Poster 122

In Vitro Activity of Omadacycline Against *Borrelia* spp. and *Bartonella henselae*

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Background

- Vector-borne pathogens present a serious challenge to public health in the US:
  - The spirochete *Borrelia burgdorferi* is the causative agent of Lyme disease, the most common vector-borne disease in the US[1]
  - *Bartonella henselae* is a gram-negative bacterium that causes cat-scratch disease (CSD), the most common form of bartonellosis, and can cause co-infections with *Borrelia* spp[2]
- Lyme disease and CSD are often under- or mis-diagnosed, and insufficient treatment of these diseases can lead to chronic illnesses[3,4]
- Doxycycline is the most commonly prescribed antibiotic for Lyme disease, yet 10-30% of patients experience treatment failure[5]
- Doxycycline is often used for CSD, but there is no standard treatment course and treatment may require combination therapy[6-7]
- Omadacycline is a semisynthetic tetracycline-class antibiotic available as once-daily PO and IV formulations, FDA-approved for adults with community-acquired bacterial pneumonia and acute bacterial skin and skin structure infection caused by susceptible microorganisms[8]

Methods

***Borrelia* spp.**

- *Borrelia burgdorferi sensu lato* strains included genetically distinct, low passage isolates of B31 (reference strain isolated from *Ixodes scapularis* ticks in New York), N40 (clinical isolate), JD1 (clinical isolate), as well as *B. garinii* IP90 (European isolate associated with neuroborreliosis)
- Following incubation for 5 days with omadacycline or doxycycline, growth was assessed by counting motile spirochetes under dark-field microscopy to determine the MIC
  - MIC = the concentration at which there was no increase in spirochete count over initial inocula
- The concentration of motile spirochetes was also counted to score viability
- To determine the MBC, B31 and N40 strains were treated for 5 days with antibiotics, followed by incubation for 5 days in antibiotic-free media
  - MBC = the lowest antibiotic concentration at which no motile spirochetes were detected after a recovery period

Bartonella henselae

- *Bartonella henselae* San Antonio 2, 267HO04 (human isolate) was tested
- Following incubation for 96 hours with omadacycline or doxycycline, the MIC was determined by optical density readings (at 600 nm) on a 96-well plate
- To determine the MBC, *B. henselae* was treated with either omadacycline or doxycycline for 96 hours followed by antibiotic-free incubation for ~14 days
- Intracellular growth was measured by infecting DH82 cells, treating with antibiotics, and then plating lysed cells on agar plates, incubating for ~10 days, and assessing viable bacteria via live/dead staining

Objective

To evaluate the in vitro activity of omadacycline against *Borrelia* spp. and *B. henselae* compared with doxycycline

Conclusions

- Omadacycline was active in vitro against all strains tested
  - Omadacycline MICs were similar to or more potent than doxycycline against *Borrelia* spp.
  - Omadacycline MICs were still low but slightly higher than doxycycline against *B. henselae,* and neither drug was sufficient to prevent intracellular growth
  - Due to the limitations of this study, further investigation is warranted

Future Directions

- Additional studies evaluating omadacycline activity against *Borrelia* spp. are warranted, including in combination with other antibiotics and in animal models
- In vitro studies with combination drug testing for *B. henselae* are warranted

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Results

- Omadacycline was 2- to 10-fold more potent than doxycycline against *Borrelia* spp. in vitro (MIC ranges 0.05 to 0.1, and 0.1 to 0.5 µg/mL, respectively; **Table 1**)
- Omadacycline demonstrated a greater reduction in *Borrelia* spp. viability vs doxycycline for each isolate
- The MBC of omadacycline was identical to that of doxycycline against the B31 strain (10 µg/mL) and was 25 µg/mL against the N40 strain

Table 1: In Vitro Activity of Omadacycline Against *Borrelia* spp.

	Omadacycline (µg/mL)				Doxycycline (µg/mL)		
Strain	MIC Average	MIC Range	MBC	Viability	MIC Average	MBC	Viability
B. burgdorferi							
B31	0.05***	0.05 - 0.1	10	1	0.5*	10	2.5
N40	0.1**	0.1 - 0.25	25	1	0.5*	ND	5
JD1	0.05*	ND	ND	0.25	0.1*	ND	0.5
B. garinii							
IP90	0.05*	ND	ND	0.1	0.1*	ND	1

1 replicate plate, **2 replicate plates, *** 3 replicate plates
ND, not determined

- Against planktonic cells, MIC values for omadacycline and doxycycline were similar against *B. henselae* (MIC ranges 0.05 to 0.1, 0.01 to 0.05 µg/mL, respectively; **Table 2**)
- MBCs of omadacycline and doxycycline were also similar to each other
- Neither drug was effective at inhibiting intracellular growth in DH82 cells, supporting previously described data for doxycycline[9]

Table 2: In Vitro Activity of Omadacycline Against *B. henselae*

			Intracellular Growth CFU at 50 µg/mL antibiotic	
Antibiotic	MIC Planktonic (µg/mL)	MBC Planktonic (µg/mL)	Replicate 1	Replicate 2
Omadacycline	0.05 - 0.1	25 to 50	36	250
Doxycycline	0.01 - 0.05	25 to 50	13	100

MIC values presented are a range of values over 2 biological / 3 technical replicates.

References

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Abbreviations

ATCC, American Type Culture Collection; CSD, cat-scratch disease; CFU, colony forming unit; IV, intravenous; MBC, minimum bactericidal concentration; MIC, minimum inhibitory concentration; ND, not determined; PO, oral; spp, species

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