Clinical trial results:
A Randomized, Double-Blind, Multi-Center Study to Evaluate the Efficacy and Safety of Intravenous to Oral Solithromycin (CEM-101) Compared to Intravenous to Oral Moxifloxacin in the Treatment of Adult Patients with Community-Acquired Bacterial Pneumonia

Summary

EudraCT number	2013-003453-13
Trial protocol	HU BG LV DE ES RO SK NL SI
Global end of trial date	07 September 2015

Results information

Result version number	v1 (current)
This version publication date	12 November 2016
First version publication date	12 November 2016

Trial information

Trial identification

Sponsor protocol code	CE01-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01968733
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cempra Pharmaceuticals, Inc.
Sponsor organisation address	6320 Quadrangle Drive, Suite 360, Chapel Hill, United States, NC 27517
Public contact	Clinical Trials Info, Cempra Pharmaceuticals, Inc., clinicaltrials@cempra.com
Scientific contact	Clinical Trials Info, Cempra Pharmaceuticals, Inc., clinicaltrials@cempra.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	29 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 September 2015
Global end of trial reached?	Yes
Global end of trial date	07 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine noninferiority (NI) in the rate of Investigator assessment of clinical success of intravenous (IV) to oral solithromycin compared to IV to oral moxifloxacin at the Short-term Follow-Up Visit (SFU), 5 -10 days after the last dose of study drug in the Intent-To-Treat (ITT) and Clinically Evaluable (CE-SFU) populations for patients with a Pneumonia Outcomes Research Team (PORT) risk class of III/IV (ie, pneumonia severity index).

Protection of trial subjects:

This study was conducted in compliance with the protocol and all regulatory requirements, in accordance with GCP, including International Conference on Harmonisation (ICH) guidelines, and in general conformity with the most recent version of the Declaration of Helsinki.

Background therapy:

A single dose of a short-acting antibiotic (penicillins, cephalosporins [not ceftriaxone], tetracyclines, or trimethoprim-sulfamethoxazole) in the 7 days prior to enrolment was permitted (number of patient limited to 25% of the population).

Evidence for comparator:

Moxifloxacin was chosen as the active comparator for multiple reasons.
It has established efficacy in the treatment of CABP, with potent activity against key pathogens associated with CABP. Moxifloxacin is recommended empiric therapy for moderately severe CABP in the EU and USA. Additionally, moxifloxacin is available in IV and oral formulations, and thus is an appropriate comparator for both this study and Study CE01-300, the Phase 3 oral solithromycin CABP trial. It was also possible to define a common moxifloxacin regimen for all countries in which the study was conducted.

Actual start date of recruitment	14 January 2014
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	Poland: 51
Country: Number of subjects enrolled	Romania: 102
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Slovenia: 16
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	Bulgaria: 80
Country: Number of subjects enrolled	Hungary: 29
Country: Number of subjects enrolled	Latvia: 17
Country: Number of subjects enrolled	Argentina: 5

Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Georgia: 63
Country: Number of subjects enrolled	Malaysia: 31
Country: Number of subjects enrolled	Peru: 9
Country: Number of subjects enrolled	Philippines: 79
Country: Number of subjects enrolled	Russian Federation: 40
Country: Number of subjects enrolled	Serbia: 88
Country: Number of subjects enrolled	South Africa: 40
Country: Number of subjects enrolled	Korea, Republic of: 10
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Ukraine: 76
Country: Number of subjects enrolled	United States: 96
Worldwide total number of subjects	863
EEA total number of subjects	314

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)	478
From 65 to 84 years	355
85 years and over	30

Subject disposition

Recruitment

Recruitment details:

A total of 863 patients were enrolled from 147 centres worldwide.
For the MAA in EU, only PORT risk class of III/IV/V patients were studied and included 661 patients (ITT-EU); among them, 454 patients in Europe, 53 patients in North America, 12 patients in Latin America, 33 patients in South Africa and 109 patient in Asia Pacific.

Pre-assignment

Screening details:

Eligible patients were males or females ≥18 years of age with an acute onset or worsening of at least 3 of the following signs and symptoms of CABP: cough, production of purulent sputum, shortness of breath (dyspnea), chest pain.
And at least 1 of the following: fever, hypothermia, presence of pulmonary rales and/or pulmonary consolidation.

Period 1

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

Blinding implementation details:

A double-dummy design was utilized, with solithromycin placebo capsules identical in appearance to solithromycin capsules and moxifloxacin placebo over-encapsulated tablets identical in appearance to moxifloxacin over-encapsulated tablets. After dosing with IV study drug was completed, an exact number of capsules needed to complete 7 days of dosing were provided in blister packs to patients who met the switch criteria.

Arms

Are arms mutually exclusive?	Yes
Arm title	Solithromycin (PORT III/IV/V)

Arm description:

Solithromycin treatment group

Arm type	Experimental
Investigational medicinal product name	Solithromycin
Investigational medicinal product code	CEM-101
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 1: Solithromycin 400 mg IV (250 mL over 60 [5/+20] minutes) followed by 400 mg IV daily until predefined oral switch criteria were met. First oral dose was 800 mg (4 x 200 mg capsules), followed by 400 mg (2 x 200 mg capsules) oral daily for the remainder of study (a total of 7 doses).

Arm title	Moxifloxacin (PORT III/IV/V)

Arm description:

Moxifloxacin treatment group

Arm type	Active comparator
Investigational medicinal product name	Moxifloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 1: Moxifloxacin 400 mg IV daily (250 mL over 60 [5/+20] minutes), followed by 400 mg IV daily until predefined oral switch criteria (clinical improvement) were met, followed by 400 mg (1×400 mg capsule) oral moxifloxacin daily for a total of 7 doses.

Number of subjects in period 1[1]	Solithromycin (PORT III/IV/V)	Moxifloxacin (PORT III/IV/V)
Started	328	333
Completed	308	318
Not completed	20	15
Adverse event, serious fatal	5	6
Consent withdrawn by subject	11	7
Adverse event, non-fatal	2	-
randomised in error	-	2
clinical failure	2	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The reporting groups refer to PORT III/IV/V patients (EU analysis).

Baseline characteristics

Reporting groups	
Reporting group title	Solithromycin (PORT III/IV/V)
Reporting group description: Solithromycin treatment group	
Reporting group title	Moxifloxacin (PORT III/IV/V)
Reporting group description: Moxifloxacin treatment group	

Reporting group values	Solithromycin (PORT III/IV/V)	Moxifloxacin (PORT III/IV/V)	Total
Number of subjects	328	333	661
Age categorical Units: Subjects			
Adults (18-64 years)	152	151	303
From 65-84 years	161	169	330
85 years and over	15	13	28
Age continuous Units: years			
arithmetic mean	64.2	64.3	
standard deviation	± 14.1	± 13.6	-
Gender categorical Units: Subjects			
Female	156	142	298
Male	172	191	363
PORT risk class Units: Subjects			
Port III	196	204	400
Port IV	130	125	255
Port V	2	4	6

End points

End points reporting groups

Reporting group title	Solithromycin (PORT III/IV/V)
Reporting group description: Solithromycin treatment group	
Reporting group title	Moxifloxacin (PORT III/IV/V)
Reporting group description: Moxifloxacin treatment group	
Subject analysis set title	Solithromycin -ITT Set (PORT III/IV/V)
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized patients with PORT III/IV/V regardless of whether or not the patient received study drug. A patient is considered randomized when the Investigator or Investigator's designee receives the IWRS-generated randomisation number.	
Subject analysis set title	Moxifloxacin - ITT Set (PORT III/IV/V)
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized patients with PORT III/IV/V regardless of whether or not the patient received study drug. A patient is considered randomized when the Investigator or Investigator's designee receives the IWRS-generated randomisation number.	
Subject analysis set title	Solithromycin - Clinically Evaluable Set (PORT III/IV/V)
Subject analysis set type	Per protocol
Subject analysis set description: All patients in the ITT population who also met the criteria listed in the SAP, among them: met key inclusion criteria, did not meet the exclusion criteria, completed the TOC Visit 5-10 days after the last dose of study drug, received ≥2 doses of study drug during the first 48 hours if the patient was a clinical failure, received ≥3 doses of study drug during the first 72 hours if the patient was a clinical success, did not receive another systemic antibacterial from the first dose of study drug through EOT (End of treatment) or through TOC with likely or documented activity against confirmed or potential CABP pathogens, received the correct study drug based on randomization assignment.	
Subject analysis set title	Moxifloxacin - Clinically evaluable Set (PORT III/IV/V)
Subject analysis set type	Per protocol
Subject analysis set description: All patients in the ITT population who also met the criteria listed in the SAP, among them: met key inclusion criteria, did not meet the exclusion criteria, completed the TOC Visit 5-10 days after the last dose of study drug, received ≥2 doses of study drug during the first 48 hours if the patient was a clinical failure, received ≥3 doses of study drug during the first 72 hours if the patient was a clinical success, did not receive another systemic antibacterial from the first dose of study drug through EOT (End of treatment) or through TOC with likely or documented activity against confirmed or potential CABP pathogens, received the correct study drug based on randomization assignment.	

Primary: Clinical response-ITT at TOC: non-inferiority hypothesis

End point title	Clinical response-ITT at TOC: non-inferiority hypothesis
End point description: Proportion of patients with clinical success of CABP symptoms. Clinical response rate at the TOC visit (or SFU visit) for the ITT Population is a co-primary endpoint of the study. Clinical response (Investigator assessment) is classified as success, failure, or indeterminate according to the definitions in the SAP.	
End point type	Primary
End point timeframe: At Test of Cure (TOC), i.e. 5-10 days after last dose of study drug.	

End point values	Solithromycin (PORT III/IV/V)	Moxifloxacin (PORT III/IV/V)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	328	333		
Units: number of patients				
success	281	293		
failure	38	30		
indeterminate	9	10		

Statistical analyses

Statistical analysis title	Non-inferiority analysis (success)-ITT

Statistical analysis description:

H0: Difference (Solithromycin treatment group minus Moxifloxacin treatment group) of clinical success rates ≤ -10%

Comparison groups	Solithromycin (PORT III/IV/V) v Moxifloxacin (PORT III/IV/V)
Number of subjects included in analysis	661
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	non-inferiority test
Parameter estimate	Difference of clinical success rates
Point estimate	-2.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	2.7

Notes:

[1] - A non-inferiority margin of 10% was used.

Primary: Clinical response - CE at TOC: non-inferiority hypothesis

End point title	Clinical response - CE at TOC: non-inferiority hypothesis

End point description:

Proportion of patients with clinical success of CABP symptoms at TOC for the Clinically Evaluable (CE) Population.
This is a co-primary endpoint of the study.
Clinical response (Investigator assessment) is classified as success, failure, or indeterminate according to the definitions in the SAP.

End point type	Primary

End point timeframe:

At TOC, i.e. 5-10 days after the last dose of study drug.

End point values	Solithromycin (PORT III/IV/V)	Moxifloxacin (PORT III/IV/V)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292[2]	300[3]		
Units: number of patients				
success	257	276		
failure	35	24		
indeterminate	0	0		

Notes:

[2] - Solithromycin- Modified Clinically Evaluable Population (PORT III/IV/V)

[3] - Moxifloxacin - Modified Clinically Evaluable Population (PORT III/IV/V)

Statistical analyses

Statistical analysis title	Non-inferiority hypotesis test (success) - CE
Statistical analysis description: H0: Differences (solithromycin minus Moxifloxacin treatment group) of clinical success rate ≤ -10%.	
Comparison groups	Solithromycin (PORT III/IV/V) v Moxifloxacin (PORT III/IV/V)
Number of subjects included in analysis	592
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in clinical success rates
Point estimate	-3.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.2
upper limit	1.2

Notes:

[4] - A non-inferiority margin of 10% was used.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first study drug administration to late follow-up (Day 28-35 after first dose of study drug).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Solithromycin - safety population (PORT III/IV/V)
Reporting group description: -	
Reporting group title	Moxifloxacin- safety population (PORT III/IV/V)
Reporting group description: -	
Reporting group title	Solithromycin-safety population (All PORT)
Reporting group description: All patients	
Reporting group title	Moxifloxacin-safety population (All PORT)
Reporting group description: Allpatients	

Serious adverse events	Solithromycin - safety population (PORT III/IV/V)	Moxifloxacin- safety population (PORT III/IV/V)	Solithromycin-safety population (All PORT)
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 327 (7.65%)	20 / 331 (6.04%)	30 / 432 (6.94%)
number of deaths (all causes)	5	6	5
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Adrenal gland cancer			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lung adenocarcinoma			

subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Lung adenocarcinoma metastatic			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Small cell lung cancer			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Hypertension			
subjects affected / exposed	1 / 327 (0.31%)	1 / 331 (0.30%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 327 (0.00%)	0 / 331 (0.00%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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 arrest			
subjects affected / exposed	2 / 327 (0.61%)	0 / 331 (0.00%)	2 / 432 (0.46%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Cardiac failure			
subjects affected / exposed	1 / 327 (0.31%)	1 / 331 (0.30%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cardiac failure congestive			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiovascular insufficiency			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Myocardial infarction			
subjects affected / exposed	2 / 327 (0.61%)	1 / 331 (0.30%)	2 / 432 (0.46%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 2
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	1 / 327 (0.31%)	1 / 331 (0.30%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
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, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 327 (0.31%)	4 / 331 (1.21%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Aspiration			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Asthmatic crisis			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 327 (0.31%)	2 / 331 (0.60%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 327 (0.61%)	0 / 331 (0.00%)	2 / 432 (0.46%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Pulmonary oedema			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
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 failure			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Upper airway obstruction			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Skin and subcutaneous tissue disorders			
Urticaria			

subjects affected / exposed	0 / 327 (0.00%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis bacterial			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (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
Lobar Pneumonia			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			

subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 327 (0.92%)	3 / 331 (0.91%)	7 / 432 (1.62%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
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 tract infection			
subjects affected / exposed	1 / 327 (0.31%)	0 / 331 (0.00%)	1 / 432 (0.23%)
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 tract infection viral			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
sepsis			
subjects affected / exposed	0 / 327 (0.00%)	1 / 331 (0.30%)	0 / 432 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	1 / 327 (0.31%)	1 / 331 (0.30%)	1 / 432 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1

Serious adverse events	Moxifloxacin-safety population (All PORT)		
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 426 (5.40%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	0		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adrenal gland cancer			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lung adenocarcinoma			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma metastatic			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small cell lung cancer			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Thrombophlebitis			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiovascular insufficiency			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Large intestine perforation			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	4 / 426 (0.94%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Aspiration			

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Asthmatic crisis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Haemoptysis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				

subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Upper airway obstruction			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Empyema			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis bacterial			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Influenza				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lobar Pneumonia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection viral				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
sepsis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Septic shock				

subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Solithromycin - safety population (PORT III/IV/V)	Moxifloxacin- safety population (PORT III/IV/V)	Solithromycin-safety population (All PORT)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 327 (42.51%)	104 / 331 (31.42%)	193 / 432 (44.68%)
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	19 / 327 (5.81%)	1 / 331 (0.30%)	28 / 432 (6.48%)
occurrences (all)	38	1	57
Vascular disorders			
hypertension			
subjects affected / exposed	5 / 327 (1.53%)	7 / 331 (2.11%)	5 / 432 (1.16%)
occurrences (all)	5	7	5
Nervous system disorders			
dizziness			
subjects affected / exposed	7 / 327 (2.14%)	2 / 331 (0.60%)	11 / 432 (2.55%)
occurrences (all)	8	2	12
headache			
subjects affected / exposed	7 / 327 (2.14%)	16 / 331 (4.83%)	15 / 432 (3.47%)
occurrences (all)	8	16	17
General disorders and administration site conditions			
Infusion site pain			
subjects affected / exposed	33 / 327 (10.09%)	6 / 331 (1.81%)	45 / 432 (10.42%)
occurrences (all)	63	6	87
Infusion site phlebitis			
subjects affected / exposed	32 / 327 (9.79%)	4 / 331 (1.21%)	43 / 432 (9.95%)
occurrences (all)	37	4	50
Infusion site erythema			
subjects affected / exposed	12 / 327 (3.67%)	2 / 331 (0.60%)	19 / 432 (4.40%)
occurrences (all)	16	6	27
Infusion site thrombosis			

subjects affected / exposed	9 / 327 (2.75%)	6 / 331 (1.81%)	9 / 432 (2.08%)
occurrences (all)	13	10	13
Infusion site paraesthesia			
subjects affected / exposed	8 / 327 (2.45%)	0 / 331 (0.00%)	9 / 432 (2.08%)
occurrences (all)	8	0	9
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 327 (3.36%)	22 / 331 (6.65%)	19 / 432 (4.40%)
occurrences (all)	11	23	19
Nausea			
subjects affected / exposed	8 / 327 (2.45%)	3 / 331 (0.91%)	14 / 432 (3.24%)
occurrences (all)	8	3	14
Psychiatric disorders			
insomnia			
subjects affected / exposed	7 / 327 (2.14%)	3 / 331 (0.91%)	9 / 432 (2.08%)
occurrences (all)	7	3	9
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	10 / 327 (3.06%)	7 / 331 (2.11%)	11 / 432 (2.55%)
occurrences (all)	10	7	11

Non-serious adverse events	Moxifloxacin-safety population (All PORT)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	125 / 426 (29.34%)		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences (all)	1		
Vascular disorders			
hypertension			
subjects affected / exposed	9 / 426 (2.11%)		
occurrences (all)	9		
Nervous system disorders			
dizziness			
subjects affected / exposed	5 / 426 (1.17%)		
occurrences (all)	6		
headache			

subjects affected / exposed	18 / 426 (4.23%)		
occurrences (all)	19		
General disorders and administration site conditions			
Infusion site pain			
subjects affected / exposed	6 / 426 (1.41%)		
occurrences (all)	6		
Infusion site phlebitis			
subjects affected / exposed	4 / 426 (0.94%)		
occurrences (all)	4		
Infusion site erythema			
subjects affected / exposed	2 / 426 (0.47%)		
occurrences (all)	6		
Infusion site thrombosis			
subjects affected / exposed	7 / 426 (1.64%)		
occurrences (all)	12		
Infusion site paraesthesia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	25 / 426 (5.87%)		
occurrences (all)	26		
Nausea			
subjects affected / exposed	7 / 426 (1.64%)		
occurrences (all)	7		
Psychiatric disorders			
insomnia			
subjects affected / exposed	5 / 426 (1.17%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	9 / 426 (2.11%)		
occurrences (all)	9		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27448679