# Clinical trial results:
# A prospective, randomized, verum controlled, open label, parallel group multi-center phase III clinical trial to demonstrate the superiority of 500 or 250 mg Aspirin® i.v. (BAY 81-8781) treatment versus 300 mg Aspirin® N tablets p.o. (BAY e4465A) in patients with Acute Coronary Syndrome, measured by time dependent thromboxane inhibition

## Summary

| | |
|---|---|
| EudraCT number | 2007-005163-94 |
| Trial protocol | DE |
| Global end of trial date | 01 July 2014 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 24 July 2016 |
| First version publication date | 10 July 2015 |
| Version creation reason | • Correction of full data set<br>Data correction due to a system error in EudraCT – Results |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | BAY81-8781/12946 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00910065 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com |

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 | 07 January 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 01 July 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate superiority of 500 milligram (mg) and 250 mg Aspirin® intravenous (IV) (BAY81-8781) treatment over oral treatment with 300 mg Aspirin® N tablets to inhibit thromboxane A2-release (measured as stable metabolite thromboxane B2 in serum [TXB2]) at 5 minutes after single dose of study drug administration.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 18 March 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: 270 |
| Worldwide total number of subjects | 270 |
| EEA total number of subjects | 270 |

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) | 166 |
| From 65 to 84 years | 96 |
| 85 years and over | 8 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Of 273 subjects enrolled, 270 subjects were randomized and treated, and the remaining 3 subjects were screen failures.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |

Arm description:

Single IV dose of aspirin at a dose of 500 mg on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Aspirin |
| Investigational medicinal product code | BAY81-8781 |
| Other name | |
| Pharmaceutical forms | Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Single IV dose of aspirin at a dose of 500 mg as bolus infusion injection in approximately 30 seconds through the vein on Day 1.

| | |
|---|---|
| **Arm title** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |

Arm description:

Single IV dose of aspirin at a dose of 250 mg on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Aspirin |
| Investigational medicinal product code | BAY81-8781 |
| Other name | |
| Pharmaceutical forms | Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Single IV dose of aspirin at a dose of 250 mg as bolus infusion injection in approximately 30 seconds through the vein on Day 1.

| | |
|---|---|
| **Arm title** | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

Arm description:

Single oral dose of aspirin tablet at a dose of 300 mg on Day 1.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Aspirin |
| Investigational medicinal product code | BAYe4465 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single oral dose of aspirin tablet at a dose of 300 mg on Day 1.

| **Number of subjects in period 1** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
|---|---|---|---|
| Started | 88 | 85 | 97 |
| Completed | 84 | 83 | 91 |
| Not completed | 4 | 2 | 6 |
| Consent withdrawn by subject | 1 | 1 | 3 |
| Death | 2 | - | 1 |
| Lost to follow-up | - | 1 | 1 |
| Missing | 1 | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |
| Reporting group description: | |
| Single IV dose of aspirin at a dose of 500 mg on Day 1. | |
| Reporting group title | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Reporting group description: | |
| Single IV dose of aspirin at a dose of 250 mg on Day 1. | |
| Reporting group title | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Reporting group description: | |
| Single oral dose of aspirin tablet at a dose of 300 mg on Day 1. | |

| Reporting group values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
|---|---|---|---|
| Number of subjects | 88 | 85 | 97 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous | | | |
| Calculated age at enrolment. | | | |
| Units: years | | | |
| arithmetic mean | 60.5 | 58.6 | 61.4 |
| standard deviation | ± 13 | ± 14.1 | ± 14.3 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 31 | 25 | 40 |
| Male | 57 | 60 | 57 |
| Smoking<br>Units: Subjects | | | |
| Non-smoker | 31 | 27 | 36 |
| Passive smoker | 0 | 0 | 1 |
| Past or present smoker | 57 | 58 | 60 |
| Current alcohol consumption<br>Units: Subjects | | | |
| Missing | 0 | 0 | 1 |
| Abstinent | 26 | 23 | 29 |
| Light alcohol consumption | 48 | 46 | 53 |
| Moderate alcohol consumption | 14 | 16 | 14 |
| Weight<br>Units: kilogram(s) | | | |
| arithmetic mean | 83.84 | 86.67 | 82.64 |
| standard deviation | ± 18.93 | ± 18.66 | ± 18.85 |
| Height<br>Units: centimeter (cm) | | | |
| arithmetic mean | 172.2 | 174.49 | 170.51 |
| standard deviation | ± 10.55 | ± 10.55 | ± 9.28 |
| Body mass index | | | |

| | | | |
|---|---|---|---|
| Units: kilogram per square meter (kg/m^2) | | | |
| arithmetic mean | 28.21 | 28.4 | 28.21 |
| standard deviation | ± 5.65 | ± 5.18 | ± 4.79 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 270 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous | | | |
| Calculated age at enrolment. | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 96 | | |
| Male | 174 | | |
| Smoking | | | |
| Units: Subjects | | | |
| Non-smoker | 94 | | |
| Passive smoker | 1 | | |
| Past or present smoker | 175 | | |
| Current alcohol consumption | | | |
| Units: Subjects | | | |
| Missing | 1 | | |
| Abstinent | 78 | | |
| Light alcohol consumption | 147 | | |
| Moderate alcohol consumption | 44 | | |
| Weight | | | |
| Units: kilogram(s) | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Height | | | |
| Units: centimeter (cm) | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Body mass index | | | |
| Units: kilogram per square meter (kg/m^2) | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |
| Reporting group description: | |
| Single IV dose of aspirin at a dose of 500 mg on Day 1. | |
| Reporting group title | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Reporting group description: | |
| Single IV dose of aspirin at a dose of 250 mg on Day 1. | |
| Reporting group title | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Reporting group description: | |
| Single oral dose of aspirin tablet at a dose of 300 mg on Day 1. | |
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Safety analysis set (N=270) included all subjects who were randomized and received study treatment after randomization. | |
| Subject analysis set title | Pharmacodynamic (PD) analysis set |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| PD analysis set (N=263) included all subjects valid for safety analysis who have a valid TXB2 measurement at baseline and at 5 minutes after study drug administration. | |

### Primary: Concentration of Thromboxane B2 (TXB2) at 5 Minutes Post-dose

| | |
|---|---|
| End point title | Concentration of Thromboxane B2 (TXB2) at 5 Minutes Post-dose |
| End point description: | |
| Values below lower limit of quantitation (LLOQ) were substituted by half of the corresponding LLOQ for the calculation of statistics. Since there was no single LLOQ value and dependent on the measurement batch, LLOQ was not specified and the LLOQ values were used in the calculations. Geometric mean and percentage geometric coefficient of variation (%CV) were reported. | |
| End point type | Primary |
| End point timeframe: | |
| 5 minutes post-dose | |

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86[1] | 82[2] | 95[3] | |
| Units: nanogram per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 3.1 (± 364.85) | 3.86 (± 580.41) | 223.74 (± 724.37) | |

Notes:

[1] - PD analysis set

[2] - PD analysis set

[3] - PD analysis set

## Statistical analyses

| Statistical analysis title | Aspirin 250 mg IV / 300 mg tablet |
|---|---|

Statistical analysis description:

Geometric means were compared using analysis of covariance (ANCOVA) models: baseline TXB2 values as covariate and use of concomitant treatment affecting the measurement up to the 5 minutes blood sample (yes/no), stratification by ST segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI)/unstable angina pectoris (UAP) at randomization as factors. Ratio of geometric means was obtained by exponentiating the differences in respective least squares (LS) mean estimates from the model.

| | |
|---|---|
| Comparison groups | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 177 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [4] |
| Method | ANCOVA |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.018 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.011 |
| upper limit | 0.03 |

Notes:

[4] - One-sided P-value

| Statistical analysis title | Aspirin 500 mg IV / 300 mg tablet |
|---|---|

Statistical analysis description:

Geometric means were compared using ANCOVA models: baseline TXB2 values as covariate and use of concomitant treatment affecting the measurement up to the 5 minutes blood sample (yes/no), stratification by STEMI and NSTEMI/UAP at randomization as factors. Ratio of geometric means was obtained by exponentiating the differences in respective LS-mean estimates from the model.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [5] |
| Method | ANCOVA |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.014 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.009 |
| upper limit | 0.023 |

Notes:

[5] - One-sided P-value

| Statistical analysis title | Aspirin 500 mg IV / 250 mg IV |
|---|---|

Statistical analysis description:

Geometric means were compared using ANCOVA models: baseline TXB2 values as covariate and use of concomitant treatment affecting the measurement up to the 5 minutes blood sample (yes/no),

stratification by STEMI and NSTEMI/UAP at randomization as factors. Ratio of geometric means was obtained by exponentiating the differences in respective LS-mean estimates from the model.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 168 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.21 [6] |
| Method | ANCOVA |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 1.37 |

Notes:

[6] - One-sided P-value

## Secondary: Concentration of Thromboxane B2 (TXB2) at 20 Minutes Post-dose

| | |
|---|---|
| End point title | Concentration of Thromboxane B2 (TXB2) at 20 Minutes Post-dose |

End point description:

Values below LLOQ were substituted by half of the corresponding LLOQ for the calculation of statistics. Since there was no single LLOQ value and dependent on the measurement batch, LLOQ was not specified and the LLOQ values were used in the calculations. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

20 minutes post-dose

| **End point values** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86[7] | 82[8] | 95[9] | |
| Units: nanogram per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 1.48 (± 260.06) | 2.08 (± 534.77) | 14.64 (± 3664.2) | |

Notes:

[7] - PD analysis set

[8] - PD analysis set

[9] - PD analysis set

### Statistical analyses

| **Statistical analysis title** | Aspirin 250 mg IV / 300 mg tablet |
|---|---|

Statistical analysis description:

Geometric means were compared using ANCOVA models: baseline TXB2 values as covariate and use of concomitant treatment affecting the measurement up to the 20 minutes blood sample (yes/no),

stratification by STEMI and NSTEMI/UAP at randomization as factors. Ratio of geometric means was obtained by exponentiating the differences in respective LS-mean estimates from the model.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 177 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [10] |
| Method | ANCOVA |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.073 |
| upper limit | 0.27 |

Notes:

[10] - One-sided P-value

| **Statistical analysis title** | Aspirin 500 mg IV / 300 mg tablet |
|---|---|

Statistical analysis description:

Geometric means were compared using ANCOVA models: baseline TXB2 values as covariate and use of concomitant treatment affecting the measurement up to the 20 minutes blood sample (yes/no), stratification by STEMI and NSTEMI/UAP at randomization as factors. Ratio of geometric means was obtained by exponentiating the differences in respective LS-mean estimates from the model.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [11] |
| Method | ANCOVA |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.099 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.054 |
| upper limit | 0.18 |

Notes:

[11] - One-sided P-value

| **Statistical analysis title** | Aspirin 500 mg IV / 250 mg IV |
|---|---|

Statistical analysis description:

Geometric means were compared using ANCOVA models: baseline TXB2 values as covariate and use of concomitant treatment affecting the measurement up to the 20 minutes blood sample (yes/no), stratification by STEMI and NSTEMI/UAP at randomization as factors. Ratio of geometric means was obtained by exponentiating the differences in respective LS-mean estimates from the model.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |

| | |
|---|---|
| Number of subjects included in analysis | 168 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.087 [12] |
| Method | ANCOVA |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 1.16 |

Notes:

[12] - One-sided P-value

## Secondary: Platelet Aggregation Inhibition (PAI) at 5 Minutes and 20 Minutes After Single Dose of Study Drug Administration Measured as Response to Treatment

| | |
|---|---|
| End point title | Platelet Aggregation Inhibition (PAI) at 5 Minutes and 20 Minutes After Single Dose of Study Drug Administration Measured as Response to Treatment |

End point description:

Percentage inhibition for platelet aggregation was assessed. In the categories listed below, 'N' signifies the number of subjects evaluable for the timepoints.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

5 and 20 minutes post-dose

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86[13] | 82[14] | 95[15] | |
| Units: percentage (%) inhibition | | | | |
| arithmetic mean (standard deviation) | | | | |
| 5 minutes post-dose (N=86, 81, 94) | 20.6 (± 12.1) | 23 (± 19) | 75.6 (± 38.5) | |
| 20 minutes post-dose (N=86, 82, 94) | 22.1 (± 13.4) | 21.6 (± 13) | 42.5 (± 34.1) | |

Notes:

[13] - PD analysis set

[14] - PD analysis set

[15] - PD analysis set

### Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Concentration of Prostacyclin Metabolite at 5 and 20 Minutes Post-dose

| | |
|---|---|
| End point title | Serum Concentration of Prostacyclin Metabolite at 5 and 20 Minutes Post-dose |

End point description:

Serum concentrations of prostacyclin metabolite, that is 6-Keto Prostaglandin F1 ALPHA (6-KETO-PGF1ALPHA) at 5 and 20 minutes post-dose, were reported. In the categories listed below, 'N' signifies the number of subjects evaluable for the timepoints.

| End point type | Secondary |
|---|---|

End point timeframe:

5 and 20 minutes post-dose

| **End point values** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86[16] | 82[17] | 95[18] | |
| Units: picogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| 5 minutes post-dose (N=84, 80, 94) | 227.2 (± 321.7) | 243.4 (± 259) | 657.5 (± 808.8) | |
| 20 minutes post-dose (N=85, 81, 93) | 199.5 (± 272.8) | 208.3 (± 270.6) | 364 (± 450.1) | |

Notes:

[16] - PD analysis set

[17] - PD analysis set

[18] - PD analysis set

## Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of the Composite Clinical Endpoint of Cardiovascular Death, Stroke and Myocardial Infarction up to Day 30 After Single Dose of Study Drug Administration

| End point title | Incidence of the Composite Clinical Endpoint of Cardiovascular Death, Stroke and Myocardial Infarction up to Day 30 After Single Dose of Study Drug Administration |
|---|---|

End point description:

The occurrence of myocardial re/infarction (MI) was assessed up to and including the 30-day time point. Serial electrocardiograms (ECGs), creatine kinase (CKs) and/or creatine kinase-muscle-brains (CK-MBs) plus/minus (+/-) 2 hours*3 were obtained for each suspected recurrent ischemic event. Ischemic stroke (IS) is defined as a new, sudden focal neurological deficit resulting from a presumed cerebrovascular cause that is not reversible or results in death within 24 hours and is not due to a readily identifiable cause, such as a tumor or seizure. Composite number of subjects with cardiovascular (CV) death, IS and MI was reported.

| End point type | Secondary |
|---|---|

End point timeframe:

Post-randomization up to 30 days after single dose of study drug administration

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[19] | 85[20] | 97[21] | |
| Units: Subjects | 2 | 0 | 3 | |

Notes:

[19] - Safety analysis set

[20] - Safety analysis set

[21] - Safety analysis set

## Statistical analyses

| Statistical analysis title | Aspirin 500 mg IV-300 mg tablet |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% confidence intervals (CI) and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.74 [22] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.3 |
| upper limit | 3.8 |

Notes:

[22] - P-value for test of difference

| Statistical analysis title | Aspirin 250 mg IV-300 mg tablet |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.075 [23] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -3 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.2 |
| upper limit | 0.3 |

Notes:

[23] - P-value for test of difference

| **Statistical analysis title** | Aspirin 500 mg IV-250 mg IV |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.17 [24] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 5.6 |

Notes:

[24] - P-value for test of difference

## Secondary: Incidence of Post-randomization Deaths From all Causes, Cardiovascular Deaths, Myocardial Re/Infarctions and Ischemic Strokes Within 24 Hours, 7 Days And 30 Days After Single Dose of Study Drug Administration

| | |
|---|---|
| End point title | Incidence of Post-randomization Deaths From all Causes, Cardiovascular Deaths, Myocardial Re/Infarctions and Ischemic Strokes Within 24 Hours, 7 Days And 30 Days After Single Dose of Study Drug Administration |

End point description:

The occurrence of MI was assessed up to and including the 30-day time point. Serial ECGs, CKs and/or CK-MBs, +/-2 hours*3 were obtained for each suspected recurrent ischemic event. IS is defined as a new, sudden focal neurological deficit resulting from a presumed cerebrovascular cause that is not reversible or results in death within 24 hours and is not due to a readily identifiable cause, such as a tumor or seizure. All deaths were considered CV in nature unless a non-CV cause was clearly shown. Number of subjects with deaths from all causes, CV deaths, MI and IS was reported.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Post-randomization up to 24 hours, 7 days and 30 days after single dose of study drug administration

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[25] | 85[26] | 97[27] | |
| Units: Subjects | | | | |
| Deaths from all causes up to 24 hours | 1 | 0 | 0 | |
| Deaths from all causes up to 7 days | 1 | 0 | 1 | |
| Deaths from all causes up to 30 days | 2 | 0 | 1 | |
| Cardiovascular deaths up to 24 hours | 1 | 0 | 0 | |
| Cardiovascular deaths up to 7 days | 1 | 0 | 1 | |
| Cardiovascular deaths up to 30 days | 1 | 0 | 1 | |
| Myocardial re/infarction up to 24 hours | 1 | 0 | 0 | |
| Myocardial re/infarction up to 7 days | 1 | 0 | 1 | |
| Myocardial re/infarction up to 30 days | 1 | 0 | 1 | |
| Ischemic strokes up to 24 hours | 0 | 0 | 1 | |
| Ischemic strokes up to 7 days | 1 | 0 | 1 | |
| Ischemic strokes up to 30 days | 1 | 0 | 1 | |

Notes:

[25] - Safety analysis set

[26] - Safety analysis set

[27] - Safety analysis set

## Statistical analyses

| Statistical analysis title | 500 mg IV-300 mg tablet: all deaths up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| Comparison groups | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |
|---|---|
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [28] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.5 |

Notes:

[28] - P-value for test of difference

| Statistical analysis title | 500 mg IV-300 mg tablet: all deaths up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-

Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.92 [29] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 3 |

Notes:

[29] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: all deaths up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.48 [30] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.3 |
| upper limit | 4.9 |

Notes:

[30] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: all deaths up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 [31] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 1.3 |

Notes:

[31] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: all deaths up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [32] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 1 |

Notes:

[32] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: all deaths up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [33] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 1 |

Notes:

[33] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: all deaths up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [34] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[34] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: all deaths up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |

| | |
|---|---|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [35] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[35] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: all deaths up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.17 [36] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 5.6 |

Notes:

[36] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: CV deaths up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [37] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.5 |

Notes:

[37] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: CV deaths up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.92 [38] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 3 |

Notes:

[38] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: CV deaths up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.92 [39] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 3 |

Notes:

[39] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: CV deaths up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 [40] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 1.3 |

Notes:

[40] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: CV deaths up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [41] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 1 |

Notes:

[41] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: CV deaths up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [42] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 1 |

Notes:

[42] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: CV deaths up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |

| | |
|---|---|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [43] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[43] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: CV deaths up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [44] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[44] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: CV deaths up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |

| | |
|---|---|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [45] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[45] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: MI events up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [46] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.5 |

Notes:

[46] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: MI events up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.92 [47] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 3 |

Notes:

[47] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: MI events up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.92 [48] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 3 |

Notes:

[48] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: MI events up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 [49] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 1.3 |

Notes:

[49] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: MI events up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [50] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 1 |

Notes:

[50] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: MI events up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.35 [51] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 1 |

Notes:

[51] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: MI events up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [52] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[52] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: MI events up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |

| | |
|---|---|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [53] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[53] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: MI events up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [54] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[54] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: IS events up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [55] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.2 |
| upper limit | 1.2 |

Notes:

[55] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: IS events up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.95 [56] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 3.2 |

Notes:

[56] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-300 mg tablet: IS events up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 185 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.95 [57] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 3.2 |

Notes:

[57] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: IS events up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [58] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.3 |
| upper limit | 1.2 |

Notes:

[58] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: IS events up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

| | |
|---|---|
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [59] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.3 |
| upper limit | 1.2 |

Notes:

[59] - P-value for test of difference

| **Statistical analysis title** | 250 mg IV-300 mg tablet: IS events up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [60] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.3 |
| upper limit | 1.2 |

Notes:

[60] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: IS events up to 24 hours |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |

| | |
|---|---|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 [61] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 1.4 |

Notes:

[61] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: IS events up to 7 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [62] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[62] - P-value for test of difference

| **Statistical analysis title** | 500 mg IV-250 mg IV: IS events up to 30 days |
|---|---|

Statistical analysis description:

Differences in incidences and their 2-sided 95% CI and p-values were calculated by stratified Mantel-Haenszel method (strata: STEMI and NSTEMI/UAP). In case of zero event in a treatment group, the correction term 0.1 (correction type: group size) was applied. The study was not powered to show statistically significant differences between the treatment groups. Consequently, these analyses are regarded as exploratory analyses.

| | |
|---|---|
| Comparison groups | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV v D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |

| | |
|---|---|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 [63] |
| Method | Mantel-Haenszel |
| Parameter estimate | % of absolute risk difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 3.6 |

Notes:

[63] - P-value for test of difference

## Other pre-specified: Number of Subjects with Treatment-emergent High Laboratory Abnormalities

| | |
|---|---|
| End point title | Number of Subjects with Treatment-emergent High Laboratory Abnormalities |

End point description:

Treatment-emergent events were defined as events started or worsened up to 24 hours after single dose of study drug administration.
Number of subjects with at least one high laboratory assessment after start of treatment was reported.
The laboratory variables were as follows:
1. Clinical chemistry laboratory variables included CK-MB, CK, creatinine, glucose, potassium, aspartate transaminase (AST), alanine transaminase (ALT), sodium, Troponin I, Troponin T;
2. Coagulation laboratory variables included prothrombin time (PT) quick method, international ratio of PT (PT-INR), partial thromboplastin time (PTT);
3. Hematology laboratory variables included hematocrit, hemoglobin, platelets, red blood cells, white blood cells.

| | |
|---|---|
| End point type | Other pre-specified |

End point timeframe:

Up to 24 hours on Day 2

| **End point values** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[64] | 85[65] | 97[66] | |
| Units: Subjects | | | | |
| CK-MB | 3 | 6 | 4 | |
| CK | 6 | 7 | 5 | |
| Creatinine | 4 | 3 | 4 | |
| Glucose | 19 | 17 | 19 | |
| Potassium | 2 | 2 | 1 | |
| AST | 3 | 7 | 6 | |
| ALT | 1 | 4 | 2 | |
| Sodium | 2 | 2 | 2 | |
| Troponin I | 1 | 3 | 0 | |
| Troponin T | 6 | 3 | 3 | |

| | | | | |
|---|---|---|---|---|
| PT quick method | 2 | 2 | 1 | |
| PT-INR | 1 | 2 | 1 | |
| PTT | 11 | 7 | 6 | |
| Hematocrit | 0 | 1 | 1 | |
| Hemoglobin | 2 | 1 | 0 | |
| Platelets | 1 | 1 | 2 | |
| Red blood cells | 1 | 1 | 1 | |
| White blood cells | 5 | 5 | 5 | |

Notes:

[64] - Safety analysis set

[65] - Safety analysis set

[66] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in Vital Signs at the End of Treatment (Day 2): Heart Rate

| End point title | Change From Baseline in Vital Signs at the End of Treatment (Day 2): Heart Rate |
|---|---|

End point description:

Heart rate was assessed at screening (Day 1) and at Day 2, and was measured in supine position if possible. Screening was defined as baseline for this endpoint. In the categories listed below, "N" signifies the number of subjects evaluable for the timepoints.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline (Day 1) and Day 2

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[67] | 85[68] | 97[69] | |
| Units: beats per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N=88, 85, 97) | 74.5 (± 14) | 77.1 (± 20.4) | 76.3 (± 15.7) | |
| Change at Day 2 (N=83, 81, 91) | -1.4 (± 11.8) | -3.6 (± 21.1) | -3.4 (± 15.9) | |

Notes:

[67] - Safety analysis set

[68] - Safety analysis set

[69] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in Vital Signs at the End of Treatment (Day 2): Blood Pressure

| End point title | Change From Baseline in Vital Signs at the End of Treatment |
|---|---|

| | |
|---|---|
| | (Day 2): Blood Pressure |

End point description:

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were assessed at screening (Day 1) and at Day 2, and were measured in supine position if possible. Screening was defined as baseline for this endpoint. In the categories listed below, "N" signifies the number of subjects evaluable for the timepoints.

| | |
|---|---|
| End point type | Other pre-specified |

End point timeframe:

Baseline (Day 1) and Day 2

| **End point values** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[70] | 85[71] | 97[72] | |
| Units: millimeter of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| SBP at baseline (N=88, 85, 97) | 140.1 (± 20.3) | 137.7 (± 23.8) | 142.2 (± 20.4) | |
| Change in SBP at Day 2 (N=83, 81, 90) | -10.5 (± 19.8) | -10.4 (± 23.3) | -12.4 (± 20.5) | |
| DBP at baseline (N=88, 85, 97) | 82.2 (± 13.8) | 78.6 (± 12.5) | 80.7 (± 12.1) | |
| Change in DBP at Day 2 (N=83, 81, 90) | -8 (± 13.4) | -6 (± 13.6) | -3.8 (± 12.5) | |

Notes:

[70] - Safety analysis set

[71] - Safety analysis set

[72] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Subjects With Abnormal Electrocardiogram (ECG) Findings

| | |
|---|---|
| End point title | Number of Subjects With Abnormal Electrocardiogram (ECG) Findings |

End point description:

ECG was performed at screening (Day 1) and at Day 2, and findings were considered 'abnormal' as per the Investigator's discretion. Screening was defined as baseline for this endpoint.

| | |
|---|---|
| End point type | Other pre-specified |

End point timeframe:

Baseline (Day 1) and Day 2

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[73] | 85[74] | 97[75] | |
| Units: Subjects | | | | |
| Baseline (Day 1) | 88 | 85 | 97 | |
| Day 2 | 80 | 78 | 81 | |

Notes:

[73] - Safety analysis set

[74] - Safety analysis set

[75] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Incidence of all Post-randomization Strokes of Unknown Etiology Until 24 Hours (Treatment-emergent), and Within 7 Days After Single Dose of Study Drug Administration

| End point title | Incidence of all Post-randomization Strokes of Unknown Etiology Until 24 Hours (Treatment-emergent), and Within 7 Days After Single Dose of Study Drug Administration |
|---|---|

End point description:

Treatment-emergent events were defined as events started or worsened up to 24 hours after single dose of study drug administration. IS is defined as a new, sudden focal neurological deficit resulting from a presumed cerebrovascular cause that is not reversible or results in death within 24 hours and is not due to a readily identifiable cause, such as a tumor or seizure. Number of subjects with post-randomization IS events of unknown etiology was reported.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Post-randomization up to 24 hours and 7 days after single dose of study drug administration

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[76] | 85[77] | 97[78] | |
| Units: Subjects | | | | |
| Up to 24 hours | 0 | 0 | 0 | |
| Up to 7 days | 0 | 0 | 1 | |

Notes:

[76] - Safety analysis set

[77] - Safety analysis set

[78] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Incidence of Composite of Post-randomization Thrombolysis in MI (TIMI) Major and Minor Bleeding, and Bleeding Requiring Medical Attention up to 24 Hours After Single Dose of Study Drug Administration

| End point title | Incidence of Composite of Post-randomization Thrombolysis in MI (TIMI) Major and Minor Bleeding, and Bleeding Requiring Medical Attention up to 24 Hours After Single Dose of Study Drug Administration |
|---|---|

End point description:

TIMI classification for bleedings was as follows:
Major: Intracranial hemorrhage; or spontaneous, bleeding at any instrumented site, retroperitoneal, or clinically significant overt hemorrhage associated with a drop in hematocrit of at least 15% or a drop in hemoglobin of at least 5 grams per deciliter (g/dL);
Minor: Clinically overt bleeding (examples: gross hematuria or hematemesis) associated with a drop in hematocrit of 9% to less than or equal to (<=) 15% or a drop in hemoglobin of 3 g/dL to <=5 g/dL;
Minimal: Any clinically overt sign of hemorrhage (including imaging) associated with a fall in hemoglobin less than (<) 3 g/dL (or, when hemoglobin is not available, a fall in hematocrit of <9%).
Bleeding requiring medical attention was defined as TIMI minimal bleeding or bleeding which was not classified above and required medical or surgical treatment.
Composite number of subjects with TIMI major and minor bleeding, and bleeding requiring medical attention was reported.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Post-randomization up to 24 hours after single dose of study drug administration

| **End point values** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[79] | 85[80] | 97[81] | |
| Units: Subjects | 6 | 3 | 6 | |

Notes:

[79] - Safety analysis set

[80] - Safety analysis set

[81] - Safety analysis set

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Hospital Mortality During the Hospitalization for Acute Coronary Syndrome

| End point title | Hospital Mortality During the Hospitalization for Acute Coronary Syndrome |
|---|---|

End point description:

Number of subjects with hospital mortality during the hospitalization period for acute coronary syndrome was reported.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

During hospital stay

| End point values | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88[82] | 85[83] | 97[84] | |
| Units: Subjects | 2 | 0 | 1 | |

Notes:

[82] - Safety analysis set

[83] - Safety analysis set

[84] - Safety analysis set

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent events including bleedings are defined as events started or worsened up to 24 hours after single dose of study drug administration.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV |

Reporting group description:

Single IV dose of aspirin at a dose of 500 mg on Day 1.

| | |
|---|---|
| Reporting group title | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV |

Reporting group description:

Single IV dose of aspirin at a dose of 250 mg on Day 1.

| | |
|---|---|
| Reporting group title | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |

Reporting group description:

Single oral dose of aspirin tablet at a dose of 300 mg on Day 1.

| Serious adverse events | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 88 (2.27%) | 1 / 85 (1.18%) | 3 / 97 (3.09%) |
| number of deaths (all causes) | 2 | 0 | 1 |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 0 / 97 (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 |
| Nervous system disorders | | | |
| Ischaemic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Sudden cardiac death | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (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 |

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

| **Non-serious adverse events** | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 500 mg IV | D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV | Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 88 (18.18%) | 10 / 85 (11.76%) | 20 / 97 (20.62%) |
| Vascular disorders | | | |
| Arteriovenous fistula | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematoma | | | |
| subjects affected / exposed | 3 / 88 (3.41%) | 3 / 85 (3.53%) | 3 / 97 (3.09%) |
| occurrences (all) | 3 | 3 | 3 |
| Hypertension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 88 (2.27%) | 1 / 85 (1.18%) | 3 / 97 (3.09%) |
| occurrences (all) | 2 | 1 | 3 |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arterial haemorrhage | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Surgical and medical procedures | | | |
| Stent placement | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 1 | 1 |
| General disorders and administration site conditions | | | |
| Injection site haematoma | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Vessel puncture site haemorrhage | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 1 / 85 (1.18%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|---|---|---|---|
| Insomnia | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Disorientation | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| High density lipoprotein decreased | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Subcutaneous haematoma | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular pseudoaneurysm | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 2 / 85 (2.35%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Headache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 88 (1.14%) | 2 / 85 (2.35%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 2 | 1 |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Ascites | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 2 / 85 (2.35%) | 2 / 97 (2.06%) |
| occurrences (all) | 1 | 2 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Cold sweat | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Renal and urinary disorders | | | |
| Renal cyst | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 1 / 85 (1.18%) | 0 / 97 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Endocrine disorders | | | |

| | | | |
|---|---|---|---|
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 1 / 85 (1.18%) | 1 / 97 (1.03%) |
| occurrences (all) | 1 | 1 | 1 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 88 (0.00%) | 0 / 85 (0.00%) | 1 / 97 (1.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 1 / 88 (1.14%) | 0 / 85 (0.00%) | 0 / 97 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 30 April 2009 | 1. Two inclusion criteria were added<br>2. Secondary efficacy and safety variables were added<br>3. Subjects were assigned to treatment groups using interactive voice response system (IVRS)<br>4. Blood samples for TXB2 analysis, serum prostacycline and platelet aggregation inhibition analysis were taken during screening period<br>5. Cardiovascular endpoints, stroke endpoints and hemorrhagic endpoints were appointed for confirmation by an Endpoint Adjudication Committee<br>6. The statistical model was ANCOVA for the analysis of the primary efficacy variable (log transformed). The ANCOVA models were stratified by region (China and Europe), by use of anticoagulant and by the stratification factor STEMI/NSTEMI and unstable angina from the randomization. |
| 03 August 2010 | It was decided to cancel the study in China and conduct it only in Germany. For this reason, the coordinating investigator was changed, the number of randomized subjects was reduced, and sample size calculations were modified accordingly. Stratification by region (China and Europe) was excluded from the planned primary and secondary efficacy analyses. Since randomization was no longer performed by Interactive Voice Response System, the method of assigning subjects to treatment was modified. Prior and concomitant medications not approved in Germany were excluded from the list of prior/concomitant therapy permitted for this study. Pregnancy test was excluded since pregnancy testing has not been routinely performed on sites. Central laboratory was not needed anymore for the purpose of the study and all laboratory evaluations were to be performed by the local laboratories. Furthermore, only local ECG performance and evaluations were to be performed.<br>Other relevant changes included the following:<br>1. Addition of statements regarding none-specific gender distribution and treatment(s) following the end of the study<br>2.Elaboration of an inclusion criterion by adding a statement on subject’s capacity to consent prior enrollment<br>3. A new definition of the time between screening and randomization (that is, the time frame was changed from “no more than 2 hours” to “as short as possible”)<br>4. Definition for sufficiently reliable safety signal of clinical relevance regarding bleeding events was added<br>5. On study definition and definitions of populations for analysis were slightly modified. |

| | |
|---|---|
| 18 October 2011 | 1. Change of one inclusion criterion to: Angina pectoris lasting for more than 20 minutes within the last 24 hours before study drug treatment (or equivalent acute symptoms such as increasing dyspnoea, diaphoresis, nausea, abdominal/epigastric pain, syncope, etc.) and at least one of the following:<br>a. ECG changes suggestive for ischemia: ST elevation or T-wave change or ST depression, new or presumed left bundle-branch block,<br>b. Elevated troponin T levels >0.01 nanogram per milliliter or any other elevated troponin levels according to local laboratory reference values,<br>c. Risk factors for acute coronary syndrome such as known coronary artery disease, diabetes mellitus, impaired renal function, peripheral artery or cerebrovascular disease, current smoking.<br>2. Change of one exclusion criterion to: Stroke within 3 months prior to study drug treatment.<br>3. Deletion of the following exclusion criterion: Other anticoagulants in the last 5 days before study drug treatment.<br>4. Addition of the following exclusion criterion: Treatment with glycoprotein IIb/IIIa inhibitors within 48 hours prior to study drug treatment and before the 20 minutes blood samples for thromboxane, prostacyclin, and platelet aggregation measurements had been taken.<br>In addition, an appropriate definition of the PD population for analysis was implemented and “haematology (full blood count)” was excluded from the safety laboratory assessments. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| Occurrence of "±” in relation with geometric CV is auto-generated and cannot be deleted. Decimal places were automatically truncated if last decimal equals zero. |

Notes: