



## 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<br>(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 unfractionated 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     |
| <b>Arm title</b>             | 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

|                  |         |
|------------------|---------|
| <b>Arm title</b> | 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

| <b>Number of subjects in period 1</b> | 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<br>Units: Subjects                                      |                |                |       |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 57.9<br>± 11.2 | 61.4<br>± 12.2 | -     |
| Gender categorical<br>Units: Subjects                                   |                |                |       |
| Female                                                                  | 9              | 14             | 23    |
| Male                                                                    | 41             | 36             | 77    |

## End points

### End points reporting groups

|                                                                                                     |         |
|-----------------------------------------------------------------------------------------------------|---------|
| Reporting group title                                                                               | Esmolol |
| Reporting group description:<br>24 hours tight heart rate Control with intravenous esmolol infusion |         |
| Reporting group title                                                                               | Placebo |
| Reporting group description:<br>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 <sup>[1]</sup> |
| End point description:<br>ITT population       |                                                                                     |
| End point type                                 | Primary                                                                             |
| End point timeframe:<br>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 <sup>[2]</sup> | 50 <sup>[3]</sup> |  |  |
| 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:<br>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 ( $\pm$ 11.8) | 9.6 ( $\pm$ 8.7) |  |  |

### Statistical analyses

No statistical analyses for this end point

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

|                                         |                                                  |
|-----------------------------------------|--------------------------------------------------|
| End point title                         | Area under the Curve (AUC) of Troponin T release |
| End point description:                  |                                                  |
| End point type                          | Secondary                                        |
| End point timeframe:<br>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 ( $\pm$ 108.3) | 119.1 ( $\pm$ 114.4) |  |  |

### 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:<br>6 weeks and 6 months |                    |



| End point values                     | Esmolol           | Placebo           |  |  |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed          | 50 <sup>[4]</sup> | 49 <sup>[5]</sup> |  |  |
| 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: Mean heart rate during study intervention

|                                                                                 |                                           |
|---------------------------------------------------------------------------------|-------------------------------------------|
| End point title                                                                 | Mean heart rate during study intervention |
| End point description:<br>Heart rate was measured at 0, 6, 12, 18 and 24 hours. |                                           |
| End point type                                                                  | Secondary                                 |
| End point timeframe:<br>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:<br>NT-proBNP: N-terminal pro brain natriuretic peptide. |                                      |
| End point type                                                                 | Secondary                            |
| End point timeframe:<br>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 ( $\pm$ 38371.8) | 86331.8 ( $\pm$ 101952.6) |  |  |

### 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 <sup>[6]</sup> | 49              |  |  |
| Units: Events               |                   |                 |  |  |
| 6 weeks                     | 7                 | 7               |  |  |
| 6 months                    | 13                | 13              |  |  |

Notes:

[6] - 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 <sup>[7]</sup> | 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:

[7] - 49 for 6 weeks, 50 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 <sup>[8]</sup> | 50 <sup>[9]</sup> |  |  |
| 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:

[8] - 49 for: ejection fr. after 6 w. and for change in ejection fr. from post-int. to 6 weeks

[9] - 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: 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 <sup>[10]</sup> | 49              |  |  |
| Units: Events               |                    |                 |  |  |
| 6 weeks                     | 4                  | 1               |  |  |
| 6 months                    | 8                  | 5               |  |  |

Notes:

[10] - 49 for 6 weeks, 50 for 60 months

## 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 <sup>[11]</sup> | 49              |  |  |
| Units: number of subjects with reinfarction |                    |                 |  |  |
| 6 weeks                                     | 0                  | 0               |  |  |
| 6 months                                    | 1                  | 1               |  |  |

Notes:

[11] - 49 for 6 weeks time point, 50 for 6 months timepoint

## Statistical analyses

No statistical analyses for this end point

## Secondary: Repeat PCI

|                                         |            |
|-----------------------------------------|------------|
| End point title                         | Repeat PCI |
| End point description:                  |            |
| PCI: percutaneous 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: 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 <sup>[12]</sup> | 50 <sup>[13]</sup> |  |  |
| Units: Events                            |                    |                    |  |  |
| Angina pectoris post-intervention CCS1/2 | 49                 | 40                 |  |  |
| Angina pectoris post-intervention 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:

[12] - 50 post intervention, 49 after 6 weeks, 50 after 6 months

[13] - 50 post-intervention, 49 after 6 weeks, 49 after 6 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 <sup>[14]</sup> |  |  |
| Units: Study events         |                 |                    |  |  |
| 6 weeks                     | 0               | 0                  |  |  |
| 6 months                    | 0               | 1                  |  |  |

Notes:

[14] - 49 subjects at 6 weeks timepoint, 48 subjects at 6 months timepoint

### 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 <sup>[15]</sup> | 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 under the Curve (AUC) creatinine kinase

|                        |                                              |
|------------------------|----------------------------------------------|
| End point title        | Area under 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:<br>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:<br>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 ( $\pm$ 3892.3) | 4909.1 ( $\pm$ 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:<br>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 ( $\pm$ 7.9) | 8.6 ( $\pm$ 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:<br>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:<br>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:<br>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:<br>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:<br>post-intervention, 6 weeks and 6 months after intervention |                                          |

| <b>End point values</b>     | Esmolol            | Placebo            |  |  |
|-----------------------------|--------------------|--------------------|--|--|
| Subject group type          | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed | 50 <sup>[16]</sup> | 50 <sup>[17]</sup> |  |  |
| 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

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

AEs from Baseline Visite 1 (0h) to Follow-up Visite 3(6mth)

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

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### Dictionary used

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|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

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|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

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

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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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported