Clinical trial results:
A Phase 3 Randomized, Double-Blind, Multi-Center Study to Compare the Safety and Efficacy of Omadacycline IV/PO to Moxifloxacin IV/PO for Treating Adult Subjects with Community-Acquired Bacterial Pneumonia (CABP)

Summary

EudraCT number	2013-004071-13
Trial protocol	SK HU CZ LV DE ES BE PL GR HR
Global end of trial date	17 February 2017

Results information

Result version number	v1 (current)
This version publication date	14 April 2018
First version publication date	14 April 2018

Trial information

Trial identification

Sponsor protocol code	PTK0796-CABP-1200

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02531438
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Paratek Pharma LLC
Sponsor organisation address	75 Park Plaza, Boston, MA, 02116, United States,
Public contact	Head of Clinical of Development, Paratek Pharma LLC, +1 6172750040,
Scientific contact	Head of Clinical of Development, Paratek Pharma LLC, +1 6172750040,

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 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 February 2017
Global end of trial reached?	Yes
Global end of trial date	17 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate that omadacycline 100 mg intravenous (iv) once every 12 hours (q12h) for 2 doses, followed by 100 mg iv/300 mg per oral (po) once every 24 hours (q24h) is non-inferior to moxifloxacin 400 mg iv/po q24h in the treatment of adults with CABP with a Pneumonia Outcomes Research Team (PORT) Risk Class of III/IV.

Protection of trial subjects:

The switching from iv to po treatment, the first dose of po therapy should begin in the morning, 24 hours after the last iv dose, to ensure the subjects continued to receive uninterrupted daily therapy. To facilitate study enrollment infusion times were adjusted to iv q12h (first 2 doses), followed by iv q24h (starting 24 hours after first dose) and switch to po q24h after at least 3 days (4 doses) of iv treatment infusion interval to achieve desired administration schedule.

Background therapy: -

Evidence for comparator:

Moxifloxacin was selected as the optimal comparator, given its long history of efficacy and tolerability. Moxifloxacin has a similar spectrum of activity with coverage against the most common typical and atypical causes of CABP. Moxifloxacin can be administered iv and po and has regulatory approval for the treatment of CABP.

Actual start date of recruitment	06 November 2015
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: 40
Country: Number of subjects enrolled	Romania: 61
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Croatia: 81
Country: Number of subjects enrolled	Bulgaria: 105
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Greece: 30
Country: Number of subjects enrolled	Hungary: 81
Country: Number of subjects enrolled	Latvia: 37
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Georgia: 26
Country: Number of subjects enrolled	Russian Federation: 26

Country: Number of subjects enrolled	Ukraine: 157
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Peru: 8
Country: Number of subjects enrolled	Philippines: 31
Country: Number of subjects enrolled	Turkey: 2
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	South Africa: 29
Country: Number of subjects enrolled	Mexico: 1
Worldwide total number of subjects	774
EEA total number of subjects	467

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)	450
From 65 to 84 years	285
85 years and over	39

Subject disposition

Recruitment

Recruitment details:

The study is designed to enroll adults with CABP. Subject randomization was stratified by PORT Risk Class (II or III/IV), receipt of an allowed antibacterial therapy in the 72 hours prior to study treatment, and geographic region. All subjects were expected to present with CABP severe enough to require a minimum of at least 3 days of iv treatment.

Pre-assignment

Screening details:

Subjects who met inclusion criteria and did not meet exclusion criteria will be randomly assigned to a treatment group, and should receive their first dose of test article within 4 hours after randomization. All subjects were expected to present with CABP PORT Risk Class II, III, or IV to require a minimum of at least 3 days of iv treatment

Period 1

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

Blinding implementation details:

Treatment phase (both iv and po) of the study was double-blind and double-dummy. In an effort to maintain blinding, each site employed shrouding of the iv bag and iv lines used for infusion of test article. To maintain double-blinding, subjects in each study arm will receive the same infusion volumes with the same blinded administration instructions and when switch to PO subjects will receive 2 tablets and 1 over-encapsulated tablet in the morning

Arms

Are arms mutually exclusive?	Yes
Arm title	Omadacycline

Arm description:

Omadacycline, 100 mg iv q12h (first 2 doses), followed by 100 mg iv q24h (starting 24 hours after first dose), with the option to switch to 300 mg (two 150 mg omadacycline tablets and 1 over-encapsulated placebo tablet matching moxifloxacin) po q24h after at least 3 days (4 doses) of iv treatment. The total duration of test article therapy (iv plus po) for all subjects was at least 7 days and no more than 14 days.

Arm type	Experimental
Investigational medicinal product name	Omadacycline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

2 doses of Omadacycline (100 mg) iv every 12 hours, followed by 100 mg iv every 24 hours, with the option to switch 300 mg po every 24 hours.

Arm title	Moxifloxacin

Arm description:

Moxifloxacin, 400 mg iv q24h (with a single placebo infusion to match the omadacycline dosing regimen 12 hours after the first dose on Day 1) with the option to switch to 400 mg (one 400 mg moxifloxacin over-encapsulated tablet and 2 placebo tablets matching omadacycline tablets) po q24h after at least 3 days (4 doses) of iv treatment. The total duration of test article therapy (iv plus po) for all subjects was at least 7 days and no more than 14 days.

Arm type	Active comparator

Investigational medicinal product name	Moxifloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Moxifloxacin 400 mg iv q24h with the option to switch to to 400 mg po q24h.

Number of subjects in period 1	Omadacycline	Moxifloxacin
Started	386	388
Completed	352	346
Not completed	34	42
Consent withdrawn by subject	4	3
Physician decision	3	9
Death	4	1
Other	6	-
Adverse event	17	28
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment period 1

Reporting group description: -

Reporting group values	Treatment period 1	Total	
Number of subjects	774	774	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	450	450	
From 65-84 years	324	324	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	347	347	
Male	427	427	

Subject analysis sets

Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population consisted of all randomized subjects regardless of whether or not the subject received test article. A subject was considered randomized when the Interactive Response System provided the test article assignment (ie, completed a randomization transaction).

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population consisted of all randomized subjects who received test article (either active or placebo). All safety analyses were conducted in this population.

Subject analysis set title	CE - EOT population
Subject analysis set type	Full analysis

Subject analysis set description:

Two CE analysis sets were defined, the CE-EOT and CE-PTE. The CE population consisted of all ITT subjects who received test article, have a qualifying CABP, an assessment of outcome, and met all other evaluability criteria.

CE-EOT: The number and percentage of subjects in each treatment group with a clinical success, clinical failure, at EOT visit occurred on the day of, or within 2 days following the last dose of test article based on the investigator’s assessment.

Subject analysis set title	microITT population

Subject analysis set type	Intention-to-treat

Subject analysis set description:

The microITT population consisted of all subjects in the ITT population who had at least 1 causative bacterial pathogen identified from a culture of a respiratory specimen (eg, respiratory fluid obtained by BAL or bronchoscopy, pleural fluid obtained by thoracentesis, or expectorated or induced sputum meeting adequacy criteria as defined by the Gram stain results), culture of blood, or from a culture-independent method (eg, positive urinary antigen test [UAT] for Streptococcus pneumoniae or Legionella pneumophila, or positive serology for Legionella pneumophila, Mycoplasma pneumoniae, or Chlamydophila pneumoniae) at Baseline.

Subject analysis set title	CE-PTE population
Subject analysis set type	Full analysis

Subject analysis set description:

Two CE analysis sets were defined, the CE-EOT and CE-PTE. The CE population consisted of all ITT subjects who received test article, have a qualifying CABP, an assessment of outcome, and met all other evaluability criteria.

CE-PTE: The number and percentage of subjects in each treatment group with a clinical success, clinical failure, and indeterminate for the overall assessment of clinical response at PTE visit. PTE visit occurred 5 to 10 days after the last dose of test article (based on the investigator's assessment) unless the subject was considered to be a clinical failure based on the investigator's assessment at the EOT visit or the subject died after EOT and before PTE.

Reporting group values	ITT population	Safety population	CE - EOT population
Number of subjects	774	770	714
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)	450		
From 65-84 years	324		
85 years and over	0		
Gender categorical Units: Subjects			
Female	347		
Male	427		

Reporting group values	microITT population	CE-PTE population	
Number of subjects	386	685	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			

85 years and over			

Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Omadacycline

Reporting group description:

Omadacycline, 100 mg iv q12h (first 2 doses), followed by 100 mg iv q24h (starting 24 hours after first dose), with the option to switch to 300 mg (two 150 mg omadacycline tablets and 1 over-encapsulated placebo tablet matching moxifloxacin) po q24h after at least 3 days (4 doses) of iv treatment. The total duration of test article therapy (iv plus po) for all subjects was at least 7 days and no more than 14 days.

Reporting group title	Moxifloxacin

Reporting group description:

Moxifloxacin, 400 mg iv q24h (with a single placebo infusion to match the omadacycline dosing regimen 12 hours after the first dose on Day 1) with the option to switch to 400 mg (one 400 mg moxifloxacin over-encapsulated tablet and 2 placebo tablets matching omadacycline tablets) po q24h after at least 3 days (4 doses) of iv treatment. The total duration of test article therapy (iv plus po) for all subjects was at least 7 days and no more than 14 days.

Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population consisted of all randomized subjects regardless of whether or not the subject received test article. A subject was considered randomized when the Interactive Response System provided the test article assignment (ie, completed a randomization transaction).

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population consisted of all randomized subjects who received test article (either active or placebo). All safety analyses were conducted in this population.

Subject analysis set title	CE - EOT population
Subject analysis set type	Full analysis

Subject analysis set description:

Two CE analysis sets were defined, the CE-EOT and CE-PTE. The CE population consisted of all ITT subjects who received test article, have a qualifying CABP, an assessment of outcome, and met all other evaluability criteria.

CE-EOT: The number and percentage of subjects in each treatment group with a clinical success, clinical failure, at EOT visit occurred on the day of, or within 2 days following the last dose of test article based on the investigator’s assessment.

Subject analysis set title	microITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The microITT population consisted of all subjects in the ITT population who had at least 1 causative bacterial pathogen identified from a culture of a respiratory specimen (eg, respiratory fluid obtained by BAL or bronchoscopy, pleural fluid obtained by thoracentesis, or expectorated or induced sputum meeting adequacy criteria as defined by the Gram stain results), culture of blood, or from a culture-independent method (eg, positive urinary antigen test [UAT] for Streptococcus pneumoniae or Legionella pneumophila, or positive serology for Legionella pneumophila, Mycoplasma pneumoniae, or Chlamydophila pneumoniae) at Baseline.

Subject analysis set title	CE-PTE population
Subject analysis set type	Full analysis

Subject analysis set description:

Two CE analysis sets were defined, the CE-EOT and CE-PTE. The CE population consisted of all ITT subjects who received test article, have a qualifying CABP, an assessment of outcome, and met all other evaluability criteria.

CE-PTE: The number and percentage of subjects in each treatment group with a clinical success, clinical failure, and indeterminate for the overall assessment of clinical response at PTE visit. PTE visit occurred

5 to 10 days after the last dose of test article (based on the investigator's assessment) unless the subject was considered to be a clinical failure based on the investigator's assessment at the EOT visit or the subject died after EOT and before PTE.

Primary: Overall Clinical Response at the EOT and PTE Visit Based on Investigator Assessments

End point title	Overall Clinical Response at the EOT and PTE Visit Based on Investigator Assessments

End point description:

At the EOT visit the investigator indicated the clinical status of the infection under study as follows: Clinical Success, Clinical Failure or Indeterminate (the clinical response to test article could not be adequately inferred).
At the PTE visit the investigator indicated 1 of the following outcomes relating to the primary infection under study: Clinical Success, Clinical Failure or Indeterminate (the clinical response to test article could not be adequately inferred). If the lower limit of the 97.5% CI for the difference in both the ITT and CE-PTE populations exceeded -10%, then the null hypothesis was rejected and the non-inferiority of omadacycline to moxifloxacin was declared.

End point type	Primary

End point timeframe:

End of Trial (EOT visit) was on the calendar day of, or within 2 days following the last dose of test article. Post Treatment Evaluation (PTE) visit was 5 to 10 days after the subject's last day of study therapy.

End point values	Omadacycline	Moxifloxacin	ITT population	CE - EOT population
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	329	331	660	616
Units: Number of subjects analysed				
Clinical success	291	282	573	574
Indeterminate	11	14	25	0
Clinical failure	27	35	62	42

End point values	CE-PTE population			
Subject group type	Subject analysis set			
Number of subjects analysed	591			
Units: Number of subjects analysed				
Clinical success	541			
Indeterminate	0			
Clinical failure	50			

Statistical analyses

Statistical analysis title	SAP dated 24 March 2017/ ITT Population

Statistical analysis description:

To test the null hypothesis, a 2-sided 97.5% CI for the observed difference in primary outcome rates (omadacycline treatment group minus moxifloxacin treatment group) was calculated for the ITT and CE-PTE populations. The 2-sided 97.5% CI for non-inferiority testing based on the difference of clinical

success rates, was computed using the method proposed with stratification.

Comparison groups	Moxifloxacin v Omadacycline
Number of subjects included in analysis	660
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Median difference (net)
Point estimate	3.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.7
upper limit	9.3
Variability estimate	Standard deviation

Notes:

[1] - The primary efficacy analyses were based on subjects with an eCRF PORT Risk Class of III/IV in the ITT and CE-PTE populations.

Statistical analysis title	SAP dated 24 March 2017/ CE-PTE Population

Statistical analysis description:

To test the null hypothesis, a 2-sided 97.5% CI for the observed difference in primary outcome rates was calculated for the ITT and CE-PTE populations. If the lower limit of the 97.5% CI for the difference in both the ITT and CE-PTE populations exceeded -10%, then the null hypothesis was rejected and the non-inferiority of omadacycline to moxifloxacin was declared. Subjects in this analysis: Omadacycline arm - 295; Moxifloxacin arm - 296; all subjects - 591

Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	660
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Median difference (net)
Point estimate	2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.2
upper limit	7.4
Variability estimate	Standard deviation

Notes:

[2] - Given that the lower limit of the 97.5% CI for the treatment difference (omadacycline – moxifloxacin) was greater than -10% in both the ITT and CE-PTE populations, omadacycline was considered non-inferior to moxifloxacin.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed from the signing of ICF to the time of the Final Follow-up assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Omadacycline

Reporting group description:

Investigational therapy: omadacycline, 100 mg iv q12h (first 2 doses), followed by 100 mg iv q24h (starting 24 hours after first dose), with the option to switch to 300 mg (two 150 mg omadacycline tablets and 1 over-encapsulated placebo tablet matching moxifloxacin) po q24h after at least 3 days (4 doses) of iv treatment.

Reporting group title	Moxifloxacin

Reporting group description:

Reference therapy: moxifloxacin, 400 mg iv q24h (with a single placebo infusion to match the omadacycline dosing regimen 12 hours after the first dose on Day 1) with the option to switch to 400 mg (one 400 mg moxifloxacin over-encapsulated tablet and 2 placebo tablets matching omadacycline tablets) po q24h after at least 3 days (4 doses) of iv treatment.

Serious adverse events	Omadacycline	Moxifloxacin	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 386 (5.96%)	26 / 388 (6.70%)	
number of deaths (all causes)	8	4	
number of deaths resulting from adverse events	8	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm			
subjects affected / exposed	2 / 386 (0.52%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatic carcinoma			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon cancer metastatic			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
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			
Multi-organ failure			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	3 / 386 (0.78%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 386 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			

subjects affected / exposed	2 / 386 (0.52%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute pulmonary oedema			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Bladder injury	Additional description: Urinary bladder damage		
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 386 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac arrest			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction	Additional description: Non ST elevation myocardial infarction		
subjects affected / exposed	2 / 386 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Cardiogenic shock			
subjects affected / exposed	2 / 386 (0.52%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Cerebrovascular accident	Additional description: Ischemic cerebrovascular accident		
subjects affected / exposed	2 / 386 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic congestion			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 386 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Lumbago			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 386 (0.26%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Influenza			
subjects affected / exposed	3 / 386 (0.78%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 386 (0.52%)	6 / 388 (1.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atypical mycobacterial pneumonia			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 386 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIV infection			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 386 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 386 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Decreased appetite	Additional description: Worsening of anorexia		
subjects affected / exposed	1 / 386 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Omadacycline	Moxifloxacin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	157 / 386 (40.67%)	188 / 388 (48.45%)	
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	15 / 386 (3.89%)	20 / 388 (5.15%)	
occurrences (all)	15	20	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	9 / 386 (2.33%)	21 / 388 (5.41%)	
occurrences (all)	9	21	
Diarrheaa			
subjects affected / exposed	4 / 386 (1.04%)	31 / 388 (7.99%)	
occurrences (all)	4	31	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic, and mediastinal disorders			
subjects affected / exposed	22 / 386 (5.70%)	29 / 388 (7.47%)	
occurrences (all)	22	29	
Infections and infestations			
Infections and infestations			
subjects affected / exposed	35 / 386 (9.07%)	41 / 388 (10.57%)	
occurrences (all)	35	41	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders			
subjects affected / exposed	15 / 386 (3.89%)	20 / 388 (5.15%)	
occurrences (all)	15	20	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2015	There was 1 amendment to the protocol (dated 27-OCT-2015 and labeled as Version 2). In addition to minor administrative changes and clarifications, the following key modifications were made: - Inclusion criterion #5 was changed to "hypoxemia (PaO2 < 60 mm Hg by ABG or oxygen saturation < 90% by pulse oximetry)" - Inclusion Criterion #9 was changed from a "highly effective method" to "an acceptable method" because of the different regional definitions of highly effective methods of birth control; postmenopausal was added as a method of birth control - In exclusion criterion #7, specific QT interval thresholds were added for clarification - In exclusion criterion #10, regarding the receipt of corticosteroids equivalent to prednisone, a reference and hyperlink to Appendix 4 was added - In exclusion criterion #10, known or suspected "active tuberculosis" was added - The Safety population definition was updated to subjects who received any amount of test article, including less than 1 complete dose - "Subjects should receive their first dose of test article within 4 hours after randomization" was added to ensure subjects received timely treatment of their infection - Population PK sampling schedule was updated to reflect blood samples for the PK analysis collected on Days 1 to 7 - Language was added to indicate that at the PTE visit, a respiratory specimen culture, and Gram stain should be obtained only for subjects who were clinical failures and required alternative antibacterial treatment for the infection under study - Urine antigen screening for Legionella pneumophila and Streptococcus pneumoniae was removed at the PTE visit - The criteria for an adequate quality sputum specimen were changed to "1) < 10 SECs/lpf (ie, 100 ×), 2) > 25 PMN/lpf (ie, 100 ×)" - The results of Cempra's solithromycin oral CABP study, the first completed study to use the ECR endpoint, reported following finalization of the original protocol and were added to the discussion

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported