] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Independent Pharmacokinetic: Drug Concentration at 24 Hours (C24h) Post-dose of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Drug Concentration at 24 Hours (C24h) Post-dose of Rivaroxaban in Plasma[213]

End point description:

Geometric and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[213] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[214]	5[215]	4[216]	11[217]
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	9.55 (± 30)	11.9 (± 77)	3.43 (± 127)	4.18 (± 64)

Notes:

[214] - PPS

[215] - PPS

[216] - PPS

[217] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[218]	5[219]		
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	12.5 (± 128)	7.44 (± 123)		

Notes:

[218] - PPS

[219] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Derived Pharmacokinetic: Drug Concentration at 24 Hours (C24h) Post-dose of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Drug Concentration at 24 Hours (C24h) Post-dose of Rivaroxaban in Plasma

End point description:

Geometric and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[220]	5[221]	4[222]	11[223]
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	7.94 (± 35.4)	9.46 (± 55.6)	3.18 (± 73.9)	3.35 (± 57.6)

Notes:

[220] - PPS

[221] - PPS

[222] - PPS

[223] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[224]	5[225]	11[226]	5[227]
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	8.46 (± 98.5)	7.18 (± 96.1)	3.27 (± 65)	5.71 (± 129)

Notes:

[224] - PPS

[225] - PPS

[226] - PPS

[227] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[228]	4[229]		
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	1.94 (± 33.5)	2.39 (± 39.9)		

Notes:

[228] - PPS

[229] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Independent Pharmacokinetic: Time to Reach Maximum Drug Concentration (tmax) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Time to Reach Maximum Drug Concentration (tmax) of Rivaroxaban in Plasma[230]

End point description:

Time to reach maximum drug concentration in the measured matrix, directly taken from analytical data. Median and range were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[230] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[231]	5[232]	4[233]	11[234]
Units: hour				
median (full range (min-max))	2.45 (0.933 to 3.37)	4.05 (0.583 to 4.73)	2.93 (2 to 8.27)	2.17 (1.02 to 8.25)

Notes:

[231] - PPS

[232] - PPS

[233] - PPS

[234] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[235]	5[236]		
Units: hour				
median (full range (min-max))	1.74 (1 to 2.5)	4.62 (3.12 to 8)		

Notes:

[235] - PPS

[236] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Derived Pharmacokinetic: Time to Reach Maximum Drug Concentration (tmax) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Time to Reach Maximum Drug Concentration (tmax) of Rivaroxaban in Plasma

End point description:

Time to reach maximum drug concentration in the measured matrix, directly taken from analytical data. Median and range were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[237]	5[238]	4[239]	11[240]
Units: hour				
median (full range (min-max))	2.57 (2.5 to 3)	2.53 (2.47 to 2.93)	2.22 (1.73 to 2.7)	2.2 (1.67 to 4.23)

Notes:

[237] - PPS

[238] - PPS

[239] - PPS

[240] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[241]	5[242]	11[243]	5[244]
Units: hour				
median (full range (min-max))	2.32 (1.87 to 2.67)	4 (3.2 to 5.13)	2.37 (1.33 to 4.67)	3.63 (1.73 to 6.2)

Notes:

[241] - PPS

[242] - PPS

[243] - PPS

[244] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[245]	4[246]		
Units: hour				
median (full range (min-max))	1.43 (1.23 to 2.33)	1.45 (1.17 to 1.6)		

Notes:

[245] - PPS

[246] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Independent Pharmacokinetic: Half Life Associated With the Terminal Slope (t1/2) of Rivaroxaban in Plasma

End point title	Model Independent Pharmacokinetic: Half Life Associated With the Terminal Slope (t1/2) of Rivaroxaban in Plasma[247]

End point description:

Half-life associated with the terminal slope. Geometric mean and percentage geometric coefficient of variation(%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

Notes:

[247] - 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: Descriptive statistics were reported only for the reporting groups specific to this endpoint.

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[248]	5[249]	4[250]	11[251]
Units: hour				
geometric mean (geometric coefficient of variation)	5.24 (± 15.7)	5.22 (± 41.1)	3.96 (± 24)	4.44 (± 16.5)

Notes:

[248] - PPS

[249] - PPS

[250] - PPS

[251] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[252]	5[253]		
Units: hour				
geometric mean (geometric coefficient of variation)	5.68 (± 39.6)	5.04 (± 30.6)		

Notes:

[252] - PPS

[253] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Model Derived Pharmacokinetic: Half Life Associated With the Terminal Slope (t1/2) of Rivaroxaban in Plasma

End point title	Model Derived Pharmacokinetic: Half Life Associated With the Terminal Slope (t1/2) of Rivaroxaban in Plasma

End point description:

Half-life associated with the terminal slope. Geometric mean and percentage geometric coefficient of variation(%CV) were reported.

End point type	Secondary

End point timeframe:

0 h (pre-dose) to 24 h post-dose

End point values	Age 12-18 Years: Tablet-Low Dose	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[254]	5[255]	4[256]	11[257]
Units: hour				
geometric mean (geometric coefficient of variation)	12.1 (± 3.09)	12.2 (± 4.39)	12 (± 4.54)	12.2 (± 3.93)

Notes:

[254] - PPS

[255] - PPS

[256] - PPS

[257] - PPS

End point values	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[258]	5[259]	11[260]	5[261]
Units: hour				
geometric mean (geometric coefficient of variation)	12.9 (± 4.67)	12.3 (± 6.41)	12.9 (± 6.32)	12.6 (± 7.31)

Notes:

[258] - PPS

[259] - PPS

[260] - PPS

[261] - PPS

End point values	Age 6 months-2 years: Suspension-Low Dose	Age 6 months-2 years: Suspension-High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[262]	4[263]		
Units: hour				
geometric mean (geometric coefficient of variation)	12.7 (± 3.66)	12.7 (± 3.08)		

Notes:

[262] - PPS

[263] - PPS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of study treatment up to 11 days

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Age 12-18 Years: Tablet-Low Dose

Reporting group description:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxabantablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

Reporting group title	Age 6-12 Years: Tablet-Low Dose

Reporting group description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 7.5 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a low dose of 10 mg.

Reporting group title	Age 6-12 Years: Suspension-Low Dose

Reporting group description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 2.5 to 5 mg.

Reporting group title	Age 12-18 Years: Tablet-High Dose

Reporting group description:

Subjects aged from 12 to 18 years were administered with a single oral dose of rivaroxaban tablet under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

Reporting group title	Age 6-12 Years: Tablet-High Dose

Reporting group description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban tabletunder fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 15 mg, and subjects with a body weight (comparable to adults) of 50 to 100 kg received a high dose of 20 mg.

Reporting group title	Age 6-12 Years: Suspension-High Dose

Reporting group description:

Subjects aged from 6 to 12 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 14 to 50 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 5 to 10 mg.

Reporting group title	Age 2-6 Years: Suspension-Low Dose

Reporting group description:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxabansuspension under fed conditions, and the dosage was adjusted based on the individual ageand body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Reporting group title	Age 2-6 Years: Suspension-High Dose

Reporting group description:

Subjects aged from 2 to 6 years were administered with a single oral dose of rivaroxabansuspension under fed conditions, and the dosage was adjusted based on the individual age andbody weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Reporting group title	Age 6 months-2 years: Suspension-Low Dose

Reporting group description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received low dose of rivaroxaban (equivalent to 10 mg in adults) ranging from 0.4 to 2.5 mg.

Reporting group title	Age 6 months-2 years: Suspension-High Dose

Reporting group description:

Subjects aged from 6 months to 2 years were administered with a single oral dose of rivaroxaban suspension under fed conditions, and the dosage was adjusted based on the individual age and body weight. Subjects with a body weight of 2 to 14 kg received high dose of rivaroxaban (equivalent to 20 mg in adults) ranging from 0.8 to 5.0 mg.

Serious adverse events	Age 12-18 Years: Tablet-Low Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (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			
Pelvic venous thrombosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (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	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose	Age 6 months-2 years: Suspension-Low Dose

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (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	Age 6 months-2 years: Suspension-High Dose		
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		
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Age 12-18 Years: Tablet-Low Dose	Age 6-12 Years: Tablet-Low Dose	Age 6-12 Years: Suspension-Low Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	4 / 11 (36.36%)
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Contusion			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Catheter site bruise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vessel puncture site bruise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

Upper respiratory tract inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	6

Non-serious adverse events	Age 12-18 Years: Tablet-High Dose	Age 6-12 Years: Tablet-High Dose	Age 6-12 Years: Suspension-High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	3 / 4 (75.00%)	0 / 5 (0.00%)
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Catheter site bruise			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Dermatitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dermatitis diaper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Age 2-6 Years: Suspension-Low Dose	Age 2-6 Years: Suspension-High Dose	Age 6 months-2 years: Suspension-Low Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	2 / 6 (33.33%)
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Catheter site bruise			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			

subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Vessel puncture site pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Age 6 months-2 years: Suspension-High Dose		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter site bruise			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vessel puncture site bruise			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vessel puncture site pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Gastritis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Skin and subcutaneous tissue disorders			
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Dermatitis diaper subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2011	A taste and texture questionnaire was introduced to assess the children's acceptance of the oral suspension in the early development phase. Clarification of exclusion criterion "history of severe allergies, severe nonallergic drug reactions, or multiple drug allergies" where severe was also added to non-allergic drug reactions. Re-screening of the children was introduced when a repeated local lab clotting test was within the normal range. Clarification of approximate total blood volume ranges were given. Single repetition of local laboratory clotting tests before administration of study drug was done. Administrative changes were done.
19 June 2013	Updates on approved indications of rivaroxaban's were given. Total number of children included were corrected. Study duration was extended due to slow enrolment. Changes to the exclusion criteria were made. Spiking experiments results to reliably predict rivaroxaban oral doses for children resulting in similar drug exposure as in adults were updated. Changes with regard to local safety lab at Visit 1, 2 and 3 were described. Changes with regard to AE reporting of adverse events (AEs) occurring between Visit 1 and Visit 2 which were not reported as AEs but recorded as medical history were made. Changes in the section on expected adverse events with reference to the most current version of the Investigators Brochure (IB) and the Company Core Data Sheet (CCDS) attached to the IB were made. Measurement of anti-Factor Xa as local lab clotting test was removed. PK sampling time windows were extended. Introduction of a new integrated flow chart compiling the information related to all age groups, from 6 months to <18 years and laboratory examinations was made. Sponsor's medical expert and medically responsible person were changed.

Notes:

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.

Baseline adjusted Emax and Etrough of anti-Xa could not be included in basic results format as the results were presented graphically. 99999=Data not calculated, Occurrence of "±" in relation with geometric CV is auto-generated and cannot be deleted.

Notes: