

Comparative Activity of Omadacycline Against Extended-spectrum Beta-lactamase Positive and Negative *Escherichia coli* and *Klebsiella pneumoniae* Strains Recovered from Urine Specimens

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Background

- Omadacycline is a novel tetracycline derivative with activity against Enterobacterales resistant to traditional tetracycline antibiotics
- Oral and intravenous (IV) omadacycline is FDA approved for treatment of community acquired pneumonia and skin and skin structure infections
- Oral omadacycline has been investigated as treatment for cystitis¹
- IV and oral omadacycline has been investigated as treatment for acute pyelonephritis²

Objective

Evaluate omadacycline in vitro activity against extended-spectrum beta-lactamase (ESBL) positive and negative Enterobacterales strains recovered from urine specimens

Methods

- Urine samples from patients with suspected urinary tract infections were quantitatively plated onto blood agar and MacConkey agar plates in the microbiology laboratory at Wake Forest Baptist Medical Center
- Following overnight incubation, colonies were identified to the species level by matrix-assisted laser desorption/ionization – time of flight (MALDI-TOF) system
- Minimum inhibitory concentrations (MIC) were performed in triplicate for isolates of *Escherichia coli* and *Klebsiella pneumoniae*
- Omadacycline and tetracycline susceptibility testing was performed by disk diffusion and gradient strip methodologies according to the manufacturer's instructions
- Results were interpreted in accordance with the Food and Drug Administration breakpoints for *Klebsiella pneumoniae*
- ESBL screening and susceptibility testing to oral antibiotics commonly prescribed for UTI were performed by the Microscan WalkAway system
- Susceptibility rates and MIC_{50/90} were calculated and subsets of isolates were analyzed using descriptive statistics

DISCLOSURE: Members of the investigational team received support for this investigator initiated study from Paratek Pharmaceuticals

Results

Table 1. Omadacycline Minimum Inhibitory Concentrations (MICs, µg/mL)

	MIC ₅₀	MIC ₉₀	Min MIC	Max MIC	Modal MIC
All <i>E. coli</i> and <i>K. pneumoniae</i> (n=204)	4	16	0.25	> 32	4
<i>E. coli</i> (n=102)	3	6	0.25	> 32	4
ESBL positive (n=51)	4	12	0.25	> 32	4
ESBL negative (n=51)	2	4	1	8	3
<i>K. pneumoniae</i> (n=102)	4	> 32	1.5	> 32	4
ESBL positive (n=51)	8	> 32	1.5	> 32	4
ESBL negative (n=51)	4	8	1.5	> 32	4
All ESBLs (n=102)	4	> 32	0.25	> 32	4
All non-ESBLs (n=102)	3	4	1	> 32	4

Table 2. Comparison of Susceptibility Results of Oral Antibiotics Used to Treat UTI (% Susceptible)

	Omadacycline	Tetracycline	Amoxicillin/ Clavulanate	Ciprofloxacin	Nitrofurantoin	Trimethoprim/ Sulfamethoxazole
<i>E. coli</i> (n=93)	87.3	47.3	73.1	45.2	92.5	49.5
ESBL positive (n=49)	74.5	26.5	63.3	10.2	91.8	26.5
ESBL negative (n=44)	100	70.5	84.1	84.1	93.2	75.0
<i>K. pneumoniae</i> (n=88)	61.8	58.0	65.9	55.7	55.7	45.5
ESBL positive (n=43)	41.2	25.6	37.2	18.6	51.2	11.6
ESBL negative (n=45)	82.3	88.9	93.3	91.1	60.0	77.8

Results (cont.)

- A total of 204 isolates, including 102 *E. coli* and 102 *K. pneumoniae* were tested
- All isolates except 1 (99.5%) exhibited categorical agreement in results generated by the strip (**Table 1**) and disk (data not shown) methods and this was considered a minor error involving an intermediate result
- Among oral options omadacycline exhibited the second highest susceptibility rate (nitrofurantoin) against ESBL positive *E. coli* and *K. pneumoniae*
- Omadacycline displayed increased susceptibility rates compared to tetracycline regardless of isolate ESBL positivity (**Table 2**)

Conclusions

- Omadacycline exhibits promising in vitro antimicrobial activity against tetracycline resistant and ESBL-positive *E. coli* and *K. pneumoniae*
- Omadacycline displays increased susceptibility rates against ESBL-positive *E. coli* when compared to ESBL-positive *K. pneumoniae*
- These data support the development of omadacycline as a much needed option in the treatment of UTI caused by ESBL-producing *E. coli* and *K. pneumoniae*

References

1. ClinicalTrials.gov Identifier NCT03425396
2. ClinicalTrials.gov Identifier NCT03757234