Clinical trial results:
Biomarker guided antibiotic treatment in Community-Acquired Pneumoni (BIO-CAP)

Summary

EudraCT number	2015-002501-11
Trial protocol	DK
Global end of trial date	30 March 2020

Results information

Result version number	v1 (current)
This version publication date	15 September 2021
First version publication date	15 September 2021

Trial information

Trial identification

Sponsor protocol code	BIO-CAP_2015

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Nordsjællands Hospital
Sponsor organisation address	Dyrehavevej 29, Hillerød, Denmark,
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of biomarker algorithms to reduce duration of antibiotic exposure in patients hospitalized with CAP compared to standard of care and to evaluate the efficacy of an algorithm based on C-reactive protein compared to an algorithm based on Procalcitonin for this purpose.

Protection of trial subjects:

Participants were treated according to guidelines in regards to choice of antibiotic agent. The intervention determined the length of treatment in the intervention groups, however, we determined a minimum treatment length according to current evidence of 72-hours. Further, the discontinuation of antibiotic treatment according to the biomarker algorithms could be overruled by the treating physician.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2017
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	Denmark: 300
Worldwide total number of subjects	300
EEA total number of subjects	300

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)	99
From 65 to 84 years	163
85 years and over	38

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 01-Mar-2017 - 01-Mar-2020.

Pre-assignment

Screening details:

Adult patients (18 years or older) admitted to Nordsjællands Hospital with symptoms compatible with Community Acquired Pneumonia (CAP) were screened for inclusion. The primay causes for no inclusion were no infiltrate on chest x-ray, inability to comprehend study material or unwillingnes to participate.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CRP-group

Arm description:

Antibiotic treatment were given for minimum 72 hours.
After this time point antibiotic treatment were continued/discontinued according to the CRP biomarker algorithm:
CRP < 50 g/dl: discontinue antibiotic treatment
CRP < 75 g/dl and CRP ≥ 50 g/dl and CRP has decreased with at least 20% within the last 24 hours: discontinue antibiotic treatment
CRP ≥ 75 g/dl: continue antibiotic treatment

Arm type	Experimental
Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency was determined by the treating physician

Investigational medicinal product name	Amoxicillin/clavulansyre
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency was determined by the treating physician

Investigational medicinal product name	Ampicillin "PCD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Dosage and frequency was determined by the treating physician

Investigational medicinal product name	Ampicillin ”PCD”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Benzylpenicillin ”Panpharma”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Cefuroxim ”Stragen”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Ciprofloxacin ”Fresenius Kabi”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Ciprofloxacin “Actavis”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Clarithromycin ”Paranova”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Clarithromycin ”Hexal”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Dicloxacillin ”Actavis”
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Doxycyclin Europharma
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Meropenem ”Fresenius Kabi”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Moxifloxacin ”Orion”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Moxifloxacin "Actavis",
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Piperacillin/Tazobactam ”Fresenius Kabi”,
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Roxithromycin ”Orifarm”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Vepicombin Novum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency were determined by the treating physician

Arm title	Control-group

Arm description:

Participant are treated according to current guidelines.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	PCT-group

Arm description:

Antibiotic treatment were given for minimum 72 hours.
After this time point antibiotic treatment were continues/discontinued according to the PCT (procalcitonin) biomarker algorithm:
PCT < 0,25 µg/l : discontinue antibiotic treatment
CRP ≥ 0,25 µg/l : continue antibiotic treatment

Arm type	intervention
Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency was determined by the treating physician

Investigational medicinal product name	Amoxicillin/clavulansyre
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency was determined by the treating physician

Investigational medicinal product name	Ampicillin "PCD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Dosage and frequency was determined by the treating physician

Investigational medicinal product name	Ampicillin ”PCD”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency was determined by the treating physician

Investigational medicinal product name	Benzylpenicillin ”Panpharma”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Cefuroxim ”Stragen”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Ciprofloxacin ”Fresenius Kabi”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Ciprofloxacin “Actavis”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Clarithromycin ”Paranova”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Dosage and frequency was determined by the treating physician	
Investigational medicinal product name	Clarithromycin ”Hexal”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Dicloxacillin ”Actavis”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	
Investigational medicinal product name	Doxycyclin Europharma
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Dosage and frequency were determined by the treating physician	

Investigational medicinal product name	Meropenem ”Fresenius Kabi”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dosage and frequency were determined by the treating physician

Investigational medicinal product name	Moxifloxacin ”Orion”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dosage and frequency were determined by the treating physician

Investigational medicinal product name	Moxifloxacin "Actavis",
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency were determined by the treating physician

Investigational medicinal product name	Piperacillin/Tazobactam ”Fresenius Kabi”,
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dosage and frequency were determined by the treating physician

Investigational medicinal product name	Roxithromycin ”Orifarm”
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency were determined by the treating physician

Investigational medicinal product name	Vepicombin Novum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and frequency were determined by the treating physician

Number of subjects in period 1	CRP-group	Control-group	PCT-group
Started	100	101	99
Completed	100	101	99

Baseline characteristics

Reporting groups	
Reporting group title	Intervention (overall period)

Reporting group description: -

Reporting group values	Intervention (overall period)	Total	
Number of subjects	300	300	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	73		
full range (min-max)	23 to 96	-	
Gender categorical Units: Subjects			
Female	155	155	
Male	145	145	

End points

End points reporting groups

Reporting group title	CRP-group

Reporting group description:

Antibiotic treatment were given for minimum 72 hours.
After this time point antibiotic treatment were continued/discontinued according to the CRP biomarker algorithm:
CRP < 50 g/dl: discontinue antibiotic treatment
CRP < 75 g/dl and CRP ≥ 50 g/dl and CRP has decreased with at least 20% within the last 24 hours: discontinue antibiotic treatment
CRP ≥ 75 g/dl: continue antibiotic treatment

Reporting group title	Control-group

Reporting group description:

Participant are treated according to current guidelines.

Reporting group title	PCT-group

Reporting group description:

Antibiotic treatment were given for minimum 72 hours.
After this time point antibiotic treatment were continues/discontinued according to the PCT (procalcitonin) biomarker algorithm:
PCT < 0,25 µg/l : discontinue antibiotic treatment
CRP ≥ 0,25 µg/l : continue antibiotic treatment

Primary: Length of antibiotic treament

End point title	Length of antibiotic treament

End point description:

End point type	Primary

End point timeframe:

Within 30 days from inclusion

End point values	CRP-group	Control-group	PCT-group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	101	99	
Units: Days	7	9	7	

Statistical analyses

Statistical analysis title	Primary outcome

Statistical analysis description:

Comparisons of length of antibiotic treatment (days) between the CRP-group and the control group

Comparison groups	CRP-group v Control-group

Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - We used the Wilcoxon Rank sum test as the assumption of a normal distribution was not met.

Statistical analysis title	Primary outcome
Comparison groups	PCT-group v CRP-group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.38
Method	Wilcoxon (Mann-Whitney)

Secondary: treatment failure	
End point title	treatment failure
End point description:	
treatment failure was defined as readmission or renewed antibiotic treatment due to pneumonia.	
End point type	Secondary
End point timeframe:	
within 30 days of inclusion	

End point values	CRP-group	Control-group	PCT-group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	101	99	
Units: yes/no	19	27	15	

Statistical analyses

Statistical analysis title	Treatment failure
Statistical analysis description:	
Number of patients who experienced treatment failure in the control-group versus the number of patients who experienced treatment failure in the CRP-group	
Comparison groups	CRP-group v Control-group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Treatment failure
Statistical analysis description: Number of patients who experienced treatment failure in the control-group versus number of patients who experienced treatment failure in the PCT-group	
Comparison groups	PCT-group v CRP-group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.56
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: May 2016 until 30-March-2021	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24
Reporting groups	
Reporting group title	CRP-group
Reporting group description: -	
Reporting group title	PCT-group
Reporting group description: -	
Reporting group title	control-group
Reporting group description: -	

Serious adverse events	CRP-group	PCT-group	control-group
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 100 (23.00%)	16 / 99 (16.16%)	25 / 101 (24.75%)
number of deaths (all causes)	4	3	5
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung cancer metastatic			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 100 (1.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (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
Acute myocardial infarction			

subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (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
Fluid overload			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (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
Nervous system disorders			
Confusional state			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (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
Social circumstances			
Death	Additional description: One patient was found death during admission, overdose was suspected, however, no autopsy was performed. Four patients died outside of hospital, all of them where known with severe chronic disorders.		
subjects affected / exposed	1 / 100 (1.00%)	2 / 99 (2.02%)	2 / 101 (1.98%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 2
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	2 / 101 (1.98%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: exacerbation		
subjects affected / exposed	1 / 100 (1.00%)	3 / 99 (3.03%)	3 / 101 (2.97%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (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
Empyema			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (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
Lung abscess			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sputum abnormal	Additional description: Hemoptysis		
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (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
Respiratory failure			
subjects affected / exposed	2 / 100 (2.00%)	1 / 99 (1.01%)	2 / 101 (1.98%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Dyspnoea			
subjects affected / exposed	1 / 100 (1.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory acidosis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Endocrine disorders			
Hypokalaemia			

subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Hip disarticulation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation	Additional description: Suspected to have venous trombosis in lower limb, rouled out with ultrasound		
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 100 (5.00%)	3 / 99 (3.03%)	9 / 101 (8.91%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 100 (2.00%)	1 / 99 (1.01%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	2 / 100 (2.00%)	0 / 99 (0.00%)	2 / 101 (1.98%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 100 (1.00%)	1 / 99 (1.01%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Influenza			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	CRP-group	PCT-group	control-group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 100 (23.00%)	29 / 99 (29.29%)	34 / 101 (33.66%)
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	0	0	0
Respiratory acidosis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 100 (2.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	1	0	1
Bradycardia			

subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Fluid overload			
subjects affected / exposed	1 / 100 (1.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences (all)	1	1	0
Chest pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Phlebitis			
subjects affected / exposed	1 / 100 (1.00%)	4 / 99 (4.04%)	0 / 101 (0.00%)
occurrences (all)	1	4	0
Anaemia			
subjects affected / exposed	1 / 100 (1.00%)	2 / 99 (2.02%)	0 / 101 (0.00%)
occurrences (all)	1	2	0
Oedema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	2 / 101 (1.98%)
occurrences (all)	1	0	2
Diarrhoea			
subjects affected / exposed	1 / 100 (1.00%)	6 / 99 (6.06%)	1 / 101 (0.99%)
occurrences (all)	1	6	1
Vomiting			
subjects affected / exposed	1 / 100 (1.00%)	1 / 99 (1.01%)	1 / 101 (0.99%)
occurrences (all)	1	1	1
Haematochezia			

subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	2 / 101 (1.98%)
occurrences (all)	0	0	2
Constipation			
subjects affected / exposed	3 / 100 (3.00%)	1 / 99 (1.01%)	4 / 101 (3.96%)
occurrences (all)	3	1	4
Abscess oral			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Liver function test	Additional description: elevated liverenzymes		
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 100 (0.00%)	2 / 99 (2.02%)	2 / 101 (1.98%)
occurrences (all)	0	2	2
Skin irritation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 100 (1.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences (all)	1	1	0
Haematuria			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Adrenal mass			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			

subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Hyperthyroidism			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
pain			
subjects affected / exposed	1 / 100 (1.00%)	3 / 99 (3.03%)	1 / 101 (0.99%)
occurrences (all)	1	4	1
Fracture			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	0 / 101 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Bacterial test positive	Additional description: Colonization with vancomcin-resistant Enterococcus		
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	2 / 101 (1.98%)
occurrences (all)	1	0	2
Lung abscess			
subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Abscess soft tissue			

subjects affected / exposed	1 / 100 (1.00%)	0 / 99 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	10 / 100 (10.00%)	7 / 99 (7.07%)	11 / 101 (10.89%)
occurrences (all)	10	7	11
Hyponatraemia			
subjects affected / exposed	0 / 100 (0.00%)	2 / 99 (2.02%)	1 / 101 (0.99%)
occurrences (all)	0	2	1
Hyperkalaemia			
subjects affected / exposed	1 / 100 (1.00%)	2 / 99 (2.02%)	0 / 101 (0.00%)
occurrences (all)	1	2	0
Hypomagnesaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	1 / 101 (0.99%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported