2020 Military Health System Research Symposium (MHSRS)

Activity of Omadacycline and Comparator Agents against Bacterial Isolates from Skin, Respiratory, and Wound Infections from United States and European Medical Centers (2014-2019)

Michael D. Huband, Michael A. Pfaller, Jennifer M. Streit, Helio S. Sader, M. Castanheira

JMI Laboratories, North Liberty, Iowa, USA

Background: Omadacycline is a novel aminomethylcycline antibacterial approved by the United States Food and Drug Administration (FDA) in 2018 for the treatment of acute bacterial skin and skin structure infection (ABSSSI) and community-acquired bacterial pneumonia (CABP) caused by indicated organism groups. Omadacycline has *in vitro* activity against most ESKAPE pathogens (except *Pseudomonas aeruginosa*) including *Enterococcus faecium, Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Enterobacter* spp. and bacterial isolates expressing common tetracycline, penicillin, fluoroquinolone, carbapenem, macrolide, and vancomycin resistance mechanisms.
Methods: Bacterial isolates were collected between 2014 and 2019 in medical centers located in the United States and Europe. These isolates included staphylococci (n=16,204), streptococci (n=8,769), enterococci (n=3,753), *Haemophilus spp*. (n=2,285), *Moraxella* spp. (n=1,155), *Enterobacterales* (n=23,069), and non-fermenters (n=7,064). One isolate per patient per infection episode was tested. Identifications were confirmed by standard microbiology methods and MALDI-TOF MS. Broth microdilution susceptibility testing was performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines M07 (2018) and M100 (2020).
Results: Omadacycline ($MIC_{50/90}$, 0.12/0.25 mg/L) was highly active against *S. aureus* isolates from skin and skin structure infection (SSSI; 99.0% susceptible [S]), respiratory tract infection (RTI; 95.2%S), and wound (98.9%S) infections (Table). Similarly, omadacycline demonstrated potent *in vitro* activity against streptococci including macrolide-R *S. pyogenes* isolates from SSSI and wound infections ($MIC_{50/90}$, 0.06/0.12 mg/L; 93.8%-98.5%S) and penicillin-resistant *S. pneumoniae* isolates from RTI ($MIC_{50/90}$, 0.06/0.12 mg/L; 98.5%S). Corresponding tetracycline susceptibilities against macrolide-R *S. pyogenes* from SSSI and pen-R *S. pneumoniae* isolates from RTI were 42.3%/42.3% (CLSI/EUCAST) and 41.9%/41.9%S (CLSI/EUCAST), respectively. Vancomycin-S and -resistant isolates of *E. faecalis* from SSSI and wound infection were susceptible to omadacycline (94.4%-97.7%S) and 97.1% of *E. faecium* isolates were inhibited by ≤0.25 mg/L of omadacycline. Tetracycline and levofloxacin susceptibilities against *E. faecalis* isolates from SSSI were 23.9%S (CLSI) and 75.9%S (CLSI), respectively, and 36.5%S (CLSI) and 10.5%S (CLSI), respectively against *E. faecium*. Against *E. cloacae* and *K. pneumoniae* isolates from SSSI and wound infection, 94.3%-94.9% and 89.1%-89.3% of isolates were susceptible to omadacycline, respectively. Similarly, 86.2% of *K. pneumoniae* isolates from RTI were susceptible to omadacycline. 99.7% of *H. influenzae* isolates from RTI were susceptible to omadacycline. 77.7% of *A. baumannii* isolates were inhibited by ≤4 mg/L of omadacycline where comparator agent susceptibilities were low and treatment options limited.
Conclusions Omadacycline demonstrated potent *in vitro* activity against gram-positive and gram-negative bacterial isolates (including drug-resistant and ESKAPE pathogens [except *P. aeruginosa*])—including *S. aureus*, *S. pyogenes*, *S. pneumoniae*, *E. faecalis* and *E. faecium*, *H. influenzae*, *Enterobacteriaceae*, and *Acinetobacter baumannii* — commonly associated with ABSSSI, CABP, and wound infections where treatment options may be limited.

		Omadacycline		Tetracycline		Levofloxacin	
Organism (no. tested)	**Infection Type[a]**	**$MIC_{50/90}$**	**%S FDA**	**$MIC_{50/90}$**	**%S CLSI/EUCAST**	**$MIC_{50/90}$**	**%S CLSI/EUCAST**
Staphylococcus aureus (6,624)	SSSI	0.12 / 0.25	99.0	≤0.5 / ≤0.5	94.1 / 92.7	0.25 / >4	72.3 / 72.3
MRSA (2,412)	SSSI	0.12 / 0.25	97.5	≤0.5 / 2	91.2 / 89.6	4 / >4	35.7 / 35.7
S. aureus (4,043)	Wound	0.12 / 0.25	98.9	≤0.5 / ≤0.5	93.7 / 92.3	0.25 / >4	73.8 / --[a]
S. aureus (3,271)	RTI	0.12 / 0.25	95.2[b]	≤0.5 / ≤0.5	94.9 / 93.1	0.25 / >4	65.6 / --[a]
MRSA (1,283)	RTI	0.12 / 0.25	90.4[b]	≤0.5 / 2	91.3 / 89.1	>4 / >4	24.5 / --[a]
MSSA (1,988)	RTI	0.12 / 0.25	98.3	≤0.5 / ≤0.5	97.1 / 95.7	0.25 / 0.5	92.1 / --[a]
Streptococcus pyogenes (768)	SSSI	0.06 / 0.12	98.3	≤0.25 / >4	82.9 / 82.5	0.5 / 1	99.7 / --[a]
S. pyogenes (97) Macrolide-R	SSSI	0.06 / 0.12	93.8	>4 / >4	42.3 / 42.3	0.5 / 2	99.0 / --[a]
S. pyogenes (548)	Wound	0.06 / 0.12	98.5	≤0.25 / >4	83.5 / 83.2	0.5 / 1	100 / --[a]
S. pneumoniae (4,229)	RTI	0.06 / 0.12	98.6	≤0.25 / >4	77.2 / 77.2	1 / 1	98.7 / --[a]
S. pneumoniae (537) Penicillin-R	RTI	0.06 / 0.12	98.5[c]	>4 / >4	41.9 / 41.9	1 / 1	98.1 / --[a]
Enterococcus faecalis (635)	SSSI	0.12 / 0.25	98.3	>8 / >8	23.9 / --	1 / >4	75.9 / 76.2
E. faecalis (344)	Wound	0.12 / 0.25	97.7	>8 / >8	22.1 / --	1 / >4	71.8 / 72.4
E. faecalis (18) Vancomycin-R	SSSI	0.12 / 0.25	94.4	>8 / >8	5.6 / --	>4 / >4	0.0 / 0.0[d]
E. faecium (1,198)	ALL	0.06 / 0.12	97.1[e]	>8 / >8	36.5 / --	>4 / >4	10.5 / 14.6
Haemophilus influenzae (2,112)	RTI	0.5 / 1	99.7	0.5 / 1	99.1 / 98.9	0.015 / 0.03	99.7 / 98.2
Carbapenem-R *Enterobacteriaceae* (494)	ALL	4 / >4	72.1[f]	8 / >16	39.1 / --	>4 / >4	10.7 / 10.7
E. cloacae sp. complex (440)	SSSI	2 / 4	94.3	2 / 16	85.5 / --	≤0.03 / 0.5	90.7 / 90.7
E. cloacae sp. complex (276)	Wound	2 / 4	94.9	2 / >16	85.1 / --	≤0.03 / 0.5	90.5 / 90.5
Klebsiella pneumoniae (543)	SSSI	2 / 8	89.1	2 / >16	65.9 / --	0.06 / >4	67.2 / 67.2
K. pneumoniae (318)	Wound	2 / 8	89.3	2 / >16	65.7 / --	0.06 / >4	66.4 / 66.4
K. pneumoniae (1,229)	RTI	2 / 8	86.2	2 / >16	67.8 / --	0.06 / >4	71.6 / 71.6
Acinetobacter baumannii (968)	ALL	4 / 8	77.7[f]	16 / >16	31.2 / --	>4 / >4	32.0 / 31.0

ALL, all infection types; SSSI, skin and skin structure infection; RTI, respiratory tract infection; BSI, bloodstream infection; MRSA, methicillin-resistant *S. aureus*; R, resistant.

[a] An arbitrary susceptible breakpoint of ≤0.001 mg/L has been published by EUCAST indicating that susceptible should not be reported for this organism-agent combination and intermediate should be interpreted as susceptible increased exposure (EUCAST 2020).

[b] Omadacycline CABP breakpoint for MSSA applied to all *S. aureus* and MRSA for comparison purposes only.

[c] Oral dosing (penicillin MIC ≥2 mg/L).

[d] Uncomplicated UTI only.

[e] Percent inhibited at ≤0.25 mg/L for comparison purposes.

[f] Percent inhibited at ≤4 mg/L for comparison purposes.

Disclaimer: This study and abstract presentation were funded by a research grant from Paratek Pharmaceuticals, Inc.

Title character count: **178** (255 characters allowed with spaces)
Abstract character count: **6,009** (8,000 characters allowed with spaces)
Abstract disclaimer character count: **115** (350 characters allowed with spaces)
Learning Objectives

1. At the end of the session, the attendee should be able to **discuss the *in vitro* activity of omadacycline against gram-positive pathogens from SSSI, wound, and RTI infections (including drug-resistant strains) and the advantage over current comparator agents.**

2. At the end of the session, the attendee should be able to **discuss the *in vitro* activity of omadacycline against *Enterobacterales* isolates from SSSI, wound, and RTI infections (including carbapenem-resistant strains) and the advantage over current comparator agents.**

3. At the end of the session, the attendee should be able to **highlight the *in vitro* activity of omadacycline over other comparator agents against *A. baumannii* where treatment options may be limited.**