



Clinical trial results: Superficial vein thrombosis (SVT) treated for forty-five days with Rivaroxaban versus Fondaparinux Summary

EudraCT number	2011-005158-73
Trial protocol	DE
Global end of trial date	31 July 2016

Results information

Result version number	v1 (current)
This version publication date	06 June 2022
First version publication date	06 June 2022

Trial information

Trial identification

Sponsor protocol code	SURPRISE-2011
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01499953
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GWT-TUD GmbH
Sponsor organisation address	Freiberger Str. 33, Dresden, Germany, 01067
Public contact	Medical Consulting, GWT-TUD GmbH, 0049 35125933100,
Scientific contact	Medical Consulting, GWT-TUD GmbH, 0049 35125933190,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2016
Global end of trial reached?	Yes
Global end of trial date	31 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of efficacy and safety of 45 days of rivaroxaban 10 mg vs. fondaparinux 2.5 mg in the treatment of superficial vein thrombosis of risk patients for major VTE complications to prove non-inferiority of oral rivaroxaban treatment

Protection of trial subjects:

The conduct of this study was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also be carried out in keeping with applicable local law(s) and regulation(s). No specific measures had to be put in place as both substances (Rivaroxaban and Fondaparinux) have a wide therapeutic window. Therefore, in case of asymptomatic overdosing without overt bleeding complications, no specific treatment actions were required and the patient should have been kept under surveillance. For rivaroxaban, gastrointestinal uptake might have been reduced by activated carbon application within 3 hours after intake of rivaroxaban. In case of bleeding complications, study treatment with rivaroxaban and fondaparinux should have been interrupted or discontinued and symptomatic therapy (mechanical compression, surgical intervention, hemodynamic stabilization with fluids or whole-blood transfusions) should have been initiated as indicated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2012
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	Germany: 472
Worldwide total number of subjects	472
EEA total number of subjects	472

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	282
From 65 to 84 years	168
85 years and over	22

Subject disposition

Recruitment

Recruitment details:

From 25/04/2012 until 18/02/2016, a total of 485 patients were screened at 23 study sites in Germany. Of them, 9 patients did not meet the eligibility criteria. For another 4 subjects, signatures either on informed consent form or data protection waiver were not provided and therefore, these 4 subjects were not included in the study.

Pre-assignment

Screening details:

472 patients were randomized to one of the two treatment groups. One patient withdrew consent after randomization but before the first study drug administration. 448 subjects completed the study (222 rivaroxaban and 226 fondaparinux).

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Rivaroxaban

Arm description: -

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

Dosage and administration details:

Patients taken rivaroxaban 10 mg once daily for 45 (± 5) days at the same time.

Arm title	Fondaparinux
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Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Fondaparinux
Investigational medicinal product code	
Other name	Arixtra®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients taken fondaparinux 2.5 mg once daily for 45 (± 5) days at the same time.

Number of subjects in period 1	Rivaroxaban	Fondaparinux
Started	236	236
Completed	222	226
Not completed	14	10
Consent withdrawn by subject	3	1
Adverse event, non-fatal	7	6
Lost to follow-up	3	1
not specified	1	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	Rivaroxaban
Reporting group description: -	
Reporting group title	Fondaparinux
Reporting group description: -	

Primary: Rate of objectively confirmed VTE (venous thromboembolism) complications

End point title	Rate of objectively confirmed VTE (venous thromboembolism) complications
End point description:	The primary efficacy outcome was the composite of death from any cause, symptomatic pulmonary embolism (PE), symptomatic deep vein thrombosis (DVT), or symptomatic extension towards the saphenofemoral junction, or symptomatic recurrence of superficial vein thrombosis (SVT) up to day 45.
End point type	Primary
End point timeframe:	day 45

End point values	Rivaroxaban	Fondaparinux		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	224		
Units: Number of patients				
number (confidence interval 95%)	3.32 (1.62 to 6.69)	1.79 (0.70 to 4.50)		

Statistical analyses

Statistical analysis title	Full Analysis
Comparison groups	Rivaroxaban v Fondaparinux
Number of subjects included in analysis	435
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0252
Method	Regression, Cox

Adverse events

Adverse events information

Timeframe for reporting adverse events:

day 0 (randomization) until day 90 (follow up)

Adverse event reporting additional description:

Patients were asked at each visit whether they have experienced adverse events (AEs) or serious adverse events (SAEs). AEs were documented from the time of first IMP application until 5 days after the last application of study treatment. AEs and SAEs were listed by primary SOC (System Organ Class).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	Overall
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Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 471 (4.03%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
subjects affected / exposed	2 / 471 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Vascular disorders			
subjects affected / exposed	4 / 471 (0.85%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	3 / 471 (0.64%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			

Surgical and medical procedures subjects affected / exposed	2 / 471 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders Nervous system disorders subjects affected / exposed	2 / 471 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders Immune system disorders subjects affected / exposed	1 / 471 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders Eye disorders subjects affected / exposed	1 / 471 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders Respiratory, thoracic and mediastinal disorders subjects affected / exposed	1 / 471 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed	1 / 471 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders Psychiatric disorders subjects affected / exposed	2 / 471 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	1 / 471 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations			
subjects affected / exposed	1 / 471 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	178 / 471 (37.79%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
subjects affected / exposed	5 / 471 (1.06%)		
occurrences (all)	5		
Vascular disorders			
Vascular disorders			
subjects affected / exposed	43 / 471 (9.13%)		
occurrences (all)	45		
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	7 / 471 (1.49%)		
occurrences (all)	7		
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	44 / 471 (9.34%)		
occurrences (all)	48		
Immune system disorders			

Immune system disorders subjects affected / exposed occurrences (all)	3 / 471 (0.64%) 3		
Reproductive system and breast disorders Reproductive system and breast disorders subjects affected / exposed occurrences (all)	7 / 471 (1.49%) 8		
Respiratory, thoracic and mediastinal disorders Respiratory, thoracic and mediastinal disorders subjects affected / exposed occurrences (all)	11 / 471 (2.34%) 12		
Psychiatric disorders Psychiatric disorders subjects affected / exposed occurrences (all)	5 / 471 (1.06%) 5		
Investigations Investigations subjects affected / exposed occurrences (all)	8 / 471 (1.70%) 10		
Injury, poisoning and procedural complications Injury, poisoning and procedural complications subjects affected / exposed occurrences (all)	8 / 471 (1.70%) 8		
Cardiac disorders Cardiac disorders subjects affected / exposed occurrences (all)	13 / 471 (2.76%) 14		
Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all)	17 / 471 (3.61%) 20		
Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	1 / 471 (0.21%) 1		

Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all)	1 / 471 (0.21%) 1		
Eye disorders Eye disorders subjects affected / exposed occurrences (all)	4 / 471 (0.85%) 4		
Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all)	35 / 471 (7.43%) 41		
Hepatobiliary disorders Hepatobiliary disorders subjects affected / exposed occurrences (all)	3 / 471 (0.64%) 3		
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	14 / 471 (2.97%) 14		
Renal and urinary disorders Renal and urinary disorders subjects affected / exposed occurrences (all)	3 / 471 (0.64%) 5		
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	33 / 471 (7.01%) 39		
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	28 / 471 (5.94%) 32		
Metabolism and nutrition disorders Metabolism and nutritional disorders subjects affected / exposed occurrences (all)	3 / 471 (0.64%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 March 2012	Protocol 2.6 dated 10 Feb 2012: Change in labelling of the primary and secondary packaging; addition of composition of the DSMB

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported