



Clinical trial results:

A Randomised, Double-Blind, Placebo-Controlled, Parallel-Group Trial to Assess Clinical Efficacy and Safety of Danegaptide in Patients with ST-Elevation Myocardial Infarction undergoing Primary Percutaneous Coronary Intervention

Summary

EudraCT number	2013-002312-27
Trial protocol	DK
Global end of trial date	04 December 2015

Results information

Result version number	v1 (current)
This version publication date	29 March 2022
First version publication date	29 March 2022

Trial information

Trial identification

Sponsor protocol code	13-031
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01977755
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Zealand Pharma A/S
Sponsor organisation address	Sydmarken 11, Soeborg, Denmark, 2860
Public contact	Clinical Operations, Zealand Pharma A/S, 45 88 77 36 00, clinicaltrials@zealandpharma.com
Scientific contact	Clinical Operations, Zealand Pharma A/S, +45 8877 3600, clinicaltrials@zealandpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2015
Global end of trial reached?	Yes
Global end of trial date	04 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the efficacy of two dose levels of Danegaptide to placebo when added to the standard treatment of STEMI in patients with single vessel disease having TIMI flow 0 or 1 prior to PCI conducted within 6 hours of symptoms debut.

Protection of trial subjects:

The trial was conducted in accordance of the World Medical Association Declaration of Helsinki, current guidelines for GCP and local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 585
Worldwide total number of subjects	585
EEA total number of subjects	585

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	363
From 65 to 84 years	217
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

This trial was conducted at one (1) site in Denmark.

Pre-assignment

Screening details:

A total of 1744 patients were screened of which 585 patients were randomized.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Investigator, all site research personnel, sponsor and CRO staff were blinded to trial treatment until the database was locked.

Arms

Are arms mutually exclusive?	Yes
Arm title	High dose danegaptide

Arm description:

Subjects in this arm received 7.5 mg bolus injection followed by 22.5 mg infused over 6 hours

Arm type	Experimental
Investigational medicinal product name	Danegaptide 2.0 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use , Intravenous use

Dosage and administration details:

Subjects received 2 bolus injections of danegaptide, followed by infusion of danegaptide over 6 hours. The dose given depended on which arm the subjects were randomised to.

Arm title	Low dose danegaptide
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Arm description:

Subjects in this arm received danegaptide as 2.5 mg bolus injection followed by 7.5 mg infused over 6 hours.

Arm type	Experimental
Investigational medicinal product name	Danegaptide 2.0 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use , Intravenous use

Dosage and administration details:

Subjects received 2 bolus injections of danegaptide, followed by infusion of danegaptide over 6 hours. The dose given depended on which arm the subjects were randomised to.

Arm title	Placebo
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Arm description:

Subjects in this arm received placebo matching the treatment given in the experimental arms.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use , Intravenous use

Dosage and administration details:

Subjects received 2 bolus injections of placebo, followed by infusion of placebo over 6 hours.

Number of subjects in period 1	High dose danegaptide	Low dose danegaptide	Placebo
Started	184	206	195
Completed	167	183	181
Not completed	17	23	14
Consent withdrawn by subject	2	6	2
Adverse event, non-fatal	-	1	-
Death	3	3	4
Other	8	6	4
Lost to follow-up	4	7	4

Baseline characteristics

Reporting groups

Reporting group title	High dose danegaptide
Reporting group description:	
Subjects in this arm received 7.5 mg bolus injection followed by 22.5 mg infused over 6 hours	
Reporting group title	Low dose danegaptide
Reporting group description:	
Subjects in this arm received danegaptide as 2.5 mg bolus injection followed by 7.5 mg infused over 6 hours.	
Reporting group title	Placebo
Reporting group description:	
Subjects in this arm received placebo matching the treatment given in the experimental arms.	

Reporting group values	High dose danegaptide	Low dose danegaptide	Placebo
Number of subjects	184	206	195
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	60.5	60.0	61.0
standard deviation	± 11.6	± 11.1	± 10.9
Gender categorical Units: Subjects			
Female	39	46	49
Male	145	160	146
Killip class			
Subject with heart failure based on Killip classification of the subject. Any symptoms consistent with Killip class II-IV were considered heart failure and were documented in the patient file and trial eCRF.			
Units: Subjects			
Killip class I	178	198	192
Killip class II	6	6	2
Killip class III	0	1	1
Not recorded	0	1	0
BMI Units: kg/m ²			
arithmetic mean	27.3	26.9	27.4
standard deviation	± 3.8	± 4.1	± 4.3

Reporting group values	Total		
Number of subjects	585		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	134		
Male	451		
Killip class			
Subject with heart failure based on Killip classification of the subject. Any symptoms consistent with Killip class II-IV were considered heart failure and were documented in the patient file and trial eCRF.			
Units: Subjects			
Killip class I	568		
Killip class II	14		
Killip class III	2		
Not recorded	1		
BMI			
Units: kg/m ²			
arithmetic mean			
standard deviation	-		

Subject analysis sets

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS was regarded as the practical implementation of the Intention-to-treat (ITT) set and comprised all ITT patients who received 1) at least one dose of trial drug and 2) had at least one valid post-baseline efficacy endpoint. The IIT, FAS and Safety Analysis set (SAS) were identical.	
Subject analysis set title	Per protocol (PP)
Subject analysis set type	Per protocol
Subject analysis set description:	
The PP set was defined as the subset of the FASimg including patients with an evaluable cardiac Magnetic Resonance Imaging (cMRI) scan at both Day 2 and Day 90, an available area at risk (AAR) for calculation of the primary endpoint and who did not have any critical protocol deviation.	

Reporting group values	Full analysis set (FAS)	Per protocol (PP)	
Number of subjects	585	169	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	60.5	56.8	
standard deviation	± 11.2	± 9.7	
Gender categorical Units: Subjects			
Female	134	31	
Male	451	138	
Killip class			
Subject with heart failure based on Killip classification of the subject. Any symptoms consistent with Killip class II-IV were considered heart failure and were documented in the patient file and trial eCRF.			
Units: Subjects			
Killip class I	568	168	
Killip class II	14	1	
Killip class III	2	0	
Not recorded	1	0	
BMI Units: kg/m ²			
arithmetic mean	27.2	27.4	
standard deviation	± 4.1	± 4.4	

End points

End points reporting groups

Reporting group title	High dose danegaptide
Reporting group description:	
Subjects in this arm received 7.5 mg bolus injection followed by 22.5 mg infused over 6 hours	
Reporting group title	Low dose danegaptide
Reporting group description:	
Subjects in this arm received danegaptide as 2.5 mg bolus injection followed by 7.5 mg infused over 6 hours.	
Reporting group title	Placebo
Reporting group description:	
Subjects in this arm received placebo matching the treatment given in the experimental arms.	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS was regarded as the practical implementation of the Intention-to-treat (ITT) set and comprised all ITT patients who received 1) at least one dose of trial drug and 2) had at least one valid post-baseline efficacy endpoint. The IIT, FAS and Safety Analysis set (SAS) were identical.	
Subject analysis set title	Per protocol (PP)
Subject analysis set type	Per protocol
Subject analysis set description:	
The PP set was defined as the subset of the FASimg including patients with an evaluable cardiac Magnetic Resonance Imaging (cMRI) scan at both Day 2 and Day 90, an available area at risk (AAR) for calculation of the primary endpoint and who did not have any critical protocol deviation.	

Primary: Myocardial Salvage Index (MSI)

End point title	Myocardial Salvage Index (MSI)
End point description:	
The difference between myocardial volume at risk in the acute phase and final infarct size at Day 90 in relation to myocardial volume at risk in the acute phase	
End point type	Primary
End point timeframe:	
Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: Myocardial Salvage Index (MSI)				
arithmetic mean (standard deviation)	63.9 (± 14.9)	65.6 (± 15.6)	66.7 (± 11.7)	65.4 (± 14.2)

Statistical analyses

Statistical analysis title	Primary efficacy analysis - placebo vs Dane. high
Statistical analysis description:	
Primary efficacy analysis of myocardial salvage index (per-protocol analysis set). The primary efficacy endpoint as analysed using an analysis of covariance model with treatment group as independent	

variable and relative infarct size at baseline, age, gender and TIMI level at Day 2 as covariates.

Comparison groups	Placebo v High dose danegaptide
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	0.8

Statistical analysis title

Primary efficacy analysis - placebo vs Dane. low

Statistical analysis description:

Primary efficacy analysis of myocardial salvage index (per-protocol analysis set). The primary efficacy endpoint as analysed using an analysis of covariance model with treatment group as independent variable and relative infarct size at baseline, age, gender and TIMI level at Day 2 as covariates.

Comparison groups	Low dose danegaptide v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.23
upper limit	2.88

Secondary: Relative infarct size Day 90

End point title	Relative infarct size Day 90
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End point description:

Relative infarct size [infarct size/left ventricle (LV) size (g/g)] × 100), as assessed by LGE cMRI, at Day 90.

End point type	Secondary
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End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: percent				
arithmetic mean (standard deviation)	14.0 ($\pm$ 7.1)	13.7 ($\pm$ 6.7)	15.4 ($\pm$ 7.7)	14.3 ($\pm$ 7.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Relative infarct size Day 2

End point title	Relative infarct size Day 2
End point description:	
End point type	Secondary
End point timeframe:	
Day 2	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	55	58	51	164
Units: percent				
arithmetic mean (standard deviation)	21.7 ($\pm$ 10.6)	21.2 ($\pm$ 9.7)	24.2 ($\pm$ 13.0)	22.3 ($\pm$ 11.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in relative infarct size

End point title	Change in relative infarct size
End point description:	
End point type	Secondary
End point timeframe:	
Change from Day 2 (baseline) to Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	55	58	51	164
Units: percent				
arithmetic mean (standard deviation)	-7.6 (± 6.6)	-7.3 (± 5.5)	-8.7 (± 8.2)	-7.8 (± 6.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute infarct size Day 90

End point title	Absolute infarct size Day 90
End point description:	
End point type	Secondary
End point timeframe:	
Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: gram(s)				
arithmetic mean (standard deviation)	19.6 (± 11.4)	18.6 (± 9.6)	21.4 (± 15.0)	19.8 (± 12.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in absolute infarct size

End point title	Change in absolute infarct size
End point description:	
End point type	Secondary
End point timeframe:	
Change from Day 2 (baseline) to Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	55	58	51	164
Units: gram(s)				
arithmetic mean (standard deviation)	-14 ($\pm$ 12.1)	-13 ($\pm$ 9.8)	-18 ($\pm$ 17.9)	-15 ($\pm$ 13.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Left ventricular ejection fraction (LVEF) Day 2

End point title	Left ventricular ejection fraction (LVEF) Day 2
End point description:	
End point type	Secondary
End point timeframe:	
Day 2	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	58	52	167
Units: percent				
arithmetic mean (standard deviation)	45.4 ($\pm$ 8.9)	47.0 ($\pm$ 8.7)	45.3 ($\pm$ 9.7)	45.9 ($\pm$ 9.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Left ventricular ejection fraction (LVEF) Day 90

End point title	Left ventricular ejection fraction (LVEF) Day 90
End point description:	
End point type	Secondary
End point timeframe:	
Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: percent				
arithmetic mean (standard deviation)	53.9 (± 9.5)	52.7 (± 10.3)	52.1 (± 10.9)	52.9 (± 10.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in left ventricular ejection fraction (LVEF)

End point title	Change in left ventricular ejection fraction (LVEF)
End point description:	
End point type	Secondary
End point timeframe:	
From Day 2 (baseline) to Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	58	52	167
Units: percent				
arithmetic mean (standard deviation)	8.6 (± 8.3)	5.7 (± 8.0)	6.8 (± 9.1)	7.0 (± 8.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in left ventricular end-systolic volume (LV-ESV) as measured by cMRI

End point title	Change in left ventricular end-systolic volume (LV-ESV) as measured by cMRI
End point description:	
End point type	Secondary
End point timeframe:	
From Day 2 (baseline) to Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	58	52	167
Units: millilitre(s)				
arithmetic mean (standard deviation)	-9.3 (± 20.5)	-3.5 (± 25.4)	-4.4 (± 30.3)	-5.8 (± 25.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in left ventricular end-diastolic volume (LV-EDV) as measured by cMRI

End point title	Change in left ventricular end-diastolic volume (LV-EDV) as measured by cMRI
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End point description:

End point type	Secondary
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End point timeframe:

From Day 2 (baseline) to Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	58	52	167
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.8 (± 29.1)	10.8 (± 26.4)	14.2 (± 29.8)	11.5 (± 28.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Relative volume with microvascular obstruction (MVO) as assessed by cMRI

End point title	Relative volume with microvascular obstruction (MVO) as assessed by cMRI
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End point description:

End point type	Secondary
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End point timeframe:

Day 2

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	55	58	51	164
Units: percent				
arithmetic mean (standard deviation)	12.6 (± 12.3)	10.9 (± 12.8)	11.0 (± 10.8)	11.5 (± 12.0)

Statistical analyses

No statistical analyses for this end point

Secondary: 90-day clinical outcome/MACE [cardiac death, new or worsening heart failure (during the initial hospitalization) and re-hospitalization due to heart failure]

End point title	90-day clinical outcome/MACE [cardiac death, new or worsening heart failure (during the initial hospitalization) and re-hospitalization due to heart failure]
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End point description:

End point type	Secondary
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End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	184	206	195	585
Units: Patients				
Cardiac death	3	2	5	10
Myocardial re-infarction	1	2	2	5
New onset or worsening heart failure	10	8	7	25
Re-admission during the 90 day FU	3	2	1	6
Stent thrombosis	1	2	2	5
Stroke	1	3	2	6

Statistical analyses

No statistical analyses for this end point

Secondary: Significant arrhythmias - Severe alerts during Telemetry Asystoli/Marked QRS pause(>4sec)

End point title	Significant arrhythmias - Severe alerts during Telemetry Asystoli/Marked QRS pause(>4sec)
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End point description:

End point type	Secondary
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End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	
Units: Patients				
Yes	0	2	2	4
No	56	48	50	154

Statistical analyses

No statistical analyses for this end point

Secondary: Significant arrhythmias - Extreme Tachycardia. HF > 180

End point title Significant arrhythmias - Extreme Tachycardia. HF > 180

End point description:

End point type Secondary

End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: Patients				
Yes	0	2	0	2
No	56	50	50	156

Statistical analyses

No statistical analyses for this end point

Secondary: Significant arrhythmias - Extreme bradycardia. HF < 30

End point title Significant arrhythmias - Extreme bradycardia. HF < 30

End point description:

End point type Secondary

End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: Patients				
Yes	2	2	2	6
No	54	50	48	152

Statistical analyses

No statistical analyses for this end point

Secondary: Significant arrhythmias - Ventricular Tachycard.VES>=5, frq. > 100

End point title	Significant arrhythmias - Ventricular Tachycard.VES>=5, frq. > 100
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End point description:

End point type	Secondary
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End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: Patients				
Yes	54	48	46	148
No	2	6	6	14

Statistical analyses

No statistical analyses for this end point

Secondary: Significant arrhythmias - Ventricular fibrillation. If VF >= 4 sec

End point title	Significant arrhythmias - Ventricular fibrillation. If VF >= 4 sec
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End point description:

End point type	Secondary
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End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: Patients				
Yes	2	2	4	8
No	54	50	48	152

Statistical analyses

No statistical analyses for this end point

Secondary: Degree of ST-segment resolution 60 minutes after PCI

End point title	Degree of ST-segment resolution 60 minutes after PCI
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End point description:

End point type	Secondary
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End point timeframe:

Measured 60 minutes post-PCI procedure on Day 0

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	135	152	151	438
Units: Patients				
<1 mm	78	87	84	249
1-2 mm	17	27	32	76
≥2 mm	40	38	35	113

Statistical analyses

No statistical analyses for this end point

Secondary: Patients with ≥70% ST-segment resolution 60 minutes after PCI

End point title	Patients with ≥70% ST-segment resolution 60 minutes after PCI
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End point description:

End point type	Secondary
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End point timeframe:

Measured 60 minutes post-PCI procedure on Day 0

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	136	153	151	440
Units: Patients				
No	47	49	58	154
Yes	89	104	93	286

Statistical analyses

No statistical analyses for this end point

Secondary: AUC₀₋₄₈ Creatine Kinase-MB

End point title	AUC ₀₋₄₈ Creatine Kinase-MB
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End point description:

End point type	Secondary
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End point timeframe:

Measured from Day 1 after PCI until discharge

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	159	179	169	507
Units: µg*h/L				
arithmetic mean (standard deviation)	3839 (± 2749)	3468 (± 2499)	3246 (± 2621)	3508 (± 2625)

Statistical analyses

No statistical analyses for this end point

Secondary: C_{max} Creatine Kinase-MB

End point title	C _{max} Creatine Kinase-MB
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End point description:

End point type	Secondary
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End point timeframe:

Measured from Day 1 after PCI until discharge

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	168	190	181	539
Units: µg/L				
arithmetic mean (standard deviation)	207 (± 159)	191 (± 144)	179 (± 148)	192 (± 150)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC,0-48 Troponin-T

End point title	AUC,0-48 Troponin-T
End point description:	
End point type	Secondary
End point timeframe:	
Measured from Day 1 after PCI until discharge	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	154	160	164	478
Units: ng*h/L				
arithmetic mean (standard deviation)	167568 (± 156757)	175173 (± 161646)	164000 (± 170992)	168889 (± 163110)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax Troponin-T

End point title	Cmax Troponin-T
End point description:	
End point type	Secondary
End point timeframe:	
Measured from Day 1 after PCI until discharge	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	163	181	179	523
Units: ng/L				
arithmetic mean (standard deviation)	5574 (± 5749)	5576 (± 5774)	5491 (± 7372)	5546 (± 6347)

Statistical analyses

No statistical analyses for this end point

Secondary: TIMI-flow as assessed immediately after the PCI procedure

End point title	TIMI-flow as assessed immediately after the PCI procedure
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End point description:

End point type	Secondary
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End point timeframe:

Assessed immediately after PCI procedure on Day 0

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Per protocol (PP)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	57	60	52	169
Units: Patients				
TIMI flow 2	1	0	2	3
TIMI flow 3	56	60	50	166

Statistical analyses

No statistical analyses for this end point

Secondary: SF36 - Physical Component Summary Score (PCS)

End point title	SF36 - Physical Component Summary Score (PCS)
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End point description:

Scale 0-100, where a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability.

End point type	Secondary
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End point timeframe:

Day 90

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	155	161	164	480
Units: Scores on a scale				
arithmetic mean (standard deviation)	40.2 (± 4.6)	41.1 (± 4.2)	40.8 (± 4.3)	40.7 (± 4.4)

Statistical analyses

No statistical analyses for this end point

Secondary: SF36 - Mental Component Summary Score (MCS)

End point title	SF36 - Mental Component Summary Score (MCS)
End point description: Scale 0-100, where a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability.	
End point type	Secondary
End point timeframe: Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	163	166	485
Units: Scores on a scale				
arithmetic mean (standard deviation)	57.0 (± 13.1)	56.5 (± 11.6)	56.6 (± 12.0)	56.7 (± 12.2)

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D-5L VAS Score

End point title	EQ-5D-5L VAS Score
End point description: Scores on a vertical visual analogue scale (VAS) that takes values between 100 (best imaginable health) and 0 (worst imaginable health).	
End point type	Secondary
End point timeframe: Day 90	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	161	167	484
Units: Scores on a scale				
arithmetic mean (standard deviation)	76.3 (± 19.0)	78.3 (± 15.7)	78.0 (± 17.7)	77.6 (± 17.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Danegaptide at the end of the PCI procedure

End point title	Plasma concentration of Danegaptide at the end of the PCI procedure
End point description:	
End point type	Secondary
End point timeframe:	
Day 1 after PCS procedure	

End point values	High dose danegaptide	Low dose danegaptide	Placebo	Full analysis set (FAS)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	183	205	192	580
Units: ng/mL				
arithmetic mean (standard deviation)	451 (± 369)	141 (± 48.4)	1.0 (± 0.0)	192 (± 279)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 until Day 90

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	High dose danegaptide
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Reporting group description:

Subjects in this arm received 7.5 mg bolus injection followed by 22.5 mg infused over 6 hours

Reporting group title	Low dose danegaptide
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Reporting group description:

Subjects in this arm received danegaptide as 2.5 mg bolus injection followed by 7.5 mg infused over 6 hours.

Reporting group title	Placebo
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Reporting group description:

Subjects in this arm received placebo matching the treatment given in the experimental arms.

Serious adverse events	High dose danegaptide	Low dose danegaptide	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 184 (16.85%)	43 / 206 (20.87%)	42 / 195 (21.54%)
number of deaths (all causes)	3	3	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma stage II			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastasis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral artery aneurysm			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery aneurysm			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	7 / 184 (3.80%)	3 / 206 (1.46%)	6 / 195 (3.08%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac death			
subjects affected / exposed	1 / 184 (0.54%)	3 / 206 (1.46%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 1
Malaise			
subjects affected / exposed	0 / 184 (0.00%)	2 / 206 (0.97%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	2 / 184 (1.09%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site thrombosis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 184 (1.09%)	5 / 206 (2.43%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary congestion			
subjects affected / exposed	1 / 184 (0.54%)	3 / 206 (1.46%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	2 / 184 (1.09%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sleep apnoea syndrome			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 184 (0.54%)	1 / 206 (0.49%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	4 / 184 (2.17%)	1 / 206 (0.49%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 184 (0.00%)	2 / 206 (0.97%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 184 (0.00%)	3 / 206 (1.46%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac arrest			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure			
subjects affected / exposed	1 / 184 (0.54%)	1 / 206 (0.49%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 184 (0.00%)	2 / 206 (0.97%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sick sinus syndrome			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			

subjects affected / exposed	1 / 184 (0.54%)	2 / 206 (0.97%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery dissection			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinoatrial block			

subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery occlusion			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dressler's syndrome			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 184 (0.00%)	2 / 206 (0.97%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroduodenitis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal discomfort			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reflux gastritis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary colic			
subjects affected / exposed	0 / 184 (0.00%)	1 / 206 (0.49%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Rash pruritic			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 184 (0.00%)	2 / 206 (0.97%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	2 / 184 (1.09%)	2 / 206 (0.97%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis externa			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 206 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 184 (0.54%)	0 / 206 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	High dose danegaptide	Low dose danegaptide	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 184 (75.54%)	154 / 206 (74.76%)	136 / 195 (69.74%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	21 / 184 (11.41%)	23 / 206 (11.17%)	21 / 195 (10.77%)
occurrences (all)	22	25	21
Blood potassium decreased			
subjects affected / exposed	10 / 184 (5.43%)	10 / 206 (4.85%)	14 / 195 (7.18%)
occurrences (all)	10	10	14
C-reactive protein increased			

subjects affected / exposed occurrences (all)	16 / 184 (8.70%) 16	8 / 206 (3.88%) 8	9 / 195 (4.62%) 9
Hemoglobin decreased subjects affected / exposed occurrences (all)	11 / 184 (5.98%) 11	13 / 206 (6.31%) 13	8 / 195 (4.10%) 8
White blood cell count increased subjects affected / exposed occurrences (all)	12 / 184 (6.52%) 12	7 / 206 (3.40%) 7	12 / 195 (6.15%) 12
ASAT increased subjects affected / exposed occurrences (all)	9 / 184 (4.89%) 9	9 / 206 (4.37%) 9	10 / 195 (5.13%) 10
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	11 / 184 (5.98%) 11	13 / 206 (6.31%) 13	22 / 195 (11.28%) 22
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	29 / 184 (15.76%) 29	32 / 206 (15.53%) 33	26 / 195 (13.33%) 26
Hypertension subjects affected / exposed occurrences (all)	8 / 184 (4.35%) 8	11 / 206 (5.34%) 11	12 / 195 (6.15%) 13
Hematoma subjects affected / exposed occurrences (all)	8 / 184 (4.35%) 8	14 / 206 (6.80%) 15	9 / 195 (4.62%) 9
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	15 / 184 (8.15%) 16	9 / 206 (4.37%) 9	15 / 195 (7.69%) 15
Ventricular tachycardia subjects affected / exposed occurrences (all)	6 / 184 (3.26%) 6	12 / 206 (5.83%) 12	10 / 195 (5.13%) 10
Bradycardia subjects affected / exposed occurrences (all)	4 / 184 (2.17%) 4	14 / 206 (6.80%) 14	8 / 195 (4.10%) 8
Angina pectoris			

subjects affected / exposed occurrences (all)	4 / 184 (2.17%) 5	12 / 206 (5.83%) 12	2 / 195 (1.03%) 2
Nervous system disorders			
Dizziness			
subjects affected / exposed	15 / 184 (8.15%)	23 / 206 (11.17%)	22 / 195 (11.28%)
occurrences (all)	16	23	23
Headache			
subjects affected / exposed	19 / 184 (10.33%)	13 / 206 (6.31%)	10 / 195 (5.13%)
occurrences (all)	21	13	11
Insomnia			
subjects affected / exposed	34 / 184 (18.48%)	31 / 206 (15.05%)	34 / 195 (17.44%)
occurrences (all)	34	31	34
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	22 / 184 (11.96%)	27 / 206 (13.11%)	29 / 195 (14.87%)
occurrences (all)	25	30	33
Fatigue			
subjects affected / exposed	37 / 184 (20.11%)	30 / 206 (14.56%)	32 / 195 (16.41%)
occurrences (all)	37	31	33
Chest discomfort			
subjects affected / exposed	18 / 184 (9.78%)	26 / 206 (12.62%)	20 / 195 (10.26%)
occurrences (all)	23	27	24
Oedema peripheral			
subjects affected / exposed	10 / 184 (5.43%)	11 / 206 (5.34%)	11 / 195 (5.64%)
occurrences (all)	11	11	11
Application site haematoma			
subjects affected / exposed	6 / 184 (3.26%)	13 / 206 (6.31%)	5 / 195 (2.56%)
occurrences (all)	7	14	5
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	19 / 184 (10.33%)	25 / 206 (12.14%)	21 / 195 (10.77%)
occurrences (all)	20	27	21
Nausea			
subjects affected / exposed	15 / 184 (8.15%)	20 / 206 (9.71%)	16 / 195 (8.21%)
occurrences (all)	16	20	16
Diarrhea			

subjects affected / exposed occurrences (all)	5 / 184 (2.72%) 5	6 / 206 (2.91%) 6	13 / 195 (6.67%) 14
Vomiting subjects affected / exposed occurrences (all)	14 / 184 (7.61%) 14	5 / 206 (2.43%) 5	6 / 195 (3.08%) 6
Respiratory, thoracic and mediastinal disorders Dyspnea subjects affected / exposed occurrences (all)	42 / 184 (22.83%) 50	45 / 206 (21.84%) 49	38 / 195 (19.49%) 41
Cough subjects affected / exposed occurrences (all)	8 / 184 (4.35%) 8	8 / 206 (3.88%) 8	12 / 195 (6.15%) 12
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	11 / 184 (5.98%) 12	4 / 206 (1.94%) 4	4 / 195 (2.05%) 4
Musculoskeletal and connective tissue disorders Groin pain subjects affected / exposed occurrences (all)	11 / 184 (5.98%) 11	11 / 206 (5.34%) 11	10 / 195 (5.13%) 10
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	12 / 184 (6.52%) 12	11 / 206 (5.34%) 11	14 / 195 (7.18%) 14

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 October 2013	Amendment 01: The reason for the amendment was to add assessments of health related quality of life and a urinary biomarker for oxidative stress.
23 January 2014	Amendment 02: Adjustments made to the protocol according to the initial experiences made during the trial and to better match the normal clinical procedures at the trial site.
05 January 2015	Amendment 03: Protocol amended to specify that patients who were not treated with PCI could be terminated from trial participation after 2-3 weeks of follow-up.
02 July 2015	Amendment 04: Number of patients estimated to be required to reach the needed sample size was reduced.
03 December 2015	Amendment 05: Addition of a supportive exploratory analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29602883>