Clinical trial results:
Atrial Fibrillation Progression Trial (ATTEST)

Summary

EudraCT number	2012-002338-35
Trial protocol	DE CZ AT SE ES IE GB
Global end of trial date	29 May 2018

Results information

Result version number	v1 (current)
This version publication date	17 May 2020
First version publication date	17 May 2020

Trial information

Trial identification

Sponsor protocol code	ATTEST

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01570361
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Johnson & Johnson Medical N.V., Biosense Webster
Sponsor organisation address	3333 Diamond Canyon Road Diamond Bar, Diamond Bar, United States, CA 91765
Public contact	Liesbeth Vanderlinden, Johnson & Johnson Medical N.V., Biosense Webster, +32 0 2 746 3446, lvanderl@its.jnj.com
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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	29 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 May 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to determine whether, in subjects with paroxysmal atrial fibrillation (PAF), early radiofrequency (RF) ablation treatment using the THERMOCOOL® Catheter Family in conjunction with the CARTO® 3, CARTO® XP, or CARTO® RMT System delays progression of atrial fibrillation (AF) compared with drug therapy (either rate or rhythm control) using current AF management guidelines.

Protection of trial subjects:

This study was performed in accordance with the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use – Good Clinical Practice (ICH-GCP) and ensure the protection of the subjects as per Declaration of Helsinki and local regulations. The safety was monitored by assessing adverse events throughout the study. Also, evaluations were done using 12-lead electrocardiograms (ECGs), Holter monitoring, event recording, transesophageal and transthoracic echocardiograms, and cardioversions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 37
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Russian Federation: 115
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Latvia: 23
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 14

Worldwide total number of subjects	255
EEA total number of subjects	126

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)	70
From 65 to 84 years	185
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first subject was enrolled on 13-Feb-2012. On 27-Feb-2018, study was terminated early due to enrollment not proceeding in accordance with expectations, independently from the study outcome. The last subject completed the last visit on 29-May-2018.

Pre-assignment

Screening details:

Before randomization and signing inform consent forms, all subjects were screened according protocol defined inclusion and exclusion criteria. Screening failures were excluded from the study and were not randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Radiofrequency (RF) ablation treatment

Arm description:

Radiofrequency (RF) ablation treatment for subjects with Paroxysmal Atrial Fibrillation (PAF) using the CARTO® 3 or CARTO® XP System, CARTO RMT, and THERMOCOOL® Catheter Family (including THERMOCOOL® SF or THERMOCOOL® SMARTTOUCH™).

Arm type	RF ablation treatment

No investigational medicinal product assigned in this arm

Arm title	Antiarrhythmic drug (AAD) therapy

Arm description:

Antiarrhythmic Drug therapy (either rate or rhythm control): Class I or class III, or AV nodal blocking agents such as beta blockers and calcium channel blockers in accordance with 2006 atrial fibrillation management guidelines. Subjects who met eligibility criteria were allowed for crossed over to RF ablation treatment (second treatment) followed by AAD therapy (first treatment).

Arm type	Active comparator
Investigational medicinal product name	Antiarrhythmic drug (AAD) therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Buccal tablet, Tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

Antiarrhythmic drug (AAD) therapy in accordance with 2006 atrial fibrillation management guidelines.

Number of subjects in period 1	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy
Started	128	127
Received Study Treatment	102	123
Cross-over (AAD therapy to RF Ablation)	0 [1]	15 [2]
AAD Therapy only	0 [3]	108

Completed	46	52
Not completed	82	75
Adverse event, serious fatal	5	4
Subject withdrew consent	14	9
Adverse event, non-fatal	2	1
Other	-	2
Sponsor closing the study	51	50
Subject discontinued	1	2
Lost to follow-up	4	4
Subject excluded	5	3

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only 15 participants were cross-over from RF Ablation arm to AAD Therapy arm.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only 15 participants were cross-over from RF Ablation arm to AAD Therapy arm.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only 15 participants were cross-over from RF Ablation arm to AAD Therapy arm.

Baseline characteristics

Reporting groups	
Reporting group title	Radiofrequency (RF) ablation treatment
Reporting group description:	
Radiofrequency (RF) ablation treatment for subjects with Paroxysmal Atrial Fibrillation (PAF) using the CARTO® 3 or CARTO® XP System, CARTO RMT, and THERMOCOOL® Catheter Family (including THERMOCOOL® SF or THERMOCOOL® SMARTTOUCH™).	
Reporting group title	Antiarrhythmic drug (AAD) therapy
Reporting group description:	
Antiarrhythmic Drug therapy (either rate or rhythm control): Class I or class III, or AV nodal blocking agents such as beta blockers and calcium channel blockers in accordance with 2006 atrial fibrillation management guidelines. Subjects who met eligibility criteria were allowed for crossed over to RF ablation treatment (second treatment) followed by AAD therapy (first treatment).	

Reporting group values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy	Total
Number of subjects	128	127	255
Age categorical Units: Subjects			
Adults (18-64 years)	35	36	71
From 65 to 84 years	93	91	184
Age Continuous Units: Year			
arithmetic mean	67.8	67.6	
standard deviation	± 4.83	± 4.64	-
Sex: Female, Male Units: Participants			
Female	74	74	148
Male	54	53	107

End points

End points reporting groups

Reporting group title	Radiofrequency (RF) ablation treatment
Reporting group description:	
Radiofrequency (RF) ablation treatment for subjects with Paroxysmal Atrial Fibrillation (PAF) using the CARTO® 3 or CARTO® XP System, CARTO RMT, and THERMOCOOL® Catheter Family (including THERMOCOOL® SF or THERMOCOOL® SMARTTOUCH™).	
Reporting group title	Antiarrhythmic drug (AAD) therapy
Reporting group description:	
Antiarrhythmic Drug therapy (either rate or rhythm control): Class I or class III, or AV nodal blocking agents such as beta blockers and calcium channel blockers in accordance with 2006 atrial fibrillation management guidelines. Subjects who met eligibility criteria were allowed for crossed over to RF ablation treatment (second treatment) followed by AAD therapy (first treatment).	

Primary: Time to Persistent Atrial Fibrillation/Atrial Tachycardia at 3 Years

End point title	Time to Persistent Atrial Fibrillation/Atrial Tachycardia at 3 Years
End point description:	
Persistent atrial fibrillation/atrial tachycardia (AF/AT) (excluding isthmus-dependent atrial flutter) was defined as AF/AT lasting longer than 7 consecutive days or requiring termination by cardioversion after 48 hours. Intent to treat population (ITT), including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received. Here '99999' signifies that due to insufficient number of participants with events, median time and 95% CI could not be estimated using Kaplan-Meier method.	
End point type	Primary
End point timeframe:	
3 years	

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Radiofrequency (RF) ablation treatment v Antiarrhythmic drug (AAD) therapy

Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0009 [1]
Method	Log Rank one sided

Notes:

[1] - Prior to the final analysis, this study had two interim analyses. Hence the alpha level is 0.0231 for the primary analysis adjusted for the two interim analyses. p-value is one sided.

Secondary: Time to Persistent Atrial Fibrillation/Atrial Tachycardia at 1 Year

End point title	Time to Persistent Atrial Fibrillation/Atrial Tachycardia at 1 Year

End point description:

Persistent atrial fibrillation/atrial tachycardia (AF/AT) (excluding isthmus-dependent atrial flutter) was defined as AF/AT lasting longer than 7 consecutive days or requiring termination by cardioversion after 48 hours. ITT, including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received. Here '99999' signifies that due to insufficient number of participants with events, Kaplan Meier (KM) estimated median time and 95% CI could not be estimated.

End point type	Secondary

End point timeframe:

1 year

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Radiofrequency (RF) ablation treatment v Antiarrhythmic drug (AAD) therapy
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0118 [2]
Method	Log Rank one sided

Notes:

[2] - The alpha level is 0.025 for this secondary endpoint.

Secondary: Time to Persistent Atrial Fibrillation/Atrial Tachycardia at 2 Years.

End point title	Time to Persistent Atrial Fibrillation/Atrial Tachycardia at 2 Years.

End point description:

Persistent atrial fibrillation/atrial tachycardia (AF/AT) (excluding isthmus-dependent atrial flutter) was

defined as AF/AT lasting longer than 7 consecutive days or requiring termination by cardioversion after 48 hours. ITT, including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received. Here '99999' signifies that due to insufficient number of participants with events, median time and 95% CI could not be estimated using Kaplan-Meier method.

End point type	Secondary

End point timeframe:

2 years

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Month				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Radiofrequency (RF) ablation treatment v Antiarrhythmic drug (AAD) therapy
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0041 [3]
Method	Log rank one sided

Notes:

[3] - The alpha level is 0.025 for this secondary endpoint.

Secondary: Percentage of Subjects with Persistent Atrial Fibrillation/Atrial Tachycardia at 1 year

End point title	Percentage of Subjects with Persistent Atrial Fibrillation/Atrial Tachycardia at 1 year

End point description:

Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 1 year were reported. The percentage of participants was calculated using Kaplan Meier (KM) rate estimate. Persistent atrial fibrillation/atrial tachycardia (AF/AT) (excluding isthmus-dependent atrial flutter) was defined as AF/AT lasting longer than 7 consecutive days or requiring termination by cardioversion after 48 hours. Intent to treat population (ITT), including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received.

End point type	Secondary

End point timeframe:

1 year

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Percentage of subjects				
number (confidence interval 95%)	1.3 (0.2 to 8.6)	6.5 (3.2 to 13.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 2 year

End point title	Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 2 year

End point description:

Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 2 year were reported. The percentage of participants was calculated using Kaplan Meier (KM) rate estimate. Persistent atrial fibrillation/atrial tachycardia (AF/AT) (excluding isthmus-dependent atrial flutter) was defined as AF/AT lasting longer than 7 consecutive days or requiring termination by cardioversion after 48 hours. Intent to treat population (ITT), including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received.

End point type	Secondary

End point timeframe:

2 years

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Percentage of participants				
number (confidence interval 95%)	2.4 (0.6 to 9.4)	12.4 (7.2 to 21.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 3 year

End point title	Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 3 year

End point description:

Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 3 year were reported. The percentage of participants was calculated using Kaplan Meier (KM) rate estimate. Persistent atrial fibrillation/atrial tachycardia (AF/AT) (excluding isthmus-dependent atrial flutter) was defined as AF/AT

lasting longer than 7 consecutive days or requiring termination by cardioversion after 48 hours. Intent to treat population (ITT), including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received.

End point type	Secondary

End point timeframe:

3 years

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Percentage of participants				
number (confidence interval 95%)	2.4 (0.6 to 9.4)	17.5 (10.7 to 27.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Persistent Atrial Fibrillation/Atrial Tachycardia at 3 Years by Number of Repeat Ablations

End point title	Percentage of Subjects with Persistent Atrial Fibrillation/Atrial Tachycardia at 3 Years by Number of Repeat Ablations[4]

End point description:

Percentage of Participants with Persistent Atrial Fibrillation/Atrial Tachycardia at 3 year by number of repeat ablations were reported. The percentage of participants was calculated using Kaplan Meier (KM) rate estimate. Persistent atrial fibrillation/atrial tachycardia (AF/AT) (excluding isthmus-dependent atrial flutter) was defined as AF/AT lasting longer than 7 consecutive days or requiring termination by cardioversion after 48 hours. Intent to treat population (ITT), including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received. Endpoint applicable only to subjects randomized into the test group (RF Ablation). Here '99999' signifies that due to insufficient number of participants with events, 95% CI could not be estimated using Kaplan-Meier method.

End point type	Secondary

End point timeframe:

3 years

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for any of the arms of this endpoint.

End point values	Radiofrequency (RF) ablation treatment			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: Percentage of subjects				
number (confidence interval 95%)				
Number of ablations = 0 (n=25)	0.0 (-99999 to 99999)			

Number of ablations = 1 (n=89) 2 or more ablations (n=14)	1.5 (0.2 to 10.4) 7.7 (1.1 to 43.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Repeat Ablations

End point title	Number of Repeat Ablations

End point description:

Number of repeat ablations refers to the total number of ablation procedures (including initial ablation procedure). If the number of repeat ablations =1 then subject only had one ablation procedure (initial ablation procedure in test group as randomized or cross-over procedure in cross-over subjects). If the number of repeat ablations is >= 2, then subject had at least one repeat procedure. ITT population includes all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received. Here 'N (number of subjects analyzed)' signifies the subjects in the Intent to treat population (ITT) who were randomized to RF ablation or who received any RF ablations as Cross-Over Patients randomized to AAD group.

End point type	Secondary

End point timeframe:

3 years

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	15		
Units: Event of ablation				
arithmetic mean (standard deviation)	0.9 (± 0.57)	1.1 (± 0.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of New Antiarrhythmic Drugs

End point title	Number of New Antiarrhythmic Drugs

End point description:

Number of new antiarrhythmic drugs were administered as per investigator's discretion and 2006 AF management guidelines. ITT population set including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received.

End point type	Secondary

End point timeframe:

3 years

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: AAD drug				
arithmetic mean (standard deviation)	0.8 (± 1.05)	1.0 (± 1.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects in Sinus Rhythm at Each Visit Throughout the Follow-up

End point title	Number of Subjects in Sinus Rhythm at Each Visit Throughout the Follow-up

End point description:

Subject in sinus rhythm: no other rhythms documented at specific visit, based on ECG, Holter and event recorder. Percentages are calculated with respect to number of subjects with data available at corresponding visit. ITT population set including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received. The number of subjects analyzed at each visit is the number of subjects with available data at the visit. Here 'n' number analyzed signifies number of subjects evaluable for specified categories.

End point type	Secondary

End point timeframe:

3 months, 6 months, 1 year, 2 years, 3 years

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Subjects				
3 months follow up (n= 69, 80)	51	55		
6 months follow up (n= 62, 60)	49	42		
1 year follow up (n= 54, 53)	41	35		
2 year follow up (n= 44, 44)	37	30		
3 year follow up (n= 27, 35)	20	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Recurrent AF/AT at Each Visit Throughout the Follow-up

End point title	Number of Subjects with Recurrent AF/AT at Each Visit Throughout the Follow-up

End point description:

Subjects with recurrent AF/AT: any AF/AT documented between previous visit up to visit analyzed at any TTM, Holter or ECG. Percentages are calculated with respect to number of subjects with data available at corresponding visit. ITT population set including all subjects randomized, where subjects were classified by the group to which they were randomized, regardless of the treatment received. Here 'n' number analyzed signifies number of subjects evaluable for specified categories.

End point type	Secondary

End point timeframe:

3 months, 6 months, 1 year, 2 year and 3 years

End point values	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Subjects				
3 months follow up (n= 101,114)	17	20		
6 months follow up (n= 96, 110)	17	45		
1 year follow up (n= 88, 87)	20	38		
2 years follow up (n= 72, 73)	16	30		
3 years follow up (n= 51, 55)	10	17		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

3 years follow up

Adverse event reporting additional description:

Adverse events are summarized using the Safety population, which includes all subjects who had undergone insertion of an ablation catheter, either as RF ablation group or cross-over subjects; subjects who had started an investigator prescribed AAD in the AAD Group and did not initiate ablation therapy.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Radiofrequency (RF) ablation treatment

Reporting group description:

Radiofrequency (RF) ablation treatment for subjects with Paroxysmal Atrial Fibrillation (PAF) using the CARTO® 3 or CARTO® XP System, CARTO RMT, and THERMOCOOL® Catheter Family (including THERMOCOOL® SF or THERMOCOOL® SMARTTOUCH™)

Reporting group title	Antiarrhythmic drug (AAD) therapy only

Reporting group description:

Antiarrhythmic Drug therapy (either rate or rhythm control): Class I or class III, or AV nodal blocking agents such as beta blockers and calcium channel blockers in accordance with 2006 atrial fibrillation management guidelines. This group includes only those subjects received AAD only.

Reporting group title	Antiarrhythmic drug (AAD) therapy - first treatment

Reporting group description:

This group of subjects received Antiarrhythmic drug (AAD) therapy first and received RF ablation treatment later. The AEs are those occurred during the AAD treatment period.

Reporting group title	Radiofrequency (RF) ablation - second treatment

Reporting group description:

This group of subjects received Antiarrhythmic drug (AAD) therapy first and received RF ablation treatment later. The AEs are those occurred during the RF treatment period.

Serious adverse events	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy only	Antiarrhythmic drug (AAD) therapy - first treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 102 (37.25%)	30 / 108 (27.78%)	7 / 15 (46.67%)
number of deaths (all causes)	5	4	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of bladder			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial carcinoma			

subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Neoplasm malignant			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer recurrent			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Vascular disorders			
Arteriovenous fistula			

subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	2 / 102 (1.96%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypertension			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Hypertensive emergency			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Surgical and medical procedures			
Abscess drainage			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ablation			
subjects affected / exposed	0 / 102 (0.00%)	0 / 108 (0.00%)	0 / 15 (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
Hernia repair			

subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 102 (2.94%)	2 / 108 (1.85%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic prolapse			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Dyspnoea			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			

subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device lead damage			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Arteriogram coronary			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Angina unstable			
subjects affected / exposed	0 / 102 (0.00%)	0 / 108 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	8 / 102 (7.84%)	7 / 108 (6.48%)	4 / 15 (26.67%)
occurrences causally related to treatment / all	2 / 13	0 / 9	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	4 / 102 (3.92%)	2 / 108 (1.85%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	4 / 102 (3.92%)	2 / 108 (1.85%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 5	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac thrombus			

subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			

subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Ventricular tachyarrhythmia			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Dizziness postural			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nerve degeneration			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Radicular syndrome			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Eye disorders			

Eyelid oedema			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Chronic gastritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Diarrhoea			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Haematemesis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Ileus			
subjects affected / exposed	0 / 102 (0.00%)	0 / 108 (0.00%)	0 / 15 (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
Inguinal hernia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Melaena			

subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic pseudocyst			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Proctalgia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Cholangitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 102 (0.00%)	2 / 108 (1.85%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Urinary retention			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Osteoarthritis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Infections and infestations			
Perineal abscess			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (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
Pneumonia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyelonephritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Radiofrequency (RF) ablation - second treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of bladder			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchial carcinoma			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasm malignant			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			

subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer recurrent				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine cancer				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Arteriovenous fistula				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematoma				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 1			
Hypertension				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive emergency				

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abscess drainage			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac ablation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hernia repair			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inflammation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pelvic prolapse			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sleep apnoea syndrome			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Major depression				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device lead damage				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device occlusion				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Arteriogram coronary				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Acetabulum fracture				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				

subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular pseudoaneurysm				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial tachycardia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				

subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac tamponade				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracardiac thrombus				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				

subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachyarrhythmia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular tachyarrhythmia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness postural				

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nerve degeneration			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radicular syndrome			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Chronic gastritis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Faeces discoloured			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Melaena			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic pseudocyst			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Proctalgia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Bile duct stenosis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Urinary retention				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Haemarthrosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Perineal abscess			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 15 (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	Radiofrequency (RF) ablation treatment	Antiarrhythmic drug (AAD) therapy only	Antiarrhythmic drug (AAD) therapy - first treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 102 (36.27%)	43 / 108 (39.81%)	6 / 15 (40.00%)
Vascular disorders			
Haematoma			

subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Haemorrhage			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Hypertension			
subjects affected / exposed	1 / 102 (0.98%)	2 / 108 (1.85%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Hypertensive crisis			
subjects affected / exposed	1 / 102 (0.98%)	2 / 108 (1.85%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Hypertensive emergency			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	2 / 102 (1.96%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 102 (1.96%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Fatigue			
subjects affected / exposed	2 / 102 (1.96%)	2 / 108 (1.85%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Vessel puncture site pain			

subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Prostatic disorder			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 102 (0.98%)	5 / 108 (4.63%)	0 / 15 (0.00%)
occurrences (all)	1	5	0
Bronchospasm			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram change			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Heart rate irregular			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Prostatic specific antigen increased			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Injury, poisoning and procedural complications			

Foot fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lower limb fracture			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Upper limb fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 102 (0.00%)	0 / 108 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Aortic valve incompetence			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	13 / 102 (12.75%)	20 / 108 (18.52%)	2 / 15 (13.33%)
occurrences (all)	14	22	2
Atrial flutter			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Atrial thrombosis			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Bradycardia			

subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	0 / 102 (0.00%)	3 / 108 (2.78%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Cardiac failure chronic			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cardiac failure congestive			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cardiac valve disease			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Coronary artery stenosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pericardial effusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Supraventricular extrasystoles			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Supraventricular tachycardia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Restless legs syndrome			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 102 (0.00%)	0 / 108 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 102 (0.00%)	0 / 108 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Large intestine polyp			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nausea			

subjects affected / exposed	1 / 102 (0.98%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Proctalgia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Thyroid disorder			
subjects affected / exposed	2 / 102 (1.96%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 108 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis bacterial			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Systemic infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 108 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 102 (0.00%)	1 / 108 (0.93%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Radiofrequency (RF) ablation - second treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypertensive crisis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypertensive emergency			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Hypotension			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Vessel puncture site pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Prostatic disorder			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Bronchospasm			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0		
Investigations Body temperature increased subjects affected / exposed occurrences (all) Electrocardiogram change subjects affected / exposed occurrences (all) Heart rate irregular subjects affected / exposed occurrences (all) Prostatic specific antigen increased subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0		
Injury, poisoning and procedural complications Foot fracture subjects affected / exposed occurrences (all) Lower limb fracture subjects affected / exposed occurrences (all) Rib fracture subjects affected / exposed occurrences (all) Upper limb fracture subjects affected / exposed occurrences (all) Vascular pseudoaneurysm subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0		
Congenital, familial and genetic disorders			

Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Aortic valve incompetence			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Atrial flutter			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Atrial thrombosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Cardiac failure			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Cardiac failure chronic			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Cardiac failure congestive			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Cardiac valve disease			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Coronary artery stenosis			

subjects affected / exposed occurrences (all) Pericardial effusion subjects affected / exposed occurrences (all) Supraventricular extrasystoles subjects affected / exposed occurrences (all) Supraventricular tachycardia subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0		
Nervous system disorders Cerebral ischaemia subjects affected / exposed occurrences (all) Neuralgia subjects affected / exposed occurrences (all) Restless legs syndrome subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0		
Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0 1 / 15 (6.67%) 1		
Eye disorders			

Dry eye subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Dry mouth subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Large intestine polyp subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Proctalgia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Haematuria subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Endocrine disorders			

Thyroid disorder subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Musculoskeletal and connective tissue disorders Bursitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Conjunctivitis bacterial subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Influenza subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Pneumonia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Systemic infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Metabolism and nutrition disorders Hyperlipidaemia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		

Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 October 2012	The language was broadened to allow all ThermoCool catheters to be used in conjunction with CARTO systems. The definition of the study locations was broadened to include North America. Further clarification of the subject population was added not to include first-line treatment subjects. The definition of paroxysmal atrial fibrillation (AF) was clarified. Clarification was added on the risk analysis for antiarrhythmic drug (AAD) drugs. Exclusion of subjects with persistent AF was added. The study entry criteria were clarified (reversible causes of AF and atrial thrombus detection technique). The definition of "lost to follow-up" was clarified. Clarification that only validated versions of the Atrial Fibrillation Effect on QualiTy-of-life (AFEQT) questionnaire in country-specific languages would be used. Clarification of subject assessments (including the table for Summary of Subject Assessments) and safety follow up for crossover subjects was added, together with the transtelephonic monitoring (TTM) start day and TTM/ transthoracic echocardiography (TTE) timelines. Blood sampling for metabolite determination was removed from the cross-over procedure. Clarified that cardioversion as part of a (re)-ablation procedure did not count as reaching the primary endpoint. Adverse event definitions/classifications were revised to comply with applicable regulations requirements, with information previously held in an appendix moved to the protocol body. The complaint reporting section was revised to comply with applicable regulations requirements. The timelines of the interim analyses were updated. Administrative responsibilities were clarified, including ethics committee (EC) approval of the study documents (protocol, amendments, informed consent form [ICF]), the monitoring procedures, and the description of source documentation. The study period was updated to include 2012.
09 April 2013	The study entry criteria were revised to enhance enrollment, reducing the required number of AF episodes from 6 to 2. A note correcting the minimum ejection fraction was added (from greater than (>)50 percent (%) to >=50%). Clarification was made regarding the time-interval related statistical deliverables to be reviewed during the interim analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
29 May 2018	The study was terminated early on 29-May-2018 due to slow enrollment.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As the study was terminated early without having met primary effectiveness or futility criteria, the study results should be interpreted with caution.

Notes: