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In vitro Activity of Omadacycline and Comparators against Gram-Positive and -Negative Clinical Isolates (including resistant organism subsets) Collected in 2017 from Patients in European Medical Centres: SENTRY Surveillance Program Results

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INTRODUCTION

- Omadacycline is an aminomethylcycline antibacterial for treating acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP) that recently completed Phase 3 clinical trials (oral and intravenous formulations)
- A new drug application was submitted February 2, 2018, to the US Food and Drug Administration for oral and intravenous omadacycline to treat ABSSSI and CABP
- Omadacycline demonstrates potent activity against a broad range of gram-positive (staphylococci, streptococci, and enterococci) and many Gram-negatives commonly associated with ABSSSI, CABP, and urinary tract infections (UTI)
- Omadacycline is highly active against bacterial clinical isolates expressing common tetracycline-, penicillin/oxacillin-, fluoroquinolone-, and macrolide-resistance mechanisms that include *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), enterococci, streptococci (*Streptococcus pneumoniae*, viridans group, and β-haemolytic streptococci), and *Enterobacteriaceae*
- The *in vitro* susceptibility results for omadacycline and comparator agents against 7,000 clinical isolates from patients in European medical centres (2017 SENTRY Surveillance Program) are presented

MATERIALS AND METHODS

- A total of 7,000 (nonduplicate) gram-positive and gram-negative bacterial clinical isolates were collected from patients with multiple infection types in 38 medical centres in 18 European countries during 2017
- Organisms tested included 1,326 *Staphylococcus aureus*, 200 CoNS, 301 β-haemolytic streptococci, 507 *Streptococcus pneumoniae*, 65 viridans group streptococci, 210 *Enterococcus faecalis,* 126 *E. faecium*, 2,959 *Enterobacteriaceae*, 172 *Acinetobacter baumannii*, 47 *Stenotrophomonas maltophilia*, 256 *Haemophilus influenzae*, and 137 *Moraxella catarrhalis*
- Only 1 isolate per patient/infection episode was included
- Bacterial isolates were initially identified by the submitting laboratories and confirmed by JMI Laboratories using a matrix-assisted laser desorption/ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany)
- Susceptibility testing was performed according to CLSI (M07, 2018) reference broth microdilution methodology and results were interpreted using EUCAST (Version 8.0, 2018) breakpoint interpretive criteria
- CLSI quality control (QC) reference strains (M100, 2018) were tested concurrently and included *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922 and ATCC 35218, *Klebsiella pneumoniae* ATCC 700603, and *Pseudomonas aeruginosa* ATCC 27853

RESULTS

- Cumulative percent inhibition data for omadacycline against staphylococci, streptococci, enterococci, *Enterobacteriaceae*, nonfermenters, and fastidious organism groups are presented in Table 1
- Site of infection incidence for the omadacycline 2017 European surveillance program is presented in Figure 1
- Omadacycline demonstrated potent *in vitro* activity against *S. aureus* isolates ($MIC_{50/90}$ 0.12/0.25 mg/L) and retained a high level of activity against isolates displaying tetracycline (doxycycline and tetracycline), fluoroquinolone (levofloxacin), macrolide (erythromycin), lincosamide (clindamycin), and/or oxacillin resistance phenotypes
  - Corresponding doxycycline, tetracycline, levofloxacin, erythromycin, clindamycin, and oxacillin resistance rates were 2.5%, 6.9%, 18.3%, 23.5%, 6.3%, and 22.1%, respectively (Table 2)
- 22.1% of *S. aureus* were methicillin resistant
- Against MRSA, omadacycline ($MIC_{50/90}$ 0.12/0.25 mg/L; highest MIC 1 mg/L) was comparable in activity to tigecycline ($MIC_{50/90}$ 0.12/0.25 mg/L, highest MIC 0.5 mg/L) and ≥8-fold more potent than doxycycline and tetracycline (MIC_{90} 2 and >8 mg/L, respectively; Table 2)
- Omadacycline and tigecycline were both active against CoNS and MRCoNS isolates with MIC_{90} values of 1 mg/L and 0.25 mg/L, respectively (Table 2)
  - Doxycycline and tetracycline were 2- and >8-fold less active than omadacycline against MRCoNS (Table 2)
- Doxycycline, tetracycline, levofloxacin, erythromycin, and clindamycin-resistance rates in CoNS were 6.0%, 12.0%, 50.0%, 56.0%, and 25.0%, respectively, and increased to 8.6%, 17.2%, 74.2%, 71.1%, and 36.7%, respectively, in MRCoNS (Table 2)

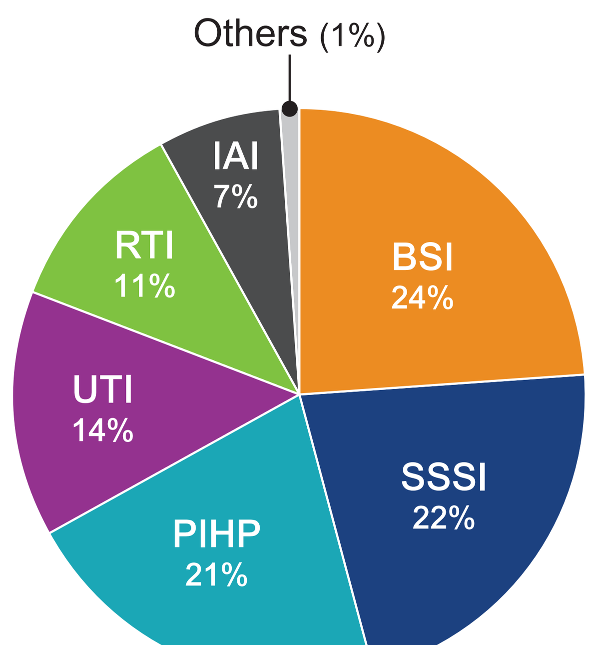
RESULTS (CONT.)

- β-haemolytic streptococci (*Streptococcus agalactiae*, *S. dysgalactiae*, and *S. pyogenes*) were very susceptible to omadacycline ($MIC_{50/90}$ 0.12/0.12 mg/L, highest MIC 0.5 mg/L)
  - These isolates were very susceptible (100.0%) to all agents tested except for tetracycline (56.1% susceptible), clindamycin (89.7% susceptible), erythromycin (78.7% susceptible), and levofloxacin (98.3% susceptible; Table 2)
- *S. pneumoniae* (including penicillin-resistant strains) and viridans group streptococci were highly susceptible to omadacycline ($MIC_{50/90}$ 0.06/0.12 mg/L; Tables 1-2), whereas 21.9% of *S. pneumoniae* isolates were resistant to tetracycline ($MIC_{50/90}$ 0.5/>4 mg/L; Table 2) and 11.2% were nonsusceptible to ceftriaxone
- Omadacycline was 2-fold more active against *E. faecium* ($MIC_{50/90}$ 0.06/0.12 mg/L) compared to *E. faecalis* ($MIC_{50/90}$ 0.12/0.25 mg/L), and its activity was unchanged against *E. faecium* isolates displaying resistance to vancomycin (Table 1)
- Omadacycline inhibited 97.3% and 74.7% of ESBL-phenotype *E. coli* and *K. pneumoniae* isolates at ≤4 mg/L, respectively, where susceptibility to comparator agents was low (Tables 1-2)
- 72.7% of *A. baumannii* isolates were inhibited by ≤4 mg/L of omadacycline (Table 1), whereas susceptibility to comparator agents ranged from 16.9% for levofloxacin to 42.4% for trimethoprim-sulfamethoxazole (Table 2)
- Isolates of *H. influenzae* (omadacycline $MIC_{50/90}$ 0.5/1 mg/L) and *M. catarrhalis* (omadacycline $MIC_{50/90}$ ≤0.12/0.25 mg/L) were susceptible to omadacycline regardless of β-lactamase production (Table 1)

CONCLUSIONS

- Omadacycline was active against *S. aureus* ($MIC_{50/90}$ 0.12/0.25 mg/L) and CoNS ($MIC_{50/90}$ 0.12/1 mg/L), including MRSA and MRCoNS isolates from Europe, and strains displaying resistance to tetracyclines (doxycycline and/or tetracycline), fluoroquinolones (levofloxacin), macrolides (erythromycin), and lincosamides (clindamycin)
- Streptococci, including *S. pneumoniae*, viridans group streptococci, and β-haemolytic streptococci, were inhibited by low levels of omadacycline (MIC_{90} values of 0.12 mg/L)
- Omadacycline was highly active against drug-resistant *S. pneumoniae* (21.9% tetracycline-resistant and 11.2% ceftriaxone-nonsusceptible) and β-haemolytic streptococci (43.2% tetracycline-resistant) isolates
- Omadacycline exhibited potent activity against *E. faecalis* ($MIC_{50/90}$ 0.12/0.25 mg/L) and vancomycin-susceptible and -nonsusceptible isolates of *E. faecium* ($MIC_{50/90}$ 0.06/0.12 mg/L), whereas tetracycline demonstrated little utility against *E. faecalis* and *E. faecium* isolates (MIC_{90} values >16 mg/L)

Figure 1 Site of infection incidence for the omadacycline 2017 European surveillance program



BSI, bloodstream infections; RTI, respiratory tract infections caused by *S. pneumoniae*, *H. influenzae*, *H. parainfluenzae*, or *M. catarrhalis*; PIHP, pneumonia in hospitalized patients; IAI, intra-abdominal infections; SSSI, skin and skin structure infections; UTI, urinary tract infections

Table 1 Antimicrobial activity of omadacycline against clinical isolates from patients in European medical centres during 2017

Organism/organism group (no. of isolates)	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	> [a]	MIC_{50}	MIC_{90}
	No. of isolates at MIC (mg/L; cumulative %)														
Staphylococcus aureus (1,326)	0 0.0	1 0.1	89 6.8	1,041 85.3	180 98.9	11 99.7	4 100.0							0.12	**0.25**
MSSA (1,033)	0 0.0	1 0.1	69 6.8	841 88.2	116 99.4	5 99.9	1 100.0							0.12	**0.25**
MRSA (293)		0 0.0	20 6.8	200 75.1	64 96.9	6 99.0	3 100.0							0.12	**0.25**
Coagulase-negative staphylococci[b] (200)	0 0.0	4 2.0	49 26.5	61 57.0	21 67.5	42 88.5	22 99.5	1 100.0						0.12	**1**
MSCoNS (72)	0 0.0	2 2.8	25 37.5	25 72.2	3 76.4	10 90.3	7 100.0							0.12	**0.5**
MRCoNS (128)	0 0.0	2 1.6	24 20.3	36 48.4	18 62.5	32 87.5	15 99.2	1 100.0						0.25	**1**
β-haemolytic streptococci[c] (301)		0 0.0	125 41.5	147 90.4	25 98.7	4 100.0								0.12	**0.12**
Streptococcus pyogenes (152)		0 0.0	96 63.2	53 98.0	3 100.0									0.06	**0.12**
Streptococcus agalactiae (100)		0 0.0	27 27.0	62 89.0	11 100.0									0.12	**0.25**
Streptococcus dysgalactiae (49)		0 0.0	2 4.1	32 69.4	11 91.8	4 100.0								0.12	**0.25**
Streptococcus pneumoniae (507)	3 0.6	70 14.4	325 78.5	102 98.6	7 100.0									0.06	**0.12**
Penicillin-susceptible oral (≤0.06 mg/L) (365)	2 0.5	58 16.4	243 83.0	57 98.6	5 100.0									0.06	**0.12**
Penicillin-intermediate oral (>0.06 mg/L and ≤1 mg/L) (85)	1 1.2	11 14.1	48 70.6	24 98.8	1 100.0									0.06	**0.12**
Penicillin-resistant oral (>1 mg/L) (57)	0 0.0	1 1.8	34 61.4	21 98.2	1 100.0									0.06	**0.12**
Viridans group streptococci[d] (65)	1 1.5	14 23.1	33 73.8	12 92.3	5 100.0									0.06	**0.12**
Enterococcus faecalis (210)	0 0.0	15 7.1	64 37.6	89 80.0	35 96.7	5 99.0	0 99.0	2 100.0						0.12	**0.25**
Enterococcus faecium (126)	0 0.0	10 7.9	70 63.5	38 93.7	7 99.2	1 100.0								0.06	**0.12**
Vancomycin-nonsusceptible (>4 mg/L) (18)	0 0.0	2 11.1	13 83.3	3 100.0										0.06	**0.12**

Organism/organism group (no. of isolates)	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	> [a]	MIC_{50}	MIC_{90}
	No. of isolates at MIC (mg/L; cumulative %)														
Enterobacteriaceae[e] (2,959)				0 0.0	56 1.9	726 26.4	886 56.4	623 77.4	292 87.3	164 92.8	123 97.0	68 99.3	21 100.0	1	**8**
Escherichia coli (1,371)				0 0.0	51 3.7	656 51.6	397 80.5	200 95.1	53 99.0	7 99.5	6 99.9	1 100.0		0.5	**2**
Non-ESBL-phenotype (1,070)				0 0.0	42 3.9	573 57.5	290 84.6	130 96.7	29 99.4	3 99.7	3 100.0			0.5	**2**
ESBL-phenotype (301)				0 0.0	9 3.0	83 30.6	107 66.1	70 89.4	24 97.3	4 98.7	3 99.7	1 100.0		1	**4**
Klebsiella pneumoniae (646)				0 0.0	1 0.2	24 3.9	233 39.9	174 66.9	107 83.4	71 94.4	24 98.1	7 99.2	5 100.0	2	**8**
Non-ESBL-phenotype (326)				0 0.0	1 0.3	14 4.6	168 56.1	94 85.0	23 92.0	19 97.9	7 100.0			1	**4**
ESBL-phenotype (320)					0 0.0	10 3.1	65 23.4	80 48.4	84 74.7	52 90.9	17 96.2	7 98.4	5 100.0	4	**8**
Enterobacter cloacae species complex[f] (204)				0 0.0	2 1.0	1 1.5	48 25.0	133 90.2	11 95.6	5 98.0	3 99.5	1 100.0		2	**2**
Acinetobacter baumannii (172)			0 0.0	5 2.9	19 14.0	9 19.2	7 23.3	33 42.4	52 72.7	38 94.8	7 98.8	2 100.0		4	**8**
Stenotrophomonas maltophilia (47)						0 0.0	2 4.3	12 29.8	22 76.6	5 87.2	5 97.9	1 100.0		4	**16**
Haemophilus influenzae (256)				0 0.0	7 2.7	151 61.7	89 96.5	8 99.6	1 100.0					0.5	**1**
β-lactamase-positive (59)				0 0.0	1 1.7	34 59.3	22 96.6	2 100.0						0.5	**1**
β-lactamase-negative (197)				0 0.0	6 3.0	117 62.4	67 96.4	6 99.5	1 100.0					0.5	**1**
Moraxella catarrhalis (137)				101 73.7	36 100.0									≤0.12	**0.25**

[a] Greater than the highest dilution tested.
[b] Organisms include: *Staphylococcus capitis* (15), *S. epidermidis* (108), *S. haemolyticus* (32), *S. hominis* (19), *S. lugdunensis* (16), *S. pettenkoferi* (1), *S. saprophyticus* (3), *S. schleiferi* (1), *S. simulans* (2), *S. warneri* (3).
[c] Organisms include: *Streptococcus agalactiae* (100), *S. dysgalactiae* (49), *S. pyogenes* (152).
[d] Organisms include: *Streptococcus anginosus* (15), *S. anginosus* group (13), *S. bovis* group (1), *S. constellatus* (3), *S. cristatus* (1), *S. gallolyticus* (4), *S. gordonii* (1), *S. massiliensis* (1), *S. mitis* (1), *S. mitis* group (12), *S. mutans* (2), *S. oralis* (2), *S. parasanguinis* (1), *S. salivarius* group (5), *S. sanguinis* (3).
[e] Organisms include: *Citrobacter amalonaticus/farmeri* (1), *C. freundii* species complex (59), *C. koseri* (53), *Enterobacter aerogenes* (74), *E. asburiae* (5), *E. cloacae* (124), *E. cloacae* species complex (71), *E. hormaechei* (2), *E. kobei* (2), *Escherichia coli* (1,371), *E. fergusonii* (1), *E. vulneris* (1), *Hafnia alvei* (19), *Klebsiella oxytoca* (140), *K. pneumoniae* (646), *K. variicola* (1), *Lelliottia amnigena* (1), *Morganella morganii* (58), *Pantoea agglomerans* (1), *Phytobacter diazotrophicus* (1), *Pluralibacter gergoviae* (1), *Proteus hauseri* (1), *P. mirabilis* (164), *P. vulgaris* (1), *P. vulgaris* group (17), *Providencia stuartii* (13), *Raoultella ornithinolytica* (4), *Serratia liquefaciens* (8), *S. marcescens* (110), *S. rubidaea* (1), unspeciated *Pantoea* (1), unspeciated *Raoultella* (7).
[f] Organisms include: *Enterobacter asburiae* (5), *E. cloacae* (124), *E. cloacae* species complex (71), *E. hormaechei* (2), *E. kobei* (2).

Table 2 *In vitro* activity of omadacycline and comparator antimicrobials against staphylococci, streptococci, and enterococci from patients in European medical centres during 2017

Organism (no. tested) antimicrobial agent	MIC_{50}	MIC_{90}	Range	EUCAST[a] %S	%I	%R
***S. aureus* (1,326)**						
Omadacycline	0.12	0.25	0.03 to 1	—	—	—
Tigecycline	0.06	0.12	≤0.015 to 0.5	100.0		0.0
Doxycycline	0.12	0.25	≤0.06 to >8	94.6	2.9	2.5
Tetracycline	≤0.5	≤0.5	≤0.5 to >8	92.8	0.2	6.9
Oxacillin	0.5	>2	≤0.06 to >2	77.9		22.1
Levofloxacin	0.25	>4	≤0.03 to >4	81.7		18.3
Erythromycin	0.12	>8	≤0.06 to >8	75.3	1.3	23.5
Clindamycin	0.06	0.06	≤0.03 to >2	93.6	0.2	6.3
Linezolid	1	2	0.25 to 4	100.0		0.0
Daptomycin	0.25	0.25	≤0.12 to 1	100.0		0.0
Vancomycin	1	1	0.25 to 2	100.0		0.0
MRSA (293)						
Omadacycline	0.12	0.25	0.06 to 1	—	—	—
Tigecycline	0.12	0.25	0.03 to 0.5	100.0		0.0
Doxycycline	0.12	2	≤0.06 to >8	86.3	6.5	7.2
Tetracycline	≤0.5	>8	≤0.5 to >8	81.9	0.7	17.4
Levofloxacin	>4	>4	0.06 to >4	30.4		69.6
Erythromycin	4	>8	≤0.06 to >8	46.4	2.0	51.5
Clindamycin	0.06	>2	≤0.03 to >2	76.8	0.0	23.2
Linezolid	1	2	0.25 to 4	100.0		0.0
Daptomycin	0.25	0.5	≤0.12 to 1	100.0		0.0
Vancomycin	1	1	0.25 to 2	100.0		0.0
CoNS[b] (200)						
Omadacycline	0.12	1	0.03 to 2	—	—	—
Tigecycline	0.06	0.25	≤0.015 to 0.5	100.0		0.0
Doxycycline	0.12	2	≤0.06 to >8	89.0	5.0	6.0
Tetracycline	≤0.5	4	≤0.5 to >8	72.0	16.0	12.0
Oxacillin	>2	>2	≤0.06 to >2	37.5		62.5
Levofloxacin	1	>4	0.06 to >4	50.0		50.0
Erythromycin	>8	>8	≤0.06 to >8	44.0	0.0	56.0
Clindamycin	0.06	>2	≤0.03 to >2	72.5	2.5	25.0
Linezolid	1	1	0.25 to >8	98.5		1.5
Daptomycin	0.25	0.5	≤0.12 to 1	100.0		0.0
Vancomycin	2	2	≤0.12 to 4	100.0		0.0
MRCoNS[c] (128)						
Omadacycline	0.25	1	0.03 to 2	—	—	—
Tigecycline	0.12	0.25	0.03 to 0.5	100.0		0.0
Doxycycline	0.5	2	≤0.06 to >8	85.2	6.2	8.6
Tetracycline	1	>8	≤0.5 to >8	64.1	18.8	17.2
Levofloxacin	>4	>4	0.12 to >4	25.8		74.2
Erythromycin	>8	>8	≤0.06 to >8	28.9	0.0	71.1
Clindamycin	0.06	>2	≤0.03 to >2	59.4	3.9	36.7
Linezolid	1	1	0.25 to >8	97.7		2.3
Daptomycin	0.25	0.5	≤0.12 to 1	100.0		0.0
Vancomycin	2	2	≤0.12 to 4	100.0		0.0
β-haemolytic streptococci[d] (301)						
Omadacycline	0.12	0.12	0.06 to 0.5	—	—	—
Tigecycline	0.06	0.12	0.03 to 0.25	100.0	0.0	0.0
Tetracycline	0.5	>4	0.12 to >4	56.1	0.7	43.2
Levofloxacin	0.5	1	0.25 to >4	98.3		1.7
Erythromycin	0.03	16	≤0.015 to >16	78.7	1.0	20.3
Clindamycin	≤0.25	1	≤0.25 to >2	89.7		10.3
Linezolid	1	2	0.5 to 2	100.0	0.0	0.0
Daptomycin	≤0.06	0.12	≤0.06 to 0.25	100.0		0.0
Vancomycin	0.5	0.5	0.25 to 1	100.0		0.0
Penicillin	0.015	0.06	≤0.008 to 0.12	100.0		0.0
***S. pneumoniae* (507)**						
Omadacycline	0.06	0.12	≤0.015 to 0.25	—	—	—
Tigecycline	0.06	0.06	0.015 to 0.12	—	—	—
Tetracycline	0.5	>4	0.12 to >4	77.7	0.4	21.9
Ceftriaxone	0.03	1	≤0.015 to >2	88.8	10.8	0.4
Levofloxacin	1	2	0.5 to >4	97.8		2.2
Erythromycin	0.03	>16	≤0.015 to >16	76.7	0.2	23.1
Clindamycin	≤0.25	>2	≤0.25 to >2	82.2		17.8
Linezolid	1	2	0.25 to 2	100.0	0.0	0.0
Vancomycin	0.25	0.5	≤0.06 to 0.5	100.0		0.0
Azithromycin	0.06	>4	≤0.03 to >4	76.7	0.2	23.1
Penicillin	0.015	2	≤0.008 to >4	72.0 72.0	 23.7	28.0 [e] 4.3 [f]
Trimethoprim-sulfamethoxazole	0.25	>4	≤0.12 to >4	78.1	2.6	19.3
***Enterococcus* spp.[g] (347)**						
Omadacycline	0.12	0.25	0.03 to 2	—	—	—
Tigecycline	0.06	0.12	≤0.015 to 0.5	99.1	0.9	0.0
Tetracycline	>16	>16	≤0.12 to >16	—	—	—
Minocycline	8	>8	≤0.06 to >8	—	—	—
Levofloxacin	4	>4	≤0.03 to >4	50.1		49.9 [h]
Linezolid	1	2	0.25 to 4	100.0		0.0
Vancomycin	1	4	0.25 to >16	93.1		6.9
Ampicillin	1	>16	≤0.12 to >16	66.3	0.6	33.1
***Escherichia coli* ESBL-phenotype (301)**						
Omadacycline	1	4	0.25 to 32	—	—	—
Tigecycline	0.25	0.5	≤0.06 to 4	99.3	0.3	0.3
Doxycycline	8	>8	0.25 to >8	—	—	—
Tetracycline	>16	>16	1 to >16	—	—	—
Minocycline	2	16	0.25 to >32	—	—	—
Ceftriaxone	>8	>8	0.12 to >8	7.0	0.7	92.4
Piperacillin-tazobactam	4	64	1 to >128	67.8	14.0	18.3
Levofloxacin	8	>16	≤0.03 to >16	23.3	1.0	75.7
Gentamicin	1	>16	0.25 to >16	69.9	1.0	29.1
Amikacin	4	16	0.5 to >32	89.7	8.6	1.7
Aztreonam	16	>16	0.12 to >16	5.0	16.3	78.7
Cefepime	>16	>16	≤0.12 to >16	14.3	13.3	72.4
Ceftazidime	16	>32	0.25 to >32	7.6	27.9	64.5
Imipenem	≤0.12	0.25	≤0.12 to >8	98.3	1.0	0.7
Trimethoprim-sulfamethoxazole	>8	>8	≤0.5 to >8	37.7	1.3	61.0
***Klebsiella pneumoniae* ESBL-phenotype (320)**						
Omadacycline	4	8	0.5 to >32	—	—	—
Tigecycline	0.5	2	0.12 to >8	81.6	10.9	7.5
Doxycycline	>8	>8	0.25 to >8	—	—	—
Tetracycline	>16	>16	0.5 to >16	—	—	—
Minocycline	4	32	0.5 to >32	—	—	—
Ceftriaxone	>8	>8	0.12 to >8	3.1	1.6	95.3
Piperacillin-tazobactam	>128	>128	0.25 to >128	21.2	10.9	67.8
Levofloxacin	16	>16	≤0.03 to >16	17.5	6.6	75.9
Gentamicin	16	>16	≤0.12 to >16	43.8	0.9	55.3
Amikacin	4	>32	0.5 to >32	65.0	10.3	24.7
Aztreonam	>16	>16	0.12 to >16	5.0	2.5	92.5
Cefepime	>16	>16	≤0.12 to >16	2.2	4.4	93.4
Ceftazidime	>32	>32	0.5 to >32	2.2	5.3	92.5
Imipenem	0.25	>8	≤0.12 to >8	67.2	12.5	20.3
Trimethoprim-sulfamethoxazole	>8	>8	≤0.5 to >8	18.8	1.2	80.0
***Acinetobacter baumannii* (172)**						
Omadacycline	4	8	0.12 to 32	—	—	—
Tigecycline	2	8	0.12 to >8	—	—	—
Doxycycline	2	>8	≤0.06 to >8	—	—	—
Tetracycline	>16	>16	2 to >16	—	—	—
Levofloxacin	16	>16	0.06 to >16	16.9	0.0	83.1
Gentamicin	>16	>16	0.25 to >16	29.7		70.3
Amikacin	>32	>32	1 to >32	23.8	0.0	76.2
Imipenem	>8	>8	≤0.12 to >8	24.4	2.9	72.7
Trimethoprim-sulfamethoxazole	8	>8	≤0.5 to >8	42.4	7.0	50.6
***Haemophilus influenzae* (256)**						
Omadacycline	0.5	1	0.25 to 4			
Tigecycline	0.25	0.25	0.06 to 1			
Tetracycline	0.5	1	0.25 to >8	98.8	0.0	1.2
Ceftriaxone	0.004	0.015	≤0.002 to 0.03	100.0		0.0
Amoxicillin-clavulanic acid	0.5	2	≤0.06 to 4	93.4		6.6
Levofloxacin	0.015	0.03	0.008 to 0.5	99.2		0.8
Ampicillin	0.25	>8	≤0.12 to >8	71.5		28.5
Azithromycin	1	2	≤0.12 to >8	98.8		[i]
Moxifloxacin	0.03	0.03	≤0.008 to 1	99.2		0.8
Trimethoprim-sulfamethoxazole	≤0.06	>4	≤0.06 to >4	62.1	3.1	34.8
***Moraxella catarrhalis* (137)**						
Omadacycline	≤0.12	0.25	≤0.12 to 0.25	—	—	—
Tigecycline	0.06	0.06	0.03 to 0.12	—	—	—
Tetracycline	0.25	0.5	≤0.06 to >8	99.3	0.0	0.7
Ceftriaxone	0.25	1	0.004 to 1	100.0	0.0	0.0
Amoxicillin-clavulanic acid	≤0.25	≤0.25	≤0.25 to 0.5	100.0		0.0
Levofloxacin	0.06	0.06	≤0.015 to 2	98.5		1.5
Azithromycin	0.015	0.03	≤0.004 to 0.03	100.0	0.0	0.0
Moxifloxacin	0.06	0.06	≤0.008 to 0.5	99.3		0.7
Trimethoprim-sulfamethoxazole	0.12	0.25	≤0.06 to 2	97.1	1.5	1.5

[a] Criteria as published by EUCAST (2018).
[b] Organisms include: *Staphylococcus capitis* (15), *S. epidermidis* (108), *S. haemolyticus* (32), *S. hominis* (19), *S. lugdunensis* (16), *S. pettenkoferi* (1), *S. saprophyticus* (3), *S. schleiferi* (1), *S. simulans* (2), *S. warneri* (3).
[c] Organisms include: *Staphylococcus capitis* (5), *S. epidermidis* (79), *S. haemolyticus* (30), *S. hominis* (7), *S. lugdunensis* (1), *S. pettenkoferi* (1), *S. saprophyticus* (3), *S. simulans* (1), *S. warneri* (1).
[d] Organisms include: *Streptococcus agalactiae* (100), *S. dysgalactiae* (49), *S. pyogenes* (152).
[e] Using meningitis breakpoints.
[f] Using nonmeningitis breakpoints.
[g] Organisms include: *Enterococcus avium* (1), *E. casseliflavus* (2), *E. faecalis* (210), *E. faecium* (126), *E. gallinarum* (6), *E. hirae* (2).
[h] Uncomplicated UTI only.
[i] Percentage of wild type based on ECV. EUCAST version 8.0 (2018).

CONCLUSIONS (CONT.)

- *Enterobacteriaceae* including ESBL-phenotype isolates of *E. coli* (97.3% inhibited) and *K. pneumoniae* (74.7% inhibited) were inhibited by ≤4 mg/L of omadacycline
- Nonfermenters that included *A. baumannii* (72.7% inhibited) and *S. maltophilia* (76.6% inhibited) isolates were inhibited by ≤4 mg/L of omadacycline where few other treatment options exist
- Omadacycline was active against fastidious organism groups, including *H. influenzae* ($MIC_{50/90}$ 0.5/1 mg/L) and *M. catarrhalis* ($MIC_{50/90}$ ≤0.12/0.25 mg/L)
- Omadacycline demonstrated potent *in vitro* activity against gram-positive and gram-negative bacterial pathogens commonly associated with ABSSSI, CABP, and UTI infections, including staphylococci, streptococci, enterococci, *Enterobacteriaceae*, some nonfermenters, and fastidious organisms
- These data support continued development of omadacycline in infections where resistant gram-positive and gram-negative isolates are likely to be found, including CABP, ABSSSI, and UTI

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