Clinical trial results:
Use of Esmolol for Tight Heart Rate Control for 24 Hours in Patients with Acute ST Elevation Myocardial Infarction: The BEtA-Blocker Therapy in Acute Myocardial Infarction (BEAT-AMI) Trial

Study Title: Herzfrequenzkontrolle nach akutem Myokardinfarkt ("Heart rate control after acute myocardial infarct")

Study Short Title: STEMI

Summary

EudraCT number	2011-000911-26
Trial protocol	DE
Global end of trial date	24 February 2014

Results information

Result version number	v1 (current)
This version publication date	18 September 2021
First version publication date	18 September 2021
Summary attachment (see zip file)	STEMI_Summary_report (STEMI_Kurzabschlussbericht_Behörden_v1-04-F_Summary_EU-CTR.pdf)

Trial information

Trial identification

Sponsor protocol code	Uni-Koeln-1392

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS number: DKRS00000766

Notes:

Sponsors

Sponsor organisation name	University of Cologne
Sponsor organisation address	Albertus-Magnus-Platz, Cologne, Germany, 50923
Public contact	Priv.-Doz. Dr. Er, Klinikum Guetersloh, Department of Internal Medicine 1, +49 54218324402, Fikret.Er@klinikum-guetersloh.de
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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	19 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 February 2014
Global end of trial reached?	Yes
Global end of trial date	24 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of esmolol-induced heart rate control as compared with placebo when used in addition to standard medical therapy in patients with acute ST elevation myocardial infarction (STEMI) in reducing final infarct size reflected by Troponin T release.

Protection of trial subjects:

The trial was conducted according to Good Clinical Practice guidelines, the applicable local laws, and in accordance with the ethical principles that have their origins in the Declaration of Helsinki.
The competent authorities approved the trial as required by national regulations.
Regulatory authorities were notified of the trial and amendments as required by national regulations.

Background therapy:

After successful percutaneous coronary intervention (PCI) all patients are getting treated in line with current national and international cardiology Guidelines. This Treatment usually consists of an ACE inhibitor, an oral beta blocker, Aspirin, an ADP receptor antagonist, a statine as well as unfractioned heparin.

Evidence for comparator: -

Actual start date of recruitment	13 October 2011
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: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	50
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date of first enrollment (FPFV): 13.10.2011
Date of last completed (LPLV): 24.02.2014

Pre-assignment

Screening details:

Patients admitted with acute ST elevation myocardial infarction were screened. Subjects underwent timely successful percutaneous intervention were identified. Eligible subjects were included and randomly allocated to receive esmolol or placebo for 24 Hours.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

Because study drug esmolol has an obvious effect on heart rate and blood pressure and due to safety reasons drug-administrating physician was not blinded. Follow up data acquisition was strictly performed in a blinded manner of physician and patient.

Arms

Are arms mutually exclusive?	Yes
Arm title	Esmolol

Arm description:

24 hours tight heart rate Control with intravenous esmolol infusion

Arm type	Experimental
Investigational medicinal product name	Esmolol
Investigational medicinal product code	
Other name	Brevibloc
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Successive, body-weight adapted i.v. administration, maximal dose 200µg/kg kg/min as maintenance dose

Arm title	Placebo

Arm description:

24 hours intravenous placebo infusion

Arm type	Placebo
Investigational medicinal product name	Placebo (NaCl 0,9%)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

250ml Infusionslösung

Number of subjects in period 1	Esmolol	Placebo
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups	
Reporting group title	Esmolol
Reporting group description:	
24 hours tight heart rate Control with intravenous esmolol infusion	
Reporting group title	Placebo
Reporting group description:	
24 hours intravenous placebo infusion	

Reporting group values	Esmolol	Placebo	Total
Number of subjects	50	50	100
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	57.9	61.4	
standard deviation	± 11.2	± 12.2	-
Gender categorical Units: Subjects			
Female	9	14	23
Male	41	36	77

End points

End points reporting groups

Reporting group title	Esmolol
Reporting group description:	
24 hours tight heart rate Control with intravenous esmolol infusion	
Reporting group title	Placebo
Reporting group description:	
24 hours intravenous placebo infusion	

Primary: Maximum change in Troponin-T-concentration from baseline to 48 hours

End point title	Maximum change in Troponin-T-concentration from baseline to 48 hours[1]
End point description:	
ITT population	
End point type	Primary
End point timeframe:	
48 hours post baseline	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: For statistical analysis see attached summary report

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[2]	50[3]		
Units: ng/ml				
arithmetic mean (standard error)	2.3 (± 3.1)	3.8 (± 4.5)		

Notes:

[2] - ITT population

[3] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to peak Troponin T

End point title	Time to peak Troponin T
End point description:	
End point type	Secondary
End point timeframe:	
baseline to 48h	

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: hours				
arithmetic mean (standard deviation)	14 (± 11.8)	9.6 (± 8.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area unter the Curve (AUC) of Troponin T release

End point title	Area unter the Curve (AUC) of Troponin T release

End point description:

End point type	Secondary

End point timeframe:
baseline to 48h

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: ng*h/ml				
arithmetic mean (standard deviation)	90.6 (± 108.3)	119.1 (± 114.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean heart rate during study intervention

End point title	Mean heart rate during study intervention

End point description:
Heart rate was measuread at 0, 6, 12, 18 and 24 hours.

End point type	Secondary

End point timeframe:
mean value from a 24 hours period

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)	68.1 (± 9.3)	72.6 (± 11.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve (AUC) NT-proBNP

End point title	Area under the curve (AUC) NT-proBNP

End point description:

NT-proBNP: N-terminal pro brain natriuretic peptide.

End point type	Secondary

End point timeframe:

within 0h (baseline) to 48 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: pg*h/ml				
arithmetic mean (standard deviation)	48873.6 (± 38371.8)	86331.8 (± 101952.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6-minute walk test

End point title	6-minute walk test

End point description:

End point type	Secondary

End point timeframe:

6 weeks and 6 months

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[4]	49[5]		
Units: meter				
arithmetic mean (standard deviation)				
6 weeks	517.3 (± 114.5)	456.0 (± 146.4)		
6 months	494.9 (± 150.2)	450.0 (± 146.9)		

Notes:

[4] - 49 for 6 weeks, 50 for 6 months

[5] - 49 for 6 weeks, 48 for 6 months

Statistical analyses

No statistical analyses for this end point

Secondary: Echocardiography-ejection fraction

End point title	Echocardiography-ejection fraction

End point description:

End point type	Secondary

End point timeframe:

post baseline, after 6 weeks, after 6 months

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[6]	50[7]		
Units: percent volume/volume				
arithmetic mean (standard deviation)				
post-intervention	58.8 (± 10.2)	55.0 (± 11.7)		
after 6 weeks	62.5 (± 8.8)	58.6 (± 9.3)		
change in ejection fr.: post-int. to 6 w.	3.5 (± 7.5)	3.3 (± 9.6)		
after 6 months	61.7 (± 9.6)	60.1 (± 10.1)		
change in ejection fr.: post-int. to 6 mths.	2.9 (± 9.3)	4.4 (± 10.0)		

Notes:

[6] - 49 for: ejection fr. after 6 w. and for change in ejection fr. from post-int. to 6 weeks

[7] - 49 for ejection fr. after 6 weeks and change post-int. to 6 w.
48 for 6 mths. values

Statistical analyses

No statistical analyses for this end point

Secondary: Rehospitalisation

End point title	Rehospitalisation

End point description:

End point type	Secondary

End point timeframe:
6 weeks and 6 months after baseline

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[8]	49		
Units: Events				
6 weeks	7	7		
6 months	13	13		

Notes:
[8] - 49 for 6 weeks, 50 for 6 months

Statistical analyses

No statistical analyses for this end point

Secondary: quality of life test

End point title	quality of life test

End point description:
Change in score between baseline and timepoint

End point type	Secondary

End point timeframe:
6 weeks and 6 months

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[9]	49		
Units: score				
arithmetic mean (standard deviation)				
6 weeks after baseline	0.0 (± 0.1)	0.0 (± 0.2)		
6 months after baseline	-0.1 (± 0.1)	0.0 (± 0.2)		

Notes:
[9] - 49 for 6 weeks, 50 for 6 months

Statistical analyses

No statistical analyses for this end point

Secondary: Repeat PCI

End point title	Repeat PCI

End point description:
PCI: percoutaneous coronary intervention

End point type	Secondary

End point timeframe:

PCI 6 weeks and 6 months after baseline

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: Events				
6 weeks	4	1		
6 months	8	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Reinfarction

End point title	Reinfarction

End point description:

End point type	Secondary

End point timeframe:

6 weeks and 6 months after baseline

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[10]	49		
Units: number of subjects with reinfarction				
6 weeks	0	0		
6 months	1	1		

Notes:

[10] - 49 for6 weeks time point, 50 for 6 months timepoint

Statistical analyses

No statistical analyses for this end point

Secondary: Reintervention

End point title	Reintervention

End point description:

End point type	Secondary

End point timeframe:

6 weeks and 6 months after baseline

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[11]	49		
Units: Events				
6 weeks	4	1		
6 months	8	5		

Notes:

[11] - 49 for 6 weeks, 50 for 60 months

Statistical analyses

No statistical analyses for this end point

Secondary: Apoplex during follow-up

End point title	Apoplex during follow-up

End point description:

End point type	Secondary

End point timeframe:

6 weeks and 6 months after baseline

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	49[12]		
Units: Study events				
6 weeks	0	0		
6 months	0	1		

Notes:

[12] - 49 subjects at 6 weeks timepoint, 48 subjects at 6 months timepoint

Statistical analyses

No statistical analyses for this end point

Secondary: Angina pectoris during follow-up

End point title	Angina pectoris during follow-up

End point description:

CCS: Canadian Cardiovascular Society

End point type	Secondary

End point timeframe:

post-intervention, after 6 weeks, after 6 months

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[13]	50[14]		
Units: Events				
Angina pectoris post-intervention CCS1/2	49	40		
Angina pectoris post-invervention CCS3/4	1	10		
Angina pectoris after 6 weeks CCS 1/2	47	43		
Angina pectoris after 6 weeks CCS 3/4	2	6		
Angina pectoris after 6 months CCS 1/2	47	41		
Angina pectoris after 6 months CCS 3/4	3	8		

Notes:

[13] - 50 post intervention, 49 after 6 weeks, 50 after 6 months

[14] - 50 post-intervention, 49 after 6 weeks, 49 after 6 months

Statistical analyses

No statistical analyses for this end point

Secondary: Death from any cause

End point title	Death from any cause

End point description:

End point type	Secondary

End point timeframe:

entire study

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: number of subjects	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to peak concentration NT-proBNP

End point title	Time to peak concentration NT-proBNP

End point description:

End point type	Secondary

End point timeframe:
baseline to 48 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: hours				
arithmetic mean (standard deviation)	28.7 (± 16)	27.1 (± 11.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Neuropsychological status

End point title	Neuropsychological status

End point description:
change in visual analogue scale (VAS) status compare to baseline

End point type	Secondary

End point timeframe:
6 weeks, 6 months

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[15]	49		
Units: mm (visual analogue scale)				
arithmetic mean (standard deviation)				
6 weeks	-1.7 (± 16.3)	1.8 (± 18.4)		
6 months	2.7 (± 17.6)	0.4 (± 18.9)		

Notes:
[15] - 49 for 6 weeks, 50 for months

Statistical analyses

No statistical analyses for this end point

Secondary: Area unter the Curve (AUC) creatinine kinase

End point title	Area unter the Curve (AUC) creatinine kinase

End point description:

End point type	Secondary

End point timeframe:
from baseline to 48 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: ng*h/ml				
arithmetic mean (standard deviation)	37152.1 (± 43683.0)	43576.4 (± 38663.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to peak creatinine kinase

End point title	Time to peak creatinine kinase

End point description:

End point type	Secondary

End point timeframe:
baseline to 48 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: hours				
arithmetic mean (standard deviation)	14.4 (± 11.5)	10.0 (± 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve (AUC) creatinine kinase MB

End point title	Area under the curve (AUC) creatinine kinase MB

End point description:

End point type	Secondary

End point timeframe:
baseline to 48 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: U*h/l				
arithmetic mean (standard deviation)	3674.7 (± 3892.3)	4909.1 (± 4076.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to peak creatinine kinase MB

End point title	Time to peak creatinine kinase MB

End point description:

End point type	Secondary

End point timeframe:
baseline to 48 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: hours				
arithmetic mean (standard deviation)	11.1 (± 7.9)	8.6 (± 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in endothelial progenitor cells CD34

End point title	Change in endothelial progenitor cells CD34

End point description:

End point type	Secondary

End point timeframe:
from baseline to 24 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: counts				
arithmetic mean (standard deviation)	130.9 (± 50.4)	63.0 (± 47.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in endothelial progenitor cells KDR

End point title	Change in endothelial progenitor cells KDR

End point description:

End point type	Secondary

End point timeframe:
baseline to 24 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: counts				
arithmetic mean (standard deviation)	40.6 (± 25.7)	18.7 (± 21.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in endothelial progenitor cells CD133

End point title	Change in endothelial progenitor cells CD133

End point description:

End point type	Secondary

End point timeframe:
baseline to 48 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: counts				
arithmetic mean (standard deviation)	104.0 (± 47.2)	49.4 (± 37.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in endothelial progenitor cells CD117

End point title	Change in endothelial progenitor cells CD117

End point description:

End point type	Secondary

End point timeframe:
baseline to 24 hours

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: counts				
arithmetic mean (standard deviation)	119.6 (± 48.5)	56.1 (± 45.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Echocardiography-wall motion abnormality

End point title	Echocardiography-wall motion abnormality

End point description:

End point type	Secondary

End point timeframe:
post-intervention, 6 weeks and 6 months after intervention

End point values	Esmolol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[16]	50[17]		
Units: patients				
post-intervention	39	46		
after 6 weeks	34	43		
after 6 months	35	44		

Notes:

[16] - 49 for 6 weeks values

[17] - 49 for 6 weeks and 6 months values

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
AEs from Baseline Visite 1 (0h) to Follow-up Visite 3(6mth)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

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

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: For Advers Event listing see attached summary report - safety

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