Omadacycline *in Vitro* Activity Against *Bacillus anthracis*

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Background

Bacillus anthracis causes cutaneous, respiratory, and intestinal anthrax. It is among the agents most likely to be used in a biologic attack[1] and is in the category of agents of greatest risk to public health and security[2]

B. anthracis can be engineered to be resistant to tetracycline and other antibiotics[3]

Omadacycline is a semisynthetic tetracycline-class antibiotic that overcomes common tetracycline resistance mechanisms[4]

Omadacycline has previously been shown to have potent *in vitro* activity against 30 strains of *B. anthracis* and to be efficacious in a preclinical post-exposure prophylaxis and a delayed treatment mouse model of inhalational anthrax[5]

Methods

Two collections of *B. anthracis* strains (100 unique strains) were examined in separate studies

- University of Florida (UF): 53 strains
- MRIGlobal: 50 strains
- Overlap of three strains (Ames, Sterne, Vollum)

The strains represented human and animal isolates from North America, Africa, Europe, Asia, and Australia

At both sites, antibiotic susceptibility testing followed Clinical Laboratory Standard Institute methods[6]

Minimum inhibitory concentrations (MICs) for omadacycline and comparators (doxycycline, ciprofloxacin, levofloxacin, moxifloxacin) were determined by broth microdilution

Results

In the MRIGlobal study, omadacycline demonstrated an MIC_{50} value of 0.06 mg/L and an MIC_{90} value of 0.06 mg/L (**Table 1**)

In the UF study, omadacycline demonstrated an MIC_{50} value of 0.015 mg/L and an MIC_{90} value of 0.03 mg/L against *B. anthracis* (**Table 1**)

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Omadacycline demonstrated potent and reproducible *in vitro* activity against 100 *B. anthracis* strains

Objectives

To evaluate the *in vitro* activity of omadacycline against a larger set of *B. anthracis* strains than previously examined

To test the reproducibility of susceptibility testing results across laboratories

Conclusions

Omadacycline showed similar *in vitro* activity against two collections of *B. anthracis* strains from two independent study sites

Omadacycline MICs were reproducible among three strains tested at the two independent sites

Based on the *in vitro* activity in both studies, omadacycline warrants further investigation as a potential treatment or prophylactic option in the event of a biothreat attack involving *B. anthracis*

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Results (continued)

All comparator MIC values were within ranges previously observed against these strains, and were similar to or higher than those of omadacycline

Against a ciprofloxacin-resistant strain (CIP MIC = 2 mg/L), omadacycline had an MIC value of 0.015 mg/L; against a doxycycline-resistant strain (DOX MIC = 4 mg/L), omadacycline had an MIC value of 0.06 mg/L

Table 1. MICs for Omadacycline and Comparators Against *B. anthracis* Strains

MIC, mg/L	OMC	DOX	CIP	LVX	MXF
MRIGlobal (n=50)					
MIC_{50}	0.06	0.015	0.06	0.125	0.06
MIC_{90}	0.06	0.03	0.125	0.125	0.125
Range	0.015–0.125	0.008–4	0.015–0.25	0.015–0.25	0.03–0.25
University of Florida (n=53)					
MIC_{50}	0.015	0.03	0.12	0.25	0.25
MIC_{90}	0.03	0.06	0.25	0.5	0.5
Range	≤0.008–0.25	≤0.008–0.25	0.015–2	0.06–2	0.06–2

CIP, ciprofloxacin; DOX, doxycycline; LVX, levofloxacin; MIC, minimal inhibitory concentration; MXF, moxifloxacin; OMA, omadacycline

Reproducibility (within one to two dilutions) was observed between the two laboratories for omadacycline *in vitro* activity against the three *B. anthracis* strains tested at both sites (**Table 2**)

Table 2. Reproducibility of Omadacycline *in Vitro* Activity Against *B. anthracis*

	B. anthracis strain		
MIC, mg/L	**Ames**	**Sterne**	**Vollum**
University of Florida	≤0.015	≤0.008	0.015
MRIGlobal	0.06	0.03	0.03

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