Clinical trial results:
Revacept, a novel inhibitor of platelet adhesion in patients with stable coronary artery disease undergoing elective percutaneous coronary interventions:
A phase II, multicentre, randomised, dose-finding, double-blind and placebo-controlled study.

Summary

EudraCT number	2015-000686-32
Trial protocol	DE
Global end of trial date	26 March 2020

Results information

Result version number	v1 (current)
This version publication date	05 May 2021
First version publication date	05 May 2021

Trial information

Trial identification

Sponsor protocol code	Revacept/CAD/02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03312855
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	German Heart Centre Munich
Sponsor organisation address	Lazarettstr. 36, Munich, Germany, 80636
Public contact	Prof. Dr. Adnan Kastrati, German Heart Centre Munich, 0049 8912184578, kastrati@dhm.mhn.de
Scientific contact	Prof. Dr. Adnan Kastrati, German Heart Centre Munich, 0049 8912184578, kastrati@dhm.mhn.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	16 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2020
Global end of trial reached?	Yes
Global end of trial date	26 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to evaluate the efficacy and safety of treatment with 2 doses (80 and 160 mg) of Revacept versus placebo.

Protection of trial subjects:

Not applicable.

Background therapy:

Patients underwent perctaneous coronary intervention and periprocedural antithrombotic therapy composed of clopidogrel, ASA and heparin was administered based on local practice and current guidelines.

Evidence for comparator:

No comparators used.

Actual start date of recruitment	14 November 2017
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	Germany: 334
Worldwide total number of subjects	334
EEA total number of subjects	334

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)	122
From 65 to 84 years	208

85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

For inclusion the patients had to fulfil the following criteria:
1) Signed written informed consent
2) Target population
a) Men and women aged >18 years
b) Diagnosis: Clinically stable coronary artery disease
c) Angiographic evidence of coronary artery disease
d) Indication for PCI

Pre-assignment period milestones

Number of subjects started	509[1]
Number of subjects completed	334

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 3
Reason: Number of subjects	Not meeting inclusion criteria, exclusion criteria: 171
Reason: Number of subjects	Organisational reason: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The pre-assignment period is completed with the screening data.
509 patients were screened and 334 patients have been randomised.

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	Investigator, Monitor, Data analyst, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Revacept 160 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Revacept 160 mg
Investigational medicinal product code	
Other name	PR-15
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single administration over 20 minutes

Arm title	Revacept 80 mg

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Revacept 80 mg
Investigational medicinal product code	
Other name	PR-15
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Single administration over 20 minutes

Arm title	Placebo

Arm description: -

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

Dosage and administration details:
Single administration over 20 minutes

Number of subjects in period 1	Revacept 160 mg	Revacept 80 mg	Placebo
Started	120	121	93
Completed	117	119	92
Not completed	3	2	1
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	1	-	1
Protocol deviation	2	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Revacept 160 mg
Reporting group description: -	
Reporting group title	Revacept 80 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Revacept 160 mg	Revacept 80 mg	Placebo
Number of subjects	120	121	93
Age categorical Units: Subjects			
Adults (18-64 years)	40	43	39
From 65-84 years	78	77	53
85 years and over	2	1	1
Age continuous Units: years			
median	67.3	67.4	67.8
inter-quartile range (Q1-Q3)	61.5 to 75.5	60.4 to 75.1	60.8 to 74.8
Gender categorical Units: Subjects			
Female	38	24	19
Male	82	97	74
Number of diseased vessels Units: Subjects			
one	19	23	15
two	41	36	28
three	60	62	50
Diabetes mellitus Units: Subjects			
Diabetes mellitus yes	32	35	22
Diabetes mellitus no	88	86	71
Smoker Units: Subjects			
Current smoker	24	20	23
Non-smoker	96	101	70
Arterial hypertension Units: Subjects			
Arterial hypertension yes	106	103	87
Arterial hypertension no	14	18	6
Hypercholesterolemia Units: Subjects			
Hypercholesterolemia yes	110	108	80
Hypercholesterolemia no	10	13	13
Myocardial infarction Units: Subjects			

Myocardial infarction yes	21	27	26
Myocardial infarction no	99	94	67
CABG			
Units: Subjects			
CABG yes	10	11	6
CABG no	110	110	87
Stroke			
Units: Subjects			
Stroke yes	2	3	3
Stroke no	118	118	90
Peripheral arterial occlusive disease			
Units: Subjects			
Peripheral arterial occlusive disease yes	11	8	7
Peripheral arterial occlusive disease no	109	113	86
COPD			
Units: Subjects			
COPD yes	8	4	5
COPD no	112	117	88
Kidney insufficiency			
Units: Subjects			
Kidney insufficiency yes	14	12	5
Kidney insufficiency no	106	109	88

Reporting group values	Total		
Number of subjects	334		
Age categorical			
Units: Subjects			
Adults (18-64 years)	122		
From 65-84 years	208		
85 years and over	4		
Age continuous			
Units: years			
median			
inter-quartile range (Q1-Q3)	-		
Gender categorical			
Units: Subjects			
Female	81		
Male	253		
Number of diseased vessels			
Units: Subjects			
one	57		
two	105		
three	172		
Diabetes mellitus			
Units: Subjects			
Diabetes mellitus yes	89		
Diabetes mellitus no	245		
Smoker			
Units: Subjects			
Current smoker	67		

Non-smoker	267		
Arterial hypertension Units: Subjects			
Arterial hypertension yes	296		
Arterial hypertension no	38		
Hypercholesterolemia Units: Subjects			
Hypercholesterolemia yes	298		
Hypercholesterolemia no	36		
Myocardial infarction Units: Subjects			
Myocardial infarction yes	74		
Myocardial infarction no	260		
CABG Units: Subjects			
CABG yes	27		
CABG no	307		
Stroke Units: Subjects			
Stroke yes	8		
Stroke no	326		
Peripheral arterial occlusive disease Units: Subjects			
Peripheral arterial occlusive disease yes	26		
Peripheral arterial occlusive disease no	308		
COPD Units: Subjects			
COPD yes	17		
COPD no	317		
Kidney insufficiency Units: Subjects			
Kidney insufficiency yes	31		
Kidney insufficiency no	303		

Subject analysis sets

Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The full-analysis set included all subjects who have been randomized in concordance with the intention-to-treat principle.

Reporting group values	Intention-to-treat		
Number of subjects	334		
Age categorical Units: Subjects			
Adults (18-64 years)	122		
From 65-84 years	208		
85 years and over	4		

Age continuous Units: years			
median	67.4		
inter-quartile range (Q1-Q3)	60.8 to 75.0		
Gender categorical Units: Subjects			
Female	81		
Male	253		
Number of diseased vessels Units: Subjects			
one	57		
two	105		
three	172		
Diabetes mellitus Units: Subjects			
Diabetes mellitus yes	89		
Diabetes mellitus no	245		
Smoker Units: Subjects			
Current smoker	67		
Non-smoker	267		
Arterial hypertension Units: Subjects			
Arterial hypertension yes	296		
Arterial hypertension no	38		
Hypercholesterolemia Units: Subjects			
Hypercholesterolemia yes	298		
Hypercholesterolemia no	36		
Myocardial infarction Units: Subjects			
Myocardial infarction yes	74		
Myocardial infarction no	260		
CABG Units: Subjects			
CABG yes	27		
CABG no	307		
Stroke Units: Subjects			
Stroke yes	8		
Stroke no	326		
Peripheral arterial occlusive disease Units: Subjects			
Peripheral arterial occlusive disease yes	26		
Peripheral arterial occlusive disease no	308		
COPD Units: Subjects			
COPD yes	17		
COPD no	317		
Kidney insufficiency			

Units: Subjects			
Kidney insufficiency yes	31		
Kidney insufficiency no	303		

End points

End points reporting groups

Reporting group title	Revacept 160 mg
Reporting group description: -	
Reporting group title	Revacept 80 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The full-analysis set included all subjects who have been randomized in concordance with the intention-to-treat principle.	

Primary: A composite end point of death or myocardial injury (defined as increase in cardiac biomarker – high-sensitivity cardiac troponin T of at least 5 times the upper limit of norm (ULN))

End point title	A composite end point of death or myocardial injury (defined as increase in cardiac biomarker – high-sensitivity cardiac troponin T of at least 5 times the upper limit of norm (ULN))
End point description:	
End point type	Primary
End point timeframe:	
within 48 hours from randomisation	

End point values	Revacept 160 mg	Revacept 80 mg	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	120	121	93	334
Units: Death or myocardial injury	29	30	21	80

Statistical analyses

Statistical analysis title	Primary end point (efficacy)
Statistical analysis description:	
Confirmatory hypothesis testing of the primary efficacy end point was performed in a sequential order. First, significance of the treatment effect across the three groups was assessed by a test for trend on a two-sided 5% significance level using a binary logistic regression model and by using the values 0, 1 and 2 to code the placebo group, the lower-dose Revacept group and the higher dose Revacept group as a continuous variable.	
Comparison groups	Revacept 160 mg v Revacept 80 mg v Placebo

Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	test for trend

Secondary: Safety end point (Bleeding BARC 2 or higher)

End point title	Safety end point (Bleeding BARC 2 or higher)

End point description:

End point type	Secondary

End point timeframe:

Within 30 days after randomisation

End point values	Revacept 160 mg	Revacept 80 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120	119	93	
Units: Bleedings BARC 2 or higher	6	7	8	

Statistical analyses

Statistical analysis title	Safety endpoint (Bleeding)
Comparison groups	Revacept 160 mg v Revacept 80 mg v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	test for trend

Secondary: Myocardial infarction

End point title	Myocardial infarction

End point description:

End point type	Secondary

End point timeframe:

Within 30 days after randomisation

End point values	Revacept 160 mg	Revacept 80 mg	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	120	121	93	334
Units: Number of patients	3	3	2	8

Statistical analyses

No statistical analyses for this end point

Secondary: Definite stent thrombosis

End point title	Definite stent thrombosis

End point description:

End point type	Secondary

End point timeframe:

Within 30 days after randomisation

End point values	Revacept 160 mg	Revacept 80 mg	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	120	121	93	334
Units: Number of patients	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Urgent coronary revascularisation

End point title	Urgent coronary revascularisation

End point description:

End point type	Secondary

End point timeframe:

Within 30 days after randomisation

End point values	Revacept 160 mg	Revacept 80 mg	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	120	121	93	334
Units: Number of patients	0	2	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Stroke

End point title	Stroke

End point description:

End point type	Secondary

End point timeframe:

Within 30 days after randomisation

End point values	Revacept 160 mg	Revacept 80 mg	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	120	121	93	334
Units: Number of patients	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: All-cause mortality

End point title	All-cause mortality

End point description:

End point type	Secondary

End point timeframe:

Within 30 days after randomization

End point values	Revacept 160 mg	Revacept 80 mg	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	120	121	93	334
Units: Number of patients	0	1	0	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Following the subject’s randomisation all adverse events were collected by the investigators. All adverse events were collected that occured until visit 3.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Revacept 160 mg
Reporting group description: -	
Reporting group title	Revacept 80 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Revacept 160 mg	Revacept 80 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 120 (10.00%)	13 / 119 (10.92%)	8 / 93 (8.60%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 120 (0.83%)	2 / 119 (1.68%)	0 / 93 (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
Troponin T increased			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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
Injury, poisoning and procedural complications			
Vascular access site haemorrhage			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			

subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access site haematoma			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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			
Hypotension			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
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	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (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
Cardiac disorders			
Myocardial haemorrhage			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (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
Acute myocardial infarction			
subjects affected / exposed	2 / 120 (1.67%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prinzmetal angina			

subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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
Ventricular fibrillation			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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
Seizure			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (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
General disorders and administration site conditions			
Therapeutic response decreased			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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
Chest pain			
subjects affected / exposed	1 / 120 (0.83%)	2 / 119 (1.68%)	4 / 93 (4.30%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Colitis microscopic			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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
Gastroenteritis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (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

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

Non-serious adverse events	Revacept 160 mg	Revacept 80 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 120 (55.00%)	58 / 119 (48.74%)	40 / 93 (43.01%)
Vascular disorders			
Blood pressure fluctuation			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Haematoma			

subjects affected / exposed	2 / 120 (1.67%)	3 / 119 (2.52%)	2 / 93 (2.15%)
occurrences (all)	2	3	2
Haemorrhage			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	1	1	0
Hypertension			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	2 / 93 (2.15%)
occurrences (all)	1	1	2
Hypotension			
subjects affected / exposed	1 / 120 (0.83%)	2 / 119 (1.68%)	0 / 93 (0.00%)
occurrences (all)	1	2	0
Phlebitis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Thrombophlebitis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Catheter site phlebitis			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	4 / 120 (3.33%)	6 / 119 (5.04%)	4 / 93 (4.30%)
occurrences (all)	4	6	5
Discomfort			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Drug intolerance			

subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	1	1	0
Fatigue			
subjects affected / exposed	2 / 120 (1.67%)	2 / 119 (1.68%)	0 / 93 (0.00%)
occurrences (all)	2	2	0
Oedema peripheral			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Therapeutic response decreased			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Menorrhagia			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 120 (0.00%)	2 / 119 (1.68%)	0 / 93 (0.00%)
occurrences (all)	0	2	0
Dyspnoea			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	1 / 120 (0.83%)	3 / 119 (2.52%)	0 / 93 (0.00%)
occurrences (all)	1	4	0
Pulmonary oedema			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Panic disorder			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			

subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Restlessness			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 120 (0.00%)	2 / 119 (1.68%)	1 / 93 (1.08%)
occurrences (all)	0	2	1
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	2 / 120 (1.67%)	2 / 119 (1.68%)	2 / 93 (2.15%)
occurrences (all)	2	2	2
Blood pressure diastolic increased			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	2 / 120 (1.67%)	1 / 119 (0.84%)	2 / 93 (2.15%)
occurrences (all)	2	1	2
Hepatic enzyme increased			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Inflammatory marker increased			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Troponin T increased			

subjects affected / exposed	0 / 120 (0.00%)	2 / 119 (1.68%)	0 / 93 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Cardiac procedure complication			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Heat stroke			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Muscle rupture			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Product administration error (not IMP)			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Subcutaneous haematoma			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Vascular access site haematoma			
subjects affected / exposed	15 / 120 (12.50%)	8 / 119 (6.72%)	7 / 93 (7.53%)
occurrences (all)	15	8	7
Vascular access site haemorrhage			
subjects affected / exposed	0 / 120 (0.00%)	2 / 119 (1.68%)	1 / 93 (1.08%)
occurrences (all)	0	2	1
Vascular access site occlusion			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	1	0	1
Vascular access site pain			

subjects affected / exposed	2 / 120 (1.67%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	2	0	1
Vascular access site pseudoaneurysm			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
Angina pectoris			
subjects affected / exposed	2 / 120 (1.67%)	2 / 119 (1.68%)	0 / 93 (0.00%)
occurrences (all)	2	2	0
Bradycardia			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Bundle branch block left			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Coronary artery dissection			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	2 / 93 (2.15%)
occurrences (all)	0	1	2
Palpitations			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	2 / 120 (1.67%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	2	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Nervous system disorders			

Carotid artery stenosis			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Cerebral artery occlusion			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Craniocervical syndrome			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	1 / 93 (1.08%)
occurrences (all)	1	1	1
Dizziness postural			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	1 / 93 (1.08%)
occurrences (all)	1	1	1
Headache			
subjects affected / exposed	1 / 120 (0.83%)	2 / 119 (1.68%)	1 / 93 (1.08%)
occurrences (all)	1	2	1
Insomnia			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Neurological symptom			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	2 / 120 (1.67%)	2 / 119 (1.68%)	0 / 93 (0.00%)
occurrences (all)	2	2	0
Presyncope			
subjects affected / exposed	5 / 120 (4.17%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	5	0	1
Sleep deficit			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenitis			

subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 120 (1.67%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Visual impairment			
subjects affected / exposed	2 / 120 (1.67%)	0 / 119 (0.00%)	2 / 93 (2.15%)
occurrences (all)	2	0	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	6 / 120 (5.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	6	1	0
Diarrhoea			
subjects affected / exposed	2 / 120 (1.67%)	2 / 119 (1.68%)	0 / 93 (0.00%)
occurrences (all)	4	3	0
Dyspepsia			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Erosive duodenitis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Gastritis erosive			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorder			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 120 (0.83%)	3 / 119 (2.52%)	3 / 93 (3.23%)
occurrences (all)	1	3	3
Paraesthesia oral			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Cold sweat			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	1	1	0
Night sweats			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Hyperthyroidism			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Arthritis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	1 / 120 (0.83%)	3 / 119 (2.52%)	3 / 93 (3.23%)
occurrences (all)	1	3	3
Joint effusion			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 120 (0.00%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	2 / 93 (2.15%)
occurrences (all)	1	1	2
Musculoskeletal pain			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	1 / 93 (1.08%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			

subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
Spinal pain			
subjects affected / exposed	1 / 120 (0.83%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	1	0	0
Tenosynovitis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 120 (9.17%)	6 / 119 (5.04%)	4 / 93 (4.30%)
occurrences (all)	11	6	4
Sinusitis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 120 (0.00%)	1 / 119 (0.84%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 120 (0.83%)	1 / 119 (0.84%)	1 / 93 (1.08%)
occurrences (all)	1	1	1
Hypokalaemia			
subjects affected / exposed	2 / 120 (1.67%)	1 / 119 (0.84%)	2 / 93 (2.15%)
occurrences (all)	2	1	2
Hyponatraemia			
subjects affected / exposed	2 / 120 (1.67%)	0 / 119 (0.00%)	0 / 93 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2016	Substantial amendment: Protocol Version 4.0 (29 Nov 2016) (not approved) - Change of the sponsor representative in Prof. Dr. A. Kastrati - Members of Steering Committee and involved parties added - Discrepancies in description of primary and secondary end points between synopsis and main protocol corrected - Revision of secondary end points - Number of study participants changed to 332 instead of 330 - Exclusion criteria described more precisely - Study duration was added - Randomisation process was amended, unblinding process added - Details of conduct of the study specified - Definitions corrected and missing definitions added in adverse event section - Data management processes described more precisely - Sample size calculation was amended and number of patients increased fom 330 to 332 - Statistical analysis amended (adapted to compare the 3 treatment groups) - Section of Data Safety Monitoring Board and Event Adjudication Committee amended - No core laboratory involved - Important definitions added for bleeding, myocardial infarction, revascularisation, acute coronary syndrome, angiographic success of PCI, diabetes mellitus, smoking status, hypercholesterolemia, multivessel disease, TIMI grade flow
21 March 2017	Substantial amendment: Protocol Version 5.0 (20 Mar 2017) - Sample size estimation and statistical analysis amended due to BfArM's request
11 May 2017	Substantial amendment: Protocol Version 6.0 (10 May 2017) - Peri-procedural treatment was changed, the dose of clopidogrel is not specified anymore, the administration is based on local practice and current guidelines - The primary and secondary end points were related to the time of randomisation - Statistical methods: Clarification, that an overall evaluation of both efficacy and safety findings will be performed - The rational for a predefined dose of clopidogrel as peri-procedural therapy was removed - Randomisation is performed with the use of an computerised system embedded in the eCRF, revision of randomisation is not allowed, section removed - In vitro bleeding test was removed - Clinical chemistry and haematoloy parameters were described more precisely - Body temperature as safety parameter was added - AE/SAE definitions adapted to CT-3 guideline - Analysis of safety end points according to modified intention to treat principle - References amended - Definitions amended (myocadial infarction, revascularisation, stable angina pectoris, arterial hypertension, complex lesions)

13 April 2018	Substantial amendment: Protocol Version 7.0 (10 Apr 2018) - Primary end point: only high-sensitive troponin T - Secondary end point: Peak high-sensitivity troponin T level within 48 hours instead of 30 days - Exclusion criteria added: o Patients with elevated high-sensitivity cardiac troponin T levels at screening o Patients receiving antithrombotic therapy with Prasugrel or Ticagrelor within 7 days prior to randomisation - It was explained more precisely that data obtained as part of the normal subject care can be used for visit 1/screening and visit 2. The screening data are considered valid only if collected within 2 days prior to randomisation. - Definition of stroke corrected
11 June 2019	Substantial amendment: Protocol Version 8.0 (11 Jun 2019) - Trial duration amended - Additional laboratory assessment: platelet related inflammatory mediators and platelet released microRNA

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/33787834