Protocol Registration Receipt
09/20/2012

Evaluation of Fondaparinux in Patients With a Heart Rhythm Disturbance Who Undergo Restoration of Normal Heart Rhythm

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00911300

Purpose

The purpose of this study is to test whether Fondaparinux is effective and safe to prevent thromboembolic events (like for example strokes) and bleeding events in patients who undergo a normalisation of their heart rhythm disturbance. Fondaparinux will be compared with Heparin and tablets containing Vitamin-K-Antagonists (Phenprocoumon, Fluindione, or Warfarin).

Condition	Intervention	Phase
Fibrillation, Atrial	Drug: fondaparinux	Phase 2

Condition	Intervention	Phase
	Drug: unfractionated heparin Drug: Vitamin-K-Antagonist	

Study Type: Interventional

Study Design: Prevention, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study

Official Title: An International, Multicentre, Randomised, Open, Controlled, Two-parallel Group, Phase II Pilot Study to Evaluate the Efficacy and Safety of ARIXTRA™ for Anticoagulation of Patients With Atrial Fibrillation Undergoing Electric Cardioversion Following Transesophageal Echocardiography

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Number of Participants With at Least One Event of Cerebral Neurologic Event, Systemic Thromboembolism, Death From Any Cause, and/or Major Bleeding Until the End of Treatment (EOT) Plus 4 Days [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants] [Designated as safety issue: No]

  Cerebral neurologic events are defined as any new neurologic disorders caused by cerebrovascular embolization, e.g., Transient Ischemic Attack (TIA), cerebral infarction. The cerebrovascular origin of the event has to be confirmed by objective procedures. Systemic thromboembolism comprises any arterial thromboembolic event (e.g., peripheral vascular embolism, mesenteric infarct, or myocardial infarction). All cerebral neurologic events were adjudicated by a Central Adjudication Committee (CAC), members of which were unaware of the participants' treatment assignment.

Secondary Outcome Measures:

- Number of Thrombus-negative and Thrombus-positive Participants (Par.) With at Least One Cerebral Neurologic Event [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)] [Designated as safety issue: No]

  Cerebral neurologic events are defined as any new neurologic disorders caused by cerebrovascular embolisation, e.g., TIA, cerebral infarction. All cerebral neurologic events were adjudicated by a CAC, members of which were unaware of the participants' treatment assignment.The cerebrovascular origin of the event was confirmed by objective procedures. A thrombus or blood clot is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets that form a platelet plug, and the activation of the humoral coagulation system (i.e., clotting factors).
- Number of Thrombus-negative and Thrombus-positive Participants With at Least One Systemic Thromboembolism [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)] [Designated as safety issue: No]

  Systemic thromboembolism comprises any arterial thromboembolic event (e.g., peripheral vascular embolism, mesenteric infarct, or myocardial infarction). All systemic thromboembolic events were adjudicated by a CAC, the members of which were unaware of the participants' treatment assignment. A thrombus or blood clot is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets that form a platelet plug, and the activation of the humoral coagulation system (i.e., clotting factors).

- Number of Thrombus-negative and Thrombus-positive Participants Who Died From Any Cause [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)] [Designated as safety issue: No]

  The cause of death was classified as due to a thromboembolic event (like cerebral infarction), bleeding, or other established diagnosis, or as unexplained. All deaths were adjudicated by an independent CAC, the members of which were unaware of the participants' treatment assignment. A thrombus or blood clot is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets that form a platelet plug, and the activation of the humoral coagulation system (i.e., clotting factors).
- Number of Thrombus-negative and Thrombus-positive Participants With at Least One Major Bleeding Event [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)] [Designated as safety issue: No]

  Major bleeding: fatal, and/or symptomatic in a critical area/ organ, causes a fall in hemoglobin of >=3 grams/deciliter compared with the pre-randomization level, or leads to the transfusion of >=2 units of whole blood/red blood cells. All bleeding events were adjudicated by a CAC, the members of which were unaware of the participants' treatment assignment. A thrombus/ blood clot is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets, and the activation of the humoral coagulation system (i.e., clotting factors).
- Number of Thrombus-negative and Thrombus-positive Participants With at Least One Minor Bleeding Event [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)] [Designated as safety issue: No]

  Minor bleeding is defined as clinically overt bleeding events that do not meet the criteria for major or clinically relevant non-major bleeding. All episodes of bleeding were adjudicated by an independent CAC, the members of which were unaware of the participants' treatment assignment.
- Number of Participants With Primary Successful Electrical Cardioversion (CV) in Sinus Rhythm [Time Frame: Day 1 until Day 3] [Designated as safety issue: No]

  CV may be performed electively to restore sinus rhythm in patients with persistent AF. The primary successful electric CV was assessed by a 12- lead electrocardiogram (ECG) directly after the CV. Results of the last cardioversion were used in cases for which more than one CV was performed.
- Number of Participants With a Thrombus in the Left Atrium (LA) or in the Left Atrial Appendage (LAA) at the Time of the Second TEE [Time Frame: At second TEE (at Day 28+/-4)] [Designated as safety issue: No]

  Atrial fibrillation (AF) causes stagnant blood in the LA or LAA and can lead to a thromboembolism. Stasis in the LAA represents the principal mechanism of thrombus formation in AF.
- Number of Thrombus-negative and Thrombus-positive Participants With Conversion to Sinus Rhythm [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Day 64 until the follow-up visit (FU) (Day 90+/-7)] [Designated as safety issue: No]

  Sinus rhythm is the normal beating of the heart, as measured by an ECG. Normal sinus rhythm not only indicates that the rhythm is normally generated by the sinus node and is traveling in a normal fashion in the heart, but it also indicates that the heart rate (the rate at which the sinus node is generating impulses) is within normal limits.
- Number of Participants Who Were Re-hospitalized [Time Frame: Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)]

[Designated as safety issue: No]

Hospitalization signifies that the participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or out-patient setting. Re-hospitalization refers to an event of hospitalization after discharge for the initial hospitilization for the cardioversion.

Enrollment: 349
Study Start Date: August 2009
Study Completion Date: September 2011
Primary Completion Date: September 2011

Arms	Assigned Interventions
Active Comparator: Arm 1: fondaparinux	Drug: fondaparinux Comparison of different drugs
Active Comparator: Arm 2: unfractionated heparin + Vitamin-K-Antagonist	Drug: unfractionated heparin Comparison of different drugs Drug: Vitamin-K-Antagonist Comparison of different drugs

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both

Inclusion Criteria:

- Male or female patients aged at least 18 years with atrial fibrillation (AF) meeting at least one of the following criteria (a, b, c): a. Acute clinical symptoms (like palpitations, chest pain, dyspnea, fatigue, lightheadedness, or syncope) for at least 48 hours and AF on baseline ECG b. Newly discovered AF persisting for >=7 days c. Recurrent AF persisting for >=7 days

Exclusion Criteria:

- No documented sinus rhythm on ECG for more than 1 year
- Acute neurological deficits (TIA, stroke, intracranial bleeding), or known disease which may cause neurological deficits (e.g., multiple sclerosis, seizure

disorder)

- Treatment with antithrombotic agents, including low-dose anticoagulation, for more than 48 hours prior to randomisation
- Treatment with oral NSAIDs or ASA at doses greater than 325 mg per day for more than 72 hours prior to randomisation
- Anticoagulant therapy required or likely to be required during the study period
- Treatment with ASA at a dose greater than 325 mg per day or oral NSAIDs (at any dose) required or likely to be required during the study period
- Treatment with two or more antiplatelet agents (e.g. clopidogrel and ASA) at any dose at the same time (i.e., within 24 hours)
- Known hypersensitivity to UFH, VKA, or Fondaparinux or one of these drugs' excipients
- Active, clinically significant bleeding or clinically significant bleeding within the past month
- Major surgery within the previous three months
- Uncontrolled arterial hypertension (persistent systolic blood pressure over 180 mm Hg or diastolic blood pressure over 110 mm Hg)
- Bacterial endocarditis
- Calculated creatinine clearance < 30 mL/min
- Body weight < 50 kg
- Planned surgery or intervention within the next 65 days

Contacts and Locations

Locations

France

GSK Investigational Site
Albi, France, 81000

GSK Investigational Site
Antony cedex, France, 92166

GSK Investigational Site
Brest Cedex, France, 29609

GSK Investigational Site
Créteil, France, 94000

GSK Investigational Site
Evecquemont, France, 78740

GSK Investigational Site
Montpellier Cedex 5, France, 34295

GSK Investigational Site
Paris cedex 12, France, 75571

GSK Investigational Site

Paris cedex 13, France, 75651

GSK Investigational Site

Pau, France, 64046

GSK Investigational Site

Pessac cedex, France, 33604

GSK Investigational Site

Poitiers cedex, France, 86021

GSK Investigational Site

Rennes Cedex 9, France, 35033

GSK Investigational Site

Toulouse Cedex 09, France, 31059

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Toulouse cedex 3, France, 31076

Germany

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Freiburg, Baden-Wuerttemberg, Germany, 79106

GSK Investigational Site

Aschaffenburg, Bayern, Germany, 63739

GSK Investigational Site

Bad Toelz, Bayern, Germany, 83646

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Simbach a. Inn, Bayern, Germany, 84359

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Berlin, Berlin, Germany, 10405

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Berlin, Berlin, Germany, 13353

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Berlin, Berlin, Germany, 10249

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Potsdam, Brandenburg, Germany, 14467

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Frankfurt, Hessen, Germany, 60488

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Bonn, Nordrhein-Westfalen, Germany, 53127
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Bonn, Nordrhein-Westfalen, Germany, 53115
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Duisburg-Huckingen, Nordrhein-Westfalen, Germany, 47259
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Unna, Nordrhein-Westfalen, Germany, 59423
GSK Investigational Site
Wesel, Nordrhein-Westfalen, Germany, 46483
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Pirna, Sachsen, Germany, 01796
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Magdeburg, Sachsen-Anhalt, Germany, 39120

Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Responsible Party:	GlaxoSmithKline
Study ID Numbers:	111418
Health Authority:	Germany: Bundesinstitut für Arzneimittel und Medizinprodukte France: Agence Française de Sécurité Sanitaire des Produits de Santé

Study Results

Participant Flow

Pre-Assignment Details

Participants (par.) were required to undergo transesophageal echocardiography (TEE) to guide cardioversion (CV). TEEs were recorded and archived to allow for later central adjudication and possible evaluation of details. At randomization (Day 1, immediately after TEE), par. were stratified to thrombus (clot)-positive and thrombus (clot)-negative.

Reporting Groups

	Description
Fondaparinux	For clot-negative (CN) participants (par.), 7.5 milligrams (mg) fondaparinux was injected once daily (OD) subcutaneously (for par. with body weight [BW] 50-100 kilograms [kg]); for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For clot-positive (CP) par. with creatinine clearance (CrCl) >= 50 milliliters (mL)/minute (min), 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
Unfractioned Heparin (UFH)/Vitamin K Antagonist (VKA)	Both CN and CP participants received an initial intravenous (i.v.) bolus injection of 70 international units (IU)/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/hour (h) (at least 1250 IU per hour). The infusion dose was adjusted to maintain an activated partial thromboplastin time (aPTT) at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target

	Description
	international normalized ratio (INR) of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Overall Study

	Fondaparinux	Unfractioned Heparin (UFH)/Vitamin K Antagonist (VKA)
Started	175	174
Completed	140	131
Not Completed	35	43
Primary Endpoint Component Occurred	1	2
Death	1	0
Thrombus Persistant in Second TEE	3	7
Adverse Event	14	6
Protocol Violation	3	2
Consent Withdrawn	4	12
Coronary Angiography Performed	1	0
Atrial Fibrillation (AF)	3	3

	Fondaparinux	Unfractioned Heparin (UFH)/Vitamin K Antagonist (VKA)
Recurrence		
Received Commercial Treatment	1	0
Recurrent Tachyarrhythmia	1	1
Recurrent Tachy-Arrhythmia Absoluta	1	1
Nurse Unavailable in Participant's City	1	0
CV Unsuccessful; Phenprocoumon Received	1	0
Participant Could Not Stay in Hospital	0	1
Investigator's Decision; New AF Episode	0	1
International Normalized Ratio Too High	0	1
Participant Refused Hospital Consulation	0	1
Underlying Disease (Myocarditis)	0	1
Physician Decision	0	1
Treatment Stopped by	0	1

	Fondaparinux	Unfractioned Heparin (UFH)/Vitamin K Antagonist (VKA)
Mistake		
Randomized; No Study Medication Received	0	2

Baseline Characteristics

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h.

	Description
	In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Baseline Measures

	Fondaparinux	UFH/VKA	Total
Number of Participants	174	170	344
Age, Continuous [1] [units: Years] Mean (Standard Deviation)	68.24 (11.09)	66.78 (11.93)	67.52 (11.52)
Gender, Male/Female [2] [units: Participants]			
Female	69	60	129
Male	105	110	215

[1] Baseline characteristic data were collected in members of the Modified Intent-to-Treat (mITT) Population, comprised of all randomized participants receiving at least one dose of study medication and for whom any post-baseline value was available.

[2] Baseline characteristic data were collected in members of the Modified Intent-to-Treat (mITT) Population, comprised of all randomized participants receiving at least one dose of study medication and for whom any post-baseline value was available.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With at Least One Event of Cerebral Neurologic Event, Systemic Thromboembolism, Death From Any Cause, and/or Major Bleeding Until the End of Treatment (EOT) Plus 4 Days
Measure Description	Cerebral neurologic events are defined as any new neurologic disorders caused by cerebrovascular embolization, e.g., Transient Ischemic Attack (TIA), cerebral infarction. The cerebrovascular origin of the event has to be confirmed by objective procedures. Systemic thromboembolism comprises any arterial thromboembolic event (e.g., peripheral vascular embolism, mesenteric infarct, or myocardial infarction). All cerebral neurologic events were adjudicated by a Central Adjudication Committee (CAC), members of which were unaware of the participants' treatment assignment.
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants
Safety Issue?	No

Analysis Population Description

Modified Intent-to-Treat (mITT) Population: all randomized participants receiving at least one dose of study medication and for whom any post-baseline value was available

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP

	Description
	par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Participants With at Least One Event of Cerebral Neurologic Event, Systemic Thromboembolism, Death From Any Cause, and/or Major Bleeding Until the End of Treatment (EOT) Plus 4 Days [units: participants]	3	2

Statistical Analysis 1 for Number of Participants With at Least One Event of Cerebral Neurologic Event, Systemic

Thromboembolism, Death From Any Cause, and/or Major Bleeding Until the End of Treatment (EOT) Plus 4 Days

Groups	Fondaparinux, UFH/VKA
Method	Fisher Exact
P-Value	1.000
Other Estimated Parameter [Percentage of participants]	0.5
95% Confidence Interval	-2.0 to 3.1

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

The estimated value is the absolute percent difference between Fondaparinux and UFH/VKA.

2. Secondary Outcome Measure:

Measure Title	Number of Thrombus-negative and Thrombus-positive Participants (Par.) With at Least One Cerebral Neurologic Event
Measure Description	Cerebral neurologic events are defined as any new neurologic disorders caused by cerebrovascular embolisation, e.g., TIA, cerebral infarction. All cerebral neurologic events were adjudicated by a CAC, members of which were unaware of the participants' treatment assignment.The cerebrovascular origin of the event was confirmed by objective procedures. A thrombus or blood clot is the final product of

	the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets that form a platelet plug, and the activation of the humoral coagulation system (i.e., clotting factors).
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to

	Description
	2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Thrombus-negative and Thrombus-positive Participants (Par.) With at Least One Cerebral Neurologic Event [units: participants]		
Thrombus-negative par. until 4 days after EOT	0	1
Thrombus-positive par. until 4 days after EOT	0	0
Thrombus-negative participants until the FU	1	1
Thrombus-positive participants until the FU	0	0

3. Secondary Outcome Measure:

Measure Title	Number of Thrombus-negative and Thrombus-positive

	Participants With at Least One Systemic Thromboembolism
Measure Description	Systemic thromboembolism comprises any arterial thromboembolic event (e.g., peripheral vascular embolism, mesenteric infarct, or myocardial infarction). All systemic thromboembolic events were adjudicated by a CAC, the members of which were unaware of the participants' treatment assignment. A thrombus or blood clot is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets that form a platelet plug, and the activation of the humoral coagulation system (i.e., clotting factors).
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the

	Description
	second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Thrombus-negative and Thrombus-positive Participants With at Least One Systemic Thromboembolism [units: participants]		
Thrombus-negative par. until 4 days after EOT	0	0
Thrombus-positive par. until 4 days after EOT	0	0
Thrombus-negative participants until the FU	0	0

	Fondaparinux	UFH/VKA
Thrombus-positive participants until the FU	0	0

4. Secondary Outcome Measure:

Measure Title	Number of Thrombus-negative and Thrombus-positive Participants Who Died From Any Cause
Measure Description	The cause of death was classified as due to a thromboembolic event (like cerebral infarction), bleeding, or other established diagnosis, or as unexplained. All deaths were adjudicated by an independent CAC, the members of which were unaware of the participants' treatment assignment. A thrombus or blood clot is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets that form a platelet plug, and the activation of the humoral coagulation system (i.e., clotting factors).
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10

	Description
	days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Thrombus-negative and Thrombus-positive Participants Who Died From Any Cause [units: participants]		

	Fondaparinux	UFH/VKA
Thrombus-negative par. until 4 days after EOT	1	0
Thrombus-positive par. until 4 days after EOT	0	0
Thrombus-negative participants until the FU	3	0
Thrombus-positive participants until the FU	0	0

5. Secondary Outcome Measure:

Measure Title	Number of Thrombus-negative and Thrombus-positive Participants With at Least One Major Bleeding Event
Measure Description	Major bleeding: fatal, and/or symptomatic in a critical area/ organ, causes a fall in hemoglobin of >=3 grams/deciliter compared with the pre-randomization level, or leads to the transfusion of >=2 units of whole blood/red blood cells. All bleeding events were adjudicated by a CAC, the members of which were unaware of the participants' treatment assignment. A thrombus/ blood clot is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets, and the activation of the humoral coagulation system (i.e., clotting factors).
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Thrombus-negative and Thrombus-positive Participants With at Least One Major Bleeding Event [units: participants]		
Thrombus-negative par. until 4 days after EOT	3	1
Thrombus-positive par. until 4 days after EOT	0	0
Thrombus-negative participants until the FU	4	1
Thrombus-positive participants until the FU	0	0

6. Secondary Outcome Measure:

Measure Title	Number of Thrombus-negative and Thrombus-positive Participants With at Least One Minor Bleeding Event
Measure Description	Minor bleeding is defined as clinically overt bleeding events that do not meet the criteria for major or clinically relevant non-major bleeding. All episodes of bleeding were adjudicated by an independent CAC, the members of which were unaware of the participants' treatment assignment.
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)

Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Thrombus-negative and Thrombus-positive Participants With at Least One Minor Bleeding Event [units: participants]		
Thrombus-negative par. until 4 days after EOT	3	4
Thrombus-positive par. until 4 days after EOT	0	0
Thrombus-negative participants until the FU	3	5
Thrombus-positive participants until the FU	1	0

7. Secondary Outcome Measure:

Measure Title	Number of Participants With Primary Successful Electrical Cardioversion (CV) in Sinus Rhythm
Measure Description	CV may be performed electively to restore sinus rhythm in patients with persistent AF. The primary successful electric CV was assessed by a 12- lead electrocardiogram (ECG) directly after the CV. Results of the last cardioversion were used in cases for which more than one CV was performed.
Time Frame	Day 1 until Day 3
Safety Issue?	No

Analysis Population Description

mITT Population. Only participants with data for primary successful electric cardioversion at the indicated timepoint were analyzed.

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	151	148
Number of Participants With Primary Successful Electrical Cardioversion (CV) in Sinus Rhythm [units: participants]	137	133

8. Secondary Outcome Measure:

Measure Title	Number of Participants With a Thrombus in the Left Atrium (LA) or in the Left Atrial Appendage (LAA) at the Time of the Second TEE
Measure Description	Atrial fibrillation (AF) causes stagnant blood in the LA or LAA and can lead to a thromboembolism. Stasis in the LAA represents the principal mechanism of thrombus formation in AF.
Time Frame	At second TEE (at Day 28+/-4)
Safety Issue?	No

Analysis Population Description

mITT Population. Only clot-positive participants at the time of the first TEE were analyzed.

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par.

	Description
	with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	14	14
Number of Participants With a Thrombus in the Left Atrium (LA) or in the Left Atrial Appendage (LAA) at the Time of the Second TEE [units: participants]	3	7

9. Secondary Outcome Measure:

Measure Title	Number of Thrombus-negative and Thrombus-positive Participants With Conversion to Sinus Rhythm
Measure Description	Sinus rhythm is the normal beating of the heart, as measured by an ECG. Normal sinus rhythm not only indicates that the rhythm is normally generated by the sinus node and is traveling in a normal fashion in the heart, but it also indicates that the heart rate (the rate at which the sinus node is generating impulses) is within normal limits.
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Day 64 until the follow-up visit (FU) (Day 90+/-7)
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total

	Description
	treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Thrombus-negative and Thrombus-positive Participants With Conversion to Sinus Rhythm [units: participants]		
Clot-negative par. until 4 days after EOT	109	115
Clot-positive par. until 4 days after EOT	5	4
Clot-negative participants until the FU	105	106
Clot-positive participants until the FU	4	5

10. Secondary Outcome Measure:

Measure Title	Number of Participants Who Were Re-hospitalized
Measure Description	Hospitalization signifies that the participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or out-patient setting. Re-hospitalization refers to an event of hospitalization after discharge for the initial hospitilization for the cardioversion.
Time Frame	Baseline (Day 1) until Day 64 (4 days after the EOT [i.e., last administration of study drug]) for CP participants; Baseline until Day 36 (4 days after the EOT) for CN participants; and from Baseline until the follow-up visit (FU) (Day 90+/-7)
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).

	Description
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Measured Values

	Fondaparinux	UFH/VKA
Number of Participants Analyzed	174	170
Number of Participants Who Were Re-hospitalized [units: participants]		
until 4 days after EOT	14	7
until the FU	18	11

Reported Adverse Events

Reporting Groups

	Description
Fondaparinux	For CN par., 7.5 mg fondaparinux was injected OD subcutaneously (for par. with BW 50-100 kg; for par. with BW >100 kg, 10 mg fondaparinux

	Description
	was administered using a disposable prefilled syringe for the first 7-10 days after randomization, followed by 3 weeks of 2.5 mg fondaparinux OD (until Day 28+/-4). For CP par. with CrCl >= 50 mL/min, 7.5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 10 mg fondaparinux was administered OD. For CP par. with CrCl 30 to <50 mL/min, 5 mg fondaparinux was injected OD (for par. with BW 50-100 kg); for par. with BW >100 kg, 7.5 mg fondaparinux was injected for 28+/-4 days. If the second TEE showed thrombus disappearance, treatment continued until 7-10 days after the second TEE followed by 3 weeks of 2.5 mg fondaparinux OD (total treatment duration: 56+/-4 days).
UFH/VKA	Both CN and CP participants received an initial i.v. bolus injection of 70 IU/kg (at least 5000 IU) UFH, followed by continuous infusion at an initial rate of 15 IU/kg/h (at least 1250 IU per h). The infusion dose was adjusted to maintain an activated partial thromboplastin aPTT at 1.5 to 2 times the reference control value. Infusion continued for at least 72 h. In parallel to UFH, treatment with VKA was started as soon as possible (preferably on Day 1). The dose of VKA was adjusted to reach a target INR of 2.0-3.0. UFH was continued until INR >2.0. Total treatment duration: 28+/-4 days. For CP participants for whom the second TEE showed thrombus disappearance, VKA was continued during cardioversion and up to a total treatment duration of 56+/-4 days.

Time Frame

Participants were analyzed for the period from randomization up to the last administration of study treatment plus four days (up to Day 56+/-4 days).

Additional Description

Serious adverse events (SAEs) and non-serious AEs were collected in members of the Safety Population, comprised of all participants included in the study, who had any post-baseline value, and who received at least one dose of study medication.

Serious Adverse Events

	Fondaparinux	UFH/VKA
Total # participants affected/at risk	30/174 (17.24%)	26/170 (15.29%)
Cardiac disorders		
Angina pectoris † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Arrhythmia supraventricular † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Atrial fibrillation † [A]		
# participants affected/at risk	12/174 (6.9%)	5/170 (2.94%)
# events		
Atrial flutter † [A]		
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
Atrioventricular block complete † [A]		
# participants affected/at	1/174 (0.57%)	0/170 (0%)

	Fondaparinux	UFH/VKA
risk		
# events		
Cardiac failure † [A]		
# participants affected/at risk	4/174 (2.3%)	3/170 (1.76%)
# events		
Cardiac failure congestive † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Cardiac valve disease † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Coronary artery disease † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Ischemic cardiomyopathy † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		

	Fondaparinux	UFH/VKA
Mitral valve incompetence † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Sinoatrial block † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Tachyarrhythmia † [A]		
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
Gastrointestinal disorders		
Colonic polyp † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Diarrhea † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Erosive esophagitis † [A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Gastrointestinal hemorrhage † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Vomiting † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
General disorders		
Death † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Infections and infestations		
Gastroenteritis † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Staphylococcal sepsis † [A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Injury, poisoning and procedural complications		
Fall †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Metabolism and nutrition disorders		
Hypokalemia †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Musculoskeletal and connective tissue disorders		
Arthralgia †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Neoplasms benign, malignant and		

	Fondaparinux	UFH/VKA
unspecified (incl cysts and polyps)		
Bronchial carcinoma † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Colon cancer † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Neoplasm skin † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Rectal cancer † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Nervous system disorders		
Cerebral infarction † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)

	Fondaparinux	UFH/VKA
# events		
Cerebrovascular accident † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Syncope † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Renal and urinary disorders		
Renal failure acute † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Respiratory, thoracic and mediastinal disorders		
Dyspnea † [A]		
# participants affected/at risk	1/174 (0.57%)	2/170 (1.18%)
# events		
Pulmonary edema † [A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Skin and subcutaneous tissue disorders		
Skin necrosis † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Vascular disorders		
Hematoma † [A]		
# participants affected/at risk	1/174 (0.57%)	2/170 (1.18%)
# events		
Hypertensive crisis † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Fondaparinux	UFH/VKA
Total # participants affected/at	68/174	70/170

	Fondaparinux	UFH/VKA
risk	(39.08%)	(41.18%)
Blood and lymphatic system disorders		
Anemia † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Cardiac disorders		
Angina pectoris † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Atrial fibrillation † [A]		
# participants affected/at risk	13/174 (7.47%)	11/170 (6.47%)
# events		
Atrial flutter † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Atrioventricular block first degree † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)

	Fondaparinux	UFH/VKA
# events		
Bradycardia † [A]		
# participants affected/at risk	2/174 (1.15%)	2/170 (1.18%)
# events		
Cardiac failure † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Mitral valve incompetence † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Palpitations † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Sinus bradycardia † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Supraventricular extrasystoles † [A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Tricuspid valve incompetence † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Ventricular tachycardia † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Ear and labyrinth disorders		
Tinnitus † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Vertigo † [A]		
# participants affected/at risk	5/174 (2.87%)	3/170 (1.76%)
# events		
Endocrine disorders		
Hyperthyroidism † [A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Hypothyroidism †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Eye disorders		
Vision blurred †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Gastrointestinal disorders		
Abdominal discomfort †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Abdominal pain †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Abdominal pain upper †[A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
Constipation †[A]		
# participants affected/at risk	3/174 (1.72%)	3/170 (1.76%)
# events		
Diarrhea †[A]		
# participants affected/at risk	3/174 (1.72%)	5/170 (2.94%)
# events		
Dry mouth †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Dysphagia †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Gastric disorder †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Gastrointestinal pain †[A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Intestinal hemorrhage †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Nausea †[A]		
# participants affected/at risk	4/174 (2.3%)	2/170 (1.18%)
# events		
Toothache †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Vomiting †[A]		
# participants affected/at risk	6/174 (3.45%)	1/170 (0.59%)
# events		
General disorders		
Asthenia †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)

	Fondaparinux	UFH/VKA
# events		
Chest discomfort † [A]		
# participants affected/at risk	0/174 (0%)	3/170 (1.76%)
# events		
Chest pain † [A]		
# participants affected/at risk	4/174 (2.3%)	2/170 (1.18%)
# events		
Edema † [A]		
# participants affected/at risk	4/174 (2.3%)	3/170 (1.76%)
# events		
Edema peripheral † [A]		
# participants affected/at risk	1/174 (0.57%)	3/170 (1.76%)
# events		
Fatigue † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Vessel puncture site hematoma † [A]		
# participants affected/at	1/174 (0.57%)	0/170 (0%)

	Fondaparinux	UFH/VKA
risk		
# events		
Infections and infestations		
Bronchitis † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Cystitis † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Gastroenteritis norovirus † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Infection † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Lung infection † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)

	Fondaparinux	UFH/VKA
# events		
Nasopharyngitis † [A]		
# participants affected/at risk	1/174 (0.57%)	2/170 (1.18%)
# events		
Onychomycosis † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Paronychia † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Sebaceous gland infection † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Urinary tract infection † [A]		
# participants affected/at risk	3/174 (1.72%)	3/170 (1.76%)
# events		
Varicella † [A]		
# participants affected/at	0/174 (0%)	1/170 (0.59%)

	Fondaparinux	UFH/VKA
risk		
# events		
Injury, poisoning and procedural complications		
Ankle fracture † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Contusion † [A]		
# participants affected/at risk	2/174 (1.15%)	0/170 (0%)
# events		
Joint sprain † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Wound † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Investigations		
Blood creatinine increased † [A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Blood potassium decreased †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
C-reactive protein increased †[A]		
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
International normalised ratio decreased †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
International normalized ratio increased †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Weight decreased †[A]		
# participants affected/at	1/174 (0.57%)	0/170 (0%)

	Fondaparinux	UFH/VKA
risk		
# events		
Metabolism and nutrition disorders		
Appetite disorder † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Gout † [A]		
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
Hypercholesterolaemia † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Hyperkalemia † [A]		
# participants affected/at risk	2/174 (1.15%)	0/170 (0%)
# events		
Hypokalemia † [A]		
# participants affected/at risk	4/174 (2.3%)	2/170 (1.18%)

	Fondaparinux	UFH/VKA
# events		
Magnesium deficiency † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Musculoskeletal and connective tissue disorders		
Arthralgia † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Back pain † [A]		
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
Musculoskeletal pain † [A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Myalgia † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		

	Fondaparinux	UFH/VKA
Osteoarthritis †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Pain in extremity †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Sensation of heaviness †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Spinal disorder †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Prostatic adenoma †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		

	Fondaparinux	UFH/VKA
Nervous system disorders		
Dizziness †[A]		
# participants affected/at risk	1/174 (0.57%)	2/170 (1.18%)
# events		
Headache †[A]		
# participants affected/at risk	7/174 (4.02%)	0/170 (0%)
# events		
Paraesthesia †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Restless legs syndrome †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Syncope †[A]		
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
Psychiatric disorders		

	Fondaparinux	UFH/VKA
Disorientation †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Insomnia †[A]		
# participants affected/at risk	1/174 (0.57%)	2/170 (1.18%)
# events		
Nightmare †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Sleep disorder †[A]		
# participants affected/at risk	2/174 (1.15%)	4/170 (2.35%)
# events		
Transient psychosis †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Renal and urinary disorders		
Renal cyst †[A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Renal failure † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Renal impairment † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Reproductive system and breast disorders		
Menstruation irregular † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Respiratory, thoracic and mediastinal disorders		
Bronchial disorder † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		

	Fondaparinux	UFH/VKA
Cough †[A]		
# participants affected/at risk	3/174 (1.72%)	1/170 (0.59%)
# events		
Dyspnea †[A]		
# participants affected/at risk	1/174 (0.57%)	4/170 (2.35%)
# events		
Epistaxis †[A]		
# participants affected/at risk	2/174 (1.15%)	2/170 (1.18%)
# events		
Hemoptysis †[A]		
# participants affected/at risk	1/174 (0.57%)	1/170 (0.59%)
# events		
Oropharyngeal pain †[A]		
# participants affected/at risk	1/174 (0.57%)	2/170 (1.18%)
# events		
Pleural effusion †[A]		
# participants affected/at risk	2/174 (1.15%)	0/170 (0%)
# events		

	Fondaparinux	UFH/VKA
Pulmonary hypertension †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Rhinalgia †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Skin and subcutaneous tissue disorders		
Alopecia †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Dermatitis allergic †[A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Drug eruption †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Hyperhidrosis †[A]		

	Fondaparinux	UFH/VKA
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Hyperkeratosis † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Pruritus † [A]		
# participants affected/at risk	3/174 (1.72%)	0/170 (0%)
# events		
Psoriasis † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Rash † [A]		
# participants affected/at risk	2/174 (1.15%)	2/170 (1.18%)
# events		
Skin hemorrhage † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		

	Fondaparinux	UFH/VKA
Surgical and medical procedures		
Skin operation † [A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		
Tooth extraction † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Vascular disorders		
Circulatory collapse † [A]		
# participants affected/at risk	0/174 (0%)	1/170 (0.59%)
# events		
Hematoma † [A]		
# participants affected/at risk	3/174 (1.72%)	2/170 (1.18%)
# events		
Hypertension † [A]		
# participants affected/at risk	4/174 (2.3%)	3/170 (1.76%)
# events		

	Fondaparinux	UFH/VKA
Hypertensive crisis †[A]		
# participants affected/at risk	0/174 (0%)	2/170 (1.18%)
# events		
Hypotension †[A]		
# participants affected/at risk	4/174 (2.3%)	0/170 (0%)
# events		
Phlebitis †[A]		
# participants affected/at risk	2/174 (1.15%)	0/170 (0%)
# events		
Thrombophlebitis †[A]		
# participants affected/at risk	1/174 (0.57%)	0/170 (0%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or

publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Limitations and Caveats:

Results Point of Contact:

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