Incidence of Hospital Admission by Age, Charlson comorbidity index (CCI), Presence of Sepsis (S), and Presence of Sepsis Symptoms (SS)

Patients < 65 years

CCI		Number of Sepsis Symptoms (SS)				Sepsis (Diagnosis)
		0	1	2	3	
0	All patients (#)	44,858	1,787	274	62	7,192
	Inpatients (%)	14.0	81.4	97.8	98.4	99.8
1	All patients (#)	9,465	999	204	61	4,437
	Inpatients (%)	28.5	92.8	100.0	100.0	99.9
2	All patients (#)	4,822	1,369	291	59	4,255
	Inpatients (%)	52.2	97.9	100.0	100.0	100.0
3	All patients (#)	1,950	839	250	53	2,479
	Inpatients (%)	63.3	98.3	100.0	100.0	100.0
4	All patients (#)	936	685	207	61	1,567
	Inpatients (%)	67.7	100.0	100.0	100.0	99.9
≥5	All patients (#)	1,320	1,353	490	117	2,812
	Inpatients (%)	75.1	99.8	99.8	100.0	99.9

Patients ≥ 65 years

CCI		Number of Sepsis Symptoms (SS)				Sepsis (Diagnosis)
		0	1	2	3	
0	All patients (#)	11,781	1,485	338	53	3,951
	Inpatients (%)	26.2	94.7	99.1	100.0	99.7
1	All patients (#)	8,845	2,195	559	87	5,812
	Inpatients (%)	48.2	97.3	99.6	100.0	100.0
2	All patients (#)	6,265	2,761	800	163	6,099
	Inpatients (%)	60.5	98.8	99.8	100.0	99.9
3	All patients (#)	4,125	2,725	847	215	5,255
	Inpatients (%)	70.2	99.0	99.8	100.0	100.0
4	All patients (#)	2,656	2,316	838	201	4,008
	Inpatients (%)	75.5	99.2	99.9	100.0	99.9
≥5	All patients (#)	4,131	4,360	1,784	494	7,476
	Inpatients (%)	82.2	99.5	99.9	100.0	99.9

CCI; Charlson Comorbidity Index

Conclusion. Nearly 1 in 5 cUTI hospital admissions may be avoidable. Given the resources associated with the management of inpatients with cUTIs, these findings highlight the critical need for healthcare systems to develop well-defined criteria for hospital admission based on presence of comorbid conditions and infection severity. Preventing avoidable hospital admissions has the potential to save the healthcare system substantial costs.

1684. Hospital Costs and Reimbursement in Patients with Resistant Enterobacteriaceae (ENT) Urinary Tract Infection (UTI) in the United States (US): A Multicenter Analysis

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Session: P-73. UTIs

Background. Rates of fluoroquinolone resistance (FQ-R) and third-generation cephalosporin resistance/extended-spectrum beta-lactamases (ESBL+) are rising. These pathogens generally retain susceptibility to intravenous (IV) carbapenems; however, the loss of susceptibility to commonly used oral (PO) antibiotics limits the opportunity to transition these patients home, leading to increased length of stay (LOS) and higher costs. Here, we evaluate the hospital LOS, costs and reimbursement for UTI hospitalizations.

Methods. We analyzed the first positive enterobacteriaceae (ENT) urine culture ≤ 3 days from hospital admission in patients with a primary or secondary UTI ICD10 discharge diagnosis from 68 US hospitals admitted October 1, 2015-2017. Patient characteristics and outcomes were categorized by ESBL+ and FQ-R status. IV to PO was identified as PO therapy after 24 hours of IV. Outcomes were stratified by resistance and PO conversion status.

Results. 16,022 patients were eligible for analysis; 5,017 (31.3%) were FQ-R, 1,763 (11.0%) were ESBL+, and 1,433 (8.9%) were both FQ-R and ESBL+; 2,367 (14.8%) were converted to PO antibiotics during their hospitalization. Overall, mean LOS, costs, and reimbursement were 5.2 days, $9,303 and $8,501 (mean difference between cost and reimbursement: -$878). Mean LOS was shorter and mean difference between cost and reimbursement was lower overall for patients converted to PO therapy vs. those who did not (4.7 vs. 5.3 days, -$532 vs. -$938). Drug resistance was associated with higher LOS and a larger difference between cost and reimbursement; patients who were FQ-R and ESBL+ and did not convert to PO had a mean LOS of 6.0 days, costs of $11,482, and reimbursement of $9,243 (difference: -$2,446). Mean LOS, costs, and reimbursement for patients who were neither FQ-R nor ESBL+ and who did convert to PO therapy were 4.6 days, $7,904, and $7,496 (difference: -$527), respectively.

Conclusion. Reduced LOS and substantial cost savings could be recognized by efficiently converting patients receiving IV antimicrobials to PO and discharging them from the hospital. Lack of PO therapies with activity against resistant pathogens has made this challenging; new PO options may help reduce hospital costs and resources required to treat these UTI patients.

1685. Inappropriate Treatment of Asymptomatic Bacteriuria in Elderly Patients: A Quality Improvement Study

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Session: P-73. UTIs

Background: Asymptomatic bacteriuria is often misdiagnosed as Urinary Tract Infection (UTI) in elderly patients. Studies suggest that 15-30% of males and 25-50% of females have asymptomatic bacteriuria. We wanted to estimate the percentage of elderly patients who are treated for UTI at our facility and if treatment was appropriate. The goal was to provide the staff with an educational opportunity and help decide if more antibiotic restriction policies would be beneficial.

Methods. A retrospective study of patients > 65 years of age who were started on antibiotics for presumed UTI at a single medical center between 7/2018 and 12/2018. Reviewed data included demographics, admitting diagnosis, presence or absence of symptoms of UTI and urine culture results. The data was presented at educational conferences and at antimicrobial stewardship meetings in our facility.

Results: 234 patients were started on antibiotics on the basis of pyuria on admission. Of these, only 47% (n=110/234) had symptoms suggestive of UTI. Positive urine cultures were more common in symptomatic patients (n=93/110) compared with asymptomatic patients (n=47/80).

In addition, ninety patients had a change in mental status on presentation and were started on antibiotics for suspected UTI. Approximately one third of these patients had eventual negative urine cultures.

Conclusion: Elderly patients with pyuria and asymptomatic bacteriuria represent a diagnostic challenge due to their inability to vocalize signs or symptoms of UTI. In addition, a percentage of patients who are asymptomatic and admitted for another reason were often started on antibiotics inappropriately on the basis of pyuria alone. Studies have shown that treating asymptomatic bacteriuria does not add a mortality benefit or lower risk of infection. The CDC emphasizes the importance of assessing for clinical symptoms of UTI before treatment is considered.

Our study highlights the importance of provider education in the management of asymptomatic bacteriuria in elderly patients. We also feel that antibiotic restriction policies may limit use of antibiotics for asymptomatic bacteriuria. This would in turn improve patient outcomes and decrease incidence of clostridium difficile associated colitis.

1686. Microbiology of Community-Onset Urinary Tract Infections in the United States, 2012-2017

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Session: P-73. UTIs

Background. Community-onset urinary tract infections (coUTIs) are one of the most common indications for antibiotic prescribing. It is important to understand patient demographic factors associated with microorganisms causing coUTI and their antibiotic resistance profiles, to tailor antibiotic prescribing practices. We analyzed microbiology data to understand factors associated with coUTI in the United States (US).

Methods. CoUTIs were identified in the Premier Healthcare Database and Cerner Health Facts among patients treated at participating healthcare facilities in the US between 2012-2017. Cases were defined by urine cultures yielding a bacterial organism and were collected in outpatient settings or within three days of hospitalization. Only the first specimen for each encounter was included in the analysis. Data on the organisms isolated, patient's age, sex, and US census regions of the submitting facilities were described and compared using chi-square tests for associations. Encounters were classified as inpatient (INPT), observation (OBS), emergency department (ED), and outpatient (OTPT) based on the setting in which the culture was submitted.

Results. Using data from 637 acute care hospitals, urine samples from 3,291,561 encounters were included, with 776,653 (25.7%) INPT, 1,063,219 (34.8%) ED, 107,760 (3.5%) OBS, and 1,092,658 (35.8%) OTPT. The pathogens most frequently associated with coUTIs were *Escherichia coli* (57.3%), *Klebsiella pneumoniae* (9.7%), *Enterococcus faecalis* (5.1%), *Proteus mirabilis* (4.9%), and *Pseudomonas aeruginosa* (2.9%). Female sex, age < 65y and OTPT and ED settings were associated with higher relative frequency of *E. coli* (all p < 0.0001). Male sex, INPT setting and age >65 y were associated with higher relative frequency of *P. aeruginosa*, *P. mirabilis* and *E. faecalis* (all p < 0.0001, Figure). *K. pneumoniae* was found at higher relative frequency in those >45y, and in INPT and OBS settings (all p < 0.0001).

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

Figure. Distribution of pathogens most frequently associated with community onset urinary tract infections
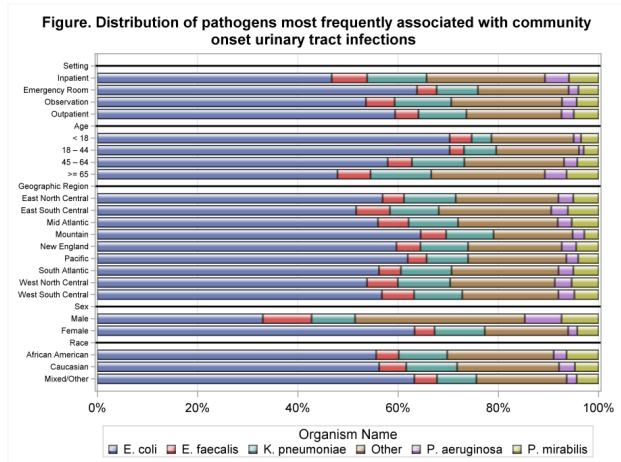
Conclusion: Understanding patient factors associated with the microbiology of coUTIs is an important step in developing treatment recommendations and antibiotic stewardship efforts. Further analyses will include assessing the impact of major antibiotic resistance phenotypes, geographic and healthcare 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 ≥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]				LEV n=74
	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	
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/m², 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.

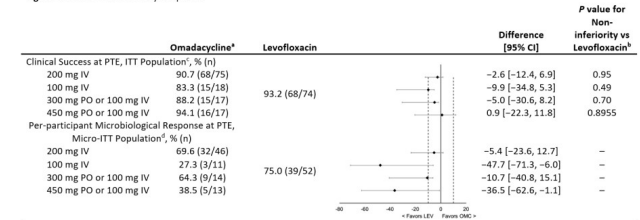[a] ITT population was all randomized participants.
[b] OMC treatment arms are described by dosing regimen for Days 2–10. All OMC treatment arms used 200 mg IV dosing on Day 1.
[c] Renal function is evaluated based on creatinine clearance at baseline, calculated from the Cockcroft–Gault equation for 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

	Omadacycline[a]	Levofloxacin		Difference [95% CI]	P value for Non-inferiority vs Levofloxacin[b]
Clinical Success at PTE, ITT Population[c], % (n)					
200 mg IV	90.7 (68/75)			−2.6 [−12.4, 6.9]	0.95
100 mg IV	83.3 (15/18)	93.2 (68/74)		−9.9 [−34.8, 5.3]	0.49
300 mg PO or 100 mg IV	88.2 (15/17)			−5.0 [−30.6, 8.2]	0.70
450 mg PO or 100 mg IV	94.1 (16/17)			0.9 [−22.3, 11.8]	0.8955
Per-participant Microbiological Response at PTE, Micro-ITT Population[d], % (n)					
200 mg IV	69.6 (32/46)			−5.4 [−23.6, 12.7]	–
100 mg IV	27.3 (3/11)	75.0 (39/52)		−47.7 [−71.3, −6.0]	–
300 mg PO or 100 mg IV	64.3 (9/14)			−10.7 [−40.8, 15.1]	–
450 mg PO or 100 mg IV	38.5 (5/13)			−36.5 [−62.6, −1.1]	–

CI, confidence interval; ITT, intent-to-treat; IV, intravenous; LEV, levofloxacin; OMC, omadacycline; 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 ≥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.