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Trial record **1 of 1** for: CSPP100A2368

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Six Months Efficacy and Safety of Aliskiren Therapy on Top of Standard Therapy, on Morbidity and Mortality in Patients With Acute Decompensated Heart Failure (ASTRONAUT)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00894387

First received: May 5, 2009
Last updated: October 15, 2013
Last verified: October 2013
History of Changes

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Results First Received: August 2, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Conditions:	Acute Decompensated Heart Failure Congestive Heart Failure
Interventions:	Drug: Aliskiren Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Of the 2134 screened patients (including 1 patient who was screened twice), 1639 patients were randomized.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Participant Flow: Overall Study

	Aliskiren	Placebo
STARTED	821 [1]	818
Safety Set	808	810
Full Analysis Set	808	807
Completed Primary Efficacy Phase (6 m)	717	707
Completed Secondary Efficacy Phase (12m)	654	640
COMPLETED	646 [2]	643
NOT COMPLETED	175	175
Adverse Event	44	45
Abnormal Laboratory values	2	2
Unsatisfactory therapeutic effect	0	1
Lost to Follow-up	3	5
Administrative problems	2	2
Death	77	76
Protocol Deviation	4	0
Patient's request	25	30
Other (Missing)	5	3
Mis-randomized	13	9
GCP non-compliance	0	2

[1] "Started" indicates all randomized patients
[2] "Completed" indicates patients whose treatment duration completed as per protocol

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.
Total	Total of all reporting groups

Baseline Measures

	Aliskiren	Placebo	Total
Number of Participants [units: participants]	**808**	**807**	**1615**
Age [units: years] Mean (Standard Deviation)	**64.7 (12.44)**	**64.5 (11.88)**	**64.6 (12.16)**

Gender [units: participants]			
Female	**171**	**197**	**368**
Male	**637**	**610**	**1247**

Outcome Measures

Hide All Outcome Measures

1. Primary: Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 6 Months [Time Frame: 6 months]

Measure Type	Primary
Measure Title	Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 6 Months
Measure Description	Time to first confirmed occurrence of either cardiovascular death or heart failure re-hospitalization within 6 months of randomization was the primary efficacy variable. For the primary efficacy analysis, an event will be considered for the analysis if it occurs on or before Day 190 (189 days from randomization). The primary composite endpoint is the the composite of cardiovascular death or heart faliure re-hospitalization within 6 months.
Time Frame	6 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set (FAS) consisted of randomized patients who had received at least one dose of study drug.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Measured Values

	Aliskiren	**Placebo**
Number of Participants Analyzed [units: participants]	**808**	**807**
Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 6 Months [units: Participants]		
Primary Composite Endpoint	**201**	**214**
Cardiovascular death	**77**	**85**
Heart faliure re-hospitalization	**153**	**166**

No statistical analysis provided for Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 6 Months

2. Secondary: Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 12 Months [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 12 Months
Measure Description	Time to first confirmed occurrence of either cardiovascular death or heart failure re-hospitalization within 12 months of randomization was the key secondary efficacy variable. For the primary efficacy analysis, an event will be considered for the analysis if it occurs on or before Day 395 (394 days from randomization). The secondary composite endpoint is the the composite of cardiovascular death or heart faliure re-hospitalization within 12 months.
Time Frame	12 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set (FAS) consisted of randomized patients who had received at least one dose of study drug.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Measured Values

	Aliskiren	**Placebo**
Number of Participants Analyzed [units: participants]	**808**	**807**
Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 12 Months [units: Participants]		
Secondary Composite Endpoint	**283**	**301**
Cardiovascular death	**126**	**137**
Heart faliure re-hospitalization	**212**	**224**

No statistical analysis provided for Time to Event Analysis: Number of Patients Experienced the First Confirmed Occurrence of Either Cardiovascular Death or Heart Failure (HF) Re-hospitalization Within 12 Months

3. Secondary: Change From Baseline in the Clinical Summary Score to 1 Month, 6 Months and 12 Months [Time Frame: Baseline, 1 months, 6 months and 12 months]

Measure Type	Secondary
Measure Title	Change From Baseline in the Clinical Summary Score to 1 Month, 6 Months and 12 Months
Measure Description	Symptom reduction and reduction in physical limitations was assessed using the clinical summary score of the Kansas City Cardiomyopathy Questionnaire (KCCQ). The KCCQ is a self-administered questionnaire and contains 23 items, covering physical function, clinical symptoms, social function, self-efficacy and knowledge, and Health-Related Quality

	of Life (QoL), including limitations, frequency, bother, change in condition, understanding, levels of enjoyment and satisfaction. Each scale score was calculated as the mean of its item scores and transformed to a 0–100 scale, with higher score indicating higher level of functioning. A score of 100 represents perfect health whereas a score of 0 represents death. A positive change in score from baseline indicates an improvement.
Time Frame	Baseline, 1 months, 6 months and 12 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set included all randomized patients who had taken at least one dose of drug. 'n' in each category indicates patients with assessable data both at baseline and corresponding time points.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Measured Values

	Aliskiren	**Placebo**
Number of Participants Analyzed [units: participants]	**808**	**807**
Change From Baseline in the Clinical Summary Score to 1 Month, 6 Months and 12 Months [units: units on a scale] Least Squares Mean (Standard Error)		
1 Month (n= 574, 571)	**24.13 (0.903)**	**23.58 (0.908)**
6 Months (n= 485, 474)	**26.54 (1.004)**	**24.51 (1.016)**
12 Months (n= 241, 230)	**24.82 (1.268)**	**24.70 (1.291)**

No statistical analysis provided for Change From Baseline in the Clinical Summary Score to 1 Month, 6 Months and 12 Months

4. Secondary: Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 6 Months [Time Frame: 6 months]

Measure Type	Secondary
Measure Title	Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 6 Months
Measure Description	A cardiovascular event defined as CV death, heart faliure re-hospitalization, non-fatal myocardial infarction (MI), nonfatal stroke, sudden death with resuscitation.
Time Frame	6 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set included all randomized patients who had taken at least one dose of drug.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Measured Values

	Aliskiren	Placebo
Number of Participants Analyzed [units: participants]	**808**	**807**
Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 6 Months [units: Participants]		
Cardiovascular event	**209**	**233**
Cardiovascular death	**77**	**85**
Heart faliure re-hospitalization	**153**	**166**
All-cause myocardial infarction	**14**	**23**
Fatal myocardial infarction	**2**	**6**
Non-fatal myocardial infarction	**12**	**22**
All-cause stroke	**13**	**22**
Fatal stroke	**6**	**4**
Non-fatal stroke	**13**	**22**
Resuscitated sudden death	**3**	**8**

No statistical analysis provided for Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 6 Months

5. Secondary: Time to Event Analysis: Number of Patients With All-cause Mortality Hospitalized for an AHF Event Within 12 Months [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Time to Event Analysis: Number of Patients With All-cause Mortality Hospitalized for an AHF Event Within 12 Months
Measure Description	No text entered.
Time Frame	12 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full ananlysis set included all randomized patients who had at least one dose of study drug.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who

	could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Measured Values

	Aliskiren	Placebo
Number of Participants Analyzed [units: participants]	**808**	**807**
Time to Event Analysis: Number of Patients With All-cause Mortality Hospitalized for an AHF Event Within 12 Months [units: Participants]	**144**	**148**

No statistical analysis provided for Time to Event Analysis: Number of Patients With All-cause Mortality Hospitalized for an AHF Event Within 12 Months

6. Secondary: Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP) Level at 1 Month, 6 Months, and 12 Months [Time Frame: Baseline, 1 month, 6 months and 12 months]

Measure Type	Secondary
Measure Title	Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP) Level at 1 Month, 6 Months, and 12 Months
Measure Description	The reported Least square means, and Confidential Interval were from a repeated measures model on log transformed NT-proBNP data containing treatment, visit, and region as factors, log baseline NT-proBNP as a continuous covariate and treatment by visit and visit by log baseline NT-proBNP as interaction terms.
Time Frame	Baseline, 1 month, 6 months and 12 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set included all randomized patients who had taken at least one dose of study drug. 'n' in each category indicates patients with assessable date at baseline and each corresponding time point.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Measured Values

	Aliskiren	Placebo
Number of Participants Analyzed [units: participants]	**808**	**807**
Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP) Level at 1 Month, 6 Months, and 12 Months [units: pg/mL] Least Squares Mean (95% Confidence Interval)		
Month 1 (n= 669, 675)	**0.86**	**0.95**

	(0.81 to 0.91)	**(0.90 to 1.00)**
Month 6 (n= 569, 556)	**0.64 (0.59 to 0.70)**	**0.76 (0.70 to 0.82)**
Month 12 (n=447, 425)	**0.62 (0.56 to 0.68)**	**0.74 (0.67 to 0.82)**

No statistical analysis provided for Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP) Level at 1 Month, 6 Months, and 12 Months

7. Secondary: Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 12 Months [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 12 Months
Measure Description	A cardiovascular event defined as CV death, heart faliure re-hospitalization, non-fatal myocardial infarction (MI), nonfatal stroke, sudden death with resuscitation.
Time Frame	12 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set included all randomized patients who had taken at least one dose of study drug.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Measured Values

	Aliskiren	**Placebo**
Number of Participants Analyzed [units: participants]	**808**	**807**
Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 12 Months [units: Participants]		
Cardiovascular event	**293**	**321**
Cardiovascular death	**126**	**137**
Heart faliure re-hospitalization	**212**	**224**
All-cause myocardial infarction	**18**	**38**

Fatal myocardial infarction	**4**	**12**
Non-fatal myocardial infarction	**16**	**36**
All-cause stroke	**18**	**27**
Fatal stroke	**6**	**7**
Non-fatal stroke	**18**	**27**
Resuscitated sudden death	**5**	**10**

No statistical analysis provided for Time to Event Analysis: Number of Patients With First Cardiovascular (CV) Event Hospitalized for an Acute Heart Faliure (AHF) Event Within 12 Months

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Serious Adverse Events

	Aliskiren	Placebo
Total, serious adverse events		
# participants affected / at risk	**421/808 (52.10%)**	**435/810 (53.70%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**6/808 (0.74%)**	**5/810 (0.62%)**
Haemorrhagic disorder † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Hilar lymphadenopathy † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Jaundice acholuric † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Leukocytosis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Lymphadenopathy † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Splenic infarction † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Thrombocytopenia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Cardiac disorders		

Acute coronary syndrome † 1		
# participants affected / at risk	**3/808 (0.37%)**	**3/810 (0.37%)**
Acute left ventricular failure † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Acute myocardial infarction † 1		
# participants affected / at risk	**9/808 (1.11%)**	**15/810 (1.85%)**
Angina pectoris † 1		
# participants affected / at risk	**9/808 (1.11%)**	**10/810 (1.23%)**
Angina unstable † 1		
# participants affected / at risk	**7/808 (0.87%)**	**6/810 (0.74%)**
Aortic valve incompetence † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Arrhythmia † 1		
# participants affected / at risk	**3/808 (0.37%)**	**3/810 (0.37%)**
Arrhythmia supraventricular † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Arteriospasm coronary † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Atrial fibrillation † 1		
# participants affected / at risk	**14/808 (1.73%)**	**16/810 (1.98%)**
Atrial flutter † 1		
# participants affected / at risk	**3/808 (0.37%)**	**2/810 (0.25%)**
Atrial tachycardia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Atrioventricular block complete † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
Bradyarrhythmia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Bradycardia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**2/810 (0.25%)**
Cardiac arrest † 1		
# participants affected / at risk	**11/808 (1.36%)**	**14/810 (1.73%)**
Cardiac failure † 1		
# participants affected / at risk	**147/808 (18.19%)**	**155/810 (19.14%)**
Cardiac failure acute † 1		
# participants affected / at risk	**58/808 (7.18%)**	**60/810 (7.41%)**
Cardiac failure chronic † 1		
# participants affected / at risk	**50/808 (6.19%)**	**62/810 (7.65%)**
Cardiac failure congestive † 1		
# participants affected / at risk	**21/808 (2.60%)**	**31/810 (3.83%)**
Cardiac tamponade † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Cardio-respiratory arrest † 1		
# participants affected / at risk	**7/808 (0.87%)**	**3/810 (0.37%)**

Cardiogenic shock † 1		
# participants affected / at risk	**7/808 (0.87%)**	**6/810 (0.74%)**
Cardiomyopathy † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Cardiopulmonary failure † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
Cardiorenal syndrome † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Congestive cardiomyopathy † 1		
# participants affected / at risk	**2/808 (0.25%)**	**2/810 (0.25%)**
Coronary artery disease † 1		
# participants affected / at risk	**4/808 (0.50%)**	**2/810 (0.25%)**
Heart valve incompetence † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Ischaemic cardiomyopathy † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Left ventricular dysfunction † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Low cardiac output syndrome † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Myocardial fibrosis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Myocardial infarction † 1		
# participants affected / at risk	**11/808 (1.36%)**	**11/810 (1.36%)**
Myocardial ischaemia † 1		
# participants affected / at risk	**3/808 (0.37%)**	**3/810 (0.37%)**
Palpitations † 1		
# participants affected / at risk	**2/808 (0.25%)**	**2/810 (0.25%)**
Pericardial effusion † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Pulseless electrical activity † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Sick sinus syndrome † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Supraventricular tachycardia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Tachyarrhythmia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Tachycardia † 1		
# participants affected / at risk	**3/808 (0.37%)**	**1/810 (0.12%)**
Ventricular arrhythmia † 1		
# participants affected / at risk	**2/808 (0.25%)**	**4/810 (0.49%)**
Ventricular dysfunction † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**

Ventricular extrasystoles † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Ventricular fibrillation † 1		
# participants affected / at risk	**4/808 (0.50%)**	**5/810 (0.62%)**
Ventricular tachycardia † 1		
# participants affected / at risk	**10/808 (1.24%)**	**6/810 (0.74%)**
Ear and labyrinth disorders		
Vertigo † 1		
# participants affected / at risk	**4/808 (0.50%)**	**2/810 (0.25%)**
Eye disorders		
Cataract † 1		
# participants affected / at risk	**3/808 (0.37%)**	**0/810 (0.00%)**
Eye haemorrhage † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Glaucoma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Retinal detachment † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Retinal haemorrhage † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Retinal vein occlusion † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Gastrointestinal disorders		
Abdominal pain † 1		
# participants affected / at risk	**3/808 (0.37%)**	**4/810 (0.49%)**
Abdominal pain upper † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Ascites † 1		
# participants affected / at risk	**0/808 (0.00%)**	**4/810 (0.49%)**
Colonic polyp † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Constipation † 1		
# participants affected / at risk	**2/808 (0.25%)**	**0/810 (0.00%)**
Diarrhoea † 1		
# participants affected / at risk	**2/808 (0.25%)**	**3/810 (0.37%)**
Diverticular perforation † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Diverticulum intestinal † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Duodenal ulcer haemorrhage † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Dyspepsia † 1		
# participants affected / at risk	**2/808 (0.25%)**	**2/810 (0.25%)**
Enteritis † 1		

# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Enterocolitis † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Gastritis † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Gastrointestinal haemorrhage † 1		
# participants affected / at risk	1/808 (0.12%)	5/810 (0.62%)
Gingival bleeding † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Haemorrhoidal haemorrhage † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Haemorrhoids † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Hiatus hernia † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Inguinal hernia † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Intestinal obstruction † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Intestinal polyp † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Lower gastrointestinal haemorrhage † 1		
# participants affected / at risk	0/808 (0.00%)	2/810 (0.25%)
Nausea † 1		
# participants affected / at risk	8/808 (0.99%)	3/810 (0.37%)
Pancreatitis acute † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Rectal haemorrhage † 1		
# participants affected / at risk	0/808 (0.00%)	2/810 (0.25%)
Small intestinal haemorrhage † 1		
# participants affected / at risk	0/808 (0.00%)	2/810 (0.25%)
Small intestinal obstruction † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Tongue oedema † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Umbilical hernia, obstructive † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Upper gastrointestinal haemorrhage † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Vomiting † 1		
# participants affected / at risk	5/808 (0.62%)	2/810 (0.25%)
General disorders		
Asthenia † 1		
# participants affected / at risk	1/808 (0.12%)	3/810 (0.37%)

Cardiac death † 1		
# participants affected / at risk	**3/808 (0.37%)**	**3/810 (0.37%)**
Chest discomfort † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Chest pain † 1		
# participants affected / at risk	**6/808 (0.74%)**	**0/810 (0.00%)**
Death † 1		
# participants affected / at risk	**21/808 (2.60%)**	**25/810 (3.09%)**
Device breakage † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Device lead issue † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Device malfunction † 1		
# participants affected / at risk	**1/808 (0.12%)**	**4/810 (0.49%)**
Drug intolerance † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Fatigue † 1		
# participants affected / at risk	**2/808 (0.25%)**	**4/810 (0.49%)**
General physical health deterioration † 1		
# participants affected / at risk	**2/808 (0.25%)**	**3/810 (0.37%)**
Generalised oedema † 1		
# participants affected / at risk	**2/808 (0.25%)**	**2/810 (0.25%)**
Implant site haematoma † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Medical device complication † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Metaplasia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Multi-organ failure † 1		
# participants affected / at risk	**1/808 (0.12%)**	**3/810 (0.37%)**
Necrosis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Non-cardiac chest pain † 1		
# participants affected / at risk	**7/808 (0.87%)**	**1/810 (0.12%)**
Oedema peripheral † 1		
# participants affected / at risk	**3/808 (0.37%)**	**6/810 (0.74%)**
Pain † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Pyrexia † 1		
# participants affected / at risk	**2/808 (0.25%)**	**2/810 (0.25%)**
Soft tissue inflammation † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Stent malfunction † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**

Sudden cardiac death † 1		
# participants affected / at risk	**5/808 (0.62%)**	**7/810 (0.86%)**
Sudden death † 1		
# participants affected / at risk	**9/808 (1.11%)**	**5/810 (0.62%)**
Hepatobiliary disorders		
Acute hepatic failure † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Cholecystitis † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
Cholelithiasis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**2/810 (0.25%)**
Hepatic cirrhosis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Hepatic cyst † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Hepatitis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Hepatitis cholestatic † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Hepatomegaly † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Hepatorenal syndrome † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Ischaemic hepatitis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Immune system disorders		
Heart transplant rejection † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Infections and infestations		
Abscess limb † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Anal abscess † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Appendicitis † 1		
# participants affected / at risk	**2/808 (0.25%)**	**0/810 (0.00%)**
Arthritis infective † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Bacteraemia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Bronchiolitis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Bronchitis † 1		
# participants affected / at risk	**6/808 (0.74%)**	**6/810 (0.74%)**
Bronchitis bacterial † 1		

# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Bronchopneumonia † 1		
# participants affected / at risk	3/808 (0.37%)	4/810 (0.49%)
Cellulitis † 1		
# participants affected / at risk	1/808 (0.12%)	3/810 (0.37%)
Citrobacter sepsis † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Clostridium difficile colitis † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Device related infection † 1		
# participants affected / at risk	1/808 (0.12%)	4/810 (0.49%)
Endocarditis † 1		
# participants affected / at risk	0/808 (0.00%)	3/810 (0.37%)
Erysipelas † 1		
# participants affected / at risk	2/808 (0.25%)	1/810 (0.12%)
Gangrene † 1		
# participants affected / at risk	2/808 (0.25%)	3/810 (0.37%)
Gastroenteritis † 1		
# participants affected / at risk	2/808 (0.25%)	3/810 (0.37%)
Gastroenteritis norovirus † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Gastrointestinal viral infection † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Hepatitis B † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Infective exacerbation of chronic obstructive airways disease † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Influenza † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Liver abscess † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Lobar pneumonia † 1		
# participants affected / at risk	1/808 (0.12%)	2/810 (0.25%)
Localised infection † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Lower respiratory tract infection † 1		
# participants affected / at risk	3/808 (0.37%)	2/810 (0.25%)
Lung infection pseudomonal † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Orchitis † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Osteomyelitis † 1		
# participants affected / at risk	1/808 (0.12%)	2/810 (0.25%)
Osteomyelitis acute † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)

Paronychia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Peritonitis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Pneumonia † 1		
# participants affected / at risk	**25/808 (3.09%)**	**27/810 (3.33%)**
Pneumonia legionella † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Postoperative wound infection † 1		
# participants affected / at risk	**1/808 (0.12%)**	**2/810 (0.25%)**
Pseudomembranous colitis † 1		
# participants affected / at risk	**2/808 (0.25%)**	**0/810 (0.00%)**
Pseudomonas bronchitis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Pulmonary sepsis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Respiratory tract infection † 1		
# participants affected / at risk	**3/808 (0.37%)**	**2/810 (0.25%)**
Sepsis † 1		
# participants affected / at risk	**8/808 (0.99%)**	**5/810 (0.62%)**
Septic shock † 1		
# participants affected / at risk	**5/808 (0.62%)**	**5/810 (0.62%)**
Skin infection † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Staphylococcal sepsis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Subacute endocarditis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Upper respiratory tract infection † 1		
# participants affected / at risk	**1/808 (0.12%)**	**4/810 (0.49%)**
Urinary tract infection † 1		
# participants affected / at risk	**4/808 (0.50%)**	**5/810 (0.62%)**
Urosepsis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Viral infection † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Wound infection pseudomonas † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Injury, poisoning and procedural complications		
Accidental overdose † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Ankle fracture † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Brain herniation † 1		

# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Contusion † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Dermatitis artefacta † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Electric shock † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Extradural haematoma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Facial bones fracture † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Fall † 1		
# participants affected / at risk	**0/808 (0.00%)**	**3/810 (0.37%)**
Femoral neck fracture † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Femur fracture † 1		
# participants affected / at risk	**4/808 (0.50%)**	**1/810 (0.12%)**
Foot fracture † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Hand fracture † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Head injury † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Hip fracture † 1		
# participants affected / at risk	**1/808 (0.12%)**	**2/810 (0.25%)**
Humerus fracture † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
In-stent arterial restenosis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Laceration † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Lower limb fracture † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Optic nerve injury † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Pelvic fracture † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Pneumothorax traumatic † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Post procedural haematoma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Procedural haemorrhage † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Pubis fracture † 1		

# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Rib fracture † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Road traffic accident † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Spinal compression fracture † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Splenic rupture † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Subcutaneous haematoma † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Subdural haematoma † 1		
# participants affected / at risk	2/808 (0.25%)	0/810 (0.00%)
Thermal burn † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Tongue injury † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Toxicity to various agents † 1		
# participants affected / at risk	2/808 (0.25%)	1/810 (0.12%)
Traumatic haematoma † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Vascular graft occlusion † 1		
# participants affected / at risk	0/808 (0.00%)	2/810 (0.25%)
Vascular graft thrombosis † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Wound necrosis † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Investigations		
Activated partial thromboplastin time prolonged † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Anticoagulation drug level above therapeutic † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Blood creatinine increased † 1		
# participants affected / at risk	3/808 (0.37%)	1/810 (0.12%)
Blood osmolarity decreased † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Blood potassium increased † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Coagulation test abnormal † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Ejection fraction decreased † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Haemoglobin decreased † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)

International normalised ratio increased † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
Renal function test abnormal † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Transaminases increased † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Urine output decreased † 1		
# participants affected / at risk	**0/808 (0.00%)**	**3/810 (0.37%)**
Weight increased † 1		
# participants affected / at risk	**1/808 (0.12%)**	**3/810 (0.37%)**
Metabolism and nutrition disorders		
Decreased appetite † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Dehydration † 1		
# participants affected / at risk	**3/808 (0.37%)**	**4/810 (0.49%)**
Diabetes mellitus † 1		
# participants affected / at risk	**1/808 (0.12%)**	**3/810 (0.37%)**
Diabetes mellitus inadequate control † 1		
# participants affected / at risk	**3/808 (0.37%)**	**3/810 (0.37%)**
Diabetic ketoacidosis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Electrolyte imbalance † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Failure to thrive † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Fluid intake reduced † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Fluid overload † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Gout † 1		
# participants affected / at risk	**2/808 (0.25%)**	**3/810 (0.37%)**
Hyperglycaemia † 1		
# participants affected / at risk	**2/808 (0.25%)**	**3/810 (0.37%)**
Hyperkalaemia † 1		
# participants affected / at risk	**12/808 (1.49%)**	**12/810 (1.48%)**
Hyperosmolar state † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Hypervolaemia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Hypocholesterolaemia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Hypoglycaemia † 1		
# participants affected / at risk	**7/808 (0.87%)**	**2/810 (0.25%)**
Hypokalaemia † 1		

# participants affected / at risk	6/808 (0.74%)	6/810 (0.74%)
Hyponatraemia † 1		
# participants affected / at risk	4/808 (0.50%)	5/810 (0.62%)
Hypovolaemia † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Type 2 diabetes mellitus † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Arthritis † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Back pain † 1		
# participants affected / at risk	1/808 (0.12%)	2/810 (0.25%)
Bursitis † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Costochondritis † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Fasciitis † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Flank pain † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Intervertebral disc protrusion † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Joint effusion † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Muscle haemorrhage † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Muscular weakness † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Musculoskeletal chest pain † 1		
# participants affected / at risk	2/808 (0.25%)	2/810 (0.25%)
Pain in extremity † 1		
# participants affected / at risk	2/808 (0.25%)	1/810 (0.12%)
Rotator cuff syndrome † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Soft tissue necrosis † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Benign bone neoplasm † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Bladder neoplasm † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Bronchial carcinoma † 1		

# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Choroid melanoma † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Chronic lymphocytic leukaemia † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Colon cancer † 1		
# participants affected / at risk	2/808 (0.25%)	1/810 (0.12%)
Colorectal cancer † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Hepatic neoplasm † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Hepatobiliary neoplasm † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Lipoma † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Liposarcoma † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Lung adenocarcinoma † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Lung neoplasm malignant † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Lung squamous cell carcinoma stage unspecified † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Multiple myeloma † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Non-small cell lung cancer metastatic † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Oesophageal neoplasm † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Ovarian cancer † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Prostate cancer † 1		
# participants affected / at risk	1/808 (0.12%)	3/810 (0.37%)
Prostate cancer metastatic † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Renal cancer † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Uterine leiomyoma † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Nervous system disorders		
Anterior spinal artery syndrome † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Aphasia † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)

Burning sensation † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Cerebellar infarction † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Cerebral haematoma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Cerebral infarction † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Cerebral ischaemia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Cerebrovascular accident † 1		
# participants affected / at risk	**9/808 (1.11%)**	**15/810 (1.85%)**
Coma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Convulsion † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Diabetic hyperglycaemic coma † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Diabetic neuropathy † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Dizziness † 1		
# participants affected / at risk	**4/808 (0.50%)**	**0/810 (0.00%)**
Dysarthria † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Embolic stroke † 1		
# participants affected / at risk	**2/808 (0.25%)**	**0/810 (0.00%)**
Epilepsy † 1		
# participants affected / at risk	**2/808 (0.25%)**	**0/810 (0.00%)**
Haemorrhagic stroke † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Hemiparesis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**3/810 (0.37%)**
Hypokinesia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Intracranial haematoma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Ischaemic stroke † 1		
# participants affected / at risk	**5/808 (0.62%)**	**9/810 (1.11%)**
Loss of consciousness † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Metabolic encephalopathy † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Myasthenia gravis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**

Myasthenia gravis crisis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Neuropathy peripheral † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Presyncope † 1		
# participants affected / at risk	**3/808 (0.37%)**	**4/810 (0.49%)**
Sensory disturbance † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Somnolence † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
Subarachnoid haemorrhage † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Syncope † 1		
# participants affected / at risk	**11/808 (1.36%)**	**13/810 (1.60%)**
Transient ischaemic attack † 1		
# participants affected / at risk	**0/808 (0.00%)**	**3/810 (0.37%)**
Trigeminal neuralgia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Unresponsive to stimuli † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Uraemic encephalopathy † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Vertebrobasilar insufficiency † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Psychiatric disorders		
Abnormal behaviour † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Alcohol abuse † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Anxiety † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Confusional state † 1		
# participants affected / at risk	**2/808 (0.25%)**	**0/810 (0.00%)**
Depression † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Depression suicidal † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Disorientation † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Insomnia † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Mental status changes † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Restlessness † 1		

# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Screaming † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Suicidal ideation † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Renal and urinary disorders		
Acute prerenal failure † 1		
# participants affected / at risk	1/808 (0.12%)	1/810 (0.12%)
Anuria † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Bladder tamponade † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Haematuria † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Nephropathy † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Obstructive uropathy † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Polyuria † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Renal artery stenosis † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Renal artery thrombosis † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Renal failure † 1		
# participants affected / at risk	6/808 (0.74%)	8/810 (0.99%)
Renal failure acute † 1		
# participants affected / at risk	20/808 (2.48%)	12/810 (1.48%)
Renal failure chronic † 1		
# participants affected / at risk	1/808 (0.12%)	3/810 (0.37%)
Renal impairment † 1		
# participants affected / at risk	5/808 (0.62%)	4/810 (0.49%)
Urinary retention † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia † 1		
# participants affected / at risk	2/808 (0.25%)	0/810 (0.00%)
Menorrhagia † 1		
# participants affected / at risk	1/808 (0.12%)	0/810 (0.00%)
Ovarian cyst † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Scrotal oedema † 1		
# participants affected / at risk	0/808 (0.00%)	1/810 (0.12%)
Respiratory, thoracic and mediastinal disorders		

Acute pulmonary oedema † 1		
# participants affected / at risk	**7/808 (0.87%)**	**4/810 (0.49%)**
Acute respiratory distress syndrome † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Acute respiratory failure † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
Asthma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Atelectasis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Bronchiectasis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Bronchitis chronic † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Bronchospasm † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Chronic obstructive pulmonary disease † 1		
# participants affected / at risk	**13/808 (1.61%)**	**5/810 (0.62%)**
Cough † 1		
# participants affected / at risk	**2/808 (0.25%)**	**2/810 (0.25%)**
Dyspnoea † 1		
# participants affected / at risk	**20/808 (2.48%)**	**18/810 (2.22%)**
Dyspnoea at rest † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Dyspnoea paroxysmal nocturnal † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Epistaxis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Haemoptysis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**3/810 (0.37%)**
Interstitial lung disease † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Lung disorder † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Obstructive airways disorder † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Pleural effusion † 1		
# participants affected / at risk	**2/808 (0.25%)**	**2/810 (0.25%)**
Pleurisy † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Pneumonitis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Pneumothorax † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**

Productive cough † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Pulmonary artery thrombosis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Pulmonary congestion † 1		
# participants affected / at risk	**1/808 (0.12%)**	**2/810 (0.25%)**
Pulmonary embolism † 1		
# participants affected / at risk	**5/808 (0.62%)**	**5/810 (0.62%)**
Pulmonary oedema † 1		
# participants affected / at risk	**4/808 (0.50%)**	**8/810 (0.99%)**
Rales † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Respiratory arrest † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Respiratory distress † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Respiratory failure † 1		
# participants affected / at risk	**6/808 (0.74%)**	**5/810 (0.62%)**
Wheezing † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Skin and subcutaneous tissue disorders		
Dermatitis † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Diabetic foot † 1		
# participants affected / at risk	**1/808 (0.12%)**	**2/810 (0.25%)**
Hyperhidrosis † 1		
# participants affected / at risk	**2/808 (0.25%)**	**0/810 (0.00%)**
Skin exfoliation † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Skin necrosis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Skin ulcer † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Skin ulcer haemorrhage † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Swelling face † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Surgical and medical procedures		
Gastric bypass † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Vascular disorders		
Circulatory collapse † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Deep vein thrombosis † 1		

# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Extremity necrosis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Haematoma † 1		
# participants affected / at risk	**1/808 (0.12%)**	**1/810 (0.12%)**
Hypertension † 1		
# participants affected / at risk	**2/808 (0.25%)**	**3/810 (0.37%)**
Hypertensive crisis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**3/810 (0.37%)**
Hypertensive emergency † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Hypotension † 1		
# participants affected / at risk	**24/808 (2.97%)**	**16/810 (1.98%)**
Intra-abdominal haematoma † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**
Orthostatic hypotension † 1		
# participants affected / at risk	**0/808 (0.00%)**	**2/810 (0.25%)**
Peripheral arterial occlusive disease † 1		
# participants affected / at risk	**4/808 (0.50%)**	**2/810 (0.25%)**
Peripheral ischaemia † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Peripheral vascular disorder † 1		
# participants affected / at risk	**2/808 (0.25%)**	**1/810 (0.12%)**
Phlebitis † 1		
# participants affected / at risk	**1/808 (0.12%)**	**0/810 (0.00%)**
Venous haemorrhage † 1		
# participants affected / at risk	**0/808 (0.00%)**	**1/810 (0.12%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Aliskiren	Randomized patients in this arm received, Aliskiren 150 mg once daily for 2 weeks. From week 2 upto 6 months , patients who could tolerate study medication were up-titrated to aliskiren 300 mg once daliy.
Placebo	Randomized patients in this arm received matching placebo of Aliskiren. At week 2, Patients who could tolerate study medication were up-titrated to matching placebo of 300 mg aliskiren.

Other Adverse Events

	Aliskiren	Placebo
Total, other (not including serious) adverse events		
# participants affected / at risk	**367/808 (45.42%)**	**333/810 (41.11%)**
Gastrointestinal disorders		
Diarrhoea † 1		
# participants affected / at risk	**49/808 (6.06%)**	**36/810 (4.44%)**
Metabolism and nutrition disorders		
Hyperkalaemia † 1		
# participants affected / at risk	**155/808 (19.18%)**	**128/810 (15.80%)**
Hypokalaemia † 1		
# participants affected / at risk	**42/808 (5.20%)**	**53/810 (6.54%)**
Nervous system disorders		
Dizziness † 1		
# participants affected / at risk	**35/808 (4.33%)**	**43/810 (5.31%)**
Renal and urinary disorders		
Renal impairment † 1		
# participants affected / at risk	**47/808 (5.82%)**	**33/810 (4.07%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**59/808 (7.30%)**	**53/810 (6.54%)**
Vascular disorders		
Hypotension † 1		
# participants affected / at risk	**117/808 (14.48%)**	**83/810 (10.25%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require

changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial or disclosure of trial results in their entirety.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300
e-mail: trialandresults.registries@novartis.com

No publications provided by Novartis

Publications automatically indexed to this study:

Gheorghiade M, Böhm M, Greene SJ, Fonarow GC, Lewis EF, Zannad F, Solomon SD, Baschiera F, Botha J, Hua TA, Gimpelewicz CR, Jaumont X, Lesogor A, Maggioni AP; ASTRONAUT Investigators and Coordinators. Effect of aliskiren on postdischarge mortality and heart failure readmissions among patients hospitalized for heart failure: the ASTRONAUT randomized trial. JAMA. 2013 Mar 20;309(11):1125-35. doi: 10.1001/jama.2013.1954. Erratum in: JAMA. 2013 Apr 10;309(14):1461.

Gheorghiade M, Albaghdadi M, Zannad F, Fonarow GC, Böhm M, Gimpelewicz C, Botha J, Moores S, Lewis EF, Rattunde H, Maggioni A; ASTRONAUT investigators and study coordinators. Rationale and design of the multicentre, randomized, double-blind, placebo-controlled Aliskiren Trial on Acute Heart Failure Outcomes (ASTRONAUT). Eur J Heart Fail. 2011 Jan;13(1):100-6. doi: 10.1093/eurjhf/hfq209. Epub 2010 Nov 30.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00894387 History of Changes
Other Study ID Numbers:	**CSPP100A2368** 2009-010236-18 (EudraCT Number)
Study First Received:	May 5, 2009
Results First Received:	August 2, 2013
Last Updated:	October 15, 2013
Health Authority:	United States: Food and Drug Administration