Activity of Omadacycline Tested against *Staphylococcus aureus* from a Global Surveillance Program (2014)

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RK FLAMM, PR RHOMBERG, MD HUBAND, DJ FARRELL
JMI Laboratories, North Liberty, IA, USA

ICAAC 2015

JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
ph. 319.665.3370, fax 319.665.3371
robert-flamm@jmilabs.com

ABSTRACT

Background: Omadacycline (OMC) is a new broad spectrum aminomethylcycline in late stage clinical development for acute bacterial skin and skin structure infections and community-acquired pneumonia as both an oral and intravenous, once-daily formulations. It has excellent activity against Gram-positive pathogens including tetracycline (TET) resistant organisms. In this report OMC and comparator agents were tested against *Staphylococcus aureus* (SA) selected from a 2014 global surveillance program and compared to the results of 2010 surveillance.

Methods: One hundred HA-MRSA (isolated >48 hours after hospital admission), 100 CA-MRSA (isolated <48 hours after hospital admission) and 50 MSSA from Europe (EU) and North America (NA) from a global surveillance program (2014) were selected for testing. Comparator agents were tested in validated dry-form panels by broth microdilution in CA-MHB following Clinical and Laboratory Standards Institute (CLSI) M07-A10 (2015) methods. OMC was tested in dry-form panels in 2010 and fresh frozen medium in 2014. QC guidelines were those of CLSI.

Results: The OMC MIC_{50}/MIC_{90} for all SA collected during 2014 was 0.12/0.12 µg/mL, respectively. The MIC_{90} was identical for MRSA, HA-MRSA and CA-MRSA (0.12 µg/mL). The MIC_{90} for isolates from 2010 for SA, MRSA, and CA-MRSA was 0.25 µg/mL (0.5 µg/mL for HA-MRSA; 87.8% were at ≤0.25 µg/mL). The MIC_{90} for all 2014 SA in NA (0.12 µg/mL) was identical to the MIC_{90} in the EU as was the MIC_{90} for all MRSA and for CA-MRSA (0.12 µg/mL). The MIC_{90} for HA-MRSA from 2014 was 0.12 µg/mL in EU and 0.5 µg/mL in NA (88.1% were at ≤0.12 µg/mL). All 2014 and 2010 MRSA isolates were vancomycin (VAN) S and ≥99.8% were daptomycin (DAP), linezolid (LZD), and tigecycline (TIG) S. TET, doxycycline (DOX), and gentamicin (GEN) S ranged from 89.1-97.5%. Erythromycin (ERY) and levofloxacin (LEV) S ranged from 15.7-26.0%.

Conclusions: The activity of OMC was unchanged between 2010 and 2014, and was similar for NA and EU isolates including MRSA (CA-MRSA or HA-MRSA).The potent activity of OMC against SA indicates that OMC merits further study in serious infections where MDR may be a concern.

INTRODUCTION

Omadacycline (PTK 0796; [7-dimethylamino, 9-(2,2-dimethyl-propyl)-aminomethylcycline]) is a novel tetracycline antibacterial agent, which is currently under clinical development for use as both an oral and intravenous formulation against acute bacterial skin and skin structure infections, community-acquired pneumonia, and urinary tract infections. Omadacycline has broad spectrum activity against Gram-positive, Gram-negative, atypical and anaerobic bacteria, including those with multi-drug resistance (MDR).

Staphylococcus aureus are extremely common causes of infection including serious infections in the hospital environment. *S. aureus* is a major cause of acute bacterial skin and skin structure infections and bloodstream infections with methicillin-resistant strains (MRSA) accounting for approximately 50% of *S. aureus.* In this report, we evaluated the activity of omadacycline tested by reference methods against *S. aureus* causing community- and hospital-acquired infections in North America and Europe in comparison to data collected in the 2010 global surveillance program.

MATERIALS AND METHODS

Organism collection: A total of 102 hospital-acquired MRSA (HA-MRSA), 100 community-acquired MRSA (CA-MRSA) and 50 MSSA from Europe and 101 HA-MRSA, 99 CA-MRSA and 50 MSSA from North America (Global surveillance, 2014; total n= 502) were selected for testing. *S. aureus* were categorized as HA-MRSA phenotype if isolated >48 hours after hospital admission and CA-MRSA if isolated <48 hours after hospital admission. The 2014 data were compared to the results from testing 7,740 *S. aureus* from the 2010 global surveillance program.

Susceptibility testing: Comparator agents were tested in validated dry-form panels manufactured by Thermo Fisher Scientific Inc. (Cleveland, Ohio, USA) by broth microdilution in cation-adjusted Mueller-Hinton broth following Clinical and Laboratory Standards Institute (CLSI) methods. Omadacycline was tested in dry-form panels in 2010 and panels with fresh frozen medium made at JMI Laboratories (North Liberty, Iowa, USA) for testing 2014 strains. Concurrent quality control (QC) testing was performed to assure proper test conditions and procedures (M07-A10, M100-S25). QC strains included: *S. aureus* American Type Culture Collection (ATCC) strain 29213 and *Enterococcus faecalis* ATCC 29212 (M100-S25). All QC results were within published ranges. Interpretive criteria used were those of CLSI (M07-A10, M100-S25) and EUCAST (2015).

RESULTS

Omadacycline: 2010 compared to 2014

- The MIC distributions for *S. aureus* from European and North American medical centers is located in **Table 1**. The MIC_{50} and MIC_{90} for all *S. aureus* in 2010 was 0.12 and 0.25 µg/mL (**Table 1**). For MSSA, the MIC_{50} and MIC_{90} for 2010 isolates was 0.12 and 0.25 µg/mL (**Table 1**). For the 2014 MSSA isolates tested, the omadacycline MIC_{50} and MIC_{90} were 0.12 and 0.12 µg/mL, respectively (**Table 1**).
- The MIC_{50} and MIC_{90} values for all MRSA were identical to the MSSA values for each year (2014 and 2010; **Table 1**).
- The MIC_{90} for CA-MRSA and HA-MRSA for 2014 isolates was 0.12 µg/mL (**Table 1**). The MIC_{90} for all CA-MRSA and all HA-MRSA from 2010 were 0.25 and 0.5 µg/mL, respectively (**Table 1**).

Omadacycline: Europe compared to North America

- Identical omadacycline MIC_{50} and MIC_{90} values (0.12 and 0.25 µg/mL, respectively) were exhibited for North American and European MSSA for 2010 isolates (**Table 1**). North American and European MSSA MIC_{50} and MIC_{90} values (0.12 and 0.12 µg/mL, respectively) were also identical for 2014 isolates (**Table 1**).
- For 2010 isolates, the MRSA MIC_{90}s were similar for Europe (0.25 µg/mL) and North America (0.5 µg/mL; however 89.9% were ≤0.25 µg/mL; **Table 1**). The MIC_{90}s for 2014 MRSA isolates were identical (0.12 µg/mL) for Europe and North America (**Table 1**).
- For HA-MRSA, MIC_{50} values were identical for 2010 and 2014 isolates from Europe and North America (0.12 µg/mL; **Table 1**). MIC_{90} values were higher in North America (0.5 µg/mL [84.9% ≤0.25 µg/mL], 2010; 0.5 µg/mL [88.1% ≤0.25 µg/mL], 2014) than in Europe (0.12 µg/mL, 2014; 0.25 µg/mL, 2010; **Table 1**).
- MIC_{50} values ranged from 0.06-0.12 µg/mL for CA-MRSA in Europe and North America for 2014 and 2010 (**Table 1**). MIC_{90}s were identical in Europe and North America in 2010 (0.25 µg/mL) and in 2014 (0.12 µg/mL; **Table 1**).

2010 compared to 2014 susceptibility

- For all *S. aureus* from 2010, susceptibility was high for daptomycin (99.9%), linezolid (>99.9%), tigecycline (>99.9%), trimethoprim-sulfamethoxazole (98.7%), and vancomycin (100%; data not shown).
- For MRSA in both 2010 and 2014, high levels of susceptibility were seen for daptomycin (99.8-99.9%), linezolid (>99.9-100.0%), tigecycline (>99.9-100.0%), trimethoprim-sulfamethoxazole (97.5-97.9%), and vancomycin (100.0%; **Table 2**). Erythromycin resistance (71.1-83.5%) and levofloxacin resistance (71.7-74.6%) were elevated (**Table 2**).

RESULTS (CONTINUED)

- For CA-MRSA and HA-MRSA in 2010 and 2014 susceptibility to daptomycin, linezolid, tigecycline, trimethoprim-sulfamethoxazole, and vancomycin was high (**Table 2**). Levofloxacin resistance ranged from 66.2-71.9% for CA-MRSA and 77.3-80.5% for HA-MRSA and erythromycin resistance from (70.9-84.7%) for CA-MRSA to 71.4-79.5% for HA-MRSA (**Table 2**).

Europe compared to North American susceptibility

- In 2010, *S. aureus* from Europe and North America exhibited a high level of susceptibility to daptomycin, linezolid, tigecycline, trimethoprim-sulfamethoxazole, and vancomycin (98.4-100.0%; data not shown). Susceptibility was high for these five agents in 2010 and 2014 for both MRSA and MSSA (**Table 3**; data not shown).
- Susceptibility was reduced for MRSA compared to MSSA in both Europe and North America for clindamycin, erythromycin and levofloxacin (**Table 3**; data not shown).
- For HA-MRSA, (2010 and 2014, Europe and North America) susceptibility was high for daptomycin, linezolid, tigecycline, trimethoprim-sulfamethoxazole, and vancomycin (96.6-100.0%; **Table 3**). Susceptibility was reduced in HA-MRSA for clindamycin, erythromycin, and levofloxacin (**Table 3**). Gentamicin susceptibility was lower for the European HA-MRSA (66.5-78.4% susceptible) than for the North American isolates (94.4-95.7% susceptible; **Table 3**).
- For the CA-MRSA, susceptibility was high for daptomycin, linezolid, tigecycline, trimethoprim-sulfamethoxazole, and vancomycin (96.0-100.0%; **Table 3**). Clindamycin, erythromycin, and gentamicin susceptibilities were reduced. Gentamicin susceptibility for CA-MRSA was lower in the European isolates (82.8-87.0% susceptible) compared to North American (96.5-98.7%; **Table 3**).

Table 2. Activity of omadacycline and comparator antimicrobial agents when tested against combined North American and European MRSA, hospital-acquired (HA) MRSA and community-acquired (CA) MRSA by year (2014 vs. 2010).

Organism group (no. tested)/ agent	2014						2010					
	CLSI[a]		EUCAST[a]		(µg/mL)		CLSI[a]		EUCAST[a]		(µg/mL)	
	%S	%R	%S	%R	$MIC_{50/90}$	MIC range	%S	%R	%S	%R	$MIC_{50/90}$	MIC range
MRSA			(402)						(3,258)			
Omadacycline	-	-	-	-	0.12/0.12	0.03 — 1	-	-	-	-	0.12/0.25	0.03 — 4
Tigecycline[b]	100.0	-	100.0	0.0	0.06/0.12	≤0.015 — 0.25	>99.9	-	>99.9	<0.1	0.12/025	≤0.03 — 1
Doxycycline	95.3	1.0	93.0	5.2	0.12/1	≤0.06 — >8	97.5	0.5	94.7	4.3	0.12/0.5	≤0.06 — >8
Tetracycline	89.1	10.2	88.3	11.7	0.12/16	≤0.03 — >16	92.6	6.8	89.4	7.6	≤0.25/2	≤0.25 — >8
Clindamycin	69.7	30.1	69.2	30.3	≤0.25/>2	≤0.25 — >2	69.5	30.4	69.0	30.5	≤0.25/>2	≤0.25 — >2
Daptomycin	99.8	-	99.8	0.2	0.25/0.5	0.12 — 2	99.9	-	99.9	0.1	0.25/0.5	≤0.06 — 2
Erythromycin	25.1	71.1	25.6	73.6	>16>16	≤0.12 — >16	15.7	83.1	15.7	83.5	>4/>4	≤0.25 — >4
Gentamicin	88.9	10.9	88.3	11.7	≤1/>8	≤1 — >8	92.0	7.8	91.2	8.8	≤1/≤1	≤1 — >8
Levofloxacin	23.9	74.6	23.9	74.6	>4/>4	≤0.12 — >4	26.0	71.7	26.0	71.7	>4/>4	≤0.5 — >4
Linezolid	100.0	0.0	100.0	0.0	1/1	≤0.12 — 2	>99.9	<0.1	>99.9	<0.1	1/1	≤0.12 — 8
TMP-SMX[c]	97.5	2.5	97.5	2.2	≤0.5/≤0.5	≤0.5 — >4	97.9	2.1	97.9	2.1	≤0.5/≤0.5	≤0.5 — >4
Vancomycin	100.0	0.0	100.0	0.0	1/1	0.25 — 2	100.0	0.0	100.0	0.0	1/1	≤0.12 — 2
HA-MRSA			(203)						(876)			
Omadacycline	-	-	-	-	0.12/0.12	0.03 — 1	-	-	-	-	0.12/0.5	0.03 — 4
Tigecycline[b]	100.0	-	100.0	0.0	0.06/0.12	≤0.015 — 0.25	100.0	-	100.0	0.0	0.12/0.25	≤0.03 — 0.5
Doxycycline	93.6	1.5	92.1	6.4	0.12/1	≤0.06 — >8	95.3	1.6	89.6	8.9	0.12/2	≤0.06 — >8
Tetracycline	87.7	11.8	86.7	13.3	0.12/16	≤0.03 — >16	87.3	12.1	82.3	12.8	≤0.25/>8	≤0.25 — >8
Clindamycin	62.6	36.9	62.1	37.4	≤0.25/>2	≤0.25 — >2	62.2	37.8	61.9	37.8	≤0.25/>2	≤0.25 — >2
Daptomycin	100.0	-	100.0	0.0	0.25/0.5	0.12 — 1	99.9	-	99.9	0.1	0.25/0.5	0.12 — 2
Erythromycin	24.6	71.4	25.1	73.9	>16/>16	≤0.12 — >16	19.5	78.8	19.5	79.5	>4/>4	≤0.25 — >4
Gentamicin	85.4	14.0	84.2	15.8	≤1/>8	≤1 — >8	83.1	16.6	82.3	17.7	≤1/>8	≤1 — >8
Levofloxacin	20.7	77.3	20.7	77.3	>4/>4	≤0.12 — >4	16.4	80.5	16.4	80.5	>4/>4	≤0.5 — >4
Linezolid	100.0	0.0	100.0	0.0	1/1	≤0.12 — 2	99.9	0.1	99.9	0.1	1/1	0.25 — 8
TMP-SMX[c]	97.5	2.5	97.5	2.0	≤0.5/≤0.5	≤0.5 — >4	97.1	2.9	97.1	2.9	≤0.5/≤0.5	≤0.5 — >4
Vancomycin	100.0	0.0	100.0	0.0	1/1	0.25 — 2	100.0	0.0	100.0	0.0	1/1	≤0.12 — 2
CA-MRSA			(199)						(1694)			
Omadacycline	-	-	-	-	0.06/0.12	0.03 — 1	-	-	-	-	0.12/0.25	0.03 — 4
Tigecycline[b]	100.0	-	100.0	0.0	0.06/0.12	0.03 — 0.25	100.0	-	100.0	0.0	0.12/0.25	≤0.03 — 0.5
Doxycycline	97.0	0.5	94.0	4.0	0.12/0.5	≤0.06 — >8	98.6	0.1	94.0	2.3	0.12/0.25	≤0.06 — >8
Tetracycline	90.5	8.5	89.9	10.1	0.12/4	≤0.03 — >16	94.4	4.8	89.9	5.8	≤0.25/0.5	≤0.25 — >8
Clindamycin	76.9	23.1	76.4	23.1	≤0.25/>2	≤0.25 — >2	73.9	25.9	76.4	26.1	≤0.25/>2	≤0.25 — >2
Daptomycin	99.5	-	99.5	0.5	0.25/0.5	0.12 — 2	99.9	-	99.5	0.1	0.25/0.5	≤0.06 — 2
Erythromycin	25.6	70.9	26.1	73.4	>16/>16	≤0.12 — >16	14.6	84.4	26.1	84.7	>4>4	≤0.25 — >4
Gentamicin	92.2	7.8	92.2	7.8	≤1/≤1	≤1 — >8	95.2	4.5	92.2	5.4	≤1/≤1	≤1 — >8
Levofloxacin	27.1	71.9	27.1	71.9	>4/>4	≤0.12 — >4	31.8	66.2	27.1	66.2	4/>4	≤0.5 — >4
Linezolid	100.0	0.0	100.0	0.0	1/1	0.25 — 2	100.0	0.0	100.0	0.0	1/1	≤0.12 — 2
TMP-SMX[c]	97.5	2.5	97.5	2.5	≤0.5/≤0.5	≤0.5 — >4	98.3	1.7	97.5	1.7	≤0.5/≤0.5	≤0.5 — >4
Vancomycin	100.0	0.0	100.0	0.0	1/1	0.25 — 2	100.0	0.0	100.0	0.0	1/1	0.25 — 2

a. Criteria as published by CLSI [2015] and EUCAST [2015].
b. Tigecycline breakpoint from FDA Package Insert (revised 12/2014) used as no CLSI breakpoint is available.
c. TMP-SMX = Trimethoprim-sulfamethoxazole.

Table 1. Cumulative frequency distribution of omadacycline MIC results for *S. aureus* for Europe (EU) and North America (NA).

Organism/region	Year	No. of Isolates	MIC in µg/mL (cumulative %): ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	MIC_{50}	MIC_{90}
S. aureus													
NA + EU	2014	502	--	11 (2.2)	207 (43.4)	253 (93.8)	9 (95.6)	10 (97.6)	12 (100.0)	--	--	0.12	0.12
NA + EU	2010	7740	2 (0.1)	41 (0.6)	589 (8.2)	4671 (68.5)	1943 (93.6)	349 (98.1)	109 (99.5)	32 (99.9)	4 (100.0)	0.12	0.25
NA	2014	250	--	2 (0.8)	125 (50.8)	102(91.6)	3 (92.8)	7 (95.6)	11 (100.0)	--	--	0.06	0.12
NA	2010	4881	--	20 (0.4)	346 (7.5)	2919 (67.3)	1247 (92.8)	215 (97.3)	101 (99.3)	29 (99.9)	4 (100.0)	0.12	0.25
EU	2014	252	--	9 (3.6)	82 (36.1)	151 (96.0)	6 (98.4)	3 (99.6)	1 (100.0)			0.12	0.12
EU	2010	2859	2 (0.1)	21 (0.8)	243 (9.3)	1752 (70.6)	696 (94.9)	134 (99.6)	8 (99.9)	3 (100.0)	--	0.12	0.25
MSSA													
NA+EU	2014	100	--	1 (1.0)	30 (31.0)	67 (98.0)	1 (99.0)	1 (100.0)	--	--	--	0.12	0.12
NA+EU	2010	4482	2 (0.1)	29 (0.7)	382 (9.2)	2790 (71.5)	1089 (95.8)	172 (99.6)	14 (99.9)	4 (100.0)	--	0.12	0.25
NA	2014	50	--	--	17 (34.0)	32 (98.0)	1 (100.0)	--	--	--	--	0.12	0.12
NA	2010	2373	--	14 (0.6)	178 (8.1)	1457 (69.5)	628 (96.0)	82 (99.4)	11 (99.9)	3 (100.0)	--	0.12	0.25
EU	2014	50	--	1 (2.0)	13 (28.0)	35 (98.0)	0 (98.0)	1 (100.0)	--	--	--	0.12	0.12
EU	2010	2109	2 (0.1)	15 (0.8)	204 (10.5)	1333 (73.7)	461 (95.5)	90 (99.8)	3 (>99.9)	1 (100.0)	--	0.12	0.25
MRSA													
NA+EU	2014	402	--	10 (2.5)	177 (46.5)	186 (92.8)	8 (94.8)	9 (97.0)	12 (100.0)	--	--	0.12	0.12
NA+EU	2010	3258	--	12 (0.4)	207 (6.7)	1881 (64.5)	854 (90.7)	177 (96.1)	95 (99.0)	28 (99.9)	4 (100.0)	0.12	0.25
NA	2014	200	--	2 (1.0)	108 (55.0)	70 (90.0)	2 (91.0)	7 (94.5)	11 (100.0)	--	--	0.06	0.12
NA	2010	2508	--	6 (0.2)	168 (6.9)	1462 (65.2)	619 (89.9)	133 (95.2)	90 (98.8)	26 (99.8)	4 (100.0)	0.12	0.5
EU	2014	202	--	8 (4.0)	69 (38.1)	116 (95.5)	6 (98.5)	2 (99.5)	1 (100.0)	--	--	0.12	0.12
EU	2010	750	--	6 (0.8)	39 (6.0)	419 (61.9)	235 (93.2)	44 (99.1)	5 (99.7)	2 (100.0)	--	0.12	0.25
Hospital-acquired MRSA													
NA+EU	2014	203	--	5 (2.5)	80 (41.9)	99 (90.6)	4 (92.6)	8 (96.6)	7 (100.0)	--	--	0.12	0.12
NA+EU	2010	876	--	2 (0.2)	41 (4.9)	488 (60.6)	238 (87.8)	56 (94.2)	40 (98.7)	10 (99.9)	1 (100.0)	0.12	0.5
NA	2014	101	--	--	45 (44.6)	44 (88.1)	0 (88.1)	6 (94.1)	6 (100.0)	--	--	0.12	0.5
NA	2010	497	--	--	28 (5.6)	280 (62.0)	114 (84.9)	29 (90.7)	36 (98.0)	9 (99.8)	1 (100.0)	0.12	0.5
EU	2014	102	--	5 (4.9)	35 (39.2)	55 (93.1)	4 (97.1)	2 (99.0)	1 (100.0)	--	--	0.12	0.12
EU	2010	379	--	2 (0.5)	13 (4.0)	208 (58.8)	124 (91.6)	27 (98.7)	4 (99.7)	1 (100.0)	--	0.12	0.25
Community-acquired MRSA													
NA+EU	2014	199	--	5 (2.5)	97 (51.3)	87 (95.0)	4 (97.0)	1 (97.5)	5 (100.0)	--	--	0.06	0.12
NA+EU	2010	1694	--	7 (0.4)	132 (8.2)	994 (66.9)	432 (92.4)	90 (97.7)	28 (99.4)	10 (99.9)	1 (100.0)	0.12	0.25
NA	2014	99	--	2 (2.0)	63 (65.7)	26 (91.9)	2 (93.9)	1 (94.9)	5 (100.0)	--	--	0.06	0.12
NA	2010	1461	--	4 (0.3)	110 (7.8)	869 (67.3)	362 (92.1)	78 (97.4)	27 (99.2)	10 (99.9)	1 (100.0)	0.12	0.25
EU	2014	100	--	3 (3.0)	34 (37.0)	61 (98.0)	2 (100.0)	--	--	--	--	0.12	0.12
EU	2010	233	--	3 (1.3)	22 (10.7)	125 (64.4)	70 (94.4)	12 (99.6)	1 (100.0)	--	--	0.12	0.25

Table 3. Activity of omadacycline and comparator antimicrobial agents when tested against North American and European MRSA, hospital-acquired MRSA and community-acquired MRSA by year (2014 vs. 2010).

Organism group (no. tested)/agent	North America 2014				North America 2010				Europe 2014				Europe 2010			
	CLSI[a] %S	EUCAST[a] %S	$MIC_{50/90}$	MIC Range	CLSI[a] %S	EUCAST[a] %S	$MIC_{50/90}$	MIC Range	CLSI[a] %S	EUCAST[a] %S	$MIC_{50/90}$	MIC Range	CLSI[a] %S	EUCAST[a] %S	$MIC_{50/90}$	MIC Range
MRSA		(200)				(2,508)				(202)				(750)		
Omadacycline	-	-	0.06/0.12	0.03 — 1	-	-	0.12/0.5	0.03 — 4	-	-	0.12/0.12	0.03 — 1	-	-	0.12/4	0.03 — 2
Tigecycline[b]	100.0	100.0	0.06/0.12	0.03 — 0.25	>99.9	>99.9	0.12/0.25	≤0.03 — 1	100.0	100.0	0.06/0.12	≤0.015 — 0.25	100.0	100.0	≤0.25/>8	≤0.03 — 0.5
Doxycycline	97.5	97.0	0.12/0.5	≤0.06 — >8	98.5	97.0	0.12/0.5	≤0.06 — >8	93.1	89.1	0.12/2	≤0.06 — >8	94.4	87.1	≤0.25/>2	≤0.06 — >8
Tetracycline	95.5	94.5	0.12/1	≤0.03 — >16	95.2	91.2	≤0.25/1	≤0.25 — >8	82.7	82.2	0.12/16	≤0.03 — >16	84.0	83.3	0.25/0.5	≤0.25 — >8
Clindamycin	66.0	66.0	≤0.25/>2	≤0.25 — >2	69.5	68.9	≤0.25/>2	≤0.25 — >2	73.3	72.3	≤0.25/>2	≤0.25 — >2	69.6	69.5	>4/>4	≤0.25 — >2
Daptomycin	99.5	99.5	0.25/0.5	0.12 — 2	99.9	99.9	0.25/0.5	≤0.06 — 2	100.0	100.0	0.25/0.5	0.12 — 1	99.9	99.9	≤1/>8	0.12 — 2
Erythromycin	10.5	11.5	>16/>16	0.25 — >16	10.5	10.5	>4/>4	≤0.25 — >4	39.6	39.6	>16/>16	≤0.12 — >16	33.1	33.1	>4/>4	≤0.25 — >4
Gentamicin	97.3	97.3	≤1/≤1	≤1 — >8	96.1	95.5	≤1/≤1	≤1 — >8	82.7	81.7	≤1/>8	≤1 — >8	78.3	76.9	1/1	≤1 — >8
Levofloxacin	28.0	28.0	4/>4	≤0.12 — >4	30.4	30.4	4/>4	≤0.5 — >4	19.8	19.8	>4/>4	≤0.12 — >4	11.3	11.3	≤0.5/≤0.5	≤0.5 — >4
Linezolid	100.0	100.0	1/1	0.5 — 1	>99.9	>99.9	1/1	≤0.12 — 8	100.0	100.0	1/1	≤0.12 — 2	100.0	100.0	1/1	0.25 — 2
TMP-SMX[c]	96.5	96.5	≤0.5/≤0.5	≤0.5 — >4	97.8	97.8	≤0.5/≤0.5	≤0.5 — >4	98.5	98.5	≤0.5/≤0.5	≤0.5 — >4	98.3	98.3	0.12/0.25	≤0.5 — >4
Vancomycin	100.0	100.0	1/1	0.25 — 2	100.0	100.0	1/1	0.25 — 2	100.0	100.0	1/1	0.25 — 2	100.0	100.0	0.12/0.25	≤0.12 — 2
Hospital-acquired MRSA		(101)				(497)				(102)				(379)		
Omadacycline	-	-	0.12/0.5	0.06 — 1	-	-	0.12/0.5	0.06 — 4	-	-	0.12/0.12	0.03 — 1	-	-	0.12/0.25	0.03 — 2
Tigecycline[b]	100.0	100.0	0.06/0.12	0.03 — 0.25	100.0	100.0	0.12/0.25	≤0.03 — 0.5	100.0	100.0	0.06/0.12	≤0.015 — 0.25	100.0	100.0	0.12/0.25	≤0.03 — 0.5
Doxycycline	97.0	97.0	0.12/0.5	≤0.06 — 8	98.2	95.8	0.12/1	≤0.06 — >8	90.2	87.3	0.12/2	≤0.06 — >8	91.6	81.5	0.12/4	≤0.06 — >8
Tetracycline	96.0	95.0	0.12/1	0.06 — >16	94.0	86.1	≤0.25/2	≤0.25 — >8	79.4	78.4	0.12/>16	≤0.03 — >16	78.6	77.3	≤0.25/>8	≤0.25 — >8
Clindamycin	55.4	55.4	≤0.25/>2	≤0.25 — >2	61.0	60.6	≤0.25/>2	≤0.25 — >2	69.6	68.6	≤0.25/>2	≤0.25 — >2	63.9	63.6	≤0.25/>2	≤0.25 — >2
Daptomycin	100.0	100.0	0.250.5	0.12 — 1	100.0	100.0	0.25/0.5	0.12 — 1	100.0	100.0	0.25/0.5	0.12 — 1	99.7	99.7	0.25/0.5	0.12 — 2
Erythromycin	8.9	9.9	>16/>16	0.25 — >16	11.5	11.5	>4/>4	≤0.25 — >4	40.2	40.2	>16>16	≤0.12 — >16	30.1	30.1	>4/>4	≤0.25 — >4
Gentamicin	95.7	95.7	≤1/≤1	≤1 — >8	94.8	94.4	≤1/≤1	≤1 — >8	78.4	76.5	≤1/>8	≤1 — >8	67.8	66.5	≤1/>8	≤1 — >8
Levofloxacin	21.8	21.8	>4/>4	≤0.12 — >4	20.9	20.9	>4/>4	≤0.5 — >4	19.6	19.6	>4/>4	≤0.12 — >4	10.6	10.6	>4/>4	≤0.5 — >4
Linezolid	100.0	100.0	1/1	0.5 — 1	99.8	99.8	1/1	0.25 — 8	100.0	100.0	1/1	≤0.12 — 2	100.0	100.0	1/1	0.25 — 2
TMP-SMX[c]	97.0	97.0	≤0.5/≤0.5	≤0.5 — >4	96.6	96.6	≤0.5/≤0.5	≤0.5 — >4	98.0	98.0	≤0.5/≤0.5	≤0.5 — >4	97.9	97.9	≤0.5/≤0.5	≤0.5 — >4
Vancomycin	100.0	0.0	1/1	0.5 — 2	100.0	100.0	1/1	0.5 — 2	100.0	100.0	1/1	0.25 — 2	100.0	100.0	1/1	≤0.12 — 2
Community-acquired MRSA		(99)				(1,461)				(100)				(233)		
Omadacycline	-	-	0.06/0.12	0.03 — 1	-	-	0.12/0.25	0.03 — 4	-	-	0.12/0.12	0.12	-	-	0.12/0.25	0.03 — 1
Tigecycline[b]	100.0	100.0	0.06/0.12	0.03 — 0.12	100.0	100.0	0.12/0.25	≤0.03 — 0.5	100.0	100.0	0.06/0.12	0.12	100.0	100.0	0.12/0.25	≤0.03 — 0.5
Doxycycline	98.0	97.0	≤0.06/0.5	≤0.06 — >8	99.0	97.9	0.12/0.25	≤0.06 — >8	96.0	91.0	0.12/1	1	96.1	90.1	0.12/1	≤0.06 — >8
Tetracycline	94.9	93.9	0.12/1	≤0.03 — >16	95.8	93.2	≤0.25/0.5	≤0.25 — >8	86.0	86.0	0.12/16	16	85.8	85.8	≤0.25/>8	≤0.25 — >8
Clindamycin	76.8	76.8	≤0.25/>2	≤0.25 — >2	74.4	73.9	≤0.25/>2	≤0.25 — >2	77.0	76.0	≤0.25/>2	>2	70.8	70.8	≤0.25/>2	≤0.25 — >2
Daptomycin	99.0	99.0	0.25/0.5	0.12 — 2	99.9	99.9	0.25/0.5	≤0.06 — 2	100.0	100.0	0.25/0.5	0.5	100.0	100.0	0.25/0.5	0.12 — 1
Erythromycin	12.1	13.1	>16/>16	0.25 — >16	11.3	11.3	>4/>4	≤0.25 — >4	39.0	39.0	>16/>16	>16	35.6	35.6	>4/>4	≤0.25 — >4
Gentamicin	98.7	98.7	≤1/≤1	≤1 — >8	97.0	96.5	≤1/≤1	≤1 — >8	87.0	87.0	≤1/>8	>8	84.1	82.8	≤1/>8	≤1 — >8
Levofloxacin	34.3	34.3	4/>4	≤0.12 — >4	35.0	35.0	4/>4	≤0.5 — >4	20.0	20.0	>4/>4	>4	11.6	11.6	>4/>4	≤0.5 — >4
Linezolid	100.0	100.0	1/1	0.5 — 1	100.0	100.0	1/1	≤0.12 — 2	100.0	100.0	1/1	1	100.0	100.0	1/1	0.25 — 2
TMP-SMX[c]	96.0	96.0	≤0.5/≤0.5	≤0.5 — >4	98.4	98.4	≤0.5/≤0.5	≤0.5 — >4	99.0	99.0	≤0.5/≤0.5	≤0.5	97.9	97.9	≤0.5/≤0.5	≤0.5 — >4
Vancomycin	100.0	100.0	1/1	0.25 — 2	100.0	100.0	1/1	0.25 — 2	100.0	100.0	1/1	1	100.0	100.0	1/1	0.25 — 2

a. Criteria as published by CLSI [2015] and EUCAST [2015].
b. Tigecycline breakpoint from FDA Package Insert (revised 12/2014) used as no CLSI breakpoint is available.
c. TMP-SMX = Trimethoprim-sulfamethoxazole.

CONCLUSIONS

- The potent in vitro activity of omadacycline remains unchanged between 2010 and 2014, and was similar for North American and European isolates including MRSA (CA-MRSA or HA-MRSA).
- Resistance to clindamycin, erythromycin, and levofloxacin was higher in MRSA than in MSSA.
- Susceptibility for a number of agents tended to be lower in HA-MRSA compared to CA-MRSA.
- The potent activity of omadacycline against *S. aureus* indicates that omadacycline merits further study in serious community-acquired infections, such as ABSSSI and CABP, where MDR may be a concern.

ACKNOWLEDGEMENT

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

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