



## Clinical trial results:

### A Phase 3b 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	2020-002986-32
Trial protocol	BG HR HU PL
Global end of trial date	27 March 2024

#### Results information

Result version number	v1 (current)
This version publication date	16 February 2025
First version publication date	16 February 2025

#### Trial information

##### Trial identification

Sponsor protocol code	PTK0796-CABP-19302
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04779242
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Paratek Pharma, LLC
Sponsor organisation address	75 Arlington Street, Suite 500, Boston, United States, 02116
Public contact	Chief Development and Regulatory, Paratek Pharma, LLC, +1 6172750040, randy.brenner@paratekpharma.com
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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	17 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 March 2024
Global end of trial reached?	Yes
Global end of trial date	27 March 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate that iv to po omadacycline was non-inferior to iv to po moxifloxacin in the treatment of adults with PORT Risk Class III and IV CABP. The secondary objectives were:

- To evaluate the safety of omadacycline in the treatment of adult subjects with CABP in the Safety population.
- To evaluate the clinical response according to the identified causative pathogen.
- To evaluate the pharmacokinetics (PK) of omadacycline in adult subjects with CABP.

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Council for Harmonisation (ICH) Harmonised Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, United States [US] Code of Federal Regulations [CFR] Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki. The investigator provided protection of the subjects by following all applicable regulations. These regulations were available upon request from the sponsor. The ICF was reviewed by the sponsor and approved by the IRB/IEC/REB. Before any procedures specified in the protocol were performed, a subject must have:

- Been informed of all pertinent aspects of the study and all elements of informed consent.
- Been given time to ask questions and time to consider the decision to participate.
- Voluntarily agreed to participate in the study.
- Signed and dated an IRB/IEC/REB approved ICF.

Background therapy:

A total of 5.0% omadacycline subjects and 2.7% moxifloxacin subjects received concomitant antibacterial medications between the first infusion of test article and the EOT visit (CE-EOT population) and 5.1% omadacycline subjects and 3.0% moxifloxacin subjects received concomitant antibacterial medications between the first infusion of test article and the PTE visit (CE-PTE population).

Evidence for comparator:

Moxifloxacin (400 mg iv every 24 hours [q24h] with the option to transition to 400 mg po q24h) was chosen as the comparator given the wide acceptance of fluoroquinolone monotherapy as a safe, first-line option for treating subjects with CABP. Moxifloxacin provides a broad spectrum of activity against respiratory pathogens that are causative agents of CABP, including typical (eg, *Streptococcus pneumoniae*) and atypical (eg, *Legionella*, *Chlamydophila*, and *Mycoplasma* spp.) pathogens, with a similar spectrum of activity to that of omadacycline. Like omadacycline, moxifloxacin has both iv and po formulation options and was administered once daily. Moxifloxacin was also the comparator in the registrational CABP trial supporting approval of Nuzyra.

Actual start date of recruitment	25 February 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Croatia: 27
Country: Number of subjects enrolled	Bulgaria: 190
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Georgia: 246
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Serbia: 91
Country: Number of subjects enrolled	Ukraine: 93
Worldwide total number of subjects	670
EEA total number of subjects	236

Notes:

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**Subjects enrolled per age group**

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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)	334
From 65 to 84 years	309
85 years and over	27

## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled at a total of 40 sites in Bulgaria (9 sites), Croatia (3 sites), Georgia (6 sites), Hungary (3 sites), Poland (2 sites), Russian Federation (2 sites), Serbia (7 sites), and Ukraine (8 sites). The first subject, first visit was on 25Feb2021.

### Pre-assignment

Screening details:

Key inclusion criteria: age  $\geq 18$  yr; at least 3 symptoms (cough, purulent sputum, dyspnea, chest pain); at least 2 abnormal vital signs (fever or hypothermia, hypotension, HR  $>90$  bpm, RR  $>20$  breaths/min); at least 1 finding associated with CABP; elevated WBC, leukopenia, or elevated immature neutrophils; PORT Risk Class III or IV.

### Period 1

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

Blinding implementation details:

The iv treatment phase: double-blind, double-dummy design with placebo infusions matched to active omadacycline and moxifloxacin infusions. All iv infusions were administered by qualified blinded personnel. The po treatment phase: double-blind, double-dummy design using omadacycline placebo comparator tablets of matching size and shape to active omadacycline tablets and matching over-encapsulated placebo and active moxifloxacin tablets.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Omadacycline

Arm description:

The ITT population included all 336 subjects randomized to the omadacycline group. The ITT population was used for analysis of demographic and baseline characteristics and efficacy. The safety population included all randomized subjects who received at least 1 dose of test article (336 subjects).

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

Dosage and administration details:

The iv-treatment phase (minimum of 2 days) followed a double-blind, double-dummy design for omadacycline. Infusions of omadacycline or matched placebo were administered continuously, without interruptions, over 30 minutes ( $\pm 5$  minutes). If once a day (QD) dosing was selected, the 200 mg infusion of omadacycline or matched placebo was administered continuously, without interruptions, over 60 minutes ( $\pm 5$  minutes). If BID dosing was selected, 100 mg infusion was administered BID on Day 1 followed by 100 mg iv on Day 2. The po treatment phase employed a double-blind, double-dummy design using omadacycline placebo comparator tablets of matching size and shape to active omadacycline tablets. The first po dose was given in the morning 12 to 24 hours after the last iv dose. To maintain investigator and subject blinding, subjects on both arms received 2 tablets and 1 over-encapsulated tablet in the morning.

