ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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Efficacy & Safety of Dronedarone Versus Amiodarone for the Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation (DIONYSOS)

This study has been completed.

Sponsor:	Sanofi
Collaborators:	
Information provided by:	Sanofi
ClinicalTrials.gov Identifier:	NCT00489736

Purpose

The objective of this study is to compare the efficacy and safety of dronedarone to that of amiodarone for the treatment of patients with atrial fibrillation.

Condition	Intervention	Phase
Atrial Fibrillation	Drug: dronedarone (SR33589) Drug: amiodarone	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Caregiver, Investigator), Randomized, Efficacy Study
Official Title: Randomized Double Blind Trial to Evaluate the Efficacy and Safety of Dronedarone (400mg BID) Versus Amiodarone (600mg Daily for 28 Days, Then 200mg Daily Thereafter) for at Least 6 Months for the Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation (AF)

Further study details as provided by Sanofi:

Primary Outcome Measure:

- Treatment Failure [Time Frame: minimum study duration is 6 months (+10 days); maximum is 15 months] [Designated as safety issue: No]
  The primary event is the treatment failure defined as the first recurrence of atrial fibrillation or premature study drug discontinuation for intolerance or lack of efficacy according to the investigator judgement. The primary efficacy analysis is performed on the time from first study drug intake to this primary event. The "Measured Values" table below presents the numbers of patients with the event at the end of the study period.

Secondary Outcome Measures:

- Occurrence of the Main Safety Endpoint (MSE) Defined as Thyroid, Hepatic, Pulmonary, Neurological, Skin, Eye, or Gastrointestinal Specific Treatment Emergent Events or Premature Study Drug Discontinuation Following Any Adverse Event [Time Frame: minimum study duration is 6 months (+10 days); maximum is 15 months] [Designated as safety issue: Yes]

  The considered event is the occurrence of the MSE defined as thyroid, hepatic, pulmonary, neurological, skin, eye, or gastrointestinal specific treatment emergent events or premature study drug discontinuation following any adverse event (AE), whichever comes first. The analysis is performed on the time from first study drug intake to this event. The "Measured Values" table below presents the numbers of patients with the event at the end of the study period.

Other Pre-specified Outcome Measures:

- Occurrence of the MSE Excluding Gastrointestinal Specific Treatment Emergent Events Defined as Diarrhoea, Nausea, Vomiting [Time Frame: minimum study duration is 6 months (+10 days); maximum is 15 months] [Designated as safety issue: Yes]

  The considered event is the occurrence of the MSE excluding gastrointestinal specific treatment emergent events defined as diarrhoea, nausea, vomiting. The analysis is performed on the time from first study drug intake to this event. The "Measured Values" table below presents the numbers of patients with the event at the end of the study period.

Enrollment: 504
Study Start Date: June 2007
Primary Completion Date: October 2008
Study Completion Date: October 2008

Arms	Assigned Interventions
Experimental: Dronedarone 400mg bid dronedarone 400mg tablets administered twice a day (bid) and matching over-encapsulated tablets of placebo of amiodarone 200mg	Drug: dronedarone (SR33589) oral administration Other Names: Multaq®
Active Comparator: Amiodarone 600mg/200mg od over-encapsulated tablets of amiodarone 200mg (600mg daily for 28 days then 200mg daily) administered once daily (od) and matching placebo of dronedarone 400mg tablets	Drug: amiodarone oral administration

Eligibility

Ages Eligible for Study: 21 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Patients with documented atrial fibrillation for more than 72 hours for whom cardioversion and antiarrhythmic treatment is indicated in the opinion of the investigator and under oral anticoagulation

Exclusion Criteria:

- Contraindication to oral anticoagulation
- Patient having received amiodarone in the past whatever the date (more than a total of twenty 200 mg tablets or more than 5 days intravenous)
- Patients known to have chronic AF, patients with atrial flutter or paroxysmal atrial fibrillation
- Severe congestive heart failure with New-York Heart Association (NYHA) class III or IV, severe bradycardia, high degree atrio-ventricular block, ongoing potentially dangerous symptoms when in AF such as angina pectoris, transient ischemic attacks, stroke, syncope, as judged by the investigator, first degree family history of sudden cardiac death below age 50 years in the absence of coronary heart disease, significant sinus node disease without a permanent pacemaker implanted
- History of torsades de pointes or long QT syndrome or QT- or QTc-interval ≥500 msecs before randomization
- Treatment with other class I or III antiarrhythmic drugs which cannot be discontinued
- Dysthyroidism or other contraindication to amiodarone

The above information are not intended to contain all the considerations relevant to a patient's potential participation in a clinical trial.

Contacts and Locations

Locations

United States, New Jersey
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Argentina
sanofi-aventis administrative office
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Diegem, Belgium
Canada
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Laval, Canada
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Santiago, Chile
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  - Praha, Czech Republic

Estonia
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  - Tallinn, Estonia

Finland
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  - Helsinki, Finland

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  - Milan, Italy

Korea, Republic of
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  - Seoul, Korea, Republic of

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  - Gouda, Netherlands

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  - Warszawa, Poland

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  - Moscow, Russian Federation

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  - Bromma, Sweden

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  - Megrine, Tunisia

Turkey
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  - Istanbul, Turkey

Investigators

Study Director:	International Clinical Development	sanofi-aventis

More Information

Responsible Party:	sanofi-aventis (International Clinical Development, Clinical Study Director)
Study ID Numbers:	EFC4968
Health Authority:	United States: Food and Drug Administration Canada: Health Canada Netherlands: Medicines Evaluation Board (MEB)

Study Results

Participant Flow

Recruitment Details	Enrollment of patients started on June 12, 2007 and was completed on October 3, 2008. The study was conducted in 112 centers in 23 countries. Minimum duration of treatment was 6 months. Minimum duration of observation was last patient's randomization plus 190 days.
Pre-Assignment Details	Planned sample size was 472. Six hundred and eighteen patients (618) were screened of which 113 did not verify one or more selection criteria. One eligible patient received a placebo capsule (morning intake in the amiodarone group) but was not randomized in the trial. This patient did not report any adverse event and was excluded from all analyses.

Reporting Groups

	Description
Dronedarone 400mg Bid	dronedarone tablets 400mg twice daily (bid)
Amiodarone 600mg/200mg od	amiodarone 600mg once daily (od) for 28 days, then amiodarone 200mg once daily (od)

Overall Study

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
Started	249 [1]	255 [1]
Completed	153 [2]	186 [2]
Not Completed	96	69
Lack of Efficacy	53	14

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
Adverse Event	32	45
Poor compliance	6	2
Not coded/ Not pre-specified	5	8

[1] Randomized and treated patients
[2] completed study drug period

Baseline Characteristics

Reporting Groups

	Description
Dronedarone 400mg Bid	dronedarone tablets 400mg twice daily (bid)
Amiodarone 600mg/200mg od	amiodarone 600mg once daily (od) for 28 days, then amiodarone 200mg once daily (od)

Baseline Measures

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od	Total
Number of Participants	249	255	504
Age, Customized [units: participants]			
18 to < 65 years	125	138	263
65 to < 75 years	76	70	146
>= 75 years	48	47	95
Age, Continuous [units: years] Mean (Standard Deviation)	64.4 (10.8)	63.7 (10.6)	64.0 (10.7)
Gender, Male/Female [units: participants]			
Female	73	73	146
Male	176	182	358

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Treatment Failure
Measure Description	The primary event is the treatment failure defined as the first recurrence of atrial fibrillation or premature study drug discontinuation for intolerance or lack of efficacy according to the investigator judgement. The primary efficacy analysis is performed on the time from first study drug intake to this primary event. The "Measured Values" table below presents the numbers of patients with the event at the end of the study period.
Time Frame	minimum study duration is 6 months (+10 days); maximum is 15 months
Safety Issue?	No

Analysis Population Description

All randomized and treated patients (receiving at least one dose of study drug) were included in the efficacy analysis according to the treatment received.

Reporting Groups

	Description
Dronedarone 400mg Bid	dronedarone tablets 400mg twice daily (bid)
Amiodarone 600mg/200mg od	amiodarone 600mg once daily (od) for 28 days, then amiodarone 200mg once daily (od)

Measured Values

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
Number of Participants Analyzed	249	255
Treatment Failure [units: participants]	184	141

Statistical Analysis 1 for Treatment Failure

Statistical Analysis Overview	Comparison Groups	Dronedarone 400mg Bid, Amiodarone 600mg/200mg od
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001

	Comments	Cumulative incidence functions in each treatment group were calculated using time-to-event non-parametric Kaplan-Meier estimate. The primary comparison was performed at the 5% level using a 2-sided Log rank test.
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.59
	Confidence Interval	(2-Sided) 95% 1.28 to 1.98
	Estimation Comments	The hazard ratio was estimated by a Cox's proportional hazard model with treatment arm factor. It provides the relative hazard of treatment failure for the dronedarone group compared with the amiodarone group.

2. Secondary Outcome Measure:

Measure Title	Occurrence of the Main Safety Endpoint (MSE) Defined as Thyroid, Hepatic, Pulmonary, Neurological, Skin, Eye, or Gastrointestinal Specific Treatment Emergent Events or Premature Study Drug Discontinuation Following Any Adverse Event
Measure Description	The considered event is the occurrence of the MSE defined as thyroid, hepatic, pulmonary, neurological, skin, eye, or gastrointestinal specific treatment emergent events or premature study drug discontinuation following any adverse event (AE), whichever comes first. The analysis is performed on the time from first study drug intake to this event. The "Measured Values" table below presents the numbers of patients with the event at the end of the study period.
Time Frame	minimum study duration is 6 months (+10 days); maximum is 15 months
Safety Issue?	Yes

Analysis Population Description

All randomized and treated patients (receiving at least one dose of study drug) were included in the safety analysis according to the treatment received.

Reporting Groups

	Description
Dronedarone 400mg Bid	dronedarone tablets 400mg twice daily (bid)
Amiodarone 600mg/200mg od	amiodarone 600mg once daily (od) for 28 days, then amiodarone 200mg once daily (od)

Measured Values

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
Number of Participants Analyzed	249	255

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
Occurrence of the Main Safety Endpoint (MSE) Defined as Thyroid, Hepatic, Pulmonary, Neurological, Skin, Eye, or Gastrointestinal Specific Treatment Emergent Events or Premature Study Drug Discontinuation Following Any Adverse Event [units: participants]	83	107

Statistical Analysis 1 for Occurrence of the Main Safety Endpoint (MSE) Defined as Thyroid, Hepatic, Pulmonary, Neurological, Skin, Eye, or Gastrointestinal Specific Treatment Emergent Events or Premature Study Drug Discontinuation Following Any Adverse Event

Statistical Analysis Overview	Comparison Groups	Dronedarone 400mg Bid, Amiodarone 600mg/200mg od
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.13
	Comments	Cumulative incidence functions in each treatment group were calculated using time-to-event non-parametric Kaplan-Meier estimate. The comparison was performed at the 5% level using a 2-sided Log rank test.
	Method	Log Rank
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.80
	Confidence Interval	(2-Sided) 95% 0.60 to 1.07
	Estimation Comments	The hazard ratio was estimated by a Cox's proportional hazard model with treatment arm factor. It provides the relative hazard of main safety event occurrence for the dronedarone group compared with the amiodarone group.

3. Other Pre-specified Outcome Measure:

Measure Title	Occurrence of the MSE Excluding Gastrointestinal Specific Treatment Emergent Events Defined as Diarrhoea, Nausea, Vomiting

Measure Description	The considered event is the occurrence of the MSE excluding gastrointestinal specific treatment emergent events defined as diarrhoea, nausea, vomiting. The analysis is performed on the time from first study drug intake to this event. The "Measured Values" table below presents the numbers of patients with the event at the end of the study period.
Time Frame	minimum study duration is 6 months (+10 days); maximum is 15 months
Safety Issue?	Yes

Analysis Population Description

All randomized and treated patients (receiving at least one dose of study drug) were included in the safety analysis according to the treatment received.

Reporting Groups

	Description
Dronedarone 400mg Bid	dronedarone tablets 400mg twice daily (bid)
Amiodarone 600mg/200mg od	amiodarone 600mg once daily (od) for 28 days, then amiodarone 200mg once daily (od)

Measured Values

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
Number of Participants Analyzed	249	255
Occurrence of the MSE Excluding Gastrointestinal Specific Treatment Emergent Events Defined as Diarrhoea, Nausea, Vomiting [units: participants]	61	99

Statistical Analysis 1 for Occurrence of the MSE Excluding Gastrointestinal Specific Treatment Emergent Events Defined as Diarrhoea, Nausea, Vomiting

Statistical Analysis Overview	Comparison Groups	Dronedarone 400mg Bid, Amiodarone 600mg/200mg od
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	Cumulative incidence functions in each treatment group were calculated using time-to-event non-parametric Kaplan-Meier estimate. The comparison was performed at the 5% level using a 2-sided Log rank test.
	Method	Log Rank

	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.61
	Confidence Interval	(2-Sided) 95% 0.44 to 0.84
	Estimation Comments	The hazard ratio was estimated by a Cox's proportional hazard model with treatment arm factor. It provides the relative hazard of MSE occurrence excluding gastrointestinal events, for the dronedarone group compared with the amiodarone group.

Reported Adverse Events

Time Frame	From first to last study drug intake +10 days i.e. end of the study.
Additional Description	The safety population was the "All randomized and treated patients" population.

Reporting Groups

	Description
Dronedarone 400mg Bid	dronedarone tablets 400mg twice daily (bid)
Amiodarone 600mg/200mg od	amiodarone 600mg once daily (od) for 28 days, then amiodarone 200mg once daily (od)

Serious Adverse Events

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Total	34/249 (13.65%)	37/255 (14.51%)
Blood and lymphatic system disorders		
Anaemia [A] *	1/249 (0.4%)	0/255 (0%)
Hypoprothrombinaemia [A] *	0/249 (0%)	1/255 (0.39%)
Cardiac disorders		
Acute coronary syndrome [A] *	0/249 (0%)	1/255 (0.39%)
Acute myocardial infarction [A] *	0/249 (0%)	1/255 (0.39%)

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Angina pectoris [A] *	1/249 (0.4%)	1/255 (0.39%)
Arteriosclerosis coronary artery [A] *	1/249 (0.4%)	0/255 (0%)
Atrioventricular block second degree [A] *	0/249 (0%)	1/255 (0.39%)
Bradycardia [A] *	1/249 (0.4%)	2/255 (0.78%)
Cardiac failure [A] *	6/249 (2.41%)	1/255 (0.39%)
Cardiac failure congestive [A] *	1/249 (0.4%)	6/255 (2.35%)
Coronary artery stenosis [A] *	0/249 (0%)	1/255 (0.39%)
Diastolic dysfunction [A] *	1/249 (0.4%)	0/255 (0%)
Left ventricular dysfunction [A] *	1/249 (0.4%)	0/255 (0%)
Pericarditis [A] *	1/249 (0.4%)	0/255 (0%)
Sick sinus syndrome [A] *	0/249 (0%)	1/255 (0.39%)
Sinus bradycardia [A] *	0/249 (0%)	1/255 (0.39%)
Gastrointestinal disorders		
Duodenal ulcer [A] *	1/249 (0.4%)	0/255 (0%)
Gastric haemorrhage [A] *	1/249 (0.4%)	0/255 (0%)
Gastrointestinal haemorrhage [A] *	0/249 (0%)	1/255 (0.39%)
Gastrointestinal necrosis [A] *	0/249 (0%)	1/255 (0.39%)
Inguinal hernia [A] *	1/249 (0.4%)	0/255 (0%)
General disorders		
Chest pain [A] *	0/249 (0%)	1/255 (0.39%)
Death [A] *	1/249 (0.4%)	0/255 (0%)
Oedema peripheral [A] *	1/249 (0.4%)	0/255 (0%)

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Sudden death [A] *	0/249 (0%)	1/255 (0.39%)
Hepatobiliary disorders		
Cholangitis [A] *	0/249 (0%)	1/255 (0.39%)
Cholecystitis acute [A] *	0/249 (0%)	1/255 (0.39%)
Hepatocellular injury [A] *	1/249 (0.4%)	0/255 (0%)
Mixed liver injury [A] *	1/249 (0.4%)	0/255 (0%)
Infections and infestations		
Bronchitis [A] *	0/249 (0%)	2/255 (0.78%)
Cellulitis [A] *	0/249 (0%)	1/255 (0.39%)
Diverticulitis [A] *	1/249 (0.4%)	1/255 (0.39%)
Ear infection [A] *	0/249 (0%)	1/255 (0.39%)
Escherichia sepsis [A] *	0/249 (0%)	1/255 (0.39%)
Gastroenteritis [A] *	0/249 (0%)	1/255 (0.39%)
Oesophageal candidiasis [A] *	0/249 (0%)	1/255 (0.39%)
Pneumonia [A] *	2/249 (0.8%)	0/255 (0%)
Septic shock [A] *	0/249 (0%)	1/255 (0.39%)
Injury, poisoning and procedural complications		
Accidental overdose [A] *	0/249 (0%)	2/255 (0.78%)
Post procedural haemorrhage [A] *	1/249 (0.4%)	0/255 (0%)
Therapeutic agent toxicity [A] *	1/249 (0.4%)	3/255 (1.18%)
Thoracic vertebral fracture [A] *	0/249 (0%)	1/255 (0.39%)
Investigations		
Blood creatinine increased [A] *	1/249 (0.4%)	1/255 (0.39%)

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Electrocardiogram PR prolongation [A] *	1/249 (0.4%)	0/255 (0%)
International normalised ratio increased [A] *	0/249 (0%)	2/255 (0.78%)
Metabolism and nutrition disorders		
Diabetic foot [A] *	1/249 (0.4%)	0/255 (0%)
Hyperkalaemia [A] *	0/249 (0%)	1/255 (0.39%)
Hypoglycaemia [A] *	1/249 (0.4%)	0/255 (0%)
Hyponatraemia [A] *	0/249 (0%)	1/255 (0.39%)
Musculoskeletal and connective tissue disorders		
Muscle haemorrhage [A] *	0/249 (0%)	1/255 (0.39%)
Symphysiolysis [A] *	1/249 (0.4%)	0/255 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adrenal adenoma [A] *	0/249 (0%)	1/255 (0.39%)
Anaplastic thyroid cancer [A] *	1/249 (0.4%)	0/255 (0%)
Bladder cancer [A] *	1/249 (0.4%)	0/255 (0%)
Carcinoma in situ of bladder [A] *	1/249 (0.4%)	0/255 (0%)
Gastrointestinal stromal tumour [A] *	0/249 (0%)	1/255 (0.39%)
Lung cancer metastatic [A] *	0/249 (0%)	1/255 (0.39%)
Lung squamous cell carcinoma stage unspecified [A] *	1/249 (0.4%)	1/255 (0.39%)
Small cell lung cancer stage unspecified [A] *	0/249 (0%)	1/255 (0.39%)
Nervous system disorders		
Cerebral ischaemia [A] *	1/249 (0.4%)	0/255 (0%)
Cerebrovascular accident [A] *	1/249 (0.4%)	0/255 (0%)

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Haemorrhage intracranial [A] *	0/249 (0%)	1/255 (0.39%)
Ischaemic stroke [A] *	1/249 (0.4%)	0/255 (0%)
Syncope [A] *	0/249 (0%)	2/255 (0.78%)
Renal and urinary disorders		
Haematuria [A] *	1/249 (0.4%)	0/255 (0%)
Urinary retention [A] *	0/249 (0%)	1/255 (0.39%)
Respiratory, thoracic and mediastinal disorders		
Acute pulmonary oedema [A] *	1/249 (0.4%)	0/255 (0%)
Bronchitis chronic [A] *	1/249 (0.4%)	0/255 (0%)
Dyspnoea [A] *	1/249 (0.4%)	0/255 (0%)
Hypoxia [A] *	0/249 (0%)	1/255 (0.39%)
Pneumonitis [A] *	1/249 (0.4%)	0/255 (0%)
Pulmonary embolism [A] *	1/249 (0.4%)	0/255 (0%)
Skin and subcutaneous tissue disorders		
Dermatitis allergic [A] *	0/249 (0%)	1/255 (0.39%)
Vascular disorders		
Pelvic venous thrombosis [A] *	0/249 (0%)	1/255 (0.39%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 11.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Total	146/249 (58.63%)	165/255 (64.71%)

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Cardiac disorders		
Any Cardiac disorders [A] *	21/249 (8.43%)	36/255 (14.12%)
Bradycardia [A] *	4/249 (1.61%)	14/255 (5.49%)
Endocrine disorders		
Any Endocrine disorders [A] *	3/249 (1.2%)	14/255 (5.49%)
Eye disorders		
Any Eye disorders [A] *	6/249 (2.41%)	13/255 (5.1%)
Gastrointestinal disorders		
Any Gastrointestinal disorders [A] *	54/249 (21.69%)	44/255 (17.25%)
Diarrhoea [A] *	23/249 (9.24%)	8/255 (3.14%)
Nausea [A] *	13/249 (5.22%)	9/255 (3.53%)
General disorders		
Any General disorders and administration site conditions [A] *	14/249 (5.62%)	26/255 (10.2%)
Oedema peripheral [A] *	6/249 (2.41%)	13/255 (5.1%)
Infections and infestations		
Any Infections and infestations [A] *	35/249 (14.06%)	35/255 (13.73%)
Injury, poisoning and procedural complications		
Any Injury, poisoning and procedural complications [A] *	8/249 (3.21%)	17/255 (6.67%)
Investigations		
Any Investigations [A] *	33/249 (13.25%)	35/255 (13.73%)
Metabolism and nutrition disorders		
Any Metabolism and nutrition disorders [A] *	8/249 (3.21%)	15/255 (5.88%)

	Dronedarone 400mg Bid	Amiodarone 600mg/200mg od
	Affected/At Risk (%)	Affected/At Risk (%)
Musculoskeletal and connective tissue disorders		
Any Musculoskeletal and connective tissue disorders [A] *	21/249 (8.43%)	22/255 (8.63%)
Nervous system disorders		
Any Nervous system disorders [A] *	17/249 (6.83%)	39/255 (15.29%)
Dizziness [A] *	8/249 (3.21%)	16/255 (6.27%)
Psychiatric disorders		
Any Psychiatric disorders [A] *	6/249 (2.41%)	23/255 (9.02%)
Sleep disorder [A] *	3/249 (1.2%)	19/255 (7.45%)
Respiratory, thoracic and mediastinal disorders		
Any Respiratory, thoracic and mediastinal disorders [A] *	21/249 (8.43%)	21/255 (8.24%)
Skin and subcutaneous tissue disorders		
Any Skin and subcutaneous tissue disorders [A] *	18/249 (7.23%)	23/255 (9.02%)
Vascular disorders		
Any Vascular disorders [A] *	9/249 (3.61%)	23/255 (9.02%)
Hypertension [A] *	7/249 (2.81%)	16/255 (6.27%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 11.0

Limitations and Caveats

[Not specified]

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.

If no publication has occurred within 12 months of the completion of the study, the Investigator shall have the right to publish/present independently the results of the study. The Investigator shall provide the Sponsor with a copy of any such publication for comment at least 45 days before any submission for publication. If requested by the Sponsor, any submission shall be delayed up to 90 days, to allow the Sponsor to preserve its proprietary rights.

Results Point of Contact:

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