IDWEEK 2016
1827
New Orleans, LA
October 26 - 30

Activity of Omadacycline when Tested against Gram-Positive Bacteria Isolated from Patients in the USA During 2015 as Part of a Global Surveillance Program

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Amended Abstract

Background: Omadacycline (OMC) is a broad spectrum aminomethylcycline in late stage clinical development for the treatment of acute bacterial skin and skin structure infections and community-acquired pneumonia that is being evaluated as both oral and intravenous, once-daily formulations.

Methods: A total of 5,102 Gram-positive (GP) organisms isolated during 2015 were selected from medical centers in the USA. Susceptibility testing (S) was performed by reference broth microdilution methods for OMC and comparators.

Results: OMC was active against *Staphylococcus aureus* (SA; $MIC_{50/90}$, 0.12/0.12 µg/ml). The $MIC_{50/90}$ for methicillin-resistant (MRSA) and MSSA isolates were identical at 0.12/0.12 µg/ml, respectively. All SA were S to tigecycline (TGC; $MIC_{50/90}$, 0.06/0.12 µg/ml), daptomycin (DAP; $MIC_{50/90}$, 0.25/0.5 µg/ml), linezolid (LZD; $MIC_{50/90}$, 1/1 µg/ml), and vancomycin (VAN; $MIC_{50/90}$, 0.5/1 µg/ml). S was lower in MRSA for levofloxacin (LEV; 29.6%), clindamycin (CLI; 71.2%), and erythromycin (ERY; 10.9/11.6%; CLSI/EUCAST). OMC ($MIC_{50/90}$, 0.12/0.5 µg/ml) and TGC ($MIC_{50/90}$, 0.06/0.12 µg/ml) were the most active agents tested against coagulase-negative staphylococci and against Enterococci (both agents $MIC_{50/90}$, 0.06/0.12 µg/ml). Against *Streptococcus pneumoniae* (SPN), the MIC_{50} and MIC_{90} for OMC (0.06/0.12 µg/ml) and TGC (0.03/0.06 µg/ml), were the lowest among the agents tested. OMC demonstrated activity against ceftriaxone (CRO) and LEV resistant isolates. OMC MIC values for SPN were 8-fold lower than CRO (MIC_{90}, 1 µg/ml) and LEV (MIC_{90}, 1 µg/ml). Against viridans group streptococci, OMC ($MIC_{50/90}$, 0.06/0.12 µg/ml) and TGC ($MIC_{50/90}$, 0.03/0.12 µg/ml; 100.0% S) were the most active agents tested. The $MIC_{50/90}$ for OMC against β-hemolytic streptococci was 0.06/0.12 µg/ml. All β-hemolytic streptococci were S to TGC, β-lactams, LZD, DAP, and VAN, however resistance to LEV (99.5/96.8% S [CLSI/EUCAST]), ERY (65.3% S), CLI (80.7/81.4% S [CLSI/EUCAST]) and tetracycline (54.5/54.3% S [CLSI/EUCAST]) occurred.

Conclusions: OMC was active against a broad range of GP bacteria including MRSA, SPN resistant to penicillin, CRO, and LEV; Enterococci, and streptococci. OMC warrants further study as therapy in infections where these organisms may occur.

Introduction

Omadacycline (formerly PTK 0796 and BAY 73-6944; 7-dimethylamino, 9-(2,2-dimethyl-propyl)-aminomethylcycline) is a novel antibacterial agent of the tetracycline family, which is currently under clinical development for the treatment of acute bacterial skin and skin structure infections and community-acquired pneumonia that is being evaluated as both oral and intravenous, once-daily formulations. This new tetracycline has shown a broad-spectrum of activity against a wide range of pathogenic bacteria, including Gram-positive and -negative isolates.

This poster compares the activity of omadacycline and currently marketed antimicrobial agents against several Gram-positive species submitted from 107 medical centers representing each of the nine Census Regions in the United States (USA). Evaluations of resistant subsets for most of the pathogen groups were included in the analysis. A total of 5,102 bacterial isolates were tested by reference Clinical and Laboratory Standards Institute (CLSI) broth microdilution methods. Categorical interpretation of comparator MIC values was performed by using the CLSI (M100-S26; 2016), European Committee on Antimicrobial Susceptibility Testing (EUCAST, 2016) and USA-Food and Drug Administration (FDA; tigecycline) breakpoint criteria, where available.

Methods

Sampling sites and Organisms: A total of 5,102 non-duplicate, single-patient Gram-positive clinical isolates that originated from the SENTRY surveillance network in North America (USA) during 2015 were received by JMI Laboratories. Isolates were obtained from hospitalized patients in 107 medical centers representing each of the nine USA Census Regions (**Figure 1**) and were responsible for a causing a variety of clinical infections including pneumonia in hospitalized patients, respiratory tract infections caused by *S. pneumoniae*, skin and skin structure infections, urinary tract infections, blood stream infections, intra-abdominal infections and other infection types (**Figure 2**).

Bacterial species were identified by the submitting laboratories and confirmed by JMI Laboratories (North Liberty, Iowa, USA) using standard bacteriologic algorithms and methodologies, including the use of matrix-assisted laser desorption/ionization-time of flight-mass spectrometry (MALDI-TOF-MS; Bruker Daltonics, Bremen, Germany).

Antimicrobial Susceptibility Testing: Reference broth microdilution methods per CLSI (M07-A10; 2015) using validated frozen-form panels produced by JMI Laboratories were utilized for susceptibility testing. Interpretive breakpoint criteria for all comparator agents were those published in CLSI (M100-S26; 2016) and EUCAST (2016), except for tigecycline where the USA-FDA breakpoints were applied (Tygacil Package Insert, 2016). Omadacycline (0.004 – 8 µg/ml MIC testing range) was supplied by Paratek Pharmaceuticals to JMI Laboratories for broth microdilution panel production. Comparator agents were selected to match previous surveillance reports for the organism groups tested. Comparator antimicrobials were acquired from their respective manufacturers, the United States Pharmacopeia (USP; Rockville, MD) or from Sigma-Aldrich (St. Louis, Missouri, USA).

Results

- MIC distributions for omadacycline against 5,102 recently collected Gram-positive clinical isolates (including resistant organism subsets) from the USA are detailed in **Table 1**.
- The *in vitro* activities and breakpoint interpretive criteria for omadacycline and comparator agents tested against 5,082 clinically significant Gram-positive isolates are detailed in **Table 2**.
- *Staphylococcus aureus* (n=2,148):
  - Omadacycline ($MIC_{50/90}$, 0.12/0.12 µg/ml) was highly active when tested against *S. aureus* isolates, possessing identical $MIC_{50/90}$ values (0.12/0.12 µg/ml) against oxacillin-susceptible (MSSA) and oxacillin-resistant (MRSA) isolates (**Table 1**).
  - All *S. aureus* isolates were susceptible to tigecycline ($MIC_{50/90}$, 0.06/0.12 µg/ml), daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/ml), linezolid ($MIC_{50/90}$, 1/1 µg/ml), and vancomycin ($MIC_{50/90}$, 0.5/1 µg/ml; **Table 2**).
  - A total of 36.5/36.5%, 53.0/55.9%, 15.0/15.3% and 0.0-3.6/2.2-6.1% (CLSI/EUCAST) of *S. aureus* isolates displayed fluoroquinolone (levofloxacin), macrolide (erythromycin), lincosamide (clindamycin), and tetracycline (doxycycline and tetracycline) resistance phenotypes, respectively (**Table 2**).
- Coagulase negative staphylococci (CoNS; n=320):
  - Omadacycline ($MIC_{50/90}$, 0.12/0.5 µg/ml) and tigecycline ($MIC_{50/90}$, 0.06/0.12 µg/ml) were the most active agents tested against CoNS.
  - The highest omadacycline MIC among the CoNS was 1 µg/ml and 98.1% of isolates were inhibited at ≤0.5 µg/ml (**Table 1**).
  - Doxycycline ($MIC_{50/90}$, 0.25/2 µg/ml; 95.6/87.2% susceptible [CLSI/EUCAST]) and tetracycline ($MIC_{50/90}$, ≤0.5/>8 µg/ml; 84.4/83.1% susceptible [CLSI/EUCAST]) were considerably less active against CoNS.
  - Overall, 62.8% of CoNS isolates were oxacillin-resistant (**Table 1**) and high levofloxacin (39.7/39.7%), erythromycin (61.6/62.8%) clindamycin (30.6/32.2%) and trimethoprim-sulfamethoxazole (25.9/9.1%) resistance rates (CLSI/EUCAST criteria) were noted among CoNS (**Table 2**).
- *Enterococcus faecalis* (n=636) and *E. faecium* (n=241):
  - Omadacycline was highly active against both *E. faecalis* and *E. faecium* isolates with $MIC_{50/90}$ values of 0.06/0.12 µg/ml. Against vancomycin-non-susceptible *E. faecium*, omadacycline was slightly less active with an MIC_{90} value of 0.25 µg/ml (**Table 1**).
  - Tigecycline was also very active against both *E. faecalis* (99.8% susceptible) and *E. faecium* (99.2% susceptible) isolates ($MIC_{50/90}$, 0.03-0.06/0.12 µg/ml) whereas tetracycline ($MIC_{50/90}$, >8/>8 µg/ml; 23.7-24.4% susceptible) demonstrated limited activity. Linezolid ($MIC_{50/90}$, 1/1 µg/ml) was active against 100.0% of the *E. faecalis* and *E. faecium* isolates tested (**Table 2**).
- *Streptococcus pneumoniae* (n=1,012):
  - Omadacycline ($MIC_{50/90}$, 0.06/0.12 µg/ml) and tigecycline ($MIC_{50/90}$, 0.03/0.06 µg/ml; 99.8% susceptible) had the lowest $MIC_{50/90}$ values among the agents tested against 1,012 *S. pneumoniae* isolates (**Table 2**).
  - $MIC_{50/90}$ values for omadacycline were unchanged ($MIC_{50/90}$, 0.06/0.12 µg/ml) against penicillin-susceptible, penicillin-intermediate and penicillin-resistant *S. pneumoniae* isolates. Tetracycline had limited activity against penicillin-intermediate (61.9% susceptible) and penicillin-resistant (37.2% susceptible) *S. pneumoniae* isolates (data not shown).
  - Omadacycline demonstrated activity against ceftriaxone- and levofloxacin-resistant *S. pneumoniae* isolates with MIC_{90} values eight-fold lower than ceftriaxone (MIC_{90}, 1 µg/ml) and levofloxacin (MIC_{90}, 1 µg/ml; **Table 2**).
- Viridans group streptococci (n=106):
  - Omadacycline ($MIC_{50/90}$, 0.06/0.12 µg/ml) and tigecycline ($MIC_{50/90}$, 0.03/0.12 µg/ml; 100.0% susceptible), were very active against viridans group streptococci whereas tetracycline ($MIC_{50/90}$, 1/>8 µg/ml; 57.1% susceptible) and erythromycin ($MIC_{50/90}$, 0.5/>4 µg/ml; 48.6% susceptible) were considerably less active (**Table 2**).
- β-hemolytic streptococci (n=619):
  - The $MIC_{50/90}$ values for omadacycline against β-hemolytic streptococci were 0.06/0.12 µg/ml (**Table 2**). All β-hemolytic streptococci were susceptible to tigecycline, amoxicillin-clavulanic acid, ceftriaxone, daptomycin, linezolid, penicillin and vancomycin, however, resistance to tetracycline ($MIC_{50/90}$, ≤0.25/>8 µg/ml; 54.3-54.5% susceptible), erythromycin ($MIC_{50/90}$, 0.06/>4 µg/ml; 65.3% susceptible), clindamycin ($MIC_{50/90}$, 0.06/>2 µg/ml; 80.7-81.4% susceptible) and levofloxacin ($MIC_{50/90}$, 0.5/1 µg/ml; 96.8-99.5% susceptible; **Table 2**) occurred.

Table 1. Omadacycline MIC distributions against the main organisms/organism groups included in this study (µg/ml).

Organisms / Organism Groups (# tested)	No. of isolates at MIC (µg/ml; cumulative %)											MIC_{50}	MIC_{90}
	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	>		
Staphylococcus aureus (2,148)		0 (0.0%)	3 (0.1%)	9 (0.6%)	760 (35.9%)	1,262 (94.7%)	41 (96.6%)	29 (98.0%)	43 (>99.9%)	1 (100.0%)		0.12	0.12
MSSA (1,206)		0 (0.0%)	1 (0.1%)	6 (0.6%)	360 (30.4%)	815 (98.0%)	13 (99.1%)	7 (99.7%)	4 (100.0%)			0.12	0.12
MRSA (942)		0 (0.0%)	2 (0.2%)	3 (0.5%)	400 (43.0%)	447 (90.4%)	28 (93.4%)	22 (95.8%)	39 (99.9%)	1 (100.0%)		0.12	0.12
Coagulase-negative staphylococci (320)		0 (0.0%)	2 (0.6%)	23 (7.8%)	104 (40.3%)	45 (54.4%)	74 (77.5%)	66 (98.1%)	6 (100.0%)			0.12	0.5
MSCoNS[a] (119)		0 (0.0%)	1 (0.8%)	14 (12.6%)	55 (58.8%)	21 (76.5%)	15 (89.1%)	12 (99.2%)	1 (100.0%)			0.06	0.5
MRCoNS[b] (201)		0 (0.0%)	1 (0.5%)	9 (5.0%)	49 (29.4%)	24 (41.3%)	59 (70.6%)	54 (97.5%)	5 (100.0%)			0.25	0.5
Enterococcus spp. (897)	0 (0.0%)	1 (0.1%)	2 (1.2%)	10 (11.5%)	92 (62.0%)	453 (92.2%)	271 (98.7%)	58 (99.8%)	10 (99.9%)	1 (100.0%)		0.06	0.12
Enterococcus faecalis (636)	0 (0.0%)	1 (0.2%)	10 (1.7%)	56 (10.5%)	305 (58.5%)	217 (92.6%)	45 (99.7%)	1 (99.8%)	1 (99.8%)	1 (100.0%)		0.06	0.12
vancomycin-susceptible (≤4) (607)	0 (0.0%)	1 (0.2%)	10 (1.8%)	55 (10.9%)	291 (58.8%)	204 (92.4%)	44 (99.7%)	1 (99.8%)	0 (99.8%)	1 (100.0%)		0.06	0.12
vancomycin-non-susceptible (>4) (29)		0 (0.0%)	0 (0.0%)	1 (3.4%)	14 (51.7%)	13 (96.6%)	1 (100.0%)					0.06	0.12
Enterococcus faecium (241)		0 (0.0%)	0 (0.0%)	32 (13.3%)	141 (71.8%)	46 (90.9%)	13 (96.3%)	8 (99.6%)	1 (100.0%)			0.06	0.12
vancomycin-susceptible (≤4) (74)		0 (0.0%)	0 (0.0%)	13 (17.6%)	46 (79.7%)	13 (97.3%)	2 (100.0%)					0.06	0.12
vancomycin-non-susceptible (>4) (167)		0 (0.0%)	0 (0.0%)	19 (11.4%)	95 (68.3%)	33 (88.6%)	11 (94.6%)	8 (99.4%)	1 (100.0%)			0.06	0.25
other *Enterococcus* spp. (20)		0 (0.0%)	0 (0.0%)	4 (20.0%)	7 (55.0%)	8 (95.0%)	0 (95.0%)	1 (100.0%)				0.06	0.12
Streptococcus pneumoniae (1,012)	0 (0.0%)	1 (0.1%)	6 (0.7%)	76 (8.2%)	667 (74.1%)	235 (97.3%)	27 (100.0%)					0.06	0.12
penicillin-susceptible (≤2) (627)		0 (0.0%)	0 (0.0%)	5 (0.8%)	67 (11.5%)	420 (78.5%)	113 (96.5%)	22 (100.0%)				0.06	0.12
penicillin-intermediate (4) (299)	0 (0.0%)	1 (0.3%)	1 (0.7%)	7 (3.0%)	196 (68.6%)	90 (98.7%)	4 (100.0%)					0.06	0.12
penicillin-resistant (>4) (86)		0 (0.0%)	0 (0.0%)	2 (2.3%)	51 (61.6%)	32 (98.8%)	1 (100.0%)					0.06	0.12
Viridans group streptococci (106)	2 (1.9%)	2 (3.8%)	4 (7.5%)	39 (44.3%)	36 (78.3%)	16 (93.4%)	7 (100.0%)					0.06	0.12
β-hemolytic streptococci (619)		0 (0.0%)	0 (0.0%)	43 (6.9%)	360 (65.1%)	185 (95.0%)	27 (99.4%)	4 (100.0%)				0.06	0.12
Streptococcus pyogenes (286)		0 (0.0%)	0 (0.0%)	30 (10.5%)	240 (94.4%)	13 (99.0%)	3 (100.0%)					0.06	0.06
Streptococcus agalactiae (261)		0 (0.0%)	0 (0.0%)	11 (4.2%)	87 (37.5%)	150 (95.0%)	12 (99.6%)	1 (100.0%)				0.12	0.12
other β-hemolytic streptococci (72)		0 (0.0%)	0 (0.0%)	2 (2.8%)	33 (48.6%)	22 (79.2%)	12 (95.8%)	3 (100.0%)				0.12	0.25

a. MSCoNS = Methicillin susceptible coagulase-negative staphylococci
b. MRCoNS = Methicillin-resistant coagulase-negative staphylococci

Table 2. Activity of omadacycline and comparator agents when tested against 5,082 Gram-positive isolates collected during 2015 in the USA.

Organism	MIC_{50}	MIC_{90}	Range	CLSI[a]			EUCAST[a]		
				%S	%I	%R	%S	%I	%R
Staphylococcus aureus (2,148)									
Omadacycline	0.12	0.12	0.015 — 2	-	-	-	-	-	-
Tigecycline	0.06	0.12	≤0.015 — 0.5	100.0	-	-[h]	100.0	-	0.0
Doxycycline	≤0.06	0.12	≤0.06 — 8	99.4	0.6	0.0	97.3	0.6	2.2
Tetracycline	≤0.5	≤0.5	≤0.5 — >8	95.3	1.1	3.6	93.5	0.4	6.1
Oxacillin	1	>2	≤0.25 —>2	56.1	-	43.9	56.1	-	43.9
Ceftriaxone	4	>8	≤0.25 — >8	56.1	-	43.9	-	-	-
Piperacillin-tazobactam	1	>16	≤0.5 —>16	56.1	-	43.9	56.1	-	43.9
Levofloxacin	0.25	>4	≤0.06 —>4	62.8	0.7	36.5	62.8	0.7	36.5
Erythromycin	>8	>8	≤0.06 —>8	41.1	5.9	53.0	42.1	2.0	55.9
Clindamycin	≤0.25	>2	≤0.25 —>2	84.7	0.2	15.0	84.6	0.1	15.3
Linezolid	1	1	0.25 — 2	100.0	-	0.0	100.0	-	0.0
Daptomycin	0.25	0.5	≤0.12 — 1	100.0	-	-	100.0	-	0.0
Vancomycin	0.5	1	≤0.12 — 2	100.0	0.0	0.0	100.0	-	0.0
Teicoplanin	≤0.5	≤0.5	≤0.5 — 4	100.0	0.0	0.0	99.9	-	0.1
Gentamicin	≤1	≤1	≤1 —>8	97.1	0.1	2.8	96.9	-	3.1
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	≤0.5 —>4	98.6	-	1.4	98.6	0.4	1.0
Coagulase-negative staphylococci (320)[c]									
Omadacycline	0.12	0.5	0.015 — 1	-	-	-	-	-	-
Tigecycline	0.06	0.12	≤0.015 — 0.5	-	-	-	100.0	-	0.0
Doxycycline	0.25	2	≤0.06 —>8	95.6	4.1	0.3	87.2	3.4	9.4
Tetracycline	≤0.5	>8	≤0.5 —>8	84.4	0.9	14.7	83.1	0.9	15.9
Oxacillin	>2	>2	≤0.25 —>2	37.2	-	62.8	37.2	-	62.8
Ceftriaxone	8	>8	≤0.25 —>8	37.2	-	62.8	-	-	-
Piperacillin-tazobactam	1	8	≤0.5 —>16	37.2	-	62.8	37.2	-	62.8
Levofloxacin	0.25	>4	≤0.06 —>4	57.8	2.5	39.7	57.8	2.5	39.7
Erythromycin	>8	>8	≤0.06 —>8	35.3	3.1	61.6	35.9	1.2	62.8
Clindamycin	≤0.25	>2	≤0.25 —>2	67.8	1.6	30.6	66.9	0.9	32.2
Linezolid	0.5	1	≤0.12 —>8	99.4	-	0.6	99.4	-	0.6
Daptomycin	0.5	0.5	≤0.12 — 1	100.0	-	-	100.0	-	0.0
Vancomycin	1	2	≤0.12 — 2	100.0	0.0	0.0	100.0	-	0.0
Teicoplanin	2	4	≤0.5 — 16	99.7	0.3	0.0	95.0	-	5.0
Gentamicin	≤1	>8	≤1 — >8	73.1	2.8	24.1	71.9	-	28.1
Trimethoprim-sulfamethoxazole	≤0.5	4	≤0.5 —>4	74.1	-	25.9	74.1	16.9	9.1
Enterococcus faecalis (636)									
Omadacycline	0.06	0.12	0.008 — 2	-	-	-	-	-	-
Tigecycline	0.06	0.12	≤0.015 — >0.5	99.8	-	-[h]	99.8	0.0	0.2
Tetracycline	>8	>8	≤1 — >8	24.4	1.4	74.2	-	-	-
Piperacillin-tazobactam	4	8	≤2 — 16	-	-	-	100.0	0.0	0.0
Levofloxacin	1	>4	≤0.5 —>4	75.5	0.0	24.5	75.5	-	24.5[d]
Linezolid	1	1	≤0.25 — 2	100.0	0.0	0.0	100.0	-	0.0
Daptomycin	1	1	≤0.25 — 4	100.0	-	-	-	-	-
Vancomycin	1	2	≤0.5 — >16	95.4	0.0	4.6	95.4	-	4.6
Teicoplanin	≤2	≤2	≤2 —>16	96.1	0.0	3.9	96.1	-	3.9
Ampicillin	≤0.5	1	≤0.5 — 2	100.0	-	0.0	100.0	0.0	0.0
Enterococcus faecium (241)									
Omadacycline	0.06	0.12	0.03 — 1	-	-	-	-	-	-
Tigecycline	0.03	0.12	≤0.015 — 0.5	-	-	-	99.2	0.8	0.0
Tetracycline	>8	>8	≤1 — >8	23.7	5.8	70.5	-	-	-
Piperacillin-tazobactam	>16	>16	≤2 — >16	-	-	-	17.4	0.4	82.2
Levofloxacin	>4	>4	≤0.5 —>4	12.9	6.2	80.9	19.1	-	80.9[e]
Linezolid	1	1	≤0.25 — 2	100.0	0.0	0.0	100.0	-	0.0
Daptomycin	1	2	≤0.25 —>8	99.6	-	-	-	-	-
Vancomycin	>16	>16	≤0.5 — >16	30.7	0.4	68.9	30.7	-	69.3
Teicoplanin	>16	>16	≤2 — >16	34.0	6.2	59.8	32.8	-	67.2
Ampicillin	>8	>8	≤0.5 — >8	17.8	-	82.2	17.4	0.4	82.2
Streptococcus pneumoniae (1,012)									
Omadacycline	0.06	0.12	0.008 — 0.25	-	-	-	-	-	-
Tigecycline	0.03	0.06	≤0.008 — 0.12	99.8	-	-[h]	-	-	-
Tetracycline	0.25	>4	≤0.12 —>4	79.6	0.1	20.3	79.6	0.1	20.3
Ceftriaxone	0.03	1	≤0.015 —>2	88.7	9.5	1.8[g]	88.7	10.6	0.7
Amoxicillin-clavulanic acid	≤0.03	2	≤0.03 —>4	95.3	2.6	2.2	-	-	-
Levofloxacin	1	1	0.25 —>4	99.5	0.0	0.5	99.5	-	0.5
Erythromycin	0.06	>2	≤0.015 —>2	55.3	0.6	44.1	55.3	0.6	44.1
Clindamycin	≤0.12	>1	≤0.12 —>1	85.9	0.6	13.5	86.5	-	13.5
Linezolid	1	1	0.25 — 2	100.0	-	-	100.0	0.0	0.0
Vancomycin	0.25	0.25	≤0.03 — 0.5	100.0	-	-	100.0	-	0.0
Penicillin	≤0.06	1	≤0.06 — 4	62.0	29.5	8.5[g]	62.0	-	38.0[e]
				62.0	-	38.0[h]	62.0	34.8	3.3[f]
				96.7	3.3	0.0	-	-	-
Trimethoprim-sulfamethoxazole	≤0.5	4	≤0.5 —>4	73.8	12.0	14.2	81.8	4.0	14.2
Viridans group streptococci (106)[i]									
Omadacycline	0.06	0.12	≤0.004 — 0.25	-	-	-	-	-	-
Tigecycline	0.03	0.12	≤0.008 — 0.25	100.0	-	-[h]	-	-	-
Tetracycline	1	>8	≤0.25 —>8	57.1	1.9	41.0	-	-	-
Ceftriaxone	0.12	1	≤0.03 — 4	97.1	1.0	1.9	89.5	-	10.5
Amoxicillin-clavulanic acid	0.06	0.5	≤0.03 —>4	-	-	-	82.9	14.3	2.9
Piperacillin-tazobactam	0.12	2	≤0.06 — 8	-	-	-	82.9	14.3	2.9
Levofloxacin	1	2	0.25 —>4	90.5	1.0	8.6	-	-	-
Erythromycin	0.5	>4	≤0.03 —>4	48.6	2.9	48.6	-	-	-
Clindamycin	0.03	>2	≤0.015 —>2	83.8	1.0	15.2	84.8	-	15.2
Linezolid	0.5	1	≤0.06 — 1	100.0	-	-	-	-	-
Daptomycin	0.5	0.5	≤0.06 — 1	100.0	-	-	-	-	-
Vancomycin	0.5	0.5	≤0.06 — 1	100.0	-	-	100.0	-	0.0
Teicoplanin	0.12	0.25	≤0.06 —0.5	-	-	-	100.0	-	0.0
Penicillin	0.06	1	≤0.03 —>4	78.1	19.0	2.9	82.9	14.3	2.9
β-hemolytic streptococci (619)[j]									
Omadacycline	0.06	0.12	0.03 — 0.5	-	-	-	-	-	-
Tigecycline	0.03	0.06	0.015 — 0.25	100.0	-	-[h]	100.0	0.0	0.0
Tetracycline	≤0.25	>8	≤0.25 —>8	54.5	1.9	43.6	54.3	0.2	45.5
Ceftriaxone	≤0.03	0.06	≤0.03 — 0.25	100.0	-	-	100.0	-	0.0
Amoxicillin-clavulanic acid	≤0.03	0.06	≤0.03 — 0.12	100.0	-	-	100.0	-	0.0
Piperacillin-tazobactam	≤0.06	0.25	≤0.06 — 0.5	-	-	-	100.0	-	0.0
Levofloxacin	0.5	1	0.12 —>4	99.5	0.2	0.3	96.8	2.8	0.5
Erythromycin	0.06	>4	≤0.03 —>4	65.3	0.6	34.0	65.3	0.6	34.0
Clindamycin	0.06	>2	≤0.015 —>2	80.7	0.6	18.6	81.4	-	18.6
Linezolid	1	1	0.5 — 1	100.0	-	-	100.0	0.0	0.0
Daptomycin	0.12	0.5	≤0.06 — 1	100.0	-	-	100.0	-	0.0
Vancomycin	0.25	0.5	0.12 — 1	100.0	-	-	100.0	-	0.0
Teicoplanin	0.12	0.25	≤0.06 —0.5	-	-	-	100.0	185	0.0
Penicillin	≤0.03	0.06	≤0.03 — 0.12	100.0	-	-	100.0	-	0.0

a. Criteria as published by CLSI [2016] and EUCAST [2016]
b. Breakpoints from FDA Package Insert [revised 01/2016]
c. Includes: *Staphylococcus auricularis* (1), *S. capitis* (13), *S. caprae* (7), *S. cohnii* (2), *S. epidermidis* (204), *S. hemolyticus* (17), *S. hominis* (22), *S. lugdunensis* (26), *S. pseudintermedius* (1), *S. pseudintermedius / intermedius / delphini* (2), *S. saprophyticus* (7), *S. schleiferi* (2), *S. simulans* (9), *S. warneri* (7)
d. Uncomplicated UTI only
e. Using Meningitis breakpoints
f. Using Non Meningitis breakpoints
g. Using Oral breakpoints
h. Using Parenteral, Meningitis breakpoints
i. Using Parenteral, Non Meningitis breakpoints
j. Includes: *Streptococcus anginosus* (30), *S. anginosus* group (6), *S. australis* (1), *S. constellatus* (2), *S. cristatus* (1), *S. gallolyticus* (5), *S. gordonii* (2), *S. infantarius* (1), *S. infantis* (1), *S. intermedius* (2), *S. lutetiensis* (1), *S. mitis* (2), *S. mitis* group (4), *S. mitis/oralis* (18), *S. mutans* (1), *S. oralis* (11), *S. parasanguinis* (9), *S. salivarius* (4), *S. salivarius* group (1), *S. sanguinis* (4)
k. Includes: *Streptococcus agalactiae* (261), *S. dysgalactiae* (72), *S. pyogenes* (286)

Figure 1. Omadacycline 2015 surveillance isolate total (%) by USA Census Region

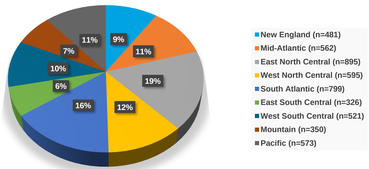
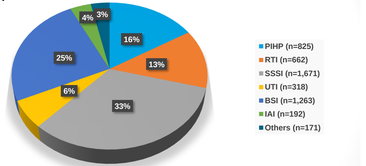


Figure 2. Omadacycline 2015 USA surveillance isolate totals (%) stratified by infection type[a]



[a] PIHP = pneumonia in hospitalized patients; RTI = respiratory tract infections cause by *S. pneumoniae*; SSSI = skin and skin structure infections; UTI = urinary tract infections; BSI = blood stream infections; IAI = intra-abdominal infections; Others = other infection types

Conclusions

- Omadacycline ($MIC_{50/90}$, 0.12/0.12 µg/ml) was highly active against *S. aureus* isolates with identical $MIC_{50/90}$ values against MSSA and MRSA isolates.
- MIC_{90} values for omadacycline were slightly higher against CoNS ($MIC_{50/90}$, 0.12/0.5 µg/ml) compared to *S. aureus* ($MIC_{50/90}$, 0.12/0.12 µg/ml). All CoNS isolates were inhibited by ≤1 µg/ml of omadacycline.
- Omadacycline displayed potent *in vitro* activity against *E. faecalis* ($MIC_{50/90}$, 0.06/0.12 µg/ml) and *E. faecium* ($MIC_{50/90}$, 0.06/0.12 µg/ml) isolates (including vancomycin-resistant strains), for which drug class comparators, such as tetracycline and doxycycline, demonstrated limited activity.
- Streptococcal isolates including *S. pneumoniae* ($MIC_{50/90}$ 0.06/0.12 µg/ml), viridans group ($MIC_{50/90}$ 0.06/0.12 µg/ml) and β-hemolytic streptococci ($MIC_{50/90}$ 0.06/0.12 µg/ml) were also very susceptible to omadacycline and all isolates were inhibited by ≤0.5 µg/ml of omadacycline.

Acknowledgements

This study was supported by a research grant from Paratek Pharmaceuticals.

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