<b>Arm title</b>	Moxifloxacin
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Arm description:

The ITT population included all 334 subjects randomized to the moxifloxacin group. The ITT population was used for analysis of demographic and baseline characteristics and efficacy. The safety population included all randomized subjects who received at least 1 administration of test article (332 subjects). Two subjects were excluded from the safety population because they did not receive test article.

Arm type	Active comparator
Investigational medicinal product name	Moxifloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion, Tablet
Routes of administration	Infusion , Oral use

**Dosage and administration details:**

The iv-treatment phase (minimum of 2 days) followed a double-blind, double-dummy design for moxifloxacin 400 mg QD and matched placebo were administered continuously without interruptions over 60 minutes ( $\pm$  5 minutes). During the first 24 hours of iv treatment, if twice a day dosing (BID) was selected, subjects on the moxifloxacin treatment arm received an additional placebo infusion to match the t=12 hours infusion. Infusions of moxifloxacin or matched placebo were administered continuously, without interruptions, over 60 minutes ( $\pm$  5 minutes). The first dose of test article was to be administered within 4 hours of randomization. The po treatment phase employed a double-blind, double-dummy design using matching over-encapsulated placebo and active moxifloxacin tablets. When switching from iv to po test article, the recommended interval between doses was maintained. The first po moxifloxacin dose was given in the morning 12 to 24 hours after the last iv dose.

<b>Number of subjects in period 1</b>	Omadacycline	Moxifloxacin
Started	336	334
Completed	316	310
Not completed	20	24
Adverse event, serious fatal	2	2
Consent withdrawn by subject	3	6
Adverse event, non-fatal	9	10
Other	6	5
Lost to follow-up	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Omadacycline
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Reporting group description:

The ITT population included all 336 subjects randomized to the omadacycline group. The ITT population was used for analysis of demographic and baseline characteristics and efficacy. The safety population included all randomized subjects who received at least 1 dose of test article (336 subjects).

Reporting group title	Moxifloxacin
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Reporting group description:

The ITT population included all 334 subjects randomized to the moxifloxacin group. The ITT population was used for analysis of demographic and baseline characteristics and efficacy. The safety population included all randomized subjects who received at least 1 administration of test article (332 subjects). Two subjects were excluded from the safety population because they did not receive test article.

Reporting group values	Omadacycline	Moxifloxacin	Total
Number of subjects	336	334	670
Age categorical			
Subjects were categorized as > 65 years of age in 48.2% and > 75 years of age in 18.8%. The overall mean age was 62.8 years.			
Units: Subjects			
Adults (18-64 years)	167	167	334
From 65-84 years	151	158	309
85 years and over	18	9	27
Age continuous			
Units: years			
arithmetic mean	63.3	62.2	
standard deviation	± 14.41	± 15.42	-
Gender categorical			
Overall in the ITT population 51.6% of subjects were male and 48.4% were female.			
Units: Subjects			
Female	158	166	324
Male	178	168	346
Ethnicity (ITT population)			
The majority of subjects were White (99.7%) and not Hispanic or Latino (98.8%).			
Units: Subjects			
Hispanic or Latino	4	4	8
Not Hispanic or Latino	332	330	662
Race			
Units: Subjects			
White	335	333	668
Asian	1	1	2
Renal function			
Units: Subjects			
normal renal function	170	188	358
mild renal impairment	123	103	226
moderate renal impairment	43	43	86
Risk factors for CABP at baseline: smoking status			
Overall, 25.7% of subjects were current smokers.			
Units: Subjects			

non-smoker	190	201	391
current smoker	88	84	172
past smoker	58	49	107
Risk factors for CABP at baseline: pneumococcal vaccine status Units: Subjects			
received pneumococcal vaccine	1	1	2
did not receive pneumococcal vaccine	335	333	668
Risk factors for CABP at baseline: COVID-19 vaccine status Units: Subjects			
received COVID-19 vaccine	90	72	162
did not receive COVID-19 vaccine	246	262	508
Risk factors for CABP at baseline: prior lung infection			
Overall, 4.5% of subjects had a prior lung infection.			
Units: Subjects			
yes prior lung infection	12	18	30
no prior lung infection	324	316	640
Risk factors for CABP at baseline: COPD			
Overall, 7.6% of subjects had COPD.			
Units: Subjects			
yes COPD	31	20	51
no COPD	305	314	619
Risk factors for CABP at baseline: asthma			
Overall, 4.6% of subjects had asthma.			
Units: Subjects			
yes asthma	10	21	31
no asthma	326	313	639
Risk factors for CABP at baseline: chronic cough Units: Subjects			
yes chronic cough	7	2	9
no chronic cough	329	332	661
CABP baseline characteristics: prior antibiotic use (as randomized)			
A prior antibiotic (ie, a single dose of a short-acting antibacterial) was used in 25.0% of omadacycline subjects and 25.7% of moxifloxacin subjects.			
Units: Subjects			
prior antibiotic use	84	84	168
no prior antibiotic use	252	250	502
CABP baseline characteristics: prior antibiotic use (actual) Units: Subjects			
prior antibiotic use	84	86	170
no prior antibiotic use	252	248	500
CABP baseline characteristics: PORT risk class (actual)			
As required per protocol, all subjects had a PORT Risk Class of III (75.6% omadacycline, 76.6% moxifloxacin) or IV (24.4% omadacycline, 23.4% moxifloxacin), with a mean PORT score of 84.9 in the omadacycline group and 84.4 in the moxifloxacin group.			
Units: Subjects			
PORT risk class III	254	256	510

PORT risk class IV	82	78	160
CABP baseline characteristics: PORT risk class (as randomized) Units: Subjects			
PORT risk class III	257	256	513
PORT risk class IV	79	78	157
CABP baseline characteristics: CURB-65 score			
Less than 36% of subjects had severe CABP based on the confusion, uremia, RR, blood pressure, and age 65 or older (CURB-65) criteria (score $\geq 2$ ).			
Units: Subjects			
CURB-65 score=0	50	51	101
CURB-65 score=1	153	149	302
CURB-65 score=2	112	124	236
CURB-65 score=3	20	9	29
CURB-65 score=4	1	1	2
CABP baseline characteristics: SIRS			
A majority of subjects had evidence of systemic inflammatory response syndrome (SIRS) at Baseline (78.1% of subjects).			
Units: Subjects			
yes SIRS	257	266	523
No SIRS	79	68	147
CABP baseline characteristics: bacteremia Units: Subjects			
yes bacteremia	12	14	26
no bacteremia	324	320	644
Radiologic assessment Units: Subjects			
chest x-ray	298	309	607
CT scan	38	25	63
Infiltrates at baseline			
All subjects had pulmonary infiltrates (which was a requirement to be enrolled in the study), which included 47.9% of omadacycline subjects and 44.6% of moxifloxacin subjects with multilobar infiltrates.			
Units: Subjects			
unilobar	175	185	360
multilobar	161	149	310
Presence of pleural effusion at baseline			
Pleural effusion was absent in most subjects (83.9% omadacycline, 81.7% moxifloxacin).			
Units: Subjects			
yes	54	61	115
no	282	273	555
Clinical symptoms of CABP at baseline: cough Units: Subjects			
mild	12	16	28
moderate	211	217	428
severe	113	101	214
Clinical symptoms of CABP at baseline: pleuritic chest pain Units: Subjects			
absent	125	130	255
mild	68	83	151
moderate	105	91	196



severe	38	30	68
Clinical symptoms of CABP at baseline: dyspnea Units: Subjects			
absent	4	4	8
mild	42	40	82
moderate	206	213	419
severe	84	77	161
Clinical symptoms of CABP at baseline: sputum production Units: Subjects			
absent	17	28	45
mild	105	87	192
moderate	179	184	363
severe	35	35	70

### Subject analysis sets

Subject analysis set title	Intent-to-Treat (ITT) set
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.

Reporting group values	Intent-to-Treat (ITT) set		
Number of subjects	670		
Age categorical			
Subjects were categorized as > 65 years of age in 48.2% and > 75 years of age in 18.8%. The overall mean age was 62.8 years.			
Units: Subjects			
Adults (18-64 years)	334		
From 65-84 years	309		
85 years and over	27		
Age continuous			
Units: years			
arithmetic mean	62.8		
standard deviation	± 14.92		
Gender categorical			
Overall in the ITT population 51.6% of subjects were male and 48.4% were female.			
Units: Subjects			
Female	324		
Male	346		
Ethnicity (ITT population)			
The majority of subjects were White (99.7%) and not Hispanic or Latino (98.8%).			
Units: Subjects			
Hispanic or Latino	8		
Not Hispanic or Latino	662		
Race			
Units: Subjects			
White	668		
Asian	2		
Renal function			

Units: Subjects			
normal renal function	358		
mild renal impairment	226		
moderate renal impairment	86		
Risk factors for CABP at baseline: smoking status			
Overall, 25.7% of subjects were current smokers.			
Units: Subjects			
non-smoker	391		
current smoker	172		
past smoker	107		
Risk factors for CABP at baseline: pneumococcal vaccine status			
Units: Subjects			
received pneumococcal vaccine	2		
did not receive pneumococcal vaccine	668		
Risk factors for CABP at baseline: COVID-19 vaccine status			
Units: Subjects			
received COVID-19 vaccine	162		
did not receive COVID-19 vaccine	508		
Risk factors for CABP at baseline: prior lung infection			
Overall, 4.5% of subjects had a prior lung infection.			
Units: Subjects			
yes prior lung infection	30		
no prior lung infection	640		
Risk factors for CABP at baseline: COPD			
Overall, 7.6% of subjects had COPD.			
Units: Subjects			
yes COPD	51		
no COPD	619		
Risk factors for CABP at baseline: asthma			
Overall, 4.6% of subjects had asthma.			
Units: Subjects			
yes asthma	31		
no asthma	639		
Risk factors for CABP at baseline: chronic cough			
Units: Subjects			
yes chronic cough	9		
no chronic cough	661		
CABP baseline characteristics: prior antibiotic use (as randomized)			
A prior antibiotic (ie, a single dose of a short-acting antibacterial) was used in 25.0% of omadacycline subjects and 25.7% of moxifloxacin subjects.			
Units: Subjects			
prior antibiotic use	168		
no prior antibiotic use	502		
CABP baseline characteristics: prior antibiotic use (actual)			
Units: Subjects			

prior antibiotic use	170		
no prior antibiotic use	500		
CABP baseline characteristics: PORT risk class (actual)			
As required per protocol, all subjects had a PORT Risk Class of III (75.6% omadacycline, 76.6% moxifloxacin) or IV (24.4% omadacycline, 23.4% moxifloxacin), with a mean PORT score of 84.9 in the omadacycline group and 84.4 in the moxifloxacin group.			
Units: Subjects			
PORT risk class III	510		
PORT risk class IV	160		
CABP baseline characteristics: PORT risk class (as randomized)			
Units: Subjects			
PORT risk class III	513		
PORT risk class IV	157		
CABP baseline characteristics: CURB-65 score			
Less than 36% of subjects had severe CABP based on the confusion, uremia, RR, blood pressure, and age 65 or older (CURB-65) criteria (score $\geq 2$ ).			
Units: Subjects			
CURB-65 score=0	101		
CURB-65 score=1	302		
CURB-65 score=2	236		
CURB-65 score=3	29		
CURB-65 score=4	2		
CABP baseline characteristics: SIRS			
A majority of subjects had evidence of systemic inflammatory response syndrome (SIRS) at Baseline (78.1% of subjects).			
Units: Subjects			
yes SIRS	523		
No SIRS	147		
CABP baseline characteristics: bacteremia			
Units: Subjects			
yes bacteremia	26		
no bacteremia	644		
Radiologic assessment			
Units: Subjects			
chest x-ray	607		
CT scan	63		
Infiltrates at baseline			
All subjects had pulmonary infiltrates (which was a requirement to be enrolled in the study), which included 47.9% of omadacycline subjects and 44.6% of moxifloxacin subjects with multilobar infiltrates.			
Units: Subjects			
unilobar	360		
multilobar	310		
Presence of pleural effusion at baseline			
Pleural effusion was absent in most subjects (83.9% omadacycline, 81.7% moxifloxacin).			
Units: Subjects			
yes	115		
no	555		
Clinical symptoms of CABP at baseline: cough			
Units: Subjects			

mild	28		
moderate	428		
severe	214		
Clinical symptoms of CABP at baseline: pleuritic chest pain Units: Subjects			
absent	255		
mild	151		
moderate	196		
severe	68		
Clinical symptoms of CABP at baseline: dyspnea Units: Subjects			
absent	8		
mild	82		
moderate	419		
severe	161		
Clinical symptoms of CABP at baseline: sputum production Units: Subjects			
absent	45		
mild	192		
moderate	363		
severe	70		

## End points

### End points reporting groups

Reporting group title	Omadacycline
Reporting group description: The ITT population included all 336 subjects randomized to the omadacycline group. The ITT population was used for analysis of demographic and baseline characteristics and efficacy. The safety population included all randomized subjects who received at least 1 dose of test article (336 subjects).	
Reporting group title	Moxifloxacin
Reporting group description: The ITT population included all 334 subjects randomized to the moxifloxacin group. The ITT population was used for analysis of demographic and baseline characteristics and efficacy. The safety population included all randomized subjects who received at least 1 administration of test article (332 subjects). Two subjects were excluded from the safety population because they did not receive test article.	
Subject analysis set title	Intent-to-Treat (ITT) set
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.	

### Primary: ECR 72-120 hr after first infusion of test article

End point title	ECR 72-120 hr after first infusion of test article
End point description: The primary efficacy outcome measure was ECR at 72 to 120 hours after administration of the first dose of test article in the ITT population. Overall, omadacycline was found to be non-inferior to moxifloxacin for the ECR assessment in the ITT population. Clinical success rates were high (89.6% omadacycline, 87.7% moxifloxacin) and comparable between both treatment groups (difference [95% CI]: 1.9 [-3.0, 6.8]). Given that the lower limit of the 95% CI for the treatment difference (omadacycline – moxifloxacin) was greater than -10%, omadacycline was considered non-inferior to moxifloxacin.	
End point type	Primary
End point timeframe: 72-120 hours after first infusion of test article	

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
clinical success	301	293		
clinical failure or indeterminate overall	35	41		
clinical failure	29	31		
indeterminate	6	10		

### Statistical analyses

Statistical analysis title	Primary efficacy analysis
Statistical analysis description: The primary efficacy analyses were based on the ITT population. The non-inferiority (NI) test was a 1-sided hypothesis test performed at the 2.5% level of significance. This NI test was based on the lower	

limit of the 2-sided 95% confidence interval (CI) (Miettinen & Nurminen method). The primary efficacy outcome was the percentage of subjects with a clinical success at the ECR Assessment (72-120 hours after the first infusion of test article).

Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk difference (RD)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	6.8

## Secondary: Overall clinical response at the PTE visit

End point title	Overall clinical response at the PTE visit
End point description:	
The number and percentage of subjects classified as clinical success, clinical failure, and indeterminate by the investigator's assessment at PTE in the ITT and CE populations calculated for each treatment group was summarized. Clinical success rates were high and similar between the treatment groups at the overall PTE visit. In the ITT population, clinical success at PTE was 86.0% for omadacycline and 87.7% for moxifloxacin (difference [95% CI]: -1.7 [-6.9, 3.4]). Similar results were observed in the CE-PTE population (clinical success was observed in 94.1% of omadacycline subjects and 95.9% of moxifloxacin subjects; difference [95% CI]: -1.8 [-5.7, 2.0]).	
End point type	Secondary
End point timeframe:	
The PTE visit occurred at 5-10 days after the last day of therapy	

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
ITT clinical success	289	293		
ITT clinical failure	27	22		
ITT indeterminate	20	19		

## Statistical analyses

Statistical analysis title	Clinical response at the PTE visit
Statistical analysis description:	
Difference was observed difference in overall clinical success rate at PTE between the omadacycline and moxifloxacin groups. Overall clinical response at the PTE was based on the investigator assessment at the EOT and PTE visits. Percentages were based on the number of subjects in each treatment group. 95% CI was constructed based on the Miettinen and Nurminen method without stratification.	
Comparison groups	Omadacycline v Moxifloxacin

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
Parameter estimate	Risk difference (RD)
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	3.4

Notes:

[1] - The 95% confidence intervals are for descriptive purposes only; no conclusion of noninferiority were made.

### Secondary: All-cause mortality at 15 & 30 days after first dose of test article lost to follow-up subjects considered deceased

End point title	All-cause mortality at 15 & 30 days after first dose of test article lost to follow-up subjects considered deceased
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End point description:

Within 15 days after the first dose of test article, 4 subjects in each treatment group died, and 1 subject in each treatment group was lost to follow-up. Within 30 days after the first dose of test article, 5 subjects in the omadacycline group and 6 subjects in the moxifloxacin group died. In addition, 2 subjects in the omadacycline group and 3 subjects in the moxifloxacin group were lost to follow-up in this time period.

End point type	Secondary
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End point timeframe:

15 and 30 days after first dose of test article

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	328	322		
Units: subjects				
15 days all-cause mortality inc lost to follow-up	5	5		
15 days deaths inc lost to follow-up	4	4		
15 days lost to follow-up	1	1		
30 days all-cause mortality inc lost to follow-up	7	9		
30 days deaths inc lost to follow-up	5	6		
30 days lost to follow-up	2	3		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Overall clinical response at PTE without resolution of all symptoms

End point title	Overall clinical response at PTE without resolution of all symptoms
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**End point description:**

Of the subjects who did not have complete resolution of symptoms at the PTE visit, a majority (83.1% omadacycline, 82.9% moxifloxacin) were determined to be clinical successes by the investigators at PTE; such subjects had residual or minimal clinical symptoms of CABP at PTE that did not require further systemic antimicrobial therapy.

End point type	Other pre-specified
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**End point timeframe:**

Post therapy evaluation (PTE; 5-10 days after the last day of therapy)

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
clinical success	49	34		
clinical failure or indeterminate	10	7		
clinical failure	10	7		
indeterminate	0	0		

**Statistical analyses**

<b>Statistical analysis title</b>	Clinical response at PTE w/o resolution of symptom
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**Statistical analysis description:**

Difference was observed difference in overall clinical success rate at PTE between the omadacycline and moxifloxacin groups. Clinical symptoms for CABP: cough, sputum production, pleuritic chest pain, and dyspnea. Resolution was defined as the absence of all baseline symptoms. Overall clinical response at the PTE was based on the investigator assessment at the EOT and PTE visits. 95% CI was constructed based on the Miettinen and Nurminen method without stratification.

Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other <sup>[2]</sup>
Parameter estimate	Risk difference (RD)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.6
upper limit	16.5

**Notes:**

[2] - The 95% confidence intervals are for descriptive purposes only; no conclusions of noninferiority were made.

**Other pre-specified: Investigator assessment of clinical response at EOT visit**

End point title	Investigator assessment of clinical response at EOT visit
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**End point description:**

Subjects classified as a clinical success, clinical failure, or indeterminate by the investigator's assessment at EOT in the ITT population. The percentage of subjects in the ITT population with clinical success was similar in the omadacycline group compared to the moxifloxacin group (90.2% and 91.3%, respectively).



End point type	Other pre-specified
End point timeframe:	
From the first dose of test article to the EOT visit.	

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
Clinical success	303	305		
Clinical failure or indeterminate	33	29		
Clinical failure	25	18		
Indeterminate	8	11		

## Statistical analyses

Statistical analysis title	Clinical response at EOT visit
Statistical analysis description:	
Difference was observed difference in investigator assessment of clinical success rate at EOT between the omadacycline and moxifloxacin groups. Two-sided unadjusted 95% CI was constructed for the observed difference in the clinical success rate based on the Miettinen and Nurminen method without stratification.	
Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	3.3

## Other pre-specified: Overall clinical response by investigator at PTE visit in subjects without resolution of all clinical symptoms (ITT population)

End point title	Overall clinical response by investigator at PTE visit in subjects without resolution of all clinical symptoms (ITT population)
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### End point description:

Analyses of shifts from Baseline to each visit (Day 2 through the PTE visit) in the clinical symptoms of CABP were performed by treatment group for the ITT population. In general, most subjects who had cough, pleuritic chest pain, dyspnea, and phlegm/sputum considered severe at Baseline were reported to have mild to no symptoms at the EOT and PTE visits. Shifts to less severe categories were also observed in the mild and moderate categories. At the PTE visit the percentage of subjects who had resolution of all clinical symptoms in the omadacycline and moxifloxacin groups were 81.0% and 86.8%, respectively. A vast majority of subjects in either treatment group did not have a new or worsening symptom (99.7% omadacycline, 99.7% moxifloxacin). Of the subjects who did not have complete resolution of symptoms at the PTE visit, a majority (83.1% omadacycline, 82.9% moxifloxacin) were

determined to be clinical successes by the investigators at PTE.

End point type	Other pre-specified
End point timeframe:	
From baseline (Day 2) to PTE visit	

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 <sup>[3]</sup>	41 <sup>[4]</sup>		
Units: subjects				
clinical success	49	34		
clinical failure or indeterminate	10	7		
clinical failure	10	7		
indeterminate	0	0		

Notes:

[3] - number of subjects without resolution of symptoms at PTE

[4] - number of subjects without resolution of symptoms at PTE

## Statistical analyses

Statistical analysis title	Response at PTE w/o resolution of all symptoms
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Statistical analysis description:

Difference was observed difference in overall clinical success rate at PTE between the omadacycline and moxifloxacin groups. Clinical symptoms for CABP: cough, sputum production, pleuritic chest pain, and dyspnea. Resolution was defined as the absence of all baseline symptoms. Overall clinical response at the PTE was based on the investigator assessment at the EOT and PTE visits. 95% CI was constructed based on the Miettinen and Nurminen method without stratification.

Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.6
upper limit	16.5

## Other pre-specified: Concordance of ECR with overall clinical response based on investigator assessment

End point title	Concordance of ECR with overall clinical response based on investigator assessment
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End point description:

Among subjects with definitive assessments (ie, not indeterminate), there was generally good concordance ( $\geq 80\%$ ) between ECR and the later clinical assessment in each treatment group. Overall, the incidences of subjects who were programmatically determined as non-responders at ECR and later deemed clinical cures at PTE by the investigators were 5.4% for omadacycline subjects and 4.5% for moxifloxacin subjects. The incidences of subjects who were responders at ECR and later deemed clinical failures at PTE were 5.7% for omadacycline subjects and 2.4% for moxifloxacin subjects. The difference

between treatment groups was driven mainly by the greater number of subjects in the omadacycline group who did not complete the PTE visit.

End point type	Other pre-specified
End point timeframe:	
72 to 120 hours to PTE visit	

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
ECR clinical success/PTE clinical success	270	275		
ECR clinical success/PTE clinical failure	19	8		
ECR clinical success/PTE indeterminate	12	10		
ECR clinical failure/PTE clinical success	18	15		
ECR clinical failure/PTE clinical failure	8	14		
ECR clinical failure/PTE indeterminate	3	2		
ECR indeterminate/PTE clinical success	1	3		
ECR indeterminate/PTE clinical failure	0	0		
ECR indeterminate/PTE indeterminate	5	7		

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Clinical response by PORT risk class

End point title	Clinical response by PORT risk class
End point description:	
ECR (at 72 to 120 hours after the first infusion of test article) and overall assessment of clinical response (based on the investigator's assessment) at the PTE visit across PORT Risk Class in the ITT population. In general, comparable results were observed between PORT Risk Class III and Class IV scores for both the ECR and PTE assessments.	
End point type	Other pre-specified
End point timeframe:	
ECR (72-120 hours after first infusion of test article) to PTE visit	

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
ECR PORT risk class III clinical success	230	229		
ECR PORT risk class IV clinical success	71	64		
PTE PORT risk class III clinical success	197	206		
PTE PORT risk class IV clinical success	60	54		

## Statistical analyses

<b>Statistical analysis title</b>	Clinical response by PORT risk class
Statistical analysis description: Difference was observed difference in early clinical success rate or overall clinical response rate at PTE between the omadacycline and moxifloxacin groups. 95% CI within each type of PORT Risk Class was constructed based on the Miettinen and Nurminen method without stratification.	
Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	6.4

## Other pre-specified: Clinical response by prior antibiotic use

End point title	Clinical response by prior antibiotic use
End point description: ECR (at 72 to 120 hours after the first infusion of test article) and overall assessment of clinical response (based on the investigator's assessment) at the PTE visit across prior antibiotic use in the ITT population. Comparable results were observed between those who did and did not receive a prior antibiotic (ie, a single dose short-acting antibiotic within 72 hours prior to the first dose of test article) for both the ECR and PTE assessments.	
End point type	Other pre-specified
End point timeframe: ECR (72-120 hours after first infusion of test article) to PTE visit	

<b>End point values</b>	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
ECR received prior antibiotics/clinical success	72	73		
ECR no prior antibiotics/clinical success	229	220		
PTE received prior antibiotics/clinical success	69	75		
PTE no prior antibiotics/clinical success	220	218		

## Statistical analyses

<b>Statistical analysis title</b>	ECR at PTE visit based on prior antibiotic use
Statistical analysis description:	
Difference was observed difference in early clinical success rate or overall clinical response rate at the PTE between the omadacycline and moxifloxacin groups. 95% CI within each type of prior antibiotics use (yes/no) was constructed based on the Miettinen and Nurminen method without stratification.	
Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	11.8

## Other pre-specified: Clinical success in subjects with SIRS and by CURB-65 score

End point title	Clinical success in subjects with SIRS and by CURB-65 score
End point description:	
In subjects with SIRS, the ECR assessment of clinical success was reported in 90.3% omadacycline subjects and 88.0% moxifloxacin subjects. At PTE, the corresponding clinical success rates were 85.2% and 87.6%. In addition, generally comparable results were observed between different CURB-65 scores, although there were relatively few subjects with CURB-65 scores of 3 or 4.	
End point type	Other pre-specified
End point timeframe:	
From ECR (72-120 after first infusion of test article) to PTE visit	

End point values	Omadacycline	Moxifloxacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	334		
Units: subjects				
SIRS at baseline ECR clinical success	232	234		
SIRS at baseline PTE clinical success	219	233		
ECR CURB-65 score=0 clinical success	46	44		
ECR CURB-65 score=1 clinical success	135	138		
ECR CURB-65 score=2 clinical success	99	103		
ECR CURB-65 score=3 clinical success	20	7		
ECR CURB-65 score=4 clinical success	1	1		

PTE CURB-65 score=0 clinical success	41	46		
PTE CURB-65 score=1 clinical success	138	137		
PTE CURB-65 score=2 clinical success	91	102		
PTE CURB-65 score=3 clinical success	18	7		
PTE CURB-65 score=4 clinical success	1	1		

## Statistical analyses

<b>Statistical analysis title</b>	ECR at PTE visit in subjects with SIRS & CURB-65
Statistical analysis description:	
Difference was observed difference in early clinical success rate or overall clinical response rate at the PTE between the omadacycline and moxifloxacin groups. 95% CI within each subgroup was constructed based on the Miettinen and Nurminen method without stratification.	
Comparison groups	Omadacycline v Moxifloxacin
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	7.8

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

A treatment-emergent AE was defined as any AE that newly appeared, increased in frequency, or worsened in severity on or after the initiation of active test article.

Adverse event reporting additional description:

The Safety population consisted of all randomized subjects who received test article. An AE was considered treatment-emergent if the AE start date and time was on or after the start date and time of the first infusion of active test article.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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### Reporting groups

Reporting group title	Omadacycline
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Reporting group description:

Safety population

Reporting group title	Moxifloxacin
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Reporting group description:

Safety population

Serious adverse events	Omadacycline	Moxifloxacin	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 336 (5.06%)	15 / 332 (4.52%)	
number of deaths (all causes)	6	6	
number of deaths resulting from adverse events	6	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to liver			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	1 / 336 (0.30%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiogenic shock			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 336 (0.00%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiopulmonary failure			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
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			
Death			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	



Multiple organ dysfunction syndrome subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Gastrointestinal haemorrhage subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic respiratory failure subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure subjects affected / exposed	0 / 336 (0.00%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 336 (0.60%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
COVID-19			
subjects affected / exposed	1 / 336 (0.30%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 336 (0.30%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphyema			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
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 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma streptococcal			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.3 %

<b>Non-serious adverse events</b>	Omadacycline	Moxifloxacin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 336 (27.68%)	78 / 332 (23.49%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Polycythaemia vera			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 336 (0.89%)	1 / 332 (0.30%)	
occurrences (all)	3	1	
Hypertensive crisis			

subjects affected / exposed	2 / 336 (0.60%)	1 / 332 (0.30%)	
occurrences (all)	2	1	
Deep vein thrombosis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Aortic dilatation			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 336 (0.89%)	0 / 332 (0.00%)	
occurrences (all)	3	0	
Catheter site related reaction			
subjects affected / exposed	2 / 336 (0.60%)	0 / 332 (0.00%)	
occurrences (all)	2	0	
Administration site reaction			
subjects affected / exposed	1 / 336 (0.30%)	3 / 332 (0.90%)	
occurrences (all)	1	3	
Oedema peripheral			
subjects affected / exposed	1 / 336 (0.30%)	1 / 332 (0.30%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Catheter site erythema			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Chest discomfort			

subjects affected / exposed	0 / 336 (0.00%)	2 / 332 (0.60%)	
occurrences (all)	0	2	
Infusion site erythema			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Infusion site reaction			
subjects affected / exposed	0 / 336 (0.00%)	2 / 332 (0.60%)	
occurrences (all)	0	2	
Malaise			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	5 / 336 (1.49%)	1 / 332 (0.30%)	
occurrences (all)	5	1	
Bronchial obstruction			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 336 (0.30%)	2 / 332 (0.60%)	
occurrences (all)	1	2	
Pleural effusion			
subjects affected / exposed	1 / 336 (0.30%)	1 / 332 (0.30%)	
occurrences (all)	1	1	
Pulmonary infarction			

subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 336 (0.60%)	7 / 332 (2.11%)	
occurrences (all)	2	7	
Delirium tremens			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Initial insomnia			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Restlessness			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Psychotic disorder			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	2	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 336 (2.08%)	0 / 332 (0.00%)	
occurrences (all)	7	0	
Alanine aminotransferase increased			

subjects affected / exposed	6 / 336 (1.79%)	1 / 332 (0.30%)
occurrences (all)	6	1
Blood creatinine increased		
subjects affected / exposed	2 / 336 (0.60%)	0 / 332 (0.00%)
occurrences (all)	2	0
Gamma-glutamyltransferase increased		
subjects affected / exposed	2 / 336 (0.60%)	1 / 332 (0.30%)
occurrences (all)	2	1
Platelet count increased		
subjects affected / exposed	2 / 336 (0.60%)	2 / 332 (0.60%)
occurrences (all)	2	2
White blood cell count increased		
subjects affected / exposed	2 / 336 (0.60%)	0 / 332 (0.00%)
occurrences (all)	2	0
Blood pressure increased		
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)
occurrences (all)	1	0
Blood urea increased		
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)
occurrences (all)	1	0
Creatinine renal clearance decreased		
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)
occurrences (all)	1	0
Electrocardiogram T wave abnormal		
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)
occurrences (all)	1	0
International normalised ratio increased		
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)
occurrences (all)	1	0
Blood creatine phosphokinase increased		
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)
occurrences (all)	0	1
Blood potassium increased		

subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Human chorionic gonadotropin increased subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Influenza A virus test positive subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Injury, poisoning and procedural complications Limb injury subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	2 / 336 (0.60%) 3	2 / 332 (0.60%) 2	
Cardiac failure subjects affected / exposed occurrences (all)	1 / 336 (0.30%) 2	1 / 332 (0.30%) 3	
Angina pectoris subjects affected / exposed occurrences (all)	1 / 336 (0.30%) 1	0 / 332 (0.00%) 0	
Cardiac failure congestive subjects affected / exposed occurrences (all)	1 / 336 (0.30%) 1	0 / 332 (0.00%) 0	
Cardiomyopathy subjects affected / exposed occurrences (all)	1 / 336 (0.30%) 1	0 / 332 (0.00%) 0	
Tachycardia subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	12 / 336 (3.57%) 12	15 / 332 (4.52%) 15	
Dizziness			



subjects affected / exposed	1 / 336 (0.30%)	2 / 332 (0.60%)	
occurrences (all)	1	2	
Brain oedema			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 336 (0.89%)	1 / 332 (0.30%)	
occurrences (all)	3	1	
Thrombocytosis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Hypochromasia			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Eye disorders			

Cataract			
subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Eye oedema			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 336 (0.89%)	0 / 332 (0.00%)	
occurrences (all)	3	0	
Nausea			
subjects affected / exposed	2 / 336 (0.60%)	5 / 332 (1.51%)	
occurrences (all)	2	5	
Abdominal pain			
subjects affected / exposed	1 / 336 (0.30%)	1 / 332 (0.30%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 336 (0.30%)	2 / 332 (0.60%)	
occurrences (all)	1	2	
Abdominal discomfort			
subjects affected / exposed	0 / 336 (0.00%)	4 / 332 (1.20%)	
occurrences (all)	0	4	
Abdominal pain upper			
subjects affected / exposed	0 / 336 (0.00%)	2 / 332 (0.60%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	0 / 336 (0.00%)	10 / 332 (3.01%)	
occurrences (all)	0	10	
Dry mouth			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	
Hepatobiliary disorders			

Hepatic cyst subjects affected / exposed occurrences (all)	1 / 336 (0.30%) 1	0 / 332 (0.00%) 0	
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Skin and subcutaneous tissue disorders			
Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 336 (0.30%) 1	0 / 332 (0.00%) 0	
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Erythema subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	3 / 332 (0.90%) 3	
Pruritus subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Rash subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	2 / 336 (0.60%) 2	0 / 332 (0.00%) 0	
Nephropathy subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Renal cyst subjects affected / exposed occurrences (all)	0 / 336 (0.00%) 0	1 / 332 (0.30%) 1	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	1 / 336 (0.30%) 1	1 / 332 (0.30%) 1	

Infections and infestations COVID-19 subjects affected / exposed occurrences (all)  Urinary tract infection subjects affected / exposed occurrences (all)  Acute sinusitis subjects affected / exposed occurrences (all)  Fungaemia subjects affected / exposed occurrences (all)  Ophthalmic herpes simplex subjects affected / exposed occurrences (all)  Cystitis subjects affected / exposed occurrences (all)  Pyelonephritis subjects affected / exposed occurrences (all)  Urinary tract candidiasis subjects affected / exposed occurrences (all)	10 / 336 (2.98%) 11  2 / 336 (0.60%) 3  1 / 336 (0.30%) 1  1 / 336 (0.30%) 1  1 / 336 (0.30%) 1  0 / 336 (0.00%) 0  0 / 336 (0.00%) 0  0 / 336 (0.00%) 0  0 / 336 (0.00%) 0	2 / 332 (0.60%) 4  1 / 332 (0.30%) 1  0 / 332 (0.00%) 0  0 / 332 (0.00%) 0  0 / 332 (0.00%) 0  1 / 332 (0.30%) 1  1 / 332 (0.30%) 1  1 / 332 (0.30%) 1	
Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all)  Gout subjects affected / exposed occurrences (all)  Hypokalaemia subjects affected / exposed occurrences (all)  Hypomagnesaemia	1 / 336 (0.30%) 1  1 / 336 (0.30%) 1  1 / 336 (0.30%) 1	0 / 332 (0.00%) 0  0 / 332 (0.00%) 0  2 / 332 (0.60%) 2	

subjects affected / exposed	1 / 336 (0.30%)	0 / 332 (0.00%)	
occurrences (all)	1	0	
Hypoproteinaemia			
subjects affected / exposed	0 / 336 (0.00%)	1 / 332 (0.30%)	
occurrences (all)	0	1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2020	Exclusion criterion 17 was expanded to include those who are allergic to any of the components of the test articles. Infusion time of omadacycline was clarified to match the US FDA-approved label. A section was added to detail the clinical events committee (CEC) that was to adjudicate all cases of mortality in the study to determine cause and relatedness to study drug. Schedule of events was updated to remove the Investigator's Assessment of Clinical Response at the Final Follow-up visit to be consistent with the body of the protocol.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported