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	v1
This version publication date	14 July 2016
First version publication date	10 July 2015

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 HealthCare AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com
Scientific contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.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 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 Units: Subjects			
Female	31	25	40
Male	57	60	57
Smoking Units: Subjects			
Non-smoker	31	27	36
Passive smoker	0	0	1
Past or present smoker	57	58	60
Current alcohol consumption Units: Subjects			
Missing	0	0	1
Abstinent	26	23	29
Light alcohol consumption	48	46	53
Moderate alcohol consumption	14	16	14
Weight Units: kilogram(s)			
arithmetic mean	83.84	86.67	82.64
standard deviation	± 18.93	± 18.66	± 18.85
Height 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	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 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.

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

subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 85 (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
General disorders and administration site conditions			
Sudden cardiac death			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 85 (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%)	1 / 97 (1.03%)	0 / 85 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 85 (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	Acetylsalicylic acid (Aspirin, BAYe4465) 300 mg Tablet	D,L-lysine acetylsalicylate (Aspirin, BAY81-8781) 250 mg IV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 88 (18.18%)	20 / 97 (20.62%)	10 / 85 (11.76%)
Vascular disorders			
Arteriovenous fistula			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	3 / 88 (3.41%)	3 / 97 (3.09%)	3 / 85 (3.53%)
occurrences (all)	3	3	3
Hypertension			

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

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

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

Hyperthyroidism			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 85 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 88 (1.14%)	1 / 97 (1.03%)	1 / 85 (1.18%)
occurrences (all)	1	1	1
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 85 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 85 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 88 (0.00%)	1 / 97 (1.03%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 85 (0.00%)
occurrences (all)	1	0	0
Hyperlipidaemia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 97 (0.00%)	0 / 85 (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 2. Secondary efficacy and safety variables were added 3. Subjects were assigned to treatment groups using interactive voice response system (IVRS) 4. Blood samples for TXB2 analysis, serum prostacycline and platelet aggregation inhibition analysis were taken during screening period 5. Cardiovascular endpoints, stroke endpoints and hemorrhagic endpoints were appointed for confirmation by an Endpoint Adjudication Committee 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. Other relevant changes included the following: 1. Addition of statements regarding none-specific gender distribution and treatment(s) following the end of the study 2.Elaboration of an inclusion criterion by adding a statement on subject’s capacity to consent prior enrollment 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”) 4. Definition for sufficiently reliable safety signal of clinical relevance regarding bleeding events was added 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: a. ECG changes suggestive for ischemia: ST elevation or T-wave change or ST depression, new or presumed left bundle-branch block, b. Elevated troponin T levels >0.01 nanogram per milliliter or any other elevated troponin levels according to local laboratory reference values, 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. 2. Change of one exclusion criterion to: Stroke within 3 months prior to study drug treatment. 3. Deletion of the following exclusion criterion: Other anticoagulants in the last 5 days before study drug treatment. 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. 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: