A Study Testing the Effectiveness of Nesiritide in Patients With Acute Decompensated Heart Failure

This study has been completed.

Sponsor:
Scios, Inc.

Information provided by (Responsible Party):
Scios, Inc.

ClinicalTrials.gov Identifier:
NCT00475852

First received: May 18, 2007
Last updated: March 1, 2013
Last verified: March 2013
History of Changes

Results First Received: September 27, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Heart Decompensation
Interventions:	Drug: Nesiritide 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
Double-Blind, Placebo-Controlled, Multicenter Acute Study of Clinical Effectiveness of Nesiritide in Subjects With Decompensated Heart Failure (ASCEND-HF)

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion:0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Participant Flow: Overall Study

	Nesiritide	**Placebo**
STARTED	**3564**	**3577**
COMPLETED	**3047**	**3029**
NOT COMPLETED	**517**	**548**
Death	**444**	**456**
Withdrawal by Subject	**19**	**24**

Lost to Follow-up	54	68

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
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion:0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Total	Total of all reporting groups

Baseline Measures

	Nesiritide	Placebo	Total
Number of Participants [units: participants]	3564	3577	7141
Age [units: participants]			
<=18 years	4	2	6
Between 18 and 65 years	1572	1597	3169
>=65 years	1988	1978	3966
Age [units: years] Mean (Standard Deviation)	65.5 (14.09)	65.4 (14.20)	65.5 (14.14)
Age, Customized [units: participants]			
<=64	1576	1599	3175
65-74	938	901	1839
>=75	1050	1077	2127
Gender [units: participants]			
Female	1197	1247	2444
Male	2367	2330	4697
Region of Enrollment [units: participants]			
ARG	108	108	216
AUS	18	16	34
BGR	35	32	67
BRA	73	77	150
CAN	240	236	476
CHL	25	25	50
CHN	154	160	314
COL	15	15	30
DEU	3	3	6
FRA	51	47	98

GRC	24	24	48
IND	499	502	1001
ISR	38	40	78
ITA	36	36	72
KOR	74	74	148
LTU	48	49	97
MEX	108	111	219
MYS	38	37	75
NLD	71	70	141
NOR	27	29	56
NZL	7	7	14
POL	134	133	267
ROU	24	28	52
RUS	148	147	295
SGP	27	26	53
SWE	2	3	5
THA	23	23	46
TWN	38	39	77
UKR	97	92	189
USA	1379	1388	2767
Baseline BMI [units: kg/cm2] Mean (Standard Deviation)	**28.9 (7.86)**	**29.1 (7.77)**	**29.0 (7.81)**

Outcome Measures

Hide All Outcome Measures

1. Primary: Composite of Rehospitalization Due to Heart Failure and All-Cause Mortality [Time Frame: Randomization to Day 30]

Measure Type	Primary
Measure Title	Composite of Rehospitalization Due to Heart Failure and All-Cause Mortality
Measure Description	No text entered.
Time Frame	Randomization to Day 30
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 141 and 164 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	Placebo

Number of Participants Analyzed [units: participants]	**3423**	**3413**
Composite of Rehospitalization Due to Heart Failure and All-Cause Mortality [units: Participants]	**321**	**345**

Statistical Analysis 1 for Composite of Rehospitalization Due to Heart Failure and All-Cause Mortality

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.313
Risk Difference (RD) [4]	-0.7
95% Confidence Interval	-2.1 to 0.7

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Stratified by geographical region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

2. Primary: Dyspnea Self-Assessment at 6 Hours After Initiation of Study Drug [Time Frame: 6 hours after initiation of study drug]

Measure Type	Primary
Measure Title	Dyspnea Self-Assessment at 6 Hours After Initiation of Study Drug
Measure Description	Dyspnea symptoms were measured by patient self-assessed Likert scale at 6 hours after study drug initiation.The Likert scale is a 7-point ordinal categorical scale (the 7 categories are markedly better, moderately better, minimally better, unchanged, minimally worse, moderately worse, and markedly worse.)
Time Frame	6 hours after initiation of study drug
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 148 and 133 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3416**	**3444**
Dyspnea Self-Assessment at 6 Hours After Initiation of Study Drug [units: Participants]		

Markedly Better	**513**	**460**
Moderately Better	**1007**	**989**
Minimally Better	**1119**	**1174**
No Change	**692**	**748**
Minimally Worse	**39**	**40**
Moderately Worse	**12**	**13**
Markedly Worse	**34**	**20**

Statistical Analysis 1 for Dyspnea Self-Assessment at 6 Hours After Initiation of Study Drug

Groups [1]	All groups
Method [2]	Van Elteren test
P Value [3]	0.030

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

3. Primary: Dyspnea Self-Assessment at 24 Hours After Initiation of Study Drug [Time Frame: 24 hours after study drug initiation]

Measure Type	Primary
Measure Title	Dyspnea Self-Assessment at 24 Hours After Initiation of Study Drug
Measure Description	Dyspnea symptoms were measured by patient self-assessed Likert scale at 24 hours after study drug initiation. The Likert scale is a 7-point ordinal categorical scale (the 7 categories are markedly better, moderately better, minimally better, unchanged, minimally worse, moderately worse, and markedly worse.)
Time Frame	24 hours after study drug initiation
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 193 and 179 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3371**	**3398**
Dyspnea Self-Assessment at 24 Hours After Initiation of Study Drug [units: Participants]		

Markedly Better	**1025**	**935**
Moderately Better	**1274**	**1313**
Minimally Better	**716**	**751**
No Change	**291**	**323**
Minimally Worse	**27**	**36**
Moderately Worse	**7**	**15**
Markedly Worse	**31**	**25**

Statistical Analysis 1 for Dyspnea Self-Assessment at 24 Hours After Initiation of Study Drug

Groups [1]	All groups
Method [2]	Van Elteren test
P Value [3]	0.007

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

4. Secondary: Overall Well-Being Self-Assessment at 6 Hours After Initiation of Study Drug [Time Frame: 6 hours after study drug initiation]

Measure Type	Secondary
Measure Title	Overall Well-Being Self-Assessment at 6 Hours After Initiation of Study Drug
Measure Description	Overall well-being was measured by patient self-assessed Likert scale at 6 hours after study drug initiation. The Likert scale is a 7-point ordinal categorical scale (the 7 categories are markedly better, moderately better, minimally better, unchanged, minimally worse, moderately worse, and markedly worse.)
Time Frame	6 hours after study drug initiation
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 158 and 147 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3406**	**3430**
Overall Well-Being Self-Assessment at 6 Hours After Initiation of Study Drug [units: Participants]		

Markedly Better	**449**	**418**
Moderately Better	**962**	**965**
Minimally Better	**1154**	**1186**
No Change	**751**	**785**
Minimally Worse	**42**	**49**
Moderately Worse	**17**	**11**
Markedly Worse	**31**	**16**

Statistical Analysis 1 for Overall Well-Being Self-Assessment at 6 Hours After Initiation of Study Drug

Groups [1]	All groups
Method [2]	Van Elteren test
P Value [3]	0.318

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

5. Secondary: Overall Well-Being Self-Assessment at 24 Hours After Initiation of Study Drug [Time Frame: 24 hours after study drug initiation]

Measure Type	Secondary
Measure Title	Overall Well-Being Self-Assessment at 24 Hours After Initiation of Study Drug
Measure Description	Overall well-being was measured by patient self-assessed Likert scale at 24 hours after study drug initiation. The Likert scale is a 7-point ordinal categorical scale (the 7 categories are markedly better, moderately better, minimally better, unchanged, minimally worse, moderately worse, and markedly worse.)
Time Frame	24 hours after study drug initiation
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 200 and 194 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3364**	**3383**
Overall Well-Being Self-Assessment at 24 Hours After Initiation of Study Drug		

[units: Participants]		
Markedly Better	**913**	**843**
Moderately Better	**1297**	**1311**
Minimally Better	**761**	**798**
No Change	**310**	**331**
Minimally Worse	**31**	**52**
Moderately Worse	**16**	**22**
Markedly Worse	**36**	**26**

Statistical Analysis 1 for Overall Well-Being Self-Assessment at 24 Hours After Initiation of Study Drug

Groups [1]	All groups
Method [2]	Van Elteren test
P Value [3]	0.018

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

6. Secondary: Composite of Persistent or Worsening Heart Failure and All-Cause Mortality [Time Frame: Randomization to hospital discharge (up to Day 30)]

Measure Type	Secondary
Measure Title	Composite of Persistent or Worsening Heart Failure and All-Cause Mortality
Measure Description	Clinical manifestations of worsening or persistent decompensated heart failure were defined by at least one of the following: new, persistent or worsening: dyspnea, orthopnea, paroxysmal nocturnal dyspnea, edema, pulmonary basilar rales/crackles, jugular venous distension, renal hypoperfusion with no other apparent cause, or radiologic evidence of worsening heart failure. And was also defined by a new therapy specifically for the treatment of worsening or persistent decompensated heart failure.
Time Frame	Randomization to hospital discharge (up to Day 30)
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 105 and 115 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**

Number of Participants Analyzed [units: participants]	**3459**	**3462**
Composite of Persistent or Worsening Heart Failure and All-Cause Mortality [units: Participants]	**147**	**165**

Statistical Analysis 1 for Composite of Persistent or Worsening Heart Failure and All-Cause Mortality

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.295
Risk Difference (RD) [4]	-0.5
95% Confidence Interval	-1.5 to 0.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

7. Secondary: Number of Days Alive and Outside the Hospital [Time Frame: Randomization to Day 30]

Measure Type	Secondary
Measure Title	Number of Days Alive and Outside the Hospital
Measure Description	No text entered.
Time Frame	Randomization to Day 30
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 182 and 188 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3382**	**3389**
Number of Days Alive and Outside the Hospital [units: Days] Mean (Standard Deviation)	**20.9 (6.88)**	**20.7 (7.05)**

Statistical Analysis 1 for Number of Days Alive and Outside the Hospital

Groups [1]	All groups
Method [2]	ANOVA
P Value [3]	0.160
Mean Difference (Net) [4]	0.2
Standard Error of the mean	(0.17)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	This analysis excluded subjects who were lost to follow-up, or withdrawal of consent before Day 30, or whose Day 30 visit occurred prior to Day 30.

8. Secondary: Composite of Cardiovascular Rehospitalization and Cardiovascular Mortality [Time Frame: Randomization to Day 30]

Measure Type	Secondary
Measure Title	Composite of Cardiovascular Rehospitalization and Cardiovascular Mortality
Measure Description	No text entered.
Time Frame	Randomization to Day 30
Safety Issue	Yes

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.
The modified intent-to-treat (MITT) population consisted of all randomized patients who received any amount of study medication and was the primary analysis population for all efficacy endpoints. 141 and 162 patients in the nesiritide and placebo groups, respectively, were not MITT population eligible or didn't have outcome measure of interest.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3423**	**3415**
Composite of Cardiovascular Rehospitalization and Cardiovascular Mortality [units: Participants]	**372**	**402**

Statistical Analysis 1 for Composite of Cardiovascular Rehospitalization and Cardiovascular Mortality

Groups [1]	All groups

Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.238
Risk Difference (RD) [4]	-0.9
95% Confidence Interval	-2.4 to 0.6

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	For subjects with a Day 30 visit prior to Day 30, information from their Day 180 visit, if available, was used to impute the mortality and rehospitalization status at Day 30.

9. Other Pre-specified: All-Cause Mortality Through Day 30 [Time Frame: Randomization to Day 30]

Measure Type	Other Pre-specified
Measure Title	All-Cause Mortality Through Day 30
Measure Description	All deaths were adjudicated by an independent Clinical Events Committee.
Time Frame	Randomization to Day 30
Safety Issue	Yes

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.
The safety population consisted of all randomized patients who received any amount of study medication. For all safety analyses, patients were analyzed according to the treatment actually received. 66 and 68 patients in the nesiritide and placebo groups, respectively, were not included in the safety population.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3498**	**3509**
All-Cause Mortality Through Day 30 [units: Participants]	**126**	**141**

No statistical analysis provided for All-Cause Mortality Through Day 30

10. Other Pre-specified: All-Cause Mortality Through Day 180 [Time Frame: Randomization to Day 180]

Measure Type	Other Pre-specified
Measure Title	All-Cause Mortality Through Day 180

Measure Description	All deaths were adjudicated by an independent Clinical Events Committee.
Time Frame	Randomization to Day 180
Safety Issue	Yes

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.
The safety population consisted of all randomized patients who received any amount of study medication. For all safety analyses, patients were analyzed according to the treatment actually received. 66 and 68 patients in the nesiritide and placebo groups, respectively, were not included in the safety population.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3498**	**3509**
All-Cause Mortality Through Day 180 [units: Participants]	**429**	**447**

No statistical analysis provided for All-Cause Mortality Through Day 180

11. Other Pre-specified: Cardiovascular Mortality Through Day 30 [Time Frame: Randomization to Day 30]

Measure Type	Other Pre-specified
Measure Title	Cardiovascular Mortality Through Day 30
Measure Description	All deaths were adjudicated by an independent Clinical Events Committee (CEC) and the cardiovascular deaths were classified by the CEC based on the primary causes.
Time Frame	Randomization to Day 30
Safety Issue	Yes

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.
The safety population consisted of all randomized patients who received any amount of study medication. For all safety analyses, patients were analyzed according to the treatment actually received. 66 and 68 patients in the nesiritide and placebo groups, respectively, were not included in the safety population.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3498**	**3509**
Cardiovascular Mortality Through Day 30 [units: Participants]		
Total Cardiovascular Deaths	**112**	**124**

Worsening Heart Failure	**68**	**80**
Myocardial Infarction	**4**	**0**
Sudden Cardiac Death	**20**	**23**
Other Cardiovascular Cause	**11**	**10**
Presumed Cardiovascular Cause	**9**	**11**

No statistical analysis provided for Cardiovascular Mortality Through Day 30

12. Other Pre-specified: Number of Patients With Renal Impairment [Time Frame: Study drug initiation to Day 30]

Measure Type	Other Pre-specified
Measure Title	Number of Patients With Renal Impairment
Measure Description	Renal impairment was defined as a greater than 25% decrease from baseline in the Modification of Diet in Renal Disease calculated glomerular filtration rate.
Time Frame	Study drug initiation to Day 30
Safety Issue	Yes

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.
The safety population consisted of all randomized patients who received any amount of study medication. For all safety analyses, patients were analyzed according to the treatment actually received. 66 and 68 patients in the nesiritide and placebo groups, respectively, were not included in the safety population.

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion 0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Measured Values

	Nesiritide	**Placebo**
Number of Participants Analyzed [units: participants]	**3498**	**3509**
Number of Patients With Renal Impairment [units: Participants]	**1032**	**968**

Statistical Analysis 1 for Number of Patients With Renal Impairment

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.109
Odds Ratio (OR) [4]	1.09
95% Confidence Interval	0.98 to 1.21

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Controlled for region.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

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

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs
Placebo	Matching placebo infusion:0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Serious Adverse Events

	Nesiritide	Placebo
Total, serious adverse events		
# participants affected / at risk	**5/3498 (0.14%)**	**2/3509 (0.06%)**
Respiratory, thoracic and mediastinal disorders		
Pneumonia * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Pulmonary Embolism * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Skin and subcutaneous tissue disorders		
Angioedema * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Vascular disorders		
Hypotension * 1		
# participants affected / at risk	**0/3498 (0.00%)**	**1/3509 (0.03%)**
Ischaemic Stroke * 1		
# participants affected / at risk	**2/3498 (0.06%)**	**1/3509 (0.03%)**

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 13.0

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	0%

Reporting Groups

	Description
Nesiritide	0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Placebo	Matching placebo infusion:0.01 mcg/kg/min IV infusion (with or without 2 mcg/kg bolus) for 24 to 168 hrs

Other Adverse Events

	Nesiritide	Placebo
Total, other (not including serious) adverse events		
# participants affected / at risk	**366/3498 (10.46%)**	**364/3509 (10.37%)**
Blood and lymphatic system disorders		
Anaemia * 1		
# participants affected / at risk	**2/3498 (0.06%)**	**4/3509 (0.11%)**
Leukocytosis * 1		
# participants affected / at risk	**0/3498 (0.00%)**	**2/3509 (0.06%)**
Thrombocytopenia * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Cardiac disorders		
Aortic Valve Stenosis * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Arrhythmia Supraventricular * 1		
# participants affected / at risk	**6/3498 (0.17%)**	**4/3509 (0.11%)**
Atrial Fibrillation * 1		
# participants affected / at risk	**46/3498 (1.32%)**	**33/3509 (0.94%)**
Atrial Flutter * 1		
# participants affected / at risk	**3/3498 (0.09%)**	**2/3509 (0.06%)**
Atrial Septal Defect * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Atrial Tachycardia * 1		
# participants affected / at risk	**0/3498 (0.00%)**	**1/3509 (0.03%)**
Atrioventricular Block Complete * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**1/3509 (0.03%)**
Bradycardia * 1		
# participants affected / at risk	**7/3498 (0.20%)**	**7/3509 (0.20%)**
Cardiac Arrest * 1		
# participants affected / at risk	**16/3498 (0.46%)**	**10/3509 (0.28%)**
Cardiac Tamponade * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Congestive Cardiomyopathy * 1		
# participants affected / at risk	**0/3498 (0.00%)**	**1/3509 (0.03%)**
Electromechanical Dissociation * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Endocarditis * 1		
# participants affected / at risk	**2/3498 (0.06%)**	**1/3509 (0.03%)**
Fluid Overload * 1		
# participants affected / at risk	**0/3498 (0.00%)**	**1/3509 (0.03%)**
Hepatic Congestion * 1		
# participants affected / at risk	**1/3498 (0.03%)**	**0/3509 (0.00%)**
Ischaemic Cardiomyopathy * 1		
# participants affected / at risk	**0/3498 (0.00%)**	**1/3509 (0.03%)**
Mitral Valve Incompetence * 1		
# participants affected / at risk	**0/3498 (0.00%)**	**1/3509 (0.03%)**
Mitral Valve Prolapse * 1		

# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Palpitations * 1		
# participants affected / at risk	0/3498 (0.00%)	3/3509 (0.09%)
Sinus Tachycardia * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Subacute Endocarditis * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Tachyarrhythmia * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Tachycardia * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Ventricular Arrhythmia * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Ventricular Extrasystoles * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Ventricular Fibrillation * 1		
# participants affected / at risk	11/3498 (0.31%)	8/3509 (0.23%)
Ventricular Septal Defect * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Ventricular Tachycardia * 1		
# participants affected / at risk	23/3498 (0.66%)	30/3509 (0.85%)
Endocrine disorders		
Carcinoid Tumour of the Appendix * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Diabetes Mellitus * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Diabetes Mellitus Inadequate Control * 1		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Diabetic Neuropathy * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Hyperglycaemia * 1		
# participants affected / at risk	2/3498 (0.06%)	2/3509 (0.06%)
Hypoglycaemia * 1		
# participants affected / at risk	5/3498 (0.14%)	8/3509 (0.23%)
Hypothyroidism * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Eye disorders		
Blindness Transient * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Vision Blurred * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Gastrointestinal disorders		
Abdominal Discomfort * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Abdominal Pain * 1		
# participants affected / at risk	5/3498 (0.14%)	1/3509 (0.03%)
Abdominal Pain Upper * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)

Anal Abscess [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Appendicitis [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Constipation [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Diarrhoea [*1]		
# participants affected / at risk	3/3498 (0.09%)	2/3509 (0.06%)
Diverticulitis [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Diverticulum [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Dysphagia [*1]		
# participants affected / at risk	2/3498 (0.06%)	1/3509 (0.03%)
Faeces Discoloured [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Gastric Ulcer [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Gastritis [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Gastroduodenitis [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Gastroenteritis [*1]		
# participants affected / at risk	3/3498 (0.09%)	2/3509 (0.06%)
Gastroenteritis Viral [*1]		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Gastrointestinal Erosion [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Gastrointestinal Obstruction [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Ileus [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Intestinal Obstruction [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Intestinal Perforation [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Nausea [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Pancreatitis Chronic [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Rectal Abscess [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Small Intestinal Obstruction [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Umbilical Hernia, Obstructive [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Vomiting [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
General disorders		

Asthenia [*1]		
# participants affected / at risk	1/3498 (0.03%)	2/3509 (0.06%)
Device Dislocation [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Device Related Infection [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Device Related Sepsis [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Hypothermia [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Infusion Site Extravasation [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Medical Device Complication [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Pyrexia [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Sudden Cardiac Death [*1]		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Sudden Death [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Hepatobiliary disorders		
Cholecystitis [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Cholecystitis Acute [*1]		
# participants affected / at risk	2/3498 (0.06%)	2/3509 (0.06%)
Cholestasis [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Hepatic Cirrhosis [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Hepatic Encephalopathy [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Hepatic Failure [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Hepatic Function Abnormal [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Hepatocellular Injury [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Immune system disorders		
Guillain-Barre Syndrome [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Transfusion Reaction [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Infections and infestations		
Bacteraemia [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Enterococcal Bacteraemia [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Infection [*1]		

# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Postoperative Wound Infection * 1		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Sepsis * 1		
# participants affected / at risk	6/3498 (0.17%)	5/3509 (0.14%)
Staphylococcal Bacteraemia * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Staphylococcal Infection * 1		
# participants affected / at risk	3/3498 (0.09%)	0/3509 (0.00%)
Staphylococcal Sepsis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Streptococcal Sepsis * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Wound Infection * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Injury, poisoning and procedural complications		
Fall * 1		
# participants affected / at risk	2/3498 (0.06%)	2/3509 (0.06%)
Road Traffic Accident * 1		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Therapeutic Agent Toxicity * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Wound Dehiscence * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Investigations		
Antimicrobial Susceptibility Test Resistant * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Blood Creatinine Increased * 1		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Blood Glucose Increased * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Catheter Culture Positive * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Fibrin D Dimer Increased * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Gastric Ph Decreased * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Hepatic Enzyme Increased * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
International Normalised Ratio Increased * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Prostatic Specific Antigen Increased * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Metabolism and nutrition disorders		
Dehydration * 1		
# participants affected / at risk	5/3498 (0.14%)	6/3509 (0.17%)
Gout * 1		
# participants affected / at risk	2/3498 (0.06%)	2/3509 (0.06%)

Hyperbilirubinaemia [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Hyperkalaemia [*1]		
# participants affected / at risk	5/3498 (0.14%)	4/3509 (0.11%)
Hypokalaemia [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Hyponatraemia [*1]		
# participants affected / at risk	1/3498 (0.03%)	2/3509 (0.06%)
Hypovolaemia [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Musculoskeletal and connective tissue disorders		
Arthritis Bacterial [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Hip Fracture [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Joint Sprain [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Lower Limb Fracture [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Monarthritis [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Musculoskeletal Pain [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Osteomyelitis [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Pain in Extremity [*1]		
# participants affected / at risk	2/3498 (0.06%)	1/3509 (0.03%)
Patella Fracture [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Pelvic Fracture [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Soft Tissue Infection [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Colonic Polyp [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Small Cell Carcinoma [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Nervous system disorders		
Confusional State [*1]		
# participants affected / at risk	4/3498 (0.11%)	2/3509 (0.06%)
Convulsion [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Dyskinesia [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Epilepsy [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Headache [*1]		
# participants affected / at risk	1/3498 (0.03%)	2/3509 (0.06%)

Loss of Consciousness * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Unresponsive to Stimuli * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Psychiatric disorders		
Acute Psychosis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Alcohol Withdrawal Syndrome * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Delirium * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Failure to Thrive * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Mental Status Changes * 1		
# participants affected / at risk	4/3498 (0.11%)	1/3509 (0.03%)
Renal and urinary disorders		
Azotaemia * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Bladder Neoplasm * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Cystitis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Haematuria * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Renal Artery Stenosis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Renal Colic * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Ureteric Haemorrhage * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Urinary Retention * 1		
# participants affected / at risk	2/3498 (0.06%)	1/3509 (0.03%)
Urinary Tract Infection * 1		
# participants affected / at risk	1/3498 (0.03%)	7/3509 (0.20%)
Urinary Tract Obstruction * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Urosepsis * 1		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Reproductive system and breast disorders		
Benign Prostatic Hyperplasia * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Breast Cancer * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Endometrial Cancer * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Orchitis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Respiratory, thoracic and mediastinal disorders		

Acute Pulmonary Oedema [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Acute Respiratory Failure [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Asthma [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Bronchitis [*1]		
# participants affected / at risk	7/3498 (0.20%)	1/3509 (0.03%)
Bronchitis Bacterial [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Chest Pain [*1]		
# participants affected / at risk	6/3498 (0.17%)	8/3509 (0.23%)
Chronic Obstructive Pulmonary Disease [*1]		
# participants affected / at risk	6/3498 (0.17%)	3/3509 (0.09%)
Dyspnoea [*1]		
# participants affected / at risk	2/3498 (0.06%)	2/3509 (0.06%)
Eosinophilic Pneumonia [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Haemoptysis [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Hypercapnia [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Hypoxia [*1]		
# participants affected / at risk	2/3498 (0.06%)	1/3509 (0.03%)
Hypoxic Encephalopathy [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Idiopathic Pulmonary Fibrosis [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Infective Exacerbation of Chronic Obstructive Airways Disease [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Influenza [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Lobar Pneumonia [*1]		
# participants affected / at risk	2/3498 (0.06%)	1/3509 (0.03%)
Lower Respiratory Tract Infection [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Lung Cancer Metastatic [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Lung Disorder [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Lung Infection [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Lung Neoplasm [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Lung Neoplasm Malignant [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Mediastinitis [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)

Mediastinum Neoplasm * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Musculoskeletal Chest Pain * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Non-Cardiac Chest Pain * 1		
# participants affected / at risk	1/3498 (0.03%)	3/3509 (0.09%)
Pharyngitis * 1		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Pleural Effusion * 1		
# participants affected / at risk	8/3498 (0.23%)	4/3509 (0.11%)
Pneumonia * 1		
# participants affected / at risk	22/3498 (0.63%)	18/3509 (0.51%)
Pneumonia Aspiration * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Pneumonia Bacterial * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Pneumonia Mycoplasmal * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Pneumonia Staphylococcal * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Pneumothorax * 1		
# participants affected / at risk	1/3498 (0.03%)	4/3509 (0.11%)
Pulmonary Embolism * 1		
# participants affected / at risk	6/3498 (0.17%)	4/3509 (0.11%)
Pulmonary Fibrosis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Pulmonary Hypertension * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Pulmonary Infarction * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Pulmonary Oedema * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Respiratory Arrest * 1		
# participants affected / at risk	2/3498 (0.06%)	2/3509 (0.06%)
Respiratory Distress * 1		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Respiratory Failure * 1		
# participants affected / at risk	2/3498 (0.06%)	9/3509 (0.26%)
Respiratory Tract Infection * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Stridor * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Upper Respiratory Tract Infection * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Skin and subcutaneous tissue disorders		
Acarodermatitis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Angioedema * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)

Cellulitis [*1]		
# participants affected / at risk	4/3498 (0.11%)	2/3509 (0.06%)
Dermatitis Allergic [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Dermatitis Exfoliative [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Diabetic Foot [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Diabetic Foot Infection [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Gangrene [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Petechiae [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Pruritus [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Subcutaneous Haematoma [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Vascular disorders		
Abdominal Wall Haematoma [*1]		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Acute Coronary Syndrome [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Angina Pectoris [*1]		
# participants affected / at risk	2/3498 (0.06%)	8/3509 (0.23%)
Angina Unstable [*1]		
# participants affected / at risk	1/3498 (0.03%)	3/3509 (0.09%)
Aortic Aneurysm [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Aortic Dissection [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Aortic Stenosis [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Arterial Haemorrhage [*1]		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Bleeding Varicose Vein [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Cardiogenic Shock [*1]		
# participants affected / at risk	14/3498 (0.40%)	16/3509 (0.46%)
Catheter Site Haemorrhage [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Cerebellar Haemorrhage [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Cerebrovascular Accident [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Colitis Ischaemic [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Coronary Artery Disease [*1]		

# participants affected / at risk	1/3498 (0.03%)	5/3509 (0.14%)
Deep Vein Thrombosis * 1		
# participants affected / at risk	4/3498 (0.11%)	3/3509 (0.09%)
Dizziness * 1		
# participants affected / at risk	0/3498 (0.00%)	4/3509 (0.11%)
Duodenal Ulcer Haemorrhage * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Embolic Stroke * 1		
# participants affected / at risk	2/3498 (0.06%)	1/3509 (0.03%)
Embolism * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Femoral Artery Occlusion * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Gastrointestinal Haemorrhage * 1		
# participants affected / at risk	4/3498 (0.11%)	8/3509 (0.23%)
Haematemesis * 1		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Haematoma * 1		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Haemorrhagic Anaemia * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Haemorrhagic Stroke * 1		
# participants affected / at risk	3/3498 (0.09%)	4/3509 (0.11%)
Haemorrhoidal Haemorrhage * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Hypertension * 1		
# participants affected / at risk	2/3498 (0.06%)	1/3509 (0.03%)
Hypertensive Crisis * 1		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Hypoperfusion * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Hypotension * 1		
# participants affected / at risk	6/3498 (0.17%)	10/3509 (0.28%)
Iliac Artery Embolism * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Iliac Artery Thrombosis * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Infusion Site Phlebitis * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Intracardiac Thrombus * 1		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Ischaemic Cerebral Infarction * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Ischaemic Hepatitis * 1		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Ischaemic Stroke * 1		
# participants affected / at risk	11/3498 (0.31%)	20/3509 (0.57%)
Lower Gastrointestinal Haemorrhage * 1		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)

Melaena [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Myocardial Infarction [*1]		
# participants affected / at risk	19/3498 (0.54%)	15/3509 (0.43%)
Myocardial Ischaemia [*1]		
# participants affected / at risk	2/3498 (0.06%)	0/3509 (0.00%)
Orthostatic Hypotension [*1]		
# participants affected / at risk	3/3498 (0.09%)	1/3509 (0.03%)
Peptic Ulcer Haemorrhage [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Peripheral Embolism [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Peripheral Ischaemia [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Phlebitis [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Post Procedural Haematoma [*1]		
# participants affected / at risk	0/3498 (0.00%)	2/3509 (0.06%)
Post Procedural Haemorrhage [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Presyncope [*1]		
# participants affected / at risk	0/3498 (0.00%)	5/3509 (0.14%)
Raynaud's Phenomenon [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Rectal Haemorrhage [*1]		
# participants affected / at risk	4/3498 (0.11%)	3/3509 (0.09%)
Retroperitoneal Haemorrhage [*1]		
# participants affected / at risk	1/3498 (0.03%)	1/3509 (0.03%)
Septic Shock [*1]		
# participants affected / at risk	3/3498 (0.09%)	3/3509 (0.09%)
Shock [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Small Intestinal Haemorrhage [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Subarachnoid Haemorrhage [*1]		
# participants affected / at risk	1/3498 (0.03%)	0/3509 (0.00%)
Syncope [*1]		
# participants affected / at risk	6/3498 (0.17%)	5/3509 (0.14%)
Systemic Inflammatory Response Syndrome [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Thrombophlebitis Superficial [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Thrombosis [*1]		
# participants affected / at risk	0/3498 (0.00%)	1/3509 (0.03%)
Transient Ischaemic Attack [*1]		
# participants affected / at risk	2/3498 (0.06%)	4/3509 (0.11%)
Upper Gastrointestinal Haemorrhage [*1]		
# participants affected / at risk	4/3498 (0.11%)	2/3509 (0.06%)

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 13.0

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
Only summary counts of deaths by group are provided for other pre-specified endpoints “All-cause mortality through Day 30” and “All-cause mortality through Day 180.” Formal statistical comparisons were not planned.

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 Executive and Steering Committees is responsible for the creation, review, and submission of publications and presentations after study completion. The Investigator agrees that all data are the property of the Sponsors and subject to confidentiality and use restrictions until results are presented in the public domain. Publications or presentations must be submitted to the Sponsors and necessary committees for review before publication, public dissemination, or review by a third-parties.

Results Point of Contact:

Name/Title: Vice President, Franchise Development
Organization: Johnson & Johnson Pharmaceutical Research & Development, LLC
phone: 610-651-6628 ext NA

No publications provided by Scios, Inc.

Publications automatically indexed to this study:

Patel PA, Heizer G, O'Connor CM, Schulte PJ, Dickstein K, Ezekowitz JA, Armstrong PW, Hasselblad V, Mills RM, McMurray JJ, Starling RC, Tang WH, Califf RM, Hernandez AF. Hypotension during hospitalization for acute heart failure is independently associated with 30-day mortality: findings from ASCEND-HF. Circ Heart Fail. 2014 Nov;7(6):918-25. doi: 10.1161/CIRCHEARTFAILURE.113.000872. Epub 2014 Oct 3.

van Deursen VM, Hernandez AF, Stebbins A, Hasselblad V, Ezekowitz JA, Califf RM, Gottlieb SS, O'Connor CM, Starling RC, Tang WH, McMurray JJ, Dickstein K, Voors AA. Nesiritide, renal function, and associated outcomes during hospitalization for acute decompensated heart failure: results from the Acute Study of Clinical Effectiveness of Nesiritide and Decompensated Heart Failure (ASCEND-HF). Circulation. 2014 Sep 16;130(12):958-65. doi: 10.1161/CIRCULATIONAHA.113.003046. Epub 2014 Jul 29.

Kaul P, Reed SD, Hernandez AF, Howlett JG, Ezekowitz JA, Li Y, Zheng Y, Rouleau JL, Starling RC, O'Connor CM, Califf RM, Armstrong PW. Differences in treatment, outcomes, and quality of life among patients with heart failure in Canada and the United States. JACC Heart Fail. 2013 Dec;1(6):523-30. doi: 10.1016/j.jchf.2013.07.004. Epub 2013 Oct 23.

Toma M, Ezekowitz JA, Bakal JA, O'Connor CM, Hernandez AF, Sardar MR, Zolty R, Massie BM, Swedberg K, Armstrong PW, Starling RC. The relationship between left ventricular ejection fraction and mortality in patients with acute heart failure: insights from the ASCEND-HF Trial. Eur J Heart Fail. 2014 Mar;16(3):334-41. doi: 10.1002/ejhf.19. Epub 2013 Dec 14.

Reed SD, Kaul P, Li Y, Eapen ZJ, Davidson-Ray L, Schulman KA, Massie BM, Armstrong PW, Starling RC, O'Connor CM, Hernandez AF, Califf RM. Medical resource use, costs, and quality of life in patients with acute decompensated heart failure: findings from ASCEND-HF. J Card Fail. 2013 Sep;19(9):611-20. doi: 10.1016/j.cardfail.2013.07.003.

Howlett JG, Ezekowitz JA, Podder M, Hernandez AF, Diaz R, Dickstein K, Dunlap ME, Corbalán R, Armstrong PW, Starling RC, O'Connor CM,

Califf RM, Fonarow GC; ASCEND-HF Investigators. Global variation in quality of care among patients hospitalized with acute heart failure in an international trial: findings from the acute study clinical effectiveness of nesiritide in decompensated heart failure trial (ASCEND-HF). Circ Cardiovasc Qual Outcomes. 2013 Sep 1;6(5):534-42. doi: 10.1161/CIRCOUTCOMES.113.000119. Epub 2013 Jul 30.

Eapen ZJ, Reed SD, Li Y, Kociol RD, Armstrong PW, Starling RC, McMurray JJ, Massie BM, Swedberg K, Ezekowitz JA, Fonarow GC, Teerlink JR, Metra M, Whellan DJ, O'Connor CM, Califf RM, Hernandez AF. Do countries or hospitals with longer hospital stays for acute heart failure have lower readmission rates?: Findings from ASCEND-HF. Circ Heart Fail. 2013 Jul;6(4):727-32. doi: 10.1161/CIRCHEARTFAILURE.112.000265. Epub 2013 Jun 14.

Ezekowitz JA, Hu J, Delgado D, Hernandez AF, Kaul P, Leader R, Proulx G, Virani S, White M, Zieroth S, O'Connor C, Westerhout CM, Armstrong PW. Acute heart failure: perspectives from a randomized trial and a simultaneous registry. Circ Heart Fail. 2012 Nov;5(6):735-41. doi: 10.1161/CIRCHEARTFAILURE.112.968974. Epub 2012 Oct 2.

Ezekowitz JA, Hernandez AF, O'Connor CM, Starling RC, Proulx G, Weiss MH, Bakal JA, Califf RM, McMurray JJ, Armstrong PW. Assessment of dyspnea in acute decompensated heart failure: insights from ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure) on the contributions of peak expiratory flow. J Am Coll Cardiol. 2012 Apr 17;59(16):1441-8. doi: 10.1016/j.jacc.2011.11.061.

O'Connor CM, Starling RC, Hernandez AF, Armstrong PW, Dickstein K, Hasselblad V, Heizer GM, Komajda M, Massie BM, McMurray JJ, Nieminen MS, Reist CJ, Rouleau JL, Swedberg K, Adams KF Jr, Anker SD, Atar D, Battler A, Botero R, Bohidar NR, Butler J, Clausell N, Corbalán R, Costanzo MR, Dahlstrom U, Deckelbaum LI, Diaz R, Dunlap ME, Ezekowitz JA, Feldman D, Felker GM, Fonarow GC, Gennevois D, Gottlieb SS, Hill JA, Hollander JE, Howlett JG, Hudson MP, Kociol RD, Krum H, Laucevicius A, Levy WC, Méndez GF, Metra M, Mittal S, Oh BH, Pereira NL, Ponikowski P, Tang WH, Tanomsup S, Teerlink JR, Triposkiadis F, Troughton RW, Voors AA, Whellan DJ, Zannad F, Califf RM. Effect of nesiritide in patients with acute decompensated heart failure. N Engl J Med. 2011 Jul 7;365(1):32-43. doi: 10.1056/NEJMoa1100171. Erratum in: N Engl J Med. 2011 Aug 25;365(8):773. Wilson, W H [corrected to Tang, W H W].

Responsible Party:	Scios, Inc.
ClinicalTrials.gov Identifier:	NCT00475852 History of Changes
Other Study ID Numbers:	**CR013954**, ASCEND-HF, A093, NATRECORAHF3002
Study First Received:	May 18, 2007
Results First Received:	September 27, 2011
Last Updated:	March 1, 2013
Health Authority:	United States: Food and Drug Administration China: Food and Drug Administration Lithuania: State Medicine Control Agency - Ministry of Health Romania: National Medicines Agency Sweden: Medical Products Agency Ukraine: State Pharmacological Center - Ministry of Health