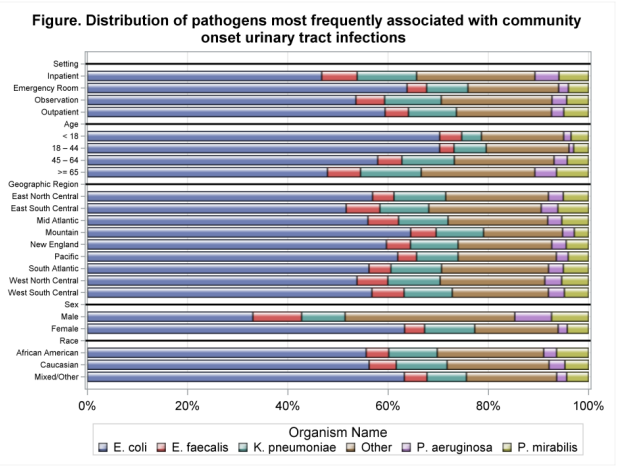
Figure. Distribution of pathogens most frequently associated with community onset urinary tract infections



Conclusion: Understanding patient factors associated with the microbiology of coUTIs is an important step in developing treatment recommendations and antibiotic stewardship efforts. Further analyses will include assessing the impact of major antibiotic resistance phenotypes, geographic and healthcare settings.

Disclosures. **All Authors**: No reported disclosures

1687. Omadacycline in Female Adults With Acute Pyelonephritis: Results from a Randomized, Double-Blind, Adaptive Phase 2 Study

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Session: P-73. UTIs

Background. Omadacycline (OMC) is a novel intravenous (IV) and oral aminomethylcycline, approved in the USA for community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections in adults. We present data from a randomized, adaptive dose–response phase 2 study of OMC in adult females with acute pyelonephritis (AP).

Methods. Females aged ≥ 18 y with acute uncomplicated pyelonephritis were initially randomized to 1 of 4 once-daily regimens of OMC vs once-daily standard regimen of IV-to-oral levofloxacin (LEV) (total therapy: 7–10 days) (NCT03757234); the randomization algorithm was subsequently adapted by the data monitoring committee (DMC; blinded to the investigators) following interim analyses of efficacy in the microbiological-intent-to-treat (micro-ITT) population (**Table 1).** Efficacy was assessed for noninferiority according to investigator's assessment of clinical response (IACR) and microbiological response at post-therapy evaluation (PTE; Day 21) and end of therapy (EOT). Treatment-emergent adverse events (TEAEs) were assessed. Results were reviewed by the DMC.

Table 1

Table 1. Study Design and Dosing Groups[a]

Group	Test Article	Study Day 1	Study Days 2–10	Interim Analysis
1	Omadacycline	200 mg IV	200 mg IV	
2	Omadacycline	200 mg IV	100 mg IV	STOPPED
3	Omadacycline	200 mg IV	300 mg PO or 100 mg IV	STOPPED
4	Omadacycline	200 mg IV	450 mg PO or 100 mg IV	STOPPED
5	Levofloxacin	750 mg IV	750 mg PO or IV	

IV, intravenous; LEV, levofloxacin; OMC, omadacycline, PO, oral.

[a] Initially, participants were randomized to 1 of 5 treatment groups. Interim analyses were conducted by the data monitoring committee (blinded to investigators) in the microbiological-intent-to-treat (micro-ITT) population (all randomized participants who had ≥1 uropathogen in baseline urine culture present at $\geq 10^5$ colony-forming units/mL, and ≤2 bacterial isolates at any colony count), at which point randomization into 3 of the 4 OMC treatment arms was stopped because of lower response rates.

Results. 201 patients were randomized. Baseline characteristics were similar across groups (**Table 2**). Among patients with an identified pathogen, the most common species was *E. coli*. For IACR at both EOT and PTE, no OMC group met noninferiority to LEV (**Figure 1**), as the lower limit of the 95% CI for the treatment difference exceeded −10% (range −12.4% to −34.8%). Responses at PTE were consistent with those at EOT. Microbiological responses in each OMC group were generally lower than LEV. OMC was well tolerated; 36.2% and 32.4% of OMC- and LEV-treated patients had ≥ 1 TEAE. The most frequently reported TEAEs (≥ 5%) in the OMC the LEV groups, respectively, were headache (10.2% vs 6.8%), asymptomatic bacteriuria (6.3% vs 1.4%), diarrhea (2.4% vs 6.8%), and nausea (5.5% vs 6.8%).

Table 2

Table 2. Demographic and Baseline Characteristics, ITT Population[a]

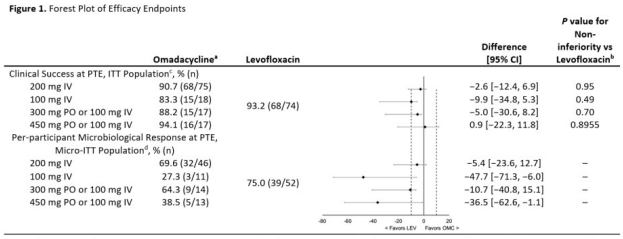
	Omadacycline[b]				
	200 mg IV n=75	100 mg IV n=18	300 mg PO or 100 mg IV n=17	450 mg PO or 100 mg IV n=17	LEV n=74
Age, years, mean (SD)	38.2 (15.0)	33.9 (14.5)	37.1 (16.0)	38.2 (17.7)	38.8 (14.7)
Race, % (n)					
White	98.7 (74)	100 (18)	100 (17)	100 (17)	100 (74)
Other	1.3 (1)	–	–	–	–
Weight, kg; mean (SD)	68.1 (15.2)	65.5 (15.5)	68.5 (14.9)	69.5 (21.2)	66.4 (13.7)
Body mass index, kg/m^2, mean (SD)	25.3 (5.7)	23.8 (6.2)	24.4 (6.0)	25.2 (7.1)	24.4 (6.0)
Renal function, n (%)[c]					
Normal renal function [>89 mL/min]	59 (78.7)	16 (88.9)	13 (76.5)	13 (76.5)	48 (64.9
Mild renal impairment [>60–89 mL/min]	12 (16.0)	1 (5.6)	3 (17.6)	4 (23.5)	20 (27.0)
Moderate renal impairment [30–60 mL/min]	4 (5.3)	1 (5.6)	1 (5.9)	0	6 (8.1)
Baseline pathogens, n (%) (micro-ITT population)[d]					
Escherichia coli	36 (78.3)	11 (100)	12 (85.7)	9 (69.2)	45 (86.5)
Klebsiella pneumoniae	6 (13.0)	0	0	0	3 (5.8)
Proteus mirabilis	1 (2.2)	0	1 (7.1)	1 (7.7)	1 (1.9)
Pseudomonas aeruginosa	0	0	0	1 (7.7)	2 (3.8)
Enterococcus faecalis	3 (6.5)	0	0	0	1 (1.9)

AP, acute pyelonephritis; ITT, intent-to-treat; IV, intravenous; LEV, levofloxacin; OMC, omadacycline; PO, oral; QD, once daily; SD, standard deviation; UTI, urinary tract infection.

[a] ITT population was all randomized participants.
[b] OMC treatment arms are described by dosing regimen for Days 2–10. All OMC treatment arms used 200 mg IV dosing on Day 1.
[c] Renal function is evaluated based on creatinine clearance at baseline, calculated from the Cockcroft–Gault equation for females and non-missing age, weight, and creatinine values.
[d] Micro-ITT: All randomized subjects who had a study-qualifying pre-treatment baseline urine culture.

Figure

Figure 1. Forest Plot of Efficacy Endpoints



CI, confidence interval; ITT, intent-to-treat; IV, intravenous; LEV, levofloxacin; OMC, omadacycline; PO, oral; PTE, post-therapy evaluation; QD, once daily.

[a] OMC treatment arms are described by dosing regimen for Days 2–10. All OMC treatment arms used 200 mg IV dosing on Day 1.
[b] Noninferiority margin was 10%. If the lower limit of the 95% CI for the difference exceeded −10%, then the null hypothesis was rejected and the noninferiority of OMC to LEV was declared for that dose. The posterior probability of noninferiority of the OMC treatment arm vs LEV was calculated.
[c] ITT population: All randomized participants.
[d] Micro-ITT population: All randomized participants who had ≥1 uropathogen in baseline urine culture present at $\geq 10^5$ colony-forming units/mL and ≤2 bacterial isolates at any colony count.

Conclusion: In this adaptive, phase 2 study, clinical success was high for both groups, although no OMC group met criteria for noninferiority to levofloxacin in AP, potentially due to pharmacokinetic/pharmacodynamic drivers of efficacy for AP. Omadacycline was well tolerated, with a safety profile consistent with its current labeling. Further evaluation is warranted to further understand the outcomes of this study.

Disclosures. J. Scott Overcash, MD, FACEP, Paratek Pharmaceuticals, Inc. (Scientific Research Study Investigator) Evan Tzanis, BS, Paratek Pharmaceuticals, Inc. (Employee, Shareholder) Amy Manley, BS, Paratek Pharmaceuticals, Inc. (Employee) Courtney Kirsch, BS, Paratek Pharmaceuticals, Inc. (Employee) Alisa W. Serio, PhD, Paratek Pharmaceuticals, Inc. (Employee, Shareholder) Tiffany White, PhD, ContraFact Corporation (Consultant, (ended Feb 2020)) Facile Therapeutics (Consultant)Paratek Pharmaceuticals, Inc. (Employee) Kelly Wright, PharmD, Paratek Pharmaceuticals, Inc. (Employee, Shareholder) Surya Chitra, PhD, Paratek Pharmaceuticals, Inc. (Consultant) Paul B. Eckburg, MD, AN2 Therapeutics (Consultant)Bugworks Research (Consultant)Curza (Advisor or Review Panel member)Paratek Pharmaceuticals, Inc. (Consultant)SNIPR Biome (Consultant)Spero Therapeutics (Consultant)

1688. Omadacycline in Female Adults With Cystitis: Results From a Randomized, Double-Blinded, Adaptive Phase 2 Study

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Session: P-73. UTIs

Background. In a previous phase 1b study, ≥ 90% of patients with cystitis treated with omadacycline (OMC), a novel intravenous (IV) and oral aminomethylcycline, achieved clinical success. We assessed the safety and efficacy of OMC vs nitrofurantoin (NIT) for treatment of cystitis in a randomized, adaptive phase 2 study.

Methods. Females ≥18 years with uncomplicated symptomatic cystitis were randomized to oral dose regimens of OMC or NIT for 7 days (NCT03425396; **Table 1**). Efficacy was assessed for noninferiority by investigator's assessment of clinical response (IACR) at post-treatment evaluation (PTE; primary endpoint; Day 14). Other endpoints included IACR, microbiologic response, and composite clinical and microbiologic response at end of treatment (EOT) and PTE. Treatment-emergent adverse events (TEAEs) were assessed. Results were reviewed by a data monitoring committee.