In Vitro Activity of Omadacycline against *Chlamydia trachomatis* Serovars

Robert J. Suchland[1], Diane M. Anastasiou[2], Alisa W. Serio[2]

[1] University of Washington, Seattle, Washington; [2] Paratek Pharmaceuticals Inc., King of Prussia, Pennsylvania

Background

Chlamydial infections are a sexually transmitted disease that most commonly affects women ≤ 24 years. Disease is most often due to *C. trachomatis.*[1]

Omadacycline is a semisynthetic tetracycline-class antibiotic that overcomes common tetracycline resistance mechanisms with *in vitro* activity including gram-postive and gram-negative aerobic pathogens and atypical pathogens.

Omadacycline is FDA approved for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and community acquired bacterial pneumonia (CABP) due to select pathogens.[2]

Methods

Omadacycline, tetracycline, and doxycycline minimal inhibitory concentrations (MIC) and minimal chlamydicidal concentrations (MCC) were determined against three sets of *C. trachomatis* strains consisting of 14 ATCC reference strains, 22 clinical isolates from the University of Washington archived collection[3], and 4 laboratory derived *tet*(C)[4] containing *C. trachomatis* strains. MIC and MCC determinations for omadacycline, tetracycline and doxycycline were performed on fresh McCoy cell monolayers with a dilution range of 125 µg/mL to 0.004 µg/mL.[5]

- MIC_{TP}: MIC Transition Point was defined as the drug concentration where ≥ 90% of visible inclusions are of abnormal size and morphology.
- MIC: The drug concentration 1-dilution higher than the MIC_{TP}.
- MCC_{TP}: MCC Transition Point was defined as the lowest concentration of drug where ≥ 90% or more of inclusions were altered in size and morphology after one tissue culture passage.
- MCC: The drug concentration 1-dilution above the MCC_{TP}

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Omadacycline demonstrated potent *in vitro* bactericidal activity against 40 *C. trachomatis*

Objectives

To access omadacycline in vitro activity against a diverse set of *C. trachomatis* strains from both ocular and genital infections including various serovars (A-K; L1-L3) and strains that exhibit tetracycline class resistance.

Conclusions

Omadacycline demonstrated potent *in vitro* bactericidal activity against all ATCC and clinical *C. trachomatis* strains.

- MICs and MCCs for omadacycline were unchanged for 4 strains with lab derived tetracycline resistance via tet(C).

Additional research is warranted to assess omadacycline as a potential treatment option for Chlamydial infections.

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Results

Omadacycline demonstrated potent activity against all 40 *C. trachomatis* strains with an MIC range of 0.016 - 0.03 µg/mL and an MCC range of 0.03 - 0.06 µg/mL, regardless of the presence of *tet*(C) (Table 1).

- Against 36 ATCC and clinical strains, the tetracycline MIC range was 0.06 - 0.12 µg/mL and the MCC range was 0.12 - 0.25 µg/mL. The tetracycline MIC and MCC values were each 8 and 16 µg/mL, respectively, for all 4 *tet*(C) strains (Table 1).
- Against 9 ATCC and clinical strains, the doxycycline MIC range was 0.03 – 0.06 µg/mL and the MCC range was 0.06 - 0.12 µg/mL. The doxycycline MIC and MCC values were 1 and 2 µg/mL, respectively against one *tet*(C) strain (Table 1).

Table 1: MICs and MCCs (µg/mL) for Omadacycline and Comparators against *C. trachomatis* Strains

	Omadacycline		Tetracycline		Doxycycline*	
Strain Set (N)	**MIC**	**MCC**	**MIC**	**MCC**	**MIC**	**MCC**
ATCC reference (14)	0.016 – 0.03	0.03 – 0.06	0.06 – 0.12	0.12 – 0.25	0.03 – 0.06	0.06 – 0.12
Clinical (22)	0.016 – 0.03	0.03 – 0.06	0.06 – 0.12	0.12 – 0.25	0.03 – 0.06	0.06 – 0.12
tet(C) (4)	0.016 – 0.03	0.03 – 0.06	8	16	1	2

* Number of strains tested against doxycycline: 2 ATCC reference, 7 clinical and 1 *tet*(C)

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Contact Information: medinfo@paratekpharma.com