Clinical trial results:
ACE inhibitor for lung protection during mechanical Ventilation for acute lung injury - pilot trial

Summary

EudraCT number	2010-020403-75
Trial protocol	DE
Global end of trial date	17 January 2016

Results information

Result version number	v1 (current)
This version publication date	26 October 2019
First version publication date	26 October 2019
Summary attachment (see zip file)	final report ACEmeVent-Pilot Trial (ACEmeVent-Pilot_Ergebnisbericht_in_Arzneimittelpruefungen_final1.0_2017-01-10.pdf)

Trial information

Trial identification

Sponsor protocol code	ACEmeVent-Pilot

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	German Clinical Trials Register: DRKS00000156

Notes:

Sponsors

Sponsor organisation name	Universität Leipzig
Sponsor organisation address	Ritterstr. 26, Leipzig, Germany, 04109
Public contact	Abteilung für Pneumologie, Universität Leipzig, Department für Innere Medizin, Neurologie und Dermatologie , 49 3419712600, ACEmeVent-Pilot@zks.uni-leipzig.de
Scientific contact	Abteilung für Pneumologie, Universität Leipzig, Department für Innere Medizin, Neurologie und Dermatologie , 49 3419712600, ACEmeVent-Pilot@zks.uni-leipzig.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 January 2016
Global end of trial reached?	Yes
Global end of trial date	17 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety concerning renal functions and cardiovascular functions as well as the occurrence of severe adverse events.
Further primary objective is efficacy of the treatment regarding the recovery of the lungs measured as ventilator free days.

Protection of trial subjects:

Patients were closely monitored by the treating staff with regard to safety during the course of the study. In addition to the detection of adverse events, this included the collection of the following parameters on the CRF: hemodynamic parameters, organ dysfunction, safety labor parameters.

Background therapy:

Standard of care

Evidence for comparator: -

Actual start date of recruitment	10 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	35
From 65 to 84 years	23

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 10.05.2012 and 28.10.2015 61 patients were randomised. Three patients had to be excluded since the informed consent process failed. N=58 patients constitute the full analysis set. All these patients were followed up until death or day 60. Accrual was slower than anticipated. The initially targeted sample size of 210 was not attainable.

Pre-assignment

Screening details:

All patients diagnosed with with acute lung failure (ALI/ARDS) in participating sites included if they meet all inclusion criteria and none of the exclusion criteria applied.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Enalaprilat

Arm description:

10mg Enalaprilat as injection solution in injection vials (10ml) or the preparation of an infusion solution (50ml). One injection vial corresponds to one daily dose. Total amount for one patient for a maximum of 28 days trial therapy and two additional daily doses as reserve.

Arm type	Experimental
Investigational medicinal product name	Enalaprilat
Investigational medicinal product code	
Other name	Enahexal
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

10mg as injection solution in injection vials (10 ml) for the preparation of an infusion solution (50 ml).

Arm title	Placebo

Arm description:

sodium chloride solution (0,9 %) in injection vials (10 ml) for the preparation of an infusion solution (50 ml). One injection vial corresponds to one daily dose. Total amount for one patient for a maximum of 28 days trial therapy and two additional daily doses as a reserve.

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

Dosage and administration details:

sodium chloride solution (0,9 %) in injection vials (10 ml) for the preparation of an infusion solution (50 ml)

Number of subjects in period 1	Enalaprilat	Placebo
Started	29	29
Completed	29	29

Baseline characteristics

Reporting groups	
Reporting group title	Enalaprilat
Reporting group description:	
10mg Enalaprilat as injection solution in injection vials (10ml) or the preparation of an infusion solution (50ml). One injection vial corresponds to one daily dose. Total amount for one patient for a maximum of 28 days trial therapy and two additional daily doses as reserve.	
Reporting group title	Placebo
Reporting group description:	
sodium chloride solution (0,9 %) in injection vials (10 ml) for the preparation of an infusion solution (50 ml). One injection vial corresponds to one daily dose. Total amount for one patient for a maximum of 28 days trial therapy and two additional daily doses as a reserve.	

Reporting group values	Enalaprilat	Placebo	Total
Number of subjects	29	29	58
Age categorical Units: Subjects			
Adults (18-64 years)	20	15	35
From 65-84 years	9	14	23
85 years and over	0	0	0
NA	0	0	0
Age continuous Units: years			
arithmetic mean	56.9	63.1	
standard deviation	± 14.1	± 13.0	-
Gender categorical Units: Subjects			
Female	5	6	11
Male	24	23	47
NA	0	0	0
Acute lung injury Units: Subjects			
yes	29	29	58
no	0	0	0
NA	0	0	0
ACE-inhibitors (within the last 7 days) Units: Subjects			
yes	2	8	10
no	27	21	48
NA	0	0	0
Cause of acute lung injury Units: Subjects			
Pneumonia	19	14	33
Sepsis	3	7	10
Aspiration	3	6	9
Trauma	1	0	1
Transfusion related lung injury	0	0	0
Other	3	2	5
NA	0	0	0

AT1 blockers Units: Subjects			
yes	4	7	11
no	25	22	47
NA	0	0	0
Height Units: cm			
arithmetic mean	175	172	
standard deviation	± 9	± 8	-
Weight Units: kg			
arithmetic mean	84	83	
standard deviation	± 15	± 18	-
Urine output Units: ml/24h			
arithmetic mean	1771	2140	
standard deviation	± 1349	± 1610	-
Maximal body temperature Units: degree Celsius			
arithmetic mean	38	38	
standard deviation	± 1	± 1	-
Arterial paCO2 Units: mmHG			
arithmetic mean	46.6	66.4	
standard deviation	± 11.2	± 64.2	-
Arterial paO2 Units: mmHg			
arithmetic mean	88.4	92.9	
standard deviation	± 41.8	± 35.0	-
FiO2 Units: percent			
arithmetic mean	0.7	0.7	
standard deviation	± 0.2	± 0.2	-
paO2/FiO2 Units: ratio			
arithmetic mean	122.0	141.4	
standard deviation	± 61.8	± 59.9	-

End points

End points reporting groups

Reporting group title	Enalaprilat
Reporting group description:	
10mg Enalaprilat as injection solution in injection vials (10ml) or the preparation of an infusion solution (50ml). One injection vial corresponds to one daily dose. Total amount for one patient for a maximum of 28 days trial therapy and two additional daily doses as reserve.	
Reporting group title	Placebo
Reporting group description:	
sodium chloride solution (0,9 %) in injection vials (10 ml) for the preparation of an infusion solution (50 ml). One injection vial corresponds to one daily dose. Total amount for one patient for a maximum of 28 days trial therapy and two additional daily doses as a reserve.	

Primary: Ventilator free days

End point title	Ventilator free days
End point description:	
Primary efficacy endpoint. Every complete day alive and without mechanical ventilation between day 0 and day 28.	
End point type	Primary
End point timeframe:	
28 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: days				
arithmetic mean (standard deviation)	12.3 (± 10.7)	8.7 (± 10.1)		

Statistical analyses

Statistical analysis title	Primary efficacy: ventilator free days
Statistical analysis description:	
comparison of ventilator-free days in the intention to treat population	
Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.185
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-3.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.12
upper limit	1.81

Primary: Renal replacement therapy free days

End point title	Renal replacement therapy free days
End point description: primary safety endpoint	
End point type	Primary
End point timeframe: 28 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: days				
arithmetic mean (standard deviation)	20 (± 11)	19 (± 11)		

Statistical analyses

Statistical analysis title	Primary: Renal replacement therapy free days
Statistical analysis description: primary safety analysis	
Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.79
Method	t-test, 2-sided

Secondary: Days alive outside ICU

End point title	Days alive outside ICU
End point description: Secondary efficacy endpoint	
End point type	Secondary
End point timeframe: 28 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: days				
arithmetic mean (standard deviation)	8.9 (± 9.4)	4.9 (± 8)		

Statistical analyses

Statistical analysis title	Secondary: days alive outside ICU
Statistical analysis description: secondary efficacy analysis	
Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.086
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	0.6

Secondary: Overall survival d28

End point title	Overall survival d28
End point description: Secondary efficacy endpoint	
End point type	Secondary
End point timeframe: 28 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: patient				
dead	6	5		
alive	23	24		

Statistical analyses

Statistical analysis title	Secondary: overall survival d28
Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chi-squared

Secondary: Overall survival d60

End point title	Overall survival d60
End point description: Secondary efficacy endpoint	
End point type	Secondary
End point timeframe: 60 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: patients				
dead	7	6		
alive	22	23		

Statistical analyses

Statistical analysis title	Secondary: overall survival d60
Statistical analysis description: secondary efficacy analysis	
Comparison groups	Placebo v Enalaprilat

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chi-squared

Secondary: Days without organ failure

End point title	Days without organ failure
End point description: Secondary efficacy endpoint. Days alive without organ failure (except lung)	
End point type	Secondary
End point timeframe: 28 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: days				
arithmetic mean (standard deviation)	20.1 (± 9.6)	21.7 (± 9.1)		

Statistical analyses

Statistical analysis title	Secondary: days without organ failure
Statistical analysis description: secondary efficacy analysis	
Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.498
Method	t-test, 2-sided

Secondary: Renal replace-ment therapy d60

End point title	Renal replace-ment therapy d60
End point description: Restricted on patients alive at day 60.	
End point type	Secondary
End point timeframe: day 60	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	23		
Units: patients				
renal replacement therapy	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean daily fluid balance

End point title	Mean daily fluid balance
End point description: Secondary safety analysis	
End point type	Secondary
End point timeframe: days 1-5	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: ml				
arithmetic mean (standard deviation)	343 (± 1644)	291 (± 1248)		

Statistical analyses

Statistical analysis title	Secondary: mean daily fluid balance
Statistical analysis description: Secondary safety analysis	
Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.89
Method	t-test, 2-sided

Secondary: Vasoactive substance free days

End point title	Vasoactive substance free days
End point description: secondary safety endpoint	
End point type	Secondary
End point timeframe: 28 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: days				
arithmetic mean (standard deviation)	16.4 (± 10.5)	16.1 (± 9.9)		

Statistical analyses

Statistical analysis title	Secondary: vasoactive substance free days
Statistical analysis description: secondary safety analysis	
Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.89
Method	t-test, 2-sided

Other pre-specified: Ventilator free days in per-protocol population

End point title	Ventilator free days in per-protocol population
End point description: Sensitivity analysis for the primary efficacy endpoint in the per-protocol-population. Every complete day alive and without mechanical ventilation between day 0 and day 28 is counted.	
End point type	Other pre-specified
End point timeframe: 28 days	

End point values	Enalaprilat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	22		
Units: days				
arithmetic mean (standard deviation)	12.5 (± 10.7)	6.8 (± 9.5)		

Statistical analyses

Statistical analysis title	Sensitivity analysis for primary efficacy endpoint

Statistical analysis description:

Several patients received additional, oral ACE Inhibitors violating the protocol. 7 patients in the Placebo arm and 5 patients in the Enalaprilat arm were treated with additional oral ACE Inhibitors. Duration of treatment with additional ACE inhibitor was 13.7±10.9 days in the Placebo and 4.6±7 days in the Enalaprilat arms (p=0.108). Since these numbers are not negligible these patients are excluded in a per-protocol sensitivity analysis.

Comparison groups	Enalaprilat v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 24h after last study drug administration	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	Enalaprilat
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Enalaprilat	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 29 (27.59%)	12 / 29 (41.38%)	
number of deaths (all causes)	7	6	
number of deaths resulting from adverse events	7	5	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prothrombin time prolonged			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural haemorrhage			

subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Low cardiac output syndrome			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Gastrointestinal disorders			
Intestinal ischaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic ischaemia			

subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Hypercapnia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	

Septic shock			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Lactic acidosis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metabolic acidosis			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Enalaprilat	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 29 (86.21%)	25 / 29 (86.21%)	
Investigations			
C-reactive protein increased			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Haemoglobin decreased			
subjects affected / exposed	0 / 29 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	3	
Platelet count decreased			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Vascular disorders			
Haemodynamic instability			
subjects affected / exposed	8 / 29 (27.59%)	2 / 29 (6.90%)	
occurrences (all)	10	3	
Hypertension			
subjects affected / exposed	0 / 29 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	5	

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	3	
Cardiac arrest			
subjects affected / exposed	3 / 29 (10.34%)	1 / 29 (3.45%)	
occurrences (all)	3	1	
Sinus bradycardia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	3	0	
Tachyarrhythmia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	9	0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Pyrexia			
subjects affected / exposed	6 / 29 (20.69%)	2 / 29 (6.90%)	
occurrences (all)	7	3	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 29 (3.45%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
Delirium			
subjects affected / exposed	2 / 29 (6.90%)	4 / 29 (13.79%)	
occurrences (all)	2	4	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	4 / 29 (13.79%)	2 / 29 (6.90%)	
occurrences (all)	4	2	
Infections and infestations			
Sepsis			
subjects affected / exposed	2 / 29 (6.90%)	2 / 29 (6.90%)	
occurrences (all)	2	3	
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	3 / 29 (10.34%)	2 / 29 (6.90%)	
occurrences (all)	3	2	
Hypophosphataemia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	
occurrences (all)	3	0	
Metabolic acidosis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2012	Exclusion criteria regarding contraindication for therapy to be used are changed: Exclusion criteria "severe renal dysfunction" and "patients with renal replacement therapy" are deleted.
09 October 2013	more precise definition of inclusion and exclusion criteria: 1. Presence of invasive mechanical ventilation and start of ventilation no longer than 60 hours ago (previously 48 hours) 2. Age at least 18 years (previously: age between 18 until 80 years) 3. patients a. after bone marrow or stem cell transplantation within the last 12 months b. after lung transplantation (previously: Patients after bone marrow, stem cell or lung transplantation)
05 February 2015	Minor adjustments to the trial protocol: for example: The project accompanying the investigation of the ACE gene polymorphism of the study has so far not been sufficiently distinguished from the study question in the trial protocol. Duration of the trial customized, because the recruitment was delayed and was expected to end in late 2015 following the recruitment of 60 patients as recommended by the DMC. Supplementing the safety endpoint: Change in renal function (CREA) by day 28

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.

The recruitment was delayed and was expected to end in late 2015 following the recruitment of 60 patients (planned: 210 patients) as recommended by the DMC.

Notes: