Clinical trial results:
A multicenter, double blind, randomized, parallel group, placebo-controlled study to evaluate the effects of intravenous serelaxin infusion on micro- and macro-vascular function in patients with coronary artery disease

Summary

EudraCT number	2012-001945-42
Trial protocol	GB
Global end of trial date	17 August 2016

Results information

Result version number	v1 (current)
This version publication date	31 August 2017
First version publication date	31 August 2017

Trial information

Trial identification

Sponsor protocol code	CRLX030A2203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01979614
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	12 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 August 2016
Global end of trial reached?	Yes
Global end of trial date	17 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effects on the coronary vasculature, as assessed by myocardial perfusion/coronary flow reserve, at the end of the treatment (EoT) of 48hr i.v. administration of 30 µg/kg/24hr serelaxin or placebo; and to evaluate the effects on AIx at the EoT of 48hr i.v. administration of 30 µg/kg/24hr serelaxin or placebo

Protection of trial subjects:

This study was conducted in compliance with the ethical principles derived from the Declaration of Helsinki and the international Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	36
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Out of the total 63 participants screened, 62 were randomized. 4 of the randomized participants did not receive study drug, and 58 did receive study drug

Pre-assignment

Screening details:

Of the 58 participants in the safety analysis set, 56 completed the treatment and follow-up period as planned (i.e. Day 30 and Day 180). Two participants, one in each treatment group, discontinued study prematurely due to AEs (unstable angina)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Serelaxin

Arm description:

Serelaxin was administered at a dose of 30 µg/kg/24h by intravenous infusion for 48 hours

Arm type	Experimental
Investigational medicinal product name	Serelaxin
Investigational medicinal product code	RLX030
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Serelaxin was administered at a dose of 30 µg/kg/24h by intravenous infusion for 48 hours

Arm title	Placebo

Arm description:

Placebo was administered by intravenous infusion for 48 hours

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	RLX030
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered by intravenous infusion for 48 hours

Number of subjects in period 1	Serelaxin	Placebo
Started	30	28
Safety Analysis Set	30	28
PK Analysis Set	30	0 [1]
PD Analysis Set	25 [2]	26 [3]
Completed	29	27
Not completed	1	1
Adverse event, non-fatal	1	1

Notes:

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

Justification: Of the 58 participants in the safety analysis set, 56 completed the treatment and follow-up period as planned (i.e. Day 30 and Day 180). Two participants, one in each treatment group, discontinued study prematurely due to AEs (unstable angina)

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

Justification: Of the 58 participants in the safety analysis set, 56 completed the treatment and follow-up period as planned (i.e. Day 30 and Day 180). Two participants, one in each treatment group, discontinued study prematurely due to AEs (unstable angina)

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

Justification: Of the 58 participants in the safety analysis set, 56 completed the treatment and follow-up period as planned (i.e. Day 30 and Day 180). Two participants, one in each treatment group, discontinued study prematurely due to AEs (unstable angina)

Baseline characteristics

Reporting groups	
Reporting group title	Serelaxin
Reporting group description:	
Serelaxin was administered at a dose of 30 µg/kg/24h by intravenous infusion for 48 hours	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered by intravenous infusion for 48 hours	

Reporting group values	Serelaxin	Placebo	Total
Number of subjects	30	28	58
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	62.6	60.1	
standard deviation	± 6.42	± 7.05	-
Gender, Male/Female Units: Subjects			
Female	3	2	5
Male	27	26	53

End points

End points reporting groups

Reporting group title	Serelaxin
Reporting group description:	
Serelaxin was administered at a dose of 30 µg/kg/24h by intravenous infusion for 48 hours	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered by intravenous infusion for 48 hours	

Primary: Statistical analysis of change from baseline to Day 3 in myocardial perfusion endpoints using ANCOVA

End point title	Statistical analysis of change from baseline to Day 3 in myocardial perfusion endpoints using ANCOVA
End point description:	
Global MPRI (Myocardial Perfusion Reserve Index) is defined as ratio between mean global myocardial blood flow values at rest and during adenosine stress Participants who did not receive study drug as per study protocol, i.e. a reduced infusion rate, were excluded from this analysis	
End point type	Primary
End point timeframe:	
baseline to Day 3	

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	25		
Units: ratio				
arithmetic mean (confidence interval 95%)				
Global Myocardial Perfusion Reserve Index (MPRI)	-0.244 (-0.454 to -0.035)	-0.133 (-0.329 to -0.064)		
Mid Perfusion Reserve Index	-0.264 (-0.519 to -0.01)	-0.075 (-0.313 to 0.164)		

Statistical analyses

Statistical analysis title	SAP for Global Myocardial Perfusion Reserve Index
Statistical analysis description:	
SAP for Global Myocardial Perfusion Reserve Index (MPRI)	
Comparison groups	Serelaxin v Placebo

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.438
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.399
upper limit	0.176

Statistical analysis title	SAP for Mid Perfusion Reserve Index
Statistical analysis description:	
SAP for Mid Perfusion Reserve Index	
Comparison groups	Serelaxin v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.28
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.16

Secondary: Change from baseline in aortic distensibility measured by MRI

End point title	Change from baseline in aortic distensibility measured by MRI
End point description:	
Summary table for measurements of arterial stiffness from cardiac MRI – Mean (SD) [n] Aortic distensibility was assessed by MRI and pulse wave velocity using the SphygmoCor device. (mmHg-1)	
End point type	Secondary
End point timeframe:	
At pre-dose on Day 1 (baseline) until Day 180 after the start of drug infusion	

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: mmHg-1				
arithmetic mean (standard deviation)				
Ascending Aorta Distensibility, Day 0 (n=24,22)	0.0017 (± 0.00158)	0.0014 (± 0.00192)		
Ascending Aorta Distensibility, Day 47 (n=23, 22)	0.0015 (± 0.00124)	0.0015 (± 0.00134)		

Descending Aorta Distensibility, Day 0 (n=24,21)	0.0023 (± 0.00146)	0.0019 (± 0.00221)		
Descending Aorta Distensibility, Day 47 (n=23,22)	0.0023 (± 0.00118)	0.0023 (± 0.00142)		
Peak Flow Velocity (cm/s), Day 0 (n=24,24)	127.994 (± 66.6941)	102.699 (± 33.894)		
Peak Flow Velocity (cm/s), Day 47 (n=23, 25)	127.981 (± 60.7571)	106.557 (± 38.9573)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in aortic velocity

End point title	Change from baseline in aortic velocity

End point description:

Summary table for measurements of arterial velocity from cardiac MRI – Mean (SD) [n] Aortic distensibility was assessed by MRI and pulse wave velocity using the SphygmoCor device. (mmHg-1)

End point type	Secondary

End point timeframe:

At pre-dose on Day 1 (baseline) until Day 180 after the start of drug infusion

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: mmHg-1				
arithmetic mean (standard deviation)				
Peak Flow Velocity (cm/s), Day 0 (n=24, 24)	127.981 (± 60.7571)	106.557 (± 38.9573)		
Peak Flow Velocity (cm/s), Day 47 (n=23, 25)	127.981 (± 60.7571)	106.557 (± 38.9573)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in augmentation index measured from Sphygmocor device

End point title	Change from baseline in augmentation index measured from Sphygmocor device

End point description:

Summary of values and change from baseline in augmentation index by time and treatment The change from baseline in Augmentation Index was analyzed using a repeated measures analysis of covariance including treatment, time, treatment by time, baseline by time interactions and baseline as fixed factors with an unstructured variance-covariance matrixStatistical analysis of change from baseline in augmentation index using repeated measures Analysis of Covariance For analysis of change from baseline, only subjects with results at both baseline and post-baseline could be included The augmentation index is a ratio calculated from the blood pressure waveform, it is a measure of wave

reflection and arterial stiffness. Augmentation index is commonly accepted as a measure of the enhancement (augmentation) of central aortic pressure by a reflected pulse wave

End point type	Secondary

End point timeframe:

At pre-dose on Day 1 (baseline) until Day 180 after the start of drug infusion

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: ratio				
arithmetic mean (standard deviation)				
DAY 1, 2h (n=23,25)	-4.12 (± 11.441)	-2.48 (± 11.56)		
DAY 1, 6h (n=24,26)	-2.99 (± 9.066)	-0.58 (± 9.551)		
DAY 2, 24h (n=24,25)	-0.82 (± 8.173)	0.22 (± 9.906)		
DAY 3, 47h (n=23,25)	3.51 (± 10.608)	0.22 (± 12.057)		
DAY 3, 50h (n=22, 24)	-0.67 (± 13.034)	-3.81 (± 9.397)		
DAY 3, 54h (n=22,25)	-1.37 (± 12.253)	-0.48 (± 11.748)		
DAY 30 (n=25, 26)	-0.83 (± 11.462)	0.58 (± 12.124)		
DAY 180 (n=24,25) end of study	0.24 (± 6.885)	0.54 (± 11.795)		

Statistical analyses

No statistical analyses for this end point

Secondary: Statistical analysis of change from baseline in augmentation index using repeated measures Analysis of Covariance

End point title	Statistical analysis of change from baseline in augmentation index using repeated measures Analysis of Covariance

End point description:

The change from baseline in Augmentation Index was analyzed using a repeated measures analysis of covariance including treatment, time, treatment by time, baseline by time interactions and baseline as fixed factors with an unstructured variance-covariance matrixStatistical analysis of change from baseline in augmentation index using repeated measures Analysis of Covariance For analysis of change from baseline, only subjects with results at both baseline and post-baseline could be included The augmentation index is a ratio calculated from the blood pressure waveform, it is a measure of wave reflection and arterial stiffness. Augmentation index is commonly accepted as a measure of the enhancement (augmentation) of central aortic pressure by a reflected pulse wave

End point type	Secondary

End point timeframe:

At pre-dose on Day 1 (baseline) until Day 180 after the start of drug infusion

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: ratio				
arithmetic mean (confidence interval 95%)				
DAY 1, 2h (n=23,25)	-4.088 (-7.967 to -0.21)	-1.97 (-5.693 to 1.753)		
DAY 1, 6h (n=24,26)	-3.277 (-6.129 to -0.425)	-0.394 (-3.139 to 2.352)		
DAY 2, 24h (n=24,25)	-0.774 (-4.016 to 2.469)	0.07 (-3.108 to 3.247)		
DAY 3, 47h (n=23,25)	3.488 (-0.47 to 7.445)	0.035 (-3.778 to 3.849)		
DAY 3, 50h (n=22, 24)	-0.764 (-5.208 to 3.68)	-4.015 (-8.273 to 0.243)		
DAY 3, 54h (n=22,25)	-1.737 (-5.915 to 2.44)	-0.753 (-4.689 to 3.182)		
DAY 30 (n=25, 26)	-0.979 (-4.912 to 2.954)	0.776 (-3.081 to 4.633)		
DAY 180 (n=24,25) end of study	0.234 (-3.066 to 3.535)	0.284 (-2.95 to 3.518)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in pulse wave velocity measured from carotid-femoral pulse wave analysis

End point title	Change from baseline in pulse wave velocity measured from carotid-femoral pulse wave analysis

End point description:

Summary of augmentation index for all visits by time and treatment Pulse wave velocity was assessed by the SphygmoCor device at pre-dose on Day1, and at 24, 47h, Day 30, and Day 180 after the start of drug infusion The augmentation index is a ratio calculated from the blood pressure waveform, it is a measure of wave reflection and arterial stiffness. Augmentation index is commonly accepted as a measure of the enhancement (augmentation) of central aortic pressure by a reflected pulse wave

End point type	Secondary

End point timeframe:

At pre-dose on Day1 (baseline) until Day 180 after the start of drug infusion

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: meters/second				
arithmetic mean (standard deviation)				
DAY 1, 0hrs (n=25,26)	7.453 (± 2.0541)	8.166 (± 1.9515)		
DAY 2, 24hrs (n=19,24)	7.051 (± 1.879)	7.677 (± 2.1361)		

DAY 3, 47hrs (n=22,23)	7.195 (± 1.9164)	8.264 (± 2.4964)		
DAY 30, 0hrs (n=23, 24)	7.989 (± 1.8151)	8.463 (± 2.4437)		
DAY 3, 47hrs (n=23,25)	29.57 (± 9.751)	26.04 (± 10.039)		
EOS (n=23,24)	8.335 (± 2.1087)	8.844 (± 2.1739)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of serelaxin

End point title	Serum concentration of serelaxin

End point description:

Summary statistics of serelaxin serum PK concentrations Blood samples were taken to measure serelaxin concentration at Pre-dose on Day 1, and at 24h, 48h, 50h, 54h, and Day 30 after the start of the 48h drug infusion. The steady state concentration was estimated using the serum concentration at the 48h timepoint

End point type	Secondary

End point timeframe:

From pre-dose on Day 1 until Day 30 after the start of drug infusion

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	0[1]		
Units: pg/mL				
arithmetic mean (standard deviation)				
DAY 1, 0hrs (n=30)	0.637 (± 3.49)	()		
DAY 2, 24hrs, (n=26)	27600 (± 79000)	()		
DAY 3, 48hrs (n=22)	26300 (± 48000)	()		
DAY 3, 50 hrs (n=21)	7940 (± 8450)	()		
DAY 3, 54hrs, (n=22)	3960 (± 3140)	()		
DAY 30 (n=30)	0 (± 0)	()		

Notes:

[1] - Summary statistics of serelaxin serum PK concentrations Blood samples were taken to measure serelaxi

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of antibodies to serelaxin

End point title	Serum concentration of antibodies to serelaxin

End point description:

Frequency and percentage of anti-Serelaxin antibodies Blood samples were taken to measure antibodies to serelaxin concentration at Pre-dose on Day 1, and at Day 30 after the start of the 48h drug infusion

N: The total number of subjects in the treatment group n: Number of subjects who are at the corresponding category m: Number of subjects with an available response at the visit

End point type	Secondary

End point timeframe:

From pre-dose on Day 1 until Day 30 after the start of drug infusion

End point values	Serelaxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	28		
Units: ratio (n/m) expressed as a percentage				
DAY 1 NEGATIVE	100	100		
DAY 1 POSITIVE	0	0		
DAY 30 NEGATIVE	100	100		
DAY 30 POSITIVE	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic clearance of serelaxin

End point title	Systemic clearance of serelaxin[2]

End point description:

Systemic clearance was estimated using the rate of serelaxin infusion and the steady state concentration

End point type	Secondary

End point timeframe:

From pre-dose on Day 1 until 48h after the start of drug infusion

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Summary statistics of serelaxin serum PK concentrations Blood samples were taken to measure serelaxin concentration at Pre-dose on Day 1, and at 24h, 48h, 50h, 54h, and Day 30 after the start of the 48h drug infusion. The steady state concentration was estimated using the serum concentration at the 48h timepoint

End point values	Serelaxin			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: CL (mL/hr/kg)				
arithmetic mean (standard deviation)	107 (± 80.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Treatment-emergent adverse events	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	Serelaxin
Reporting group description: Serelaxin	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	Serelaxin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 30 (16.67%)	7 / 28 (25.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Cardiac procedure complication			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular procedure complication			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			

subjects affected / exposed	1 / 30 (3.33%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 30 (3.33%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Type IV hypersensitivity reaction			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Serelaxin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 30 (53.33%)	18 / 28 (64.29%)	
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Peripheral coldness			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Feeling cold			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Dyspnoea exertional			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Pulmonary mass			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Pulmonary oedema			

subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Throat tightness			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Depressed mood			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Investigations			
Amylase increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Blood cholesterol increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Blood sodium decreased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Electrocardiogram Q wave abnormal			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Glomerular filtration rate decreased			

subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Haematocrit decreased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Haemoglobin decreased			
subjects affected / exposed	2 / 30 (6.67%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
Lipase increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Platelet count increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
QRS axis abnormal			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Red blood cell count decreased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Extrasystoles			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 30 (6.67%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
Headache			

subjects affected / exposed	2 / 30 (6.67%)	4 / 28 (14.29%)	
occurrences (all)	2	4	
Presyncope			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Skin exfoliation			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue			

disorders			
Muscle spasms			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Muscle tightness			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Wound infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Hypomagnesaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Type 2 diabetes mellitus			

subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 28 (3.57%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported