



Clinical trial results:

Reduction of Ischemic Myocardium with Ranolazine-Treatment in patients with acute myocardial Ischemia – RIMINI-Pilot-Trial

Summary

EudraCT number	2013-000030-35
Trial protocol	DE
Global end of trial date	05 June 2015

Results information

Result version number	v1 (current)
This version publication date	10 September 2022
First version publication date	10 September 2022
Summary attachment (see zip file)	RIMINI_Synopsis Final Report (CTC11599 Synopse CSR 2015_12_15 Version 1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	RIMINI-Pilot
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01797484
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Hamburg-Eppendorf
Sponsor organisation address	Martinistr. 52, Hamburg, Germany, 20246
Public contact	Dr. Peter Clemmensen, University Medical Center Hamburg-Eppendorf, +49 40741053979, p.clemmensen@uke.de
Scientific contact	Dr. Peter Clemmensen, University Medical Center Hamburg-Eppendorf, +49 40741053979, p.clemmensen@uke.de

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	15 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2015
Global end of trial reached?	Yes
Global end of trial date	05 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Area of ischemic myocardium/cm² (longitudinal strain, radial/circumferential strain) after 42 days treatment with Ranolazine

Protection of trial subjects:

Concerning risk/benefit consideration it is important to state that in the present trial the IMP was used within its approval according to the SmPC. Therefore an excessive risk for participating patients was not expected.

Each participant was involved in the study for a maximum of 42 days. Patients needed to attend on 3 occasions. There was the possibility of additional visits at the request of the subject or if this was considered clinically necessary.

Specific inclusion and exclusion criteria and a defined visit plan for monitoring the patients were included in the protocol.

Screening/Enrolment/Day 0 Written informed consent, blood sampling, echocardiography, medical history

Visit 1 (week 1) assessment, dosage increase

Visit 2 (week 2) assessment, blood sampling

Visit 3 (week 6) assessment, echocardiography, ECG

Criteria for Discontinuation Study Treatment for all patients

Discontinue study medication in the following instances:

- Discontinuation of study at the request of sponsor, Regulatory Agency or an EC
- Termination of study by Sponsor
- Medication-related toxicity > Grade 4 in more than 10 % of study population
- More than 2 Serious Adverse Events or SUSARs, which were judged as related to the study medication
- Indication that either of the study arms is associated with an accelerated clinical progression (stop of study at the decision of Investigator after discussion with Sponsor)

Criteria for Discontinuation of Study Treatment for the Single Patient

- Any clinical AE, laboratory abnormality or intercurrent illness, which in opinion of the Investigator, indicates that continued treatment with study therapy is not in the best interest of the subject
- Subject withdraws consent
- Pregnancy or breast-feeding during study
- Imprisonment or the compulsory detention for treatment of either a psychiatric or physical (e. g., infectious disease) illness.
- Discontinuations mandated by protocol defined safety parameters
- Requirement

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2013
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	Germany: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	10
From 65 to 84 years	9
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

First patient enrolled: 05-Aug-2013

Last patient finished: 05-Jun-2015

All patients were enrolled at the University Heart Centre Hamburg Eppendorf. A total of 20 patients with acute coronary syndrome and proof of myocardial dyskinesia were enrolled.

Pre-assignment

Screening details:

Proof of acute cardiac ischemia (elevated serum Troponine)

Proof of myocardial dyskinesia with functional ECG ("speckle tracking")

Stable angina pectoris \geq CCS II in patient history

Stabilized patients after coronary angioplasty or angiography

coronary angioplasty or angiography not older than 48h

Established standard therapy for CAD

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Only the cardiology specialist performing speckle-tracking ECG was blinded to the treatment regime of the patient undergoing examination.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Ranolazine
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ranolazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ranolazine was administered as one tablet orally twice a day. Dosage started with 500mg bid and was increased to 750mg bid after seven days of treatment as described in the Summary of Product Characteristics. Duration of treatment was 42 days.

Arm title	no additional medication
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Arm description: -

Arm type	no additional medication
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Ranolazine	no additional medication
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups

Reporting group title	Ranolazine
Reporting group description: -	
Reporting group title	no additional medication
Reporting group description: -	

Reporting group values	Ranolazine	no additional medication	Total
Number of subjects	10	10	20
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			
median	68	72	
standard deviation	± 9	± 7	-
Gender categorical Units: Subjects			
Female	4	5	9
Male	6	5	11

End points

End points reporting groups

Reporting group title	Ranolazine
Reporting group description: -	
Reporting group title	no additional medication
Reporting group description: -	

Primary: Area of ischemic Myocardium/cm² (longitudinal strain, radial/circumferential strain) after 42 days treatment with Ranolazine

End point title	Area of ischemic Myocardium/cm ² (longitudinal strain, radial/circumferential strain) after 42 days treatment with Ranolazine
End point description:	
End point type	Primary
End point timeframe:	
42 days after first dose of Ranolazine	

End point values	Ranolazine	no additional medication		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Left Ventricular Global Strain Rate				
number (not applicable)	10	10		

Statistical analyses

Statistical analysis title	Baseline Adjusted Analysis
Statistical analysis description:	
Analysis between Ranolazine treatment and no additional treatment were carried out using paired t-test. Non-parametric Mann-Whitney test were used for data that are not normally distributed. Categorical parameters were analyzed using χ^2 and exact Fisher's test.	
Comparison groups	Ranolazine v no additional medication
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[1] - proof of concept

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

AEs were collected for all patients from first dose of protocol treatment until 30 days after the last dose of treatment with a protocol IMP.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	na

Reporting groups

Reporting group title	Ranolazine
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Reporting group description: -

Reporting group title	no additional medication
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Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: AEs were collected for all patients from first dose of protocol treatment until 30 days after the last dose of treatment with a protocol IMP.

Information about AEs, whether volunteered by the patient, discovered by the investigator questioning or detected through physical examination, laboratory test or other investigation were collected and recorded in the study files. No reporting of AEs.

Serious adverse events	Ranolazine	no additional medication	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Retroperitoneal haematoma			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Shortness of breath			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ranolazine	no additional medication	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	

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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29938533>