



## Clinical trial results:

### A Randomized, Double-Blinded, Adaptive Phase 2 Study to Evaluate the Safety and Efficacy of IV or IV/PO Omadacycline and IV/PO Levofloxacin in the Treatment of Adults with Acute Pyelonephritis.

#### Summary

EudraCT number	2018-000037-13
Trial protocol	LV
Global end of trial date	24 July 2019

#### Results information

Result version number	v1 (current)
This version publication date	10 June 2021
First version publication date	10 June 2021

#### Trial information

##### Trial identification

Sponsor protocol code	PTK0796-AP-17202
-----------------------	------------------

##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03757234
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Paratek Pharmaceuticals Inc
Sponsor organisation address	75 Park Plaza, 4th Floor, Boston, Massachusetts, United States, 02116
Public contact	Paratek Medical Information, Paratek Pharmaceuticals Inc, 1 833-727-2835, medinfo@paratekpharma.com
Scientific contact	Paratek Medical Information, Paratek Pharmaceuticals Inc, 1 833-727-2835, medinfo@paratekpharma.com

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2019
Global end of trial reached?	Yes
Global end of trial date	24 July 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety and efficacy of intravenous (iv) or iv/per oral (po) omadacycline as compared to iv or iv/po levofloxacin in the treatment of female adults with acute pyelonephritis.

Protection of trial subjects:

The study was designed, implemented, and reported in accordance with the International Council for Harmonisation Harmonized Tripartite Guideline for Good Clinical Practice, with applicable local regulations (including European Directive 2001/20/EC, United States Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2018
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	Georgia: 51
Country: Number of subjects enrolled	Russian Federation: 73
Country: Number of subjects enrolled	Ukraine: 54
Country: Number of subjects enrolled	Latvia: 23
Worldwide total number of subjects	201
EEA total number of subjects	23

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)	201
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 207 subjects were screened for entry into the study. Of these, 6 subjects failed screening, and 201 subjects were enrolled and randomized in the study.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Omadacycline 200 iv/200 iv

Arm description:

On Day 1, participants received omadacycline 200 milligrams intravenously (iv). On Days 2 through 7, participants continued to receive omadacycline 200 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.

Arm type	Experimental
Investigational medicinal product name	Omadacycline
Investigational medicinal product code	PTK 0796
Other name	Nuzyra
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 iv: 200 milligrams omadacycline reconstituted in 150 milliliters normal saline

<b>Arm title</b>	Omadacycline 200 iv/100 iv
------------------	----------------------------

Arm description:

On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.

Arm type	Experimental
Investigational medicinal product name	Omadacycline
Investigational medicinal product code	PTK 0796
Other name	Nuzyra
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 iv: 100 milligrams omadacycline reconstituted in 150 milliliters normal saline; 200 iv: 200 milligrams omadacycline reconstituted in 150 milliliters normal saline

<b>Arm title</b>	Omadacycline 200 iv/300 po or 100 iv
------------------	--------------------------------------

Arm description:

On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 300 milligrams per oral (po). All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	Omadacycline
Investigational medicinal product code	PTK 0796
Other name	Nuzyra
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 po: 2 tablets of 150 milligrams omadacycline were taken with water in fasted state

Investigational medicinal product name	Omadacycline
Investigational medicinal product code	PTK 0796
Other name	Nuzyra
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 iv: 100 milligrams omadacycline reconstituted in 150 milliliters normal saline; 200 iv: 200 milligrams omadacycline reconstituted in 150 milliliters normal saline

<b>Arm title</b>	Omadacycline 200 iv/450 po or 100 iv
------------------	--------------------------------------

Arm description:

On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 450 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.

Arm type	Experimental
Investigational medicinal product name	Omadacycline
Investigational medicinal product code	PTK 0796
Other name	Nuzyra
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

450 po: 3 tablets of 150 milligrams omadacycline were taken with water in fasted state

Investigational medicinal product name	Omadacycline
Investigational medicinal product code	PTK 0796
Other name	Nuzyra
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 iv: 100 milligrams omadacycline reconstituted in 150 milliliters normal saline; 200 iv: 200 milligrams omadacycline reconstituted in 150 milliliters normal saline

<b>Arm title</b>	Levofloxacin 750 iv/750 po or iv
------------------	----------------------------------

Arm description:

On Day 1, participants received levofloxacin 750 milligrams iv. On Days 2 through 7, participants received levofloxacin 750 milligrams iv or levofloxacin 750 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.

Arm type	Experimental
Investigational medicinal product name	Levofloxacin
Investigational medicinal product code	
Other name	Levaquin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

750 iv: 750 milligrams levofloxacin reconstituted in 150 milliliters normal saline

Investigational medicinal product name	Levofloxacin
Investigational medicinal product code	
Other name	Levaquin
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

750 po: 3 tablets of 250 milligrams levofloxacin were taken with water in fasted state

<b>Number of subjects in period 1</b>	Omadacycline 200 iv/200 iv	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/300 po or 100 iv
Started	75	18	17
Completed PTE visit	72	16	17
Completed	72	16	17
Not completed	3	2	0
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	-	-	-
Other	1	1	-
Lost to follow-up	1	-	-

<b>Number of subjects in period 1</b>	Omadacycline 200 iv/450 po or 100 iv	Levofloxacin 750 iv/750 po or iv
Started	17	74
Completed PTE visit	16	71
Completed	16	70
Not completed	1	4
Consent withdrawn by subject	1	2
Adverse event, non-fatal	-	1
Other	-	-
Lost to follow-up	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Omadacycline 200 iv/200 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams intravenously (iv). On Days 2 through 7, participants continued to receive omadacycline 200 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.	
Reporting group title	Omadacycline 200 iv/100 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.	
Reporting group title	Omadacycline 200 iv/300 po or 100 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 300 milligrams per oral (po). All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.	
Reporting group title	Omadacycline 200 iv/450 po or 100 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 450 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.	
Reporting group title	Levofloxacin 750 iv/750 po or iv
Reporting group description: On Day 1, participants received levofloxacin 750 milligrams iv. On Days 2 through 7, participants received levofloxacin 750 milligrams iv or levofloxacin 750 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.	

Reporting group values	Omadacycline 200 iv/200 iv	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/300 po or 100 iv
Number of subjects	75	18	17
Age categorical Units:			

Age continuous Units: years arithmetic mean standard deviation	38.2 ± 14.97	33.9 ± 14.48	37.1 ± 15.97
Gender categorical Units: Subjects			
Female	75	18	17
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0

White	74	18	17
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	74	18	17
Unknown or Not Reported	0	0	0

Reporting group values	Omadacycline 200 iv/450 po or 100 iv	Levofloxacin 750 iv/750 po or iv	Total
Number of subjects	17	74	201
Age categorical			
Units:			

Age continuous			
Units: years			
arithmetic mean	38.2	38.8	
standard deviation	± 17.66	± 14.74	-
Gender categorical			
Units: Subjects			
Female	17	74	201
Male	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	17	74	200
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	17	74	200
Unknown or Not Reported	0	0	0



## End points

### End points reporting groups

Reporting group title	Omadacycline 200 iv/200 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams intravenously (iv). On Days 2 through 7, participants continued to receive omadacycline 200 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.	
Reporting group title	Omadacycline 200 iv/100 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.	
Reporting group title	Omadacycline 200 iv/300 po or 100 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 300 milligrams per oral (po). All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.	
Reporting group title	Omadacycline 200 iv/450 po or 100 iv
Reporting group description: On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 450 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.	
Reporting group title	Levofloxacin 750 iv/750 po or iv
Reporting group description: On Day 1, participants received levofloxacin 750 milligrams iv. On Days 2 through 7, participants received levofloxacin 750 milligrams iv or levofloxacin 750 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.	

### Primary: Number of Participants With an Investigator Assessment of Clinical Response at the Post Therapy Evaluation (PTE) Visit (ITT Population)

End point title	Number of Participants With an Investigator Assessment of Clinical Response at the Post Therapy Evaluation (PTE) Visit (ITT Population)
End point description: Clinical response was determined by the investigator at the PTE visit by assessing whether or not the participant met the clinical outcome of Clinical Success, Clinical Failure, or Indeterminate. Clinical Success was defined as the complete resolution or significant improvement of the baseline AP signs and symptoms at the PTE visit such that no additional antimicrobial therapy is required for the current infection. Clinical Failure was defined as no apparent response to therapy or persistence of signs and symptoms of infection or reappearance of signs and symptoms at or before the PTE visit such that use of additional systemic antimicrobial therapy for the current infection was required or death at or before the PTE visit. The clinical outcome was deemed as Indeterminate when the PTE visit was not completed.	
End point type	Primary
End point timeframe: Day 21 (A PTE occurred on Day 21 ± 2 days after the participant's first dose of study drug).	

End point values	Omadacycline 200 iv/200 iv	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/300 po or 100 iv	Omadacycline 200 iv/450 po or 100 iv
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	18	17	17
Units: participants				
number (not applicable)				
Clinical Success	68	15	15	16
Clinical Failure	5	1	2	0
Indeterminate	2	2	0	1

End point values	Levofloxacin 750 iv/750 po or iv			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: participants				
number (not applicable)				
Clinical Success	69			
Clinical Failure	1			
Indeterminate	4			

### Statistical analyses

<b>Statistical analysis title</b>	Clinical Response
Comparison groups	Omadacycline 200 iv/200 iv v Levofloxacin 750 iv/750 po or iv
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Parameter estimate	Treatment difference
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4
upper limit	6.9

Notes:

[1] - Non-inferiority margin for comparison of the doses was set at 10%.

<b>Statistical analysis title</b>	Clinical Response
Comparison groups	Omadacycline 200 iv/100 iv v Levofloxacin 750 iv/750 po or iv

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[2]</sup>
Parameter estimate	Treatment difference
Point estimate	-9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.8
upper limit	5.3

Notes:

[2] - Non-inferiority margin for comparison of the doses was set at 10%.

<b>Statistical analysis title</b>	Clinical Response
Comparison groups	Omadacycline 200 iv/300 po or 100 iv v Levofloxacin 750 iv/750 po or iv
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[3]</sup>
Parameter estimate	Treatment difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.6
upper limit	8.2

Notes:

[3] - Non-inferiority margin for comparison of the doses was set at 10%.

<b>Statistical analysis title</b>	Clinical Response
Comparison groups	Omadacycline 200 iv/450 po or 100 iv v Levofloxacin 750 iv/750 po or iv
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[4]</sup>
Parameter estimate	Treatment Difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.4
upper limit	11.8

Notes:

[4] - Non-inferiority margin for comparison of the doses was set at 10%.

### **Primary: Number of Participants With a Microbiological Response at the PTE Visit (Micro-ITT Population)**

End point title	Number of Participants With a Microbiological Response at the PTE Visit (Micro-ITT Population)
-----------------	--

End point description:

Microbiological response was determined programmatically at the PTE visit by assessing whether or not

the participant met the microbiological outcome of 'Success', 'Failure', or 'Indeterminate'. Participants were considered to have a microbiological response of 'Success' if the outcomes of each baseline pathogens were eradication at the PTE visit. Participants were considered to have a microbiological response of 'Failure' if the outcome for any pathogen was persistence. Participants were considered to have a microbiological response of 'Indeterminate', if the outcome of at least 1 baseline pathogen was indeterminate and there was no outcome of persistence for any baseline pathogen.

End point type	Primary
----------------	---------

End point timeframe:

Day 21 (A PTE occurred on Day 21 ± 2 days after the participant's first dose of study drug).

End point values	Omadacycline 200 iv/200 iv	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/300 po or 100 iv	Omadacycline 200 iv/450 po or 100 iv
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	11	14	13
Units: participants				
number (not applicable)				
Clinical Success	32	3	9	5
Clinical Failure	13	7	5	7
Indeterminate	1	1	0	1

End point values	Levofloxacin 750 iv/750 po or iv			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: participants				
number (not applicable)				
Clinical Success	39			
Clinical Failure	11			
Indeterminate	2			

## Statistical analyses

Statistical analysis title	Clinical Response
Comparison groups	Omadacycline 200 iv/200 iv v Levofloxacin 750 iv/750 po or iv
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[5]</sup>
Parameter estimate	Treatment difference
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.6
upper limit	12.7

Notes:

[5] - Non-inferiority margin for comparison of the doses was set at 10%.

<b>Statistical analysis title</b>	Clinical Response
Comparison groups	Omadacycline 200 iv/100 iv v Levofloxacin 750 iv/750 po or iv
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[6]</sup>
Parameter estimate	Treatment difference
Point estimate	-47.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.3
upper limit	-6

Notes:

[6] - Non-inferiority margin for comparison of the doses was set at 10%.

<b>Statistical analysis title</b>	Clinical Response
Comparison groups	Omadacycline 200 iv/300 po or 100 iv v Levofloxacin 750 iv/750 po or iv
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[7]</sup>
Parameter estimate	Treatment difference
Point estimate	-10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.8
upper limit	15.1

Notes:

[7] - Non-inferiority margin for comparison of the doses was set at 10%.

<b>Statistical analysis title</b>	Clinical Response
Comparison groups	Omadacycline 200 iv/450 po or 100 iv v Levofloxacin 750 iv/750 po or iv
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[8]</sup>
Parameter estimate	Treatment difference
Point estimate	-36.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.6
upper limit	-1.1

Notes:

[8] - Non-inferiority margin for comparison of the doses was set at 10%.

**Primary: Number of Participants With Resolution of All AP Signs and Clinical Symptoms at PTE Visit (ITT Population)**

End point title	Number of Participants With Resolution of All AP Signs and Clinical Symptoms at PTE Visit (ITT Population) <sup>[9]</sup>
-----------------	---

## End point description:

Participants recorded their assessments using the Modified Patient Symptom Assessment Questionnaire (mPSAQ), a 6-item questionnaire that assessed the levels of 'severity' and 'bothersomeness' for six pyelonephritis signs and symptoms. The sub-scale responses were recorded as 'did not have', 'mild', 'moderate', and 'severe' for 'severity'; and 'not at all', 'a little', 'moderately', and 'a lot' for 'bothersomeness', both scored 0–3. Total scores were calculated by summing the non-missing scores of the 6 items, divided by the number of non-missing items, and then multiplied by 6. For each sub-scale, the total score ranged from 0 (least Severe/ least bothersome) and 18 (worst severity/most bothersome). Number of participants with resolution of all symptoms, without occurrence of new symptoms is reported. Resolution was defined as absence of all baseline symptoms.

End point type	Primary
----------------	---------

## End point timeframe:

Day 21 (A PTE occurred on Day 21 ± 2 days after the participant's first dose of study drug).

## Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were summarized for this primary endpoint.

End point values	Omadacycline 200 iv/200 iv	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/300 po or 100 iv	Omadacycline 200 iv/450 po or 100 iv
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	16	16	16
Units: participants				
number (not applicable)	51	15	14	13

End point values	Levofloxacin 750 iv/750 po or iv			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: participants				
number (not applicable)	54			

**Statistical analyses**

No statistical analyses for this end point

**Primary: Number of Participants With No Worsening and Absence of New AP Signs and Clinical Symptoms at PTE Visit (ITT Population)**

End point title	Number of Participants With No Worsening and Absence of New AP Signs and Clinical Symptoms at PTE Visit (ITT Population) <sup>[10]</sup>
-----------------	--

## End point description:

Participants recorded their assessments using the mPSAQ, a 6-item questionnaire that assessed the levels of 'severity' and 'bothersomeness' for six pyelonephritis signs and symptoms. The sub-scale responses were recorded as 'did not have', 'mild', 'moderate', and 'severe' for 'severity'; and 'not at all', 'a little', 'moderately', and 'a lot' for 'bothersomeness', both scored 0–3. Total scores were calculated by summing the non-missing scores of the 6 items, divided by the number of non-missing items, and then

multiplied by 6. For each sub-scale, the total score ranged from 0 (least Severe/ least bothersome) and 18 (worst severity/most bothersome). Number of participants with no worsening and absence of AP signs and clinical symptoms is reported. No worsening meant that each question score is same or better at post baseline.

End point type	Primary
End point timeframe:	
Day 21 (A PTE occurred on Day 21 ± 2 days after the participant's first dose of study drug).	

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were summarized for this primary endpoint.

End point values	Omadacycline 200 iv/200 iv	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/300 po or 100 iv	Omadacycline 200 iv/450 po or 100 iv
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	16	16	16
Units: participants				
number (not applicable)	62	16	16	15

End point values	Levofloxacin 750 iv/750 po or iv			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: participants				
number (not applicable)	65			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Treatment Emergent Adverse Events and Serious Adverse Events

End point title	Number of Participants With Treatment Emergent Adverse Events and Serious Adverse Events
-----------------	--

End point description:

An adverse event is any untoward, undesired, or unplanned event in the form of signs, symptoms, disease, or laboratory or physiologic observations occurring in a person given a study drug or in a clinical study. A treatment-emergent adverse event was defined as any adverse event that newly appeared, increased in frequency, or worsened in severity on or after the initiation of the study drug.

End point type	Secondary
End point timeframe:	
Up to approximately 28 days	

<b>End point values</b>	Omadacycline 200 iv/200 iv	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/300 po or 100 iv	Omadacycline 200 iv/450 po or 100 iv
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	18	17	17
Units: participants				
number (not applicable)				
Treatment Emergent Adverse Events	23	6	9	8
Treatment Emergent Serious Adverse Events	0	0	2	2

<b>End point values</b>	Levofloxacin 750 iv/750 po or iv			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: participants				
number (not applicable)				
Treatment Emergent Adverse Events	24			
Treatment Emergent Serious Adverse Events	2			

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to approximately 28 days

Adverse event reporting additional description:

The Safety Population consisted of all randomized participants who received at least one dose of study drug.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20.1
--------------------	------

### Reporting groups

Reporting group title	Omadacycline 200 iv/100 iv
-----------------------	----------------------------

Reporting group description:

On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.

Reporting group title	Omadacycline 200 iv/450 po or 100 iv
-----------------------	--------------------------------------

Reporting group description:

On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 450 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.

Reporting group title	Omadacycline 200 iv/200 iv
-----------------------	----------------------------

Reporting group description:

On Day 1, participants received omadacycline 200 milligrams intravenously (iv). On Days 2 through 7, participants continued to receive omadacycline 200 milligrams iv. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes.

Reporting group title	Levofloxacin 750 iv/750 po or iv
-----------------------	----------------------------------

Reporting group description:

On Day 1, participants received levofloxacin 750 milligrams iv. On Days 2 through 7, participants received levofloxacin 750 milligrams iv or levofloxacin 750 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline as continuous infusions over 90 minutes. All oral doses were taken in a fasted state.

Reporting group title	Omadacycline 200 iv/300 po or 100 iv
-----------------------	--------------------------------------

Reporting group description:

On Day 1, participants received omadacycline 200 milligrams iv. On Days 2 through 7, participants received omadacycline 100 milligrams iv or omadacycline 300 milligrams po. All doses were administered once-per-day and iv doses were administered in 150 milliliters of normal saline. All oral doses were taken in a fasted state.

Serious adverse events	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/450 po or 100 iv	Omadacycline 200 iv/200 iv
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)	0 / 75 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Renal abscess			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Levofloxacin 750 iv/750 po or iv	Omadacycline 200 iv/300 po or 100 iv	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 74 (2.70%)	2 / 17 (11.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 74 (1.35%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal disorders</b>			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 74 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Renal abscess			
subjects affected / exposed	0 / 74 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 74 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Omadacycline 200 iv/100 iv	Omadacycline 200 iv/450 po or 100 iv	Omadacycline 200 iv/200 iv
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 18 (33.33%)	8 / 17 (47.06%)	21 / 75 (28.00%)
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 75 (1.33%)
occurrences (all)	1	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	3 / 75 (4.00%)
occurrences (all)	0	0	3
Dysgeusia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	8 / 75 (10.67%)
occurrences (all)	0	3	9
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	2 / 75 (2.67%)
occurrences (all)	0	0	2
Hyperthermia			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 75 (0.00%) 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	1 / 75 (1.33%)
occurrences (all)	1	1	1
Nausea			
subjects affected / exposed	0 / 18 (0.00%)	4 / 17 (23.53%)	3 / 75 (4.00%)
occurrences (all)	0	4	4
Vomiting			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	2 / 75 (2.67%)
occurrences (all)	0	0	2
Rash erythematous			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	3 / 75 (4.00%)
occurrences (all)	0	0	6
Urticaria			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	2 / 75 (2.67%)
occurrences (all)	0	0	3
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	2 / 18 (11.11%)	1 / 17 (5.88%)	3 / 75 (4.00%)
occurrences (all)	2	1	3
Oral herpes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0

Viral rhinitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Levofloxacin 750 iv/750 po or iv	Omadacycline 200 iv/300 po or 100 iv	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 74 (21.62%)	7 / 17 (41.18%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Body temperature increased			
subjects affected / exposed	1 / 74 (1.35%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 74 (1.35%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 74 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 74 (0.00%)</p> <p>0</p> <p>5 / 74 (6.76%)</p> <p>5</p>	<p>1 / 17 (5.88%)</p> <p>1</p> <p>2 / 17 (11.76%)</p> <p>2</p>	
<p>General disorders and administration site conditions</p> <p>Asthenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hyperthermia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 74 (1.35%)</p> <p>1</p> <p>0 / 74 (0.00%)</p> <p>0</p>	<p>0 / 17 (0.00%)</p> <p>0</p> <p>0 / 17 (0.00%)</p> <p>0</p>	
<p>Gastrointestinal disorders</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 74 (6.76%)</p> <p>5</p> <p>5 / 74 (6.76%)</p> <p>6</p> <p>1 / 74 (1.35%)</p> <p>1</p>	<p>0 / 17 (0.00%)</p> <p>0</p> <p>0 / 17 (0.00%)</p> <p>0</p> <p>0 / 17 (0.00%)</p> <p>0</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 74 (0.00%)</p> <p>0</p>	<p>2 / 17 (11.76%)</p> <p>2</p>	
<p>Skin and subcutaneous tissue disorders</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash erythematous</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 74 (0.00%)</p> <p>0</p> <p>0 / 74 (0.00%)</p> <p>0</p> <p>0 / 74 (0.00%)</p> <p>0</p>	<p>0 / 17 (0.00%)</p> <p>0</p> <p>0 / 17 (0.00%)</p> <p>0</p> <p>0 / 17 (0.00%)</p> <p>0</p>	

Infections and infestations Asymptomatic bacteriuria subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 1	2 / 17 (11.76%) 2	
Oral herpes subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0	1 / 17 (5.88%) 1	
Pharyngitis subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0	0 / 17 (0.00%) 0	
Viral rhinitis subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0	1 / 17 (5.88%) 1	
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0	1 / 17 (5.88%) 1	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In May 2019, the DMC modified the randomization algorithm based on their review of the data. After this change, participants were randomized in a 1:1 ratio to either the omadacycline 200 iv/200 iv or levofloxacin arms.
--

Notes: