In Vitro Activity of omadacycline against *Chlamydia pneumoniae*

S. Kohlhoff[#] , N.A. Huerta, M.R. Hammerschlag

Department of Pediatrics, Division of Infectious Diseases, SUNY Downstate Medical Center, Brooklyn , NY

Corresponding author: Stephan A. Kohlhoff, MD
Tel: 718-270-2271 Email: stephan.kohlhoff@downstate.edu

Poster # SATURDAY-626

Abstract:

Background: Omadacycline (PTK 0796) is a new aminomethylcycline with potent *in vitro* antibacterial activity against a broad range of bacteria causing respiratory infections, including *Chlamydia spp.*. *C. pneumoniae* is a frequent cause of community-acquired respiratory infections, including pneumonia and bronchitis, in adults.

Method: 15 respiratory isolates of *C. pneumoniae* were tested against omadacycline, azithromycin, doxycycline, moxifloxacin and levofloxacin. Susceptibility testing of *C. pneumoniae* was performed in cell culture using HEp-2 cells grown in supplemented DMEM media followed by infection with 10^3 – 10^4 IFU/ml and included both MIC and MBC determinations.

Background: The activities of omadacycline and comparator antibacterials against 15 isolates of *C. pneumoniae* are shown in the table below.

Drug	MIC range (µg/ml)	MIC50 (µg/ml)	MIC90 (µg/ml)	MBC range (µg/ml)	MBC90 (µg/ml)
Omadacycline	0.03-0.5	0.06	0.25	0.06-0.5	0.5
Azithromycin	0.03-0.06	0.06	0.06	0.06-0.25	0.25
Levofloxacin	0.25-0.5	0.5	0.5	0.25-2	2
Moxifloxacin	0.25-1	0.5	1	0.5-1	1
Doxycycline	0.06-0.25	0.125	0.125	0.25-0.5	0.5

Conclusions: Omadacycline had potent in vitro activity against *C. pneumoniae*. The high in vitro activity supports further clinical investigations with omadacycline against *C. pneumoniae* especially community-acquired bacterial pneumonia including infections due to *C. pneumoniae.*

Introduction

- Omadacycline (PTK 0796) is a new aminomethylcycline with potent *in vitro* antibacterial activity against a broad range of bacteria causing respiratory infections
- We compared the in vitro activity of omadacycline, azithromycin, levofloxacin, moxifloxacin and doxycycline against clinical and laboratory isolates of *C. pneumoniae.*

Methods

- *C. pneumoniae* isolates tested were: 2 isolates from ATCC® (Manassas, VA): TW-183 (VR-2282), CM-1 (VR-1360), and 13 human isolates from patients with community-acquired pneumonia (CAP) including BAL specimens from the United States.
- Susceptibility testing was done in tissue culture as previously described[1].
- HEp-2 cells were grown in 96-well microtiter plates and infected with 10^4 IFU/ml of the chlamydia isolate.
- After 72 hrs incubation cultures were fixed and stained with a fluorescein-conjugated anti-chlamydia LPS antibody and examined for the presence of inclusions.
- The MIC was lowest antibiotic concentration without visible inclusions
- MBC was determined by removing antibiotic-containing medium and adding antibiotic-free medium; infected cells were frozen at -70°C, thawed, passed onto new cells, incubated for 72h, and then fixed and stained as described above; the MBC was the lowest antibiotic concentration that resulted in no inclusions after passage.

Results

- The MICs and MBCs of Omadacycline and comparators for 15 isolates of *C. pneumoniae* are shown in Table 1 and 2, respectively below.

Table 1

MIC (µg/ml)			
Drug	Range	50%	90%
Omadacycline	0.03-0.5	0.06	0.25
Azithromycin	0.03-0.06	0.06	0.06
Levofloxacin	0.25-0.5	0.5	0.5
Moxifloxacin	0.25-1.0	0.5	1.0
Doxycycline	0.06-0.25	0.125	0.125

Table 2

MBC (µg/ml)		
Drug	Range	90%
Omadacycline	0.06-0.5	0.5
Azithromycin	0.06-0.25	0.25
Levofloxacin	0.25-2	2
Moxifloxacin	0.5-1.0	1.0
Doxycycline	0.25-0.5	0.5

Discussion

- The *in vitro* activity of omadacycline is comparable to that of several antibiotics with proven clinical efficacy.
- Omadacycline achieves high, sustained concentrations in plasma, epithelial lining fluid and alveolar cells suggesting that it will be effective in the treatment of pulmonary infections, including those due to intracellular organisms, including *C. pneumoniae* [2]
- Omadacycline has received qualified infectious disease product status from the US Food and Drug Administration for the treatment of CAP
- In a phase 3 study omadacycline was non-inferior to moxifloxacin in the treatment of community-acquired bacterial pneumonia [3]
- The role of omadacycline in the treatment of *C. pneumoniae* infections will depend on the results of clinical studies that assess microbiologic efficacy [4]

References

1. Kohlhoff SA, Huband MD, Hammerschlag MR. In vitro activity of AZD0914, a novel DNA gyrase inhibitor, against *Chlamydia trachomatis* and *Chlamydia pneumoniae.* Antimicrob Agents Chemother 2014; 58:7595-7596.
2. Gotfried MH, Horn K, Garrity-Ryan L, et al. Comparison of omadacycline and tygecycline pharmacokinetics in the plasma, epithelial lining fluid and alveolar cells of healthy adults. Antimicrob Agents Chemother 2018; 61:e01135-17.
3. R. Stets, M. Popescu, J. Gonong, et al (2017) A Phase 3, Randomized, Double-Blind, Multi-Center Study to Compare the Safety and Efficacy of IV to Oral Omadacycline to Moxifloxacin for the Treatment of Adult Patients With CABP (The OPTIC Study). Poster 1883. IDWeek 2017, San Diego, CA.]
4. Kohlhoff SA, Hammerschlag MR. Treatment of chlamydial infections: 2014 update. Expert Opin Pharmacother 2014;16:2015-21.

Acknowledgments

This study was supported in part by a grant from Paratek Pharmaceuticals, Inc.