IDWeek 2019
Poster #665

In vitro Activity of Omadacycline against Recent (2018) Bacterial Pathogens from the United States and Europe Obtained from Skin and Skin Structure, Respiratory, and Urinary Tract Infections

Michael D. Huband, Michael A. Pfaller, Jennifer M. Streit, Helio S. Sader, Robert K. Flamm
JMI Laboratories, North Liberty, Iowa, USA

To obtain a PDF of this poster:

Scan the QR code or visit https://paratekpharma.com/media/1684/idweek-2019-665-huband-omc-sentry-2018.pdf

Charges may apply. No personal information is store.

Contact Information:
Michael D. Huband, B.S.
JMI Laboratories
345 Beaver Kreek Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Fax: (319) 665-3371
Email: michael-huband@jmilabs.com

INTRODUCTION

- Omadacycline is a broad-spectrum aminomethylcycline bacterial protein synthesis inhibitor approved by the Food and Drug Administration (FDA; oral and intravenous formulations) in 2018 for the treatment of adults with acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP) caused by indicated organisms
- An omadacycline phase 2 clinical trial for the treatment of uncomplicated urinary tract infection (uUTI; NCT03425396) was recently completed and an omadacycline acute pyelonephritis clinical trial (NCT03757234) is ongoing
- The spectrum of omadacycline includes potent *in vitro* activity against gram-positive (staphylococci, streptococci, and enterococci) and gram-negative (*Enterobacter cloacae*, *Haemophilus influenzae*, and *Klebsiella pneumoniae*) bacterial pathogens commonly associated with skin and skin structure infection (SSSI), CABP, and UTI
- Omadacycline is active against bacterial isolates expressing common tetracycline-, penicillin/oxacillin-, fluoroquinolone-, and macrolide-resistance mechanisms that include *Staphylococcus aureus*, coagulase-negative staphylococci (*Staphylococcus lugdunensis*), *Enterococcus faecalis*, streptococci (*Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus anginosus*), *Enterobacteriaceae* (*E. cloacae* and *K. pneumoniae*), and *Haemophilus* spp.
- *In vitro* activity of omadacycline and comparator agents against 14,000 gram-positive and -negative bacterial clinical isolates collected from patients in United States and European medical centers during 2018 (SENTRY Antimicrobial Surveillance Program) is presented
  - Isolates were collected from patients with SSSI (3,134 isolates; 22.4%), bloodstream infection (3,600 isolates; 25.7%), community-acquired respiratory tract infection (CARTI—1,420 isolates; 10.1%), intra-abdominal infection (801 isolates; 5.7%), pneumonia in hospitalized patients (2,946 isolates; 21.0%), UTI (1,808 isolates; 12.9%), and other infection types (291 isolates; 2.1%) (Figure 1)

MATERIALS AND METHODS

- A total of 14,000 (non-duplicate) gram-positive and gram-negative bacterial isolates were collected from patients with multiple infection types in the United States (31 medical centers) and Europe (38 medical centers) that included 3,458 staphylococci, 1,551 streptococci, 746 enterococci, 574 *Haemophilus* spp., and 7,406 *Enterobacterales* isolates
- Only 1 isolate per patient infection episode was tested
- Bacterial isolate identifications were 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 Clinical and Laboratory Standards Institute (CLSI; 2018) reference broth microdilution methodology and results were interpreted using CLSI (2019), European Committee on Antimicrobial Susceptibility Testing (EUCAST; v9.0, 2019), and FDA (omadacycline and tigecycline) breakpoint interpretive criteria
  - CLSI quality control (QC) reference strains (2019) were tested concurrently and included *S. aureus* ATCC 29213; *E. faecalis* ATCC 29212; *Escherichia coli* ATCC 25922, ATCC 35218, and NCTC 13353; *K. pneumoniae* ATCC 700603, ATCC BAA-1705, and ATCC BAA-2814; *S. pneumoniae* ATCC 49619; *H. influenzae* ATCC 49247 and ATCC 49766; and *Pseudomonas aeruginosa* ATCC 27853

RESULTS

- Cumulative percent inhibition and susceptibility data for omadacycline against key gram-positive and gram-negative pathogens collected from patients with SSSI, CABP, or UTI in the United States and Europe during 2018 is presented in Table 1 and from patients with multiple infection types in Table 2

RESULTS (CONT.)

- Omadacycline demonstrated potent *in vitro* activity against *S. aureus* isolates from SSSI and MSSA from CARTI with $MIC_{50/90}$ values of 0.12/0.25 µg/mL and corresponding susceptibility (S) values of 99.3%S and 98.4%S (Table 1)
- Against *S. aureus* isolates collected from multiple infection sites, omadacycline ($MIC_{50/90}$, 0.12/0.25 µg/mL) was comparable in activity to tigecycline ($MIC_{50/90}$, 0.12/0.12 µg/mL), inhibiting 98.7% and 99.9%, respectively, of all isolates at ≤0.5 µg/mL (Table 2)
  - Overall susceptibilities for tetracycline ($MIC_{50/90}$, ≤0.5/≤0.5 µg/mL) and levofloxacin ($MIC_{50/90}$, 0.25/>4 µg/mL) against *S. aureus* were 94.6%S and 74.0%S, respectively (Table 2)

RESULTS (CONT.)

- Omadacycline ($MIC_{50/90}$, 0.12/0.25 µg/mL) was similarly active against methicillin-resistant *S. aureus* (MRSA) isolates from SSSI (97.7%S) and multiple infection types (96.3% inhibited at ≤0.5 µg/mL) (Tables 1-2)
  - Levofloxacin susceptibility was low (32.9%S) against MRSA (Table 2)
- All *S. lugdunensis* ($MIC_{50/90}$, 0.06/0.06 µg/mL) isolates from SSSI were susceptible to omadacycline (Table 1) and 97.4% of *S. lugdunensis* ($MIC_{50/90}$, 0.06/0.12 µg/mL) isolates from multiple infection types were inhibited by ≤0.12 µg/mL of omadacycline (Table 2)

RESULTS (CONT.)

- Omadacycline was very active against streptococci from SSSI, including *S. anginosus* group ($MIC_{50/90}$, 0.06/0.12 µg/mL; 100.0%S) and *S. pyogenes* ($MIC_{50/90}$, 0.06/0.12 µg/mL; 97.6%S)
  - Macrolide-resistant (R) and tetracycline-R *S. pyogenes* isolates from SSSI were slightly less susceptible with $MIC_{50/90}$ values of 0.12/0.25 µg/mL and 87.5%S
- Omadacycline was equally active against *S. pneumoniae* isolates from RTI and multiple infection types ($MIC_{50/90}$, 0.06/0.12 µg/mL; 98.0%S or inhibited at ≤0.12 µg/mL) including penicillin-R and tetracycline-R strains ($MIC_{50/90}$, 0.06/0.12 µg/mL; 94.2%-95.1%S or inhibited at ≤0.12 µg/mL) (Tables 1-2)

RESULTS (CONT.)

- Omadacycline ($MIC_{50/90}$, 0.12/0.25 µg/mL) was active against 99.0% of *E. faecalis* isolates from SSSI and inhibited 98.5% of *E. faecalis* isolates from multiple infection sites at ≤0.25 µg/mL (Tables 1-2)
  - Similarly, 97.4% of *Enterococcus faecium* isolates from SSSI, 100.0% of vancomycin-R *E. faecium* isolates from SSSI, and 98.8% of *E. faecium* isolates from multiple infection sites were inhibited by ≤0.25 µg/mL of omadacycline (Tables 1-2)
- 99.8% of *H. influenzae* isolates and 88.9% of *Haemophilus parainfluenzae* isolates from RTI were susceptible to omadacycline whereas 99.8% of *H. influenzae* and 93.6% of *H. parainfluenzae* isolates from multiple infection sites were inhibited by ≤2 µg/mL of omadacycline (Tables 1-2)
- 92.1% of *E. cloacae* and 89.4% of *K. pneumoniae* isolates from SSSI were susceptible to omadacycline as were 86.2% of *K. pneumoniae* isolates from RTI (Table 1)
- 99.0%-99.3% of *E. coli* isolates from SSSI, RTI, and UTI were inhibited by ≤4 µg/mL of omadacycline (Table 1)

Table 1 Antimicrobial activity of omadacycline and comparators against SSSI, RTI, and UTI pathogens collected from medical centers in the United States and Europe during 2018

Organisms (no. tested)	Infection type	No. of isolates at MIC (µg/mL; cumulative % inhibited)											MIC_{50}	MIC_{90}
		≤0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	>		
Staphylococcus aureus (1,475)	SSSI	0	2	2	113	1,141	**183**	23	8	3					0.12	**0.25**
		0.0	0.1	0.3	7.9	85.3	**97.7**	99.3	99.8	100.0						
MRSA (432)	SSSI	0	1	0	39	318	**49**	15	7	3					0.12	**0.25**
		0.0	0.2	0.2	9.3	82.9	**94.2**	97.7	99.3	100.0						
MSSA (1,043)	SSSI	0	1	2	74	823	**134**	8	1						0.12	**0.25**
		0.0	0.1	0.3	7.4	86.3	**99.1**	99.9	100.0							
S. aureus (283)	CARTI	0	1	3	28	197	**39**	3	11	0	0	1			0.12	**0.25**
		0.0	0.4	1.4	11.3	80.9	**94.7**	95.8	99.6	99.6	99.6	100.0				
MRSA (101)	CARTI			0	7	71	**11**	**2**	9	0	0	1			0.12	**0.5**
				0.0	6.9	77.2	88.1	**90.1**	99.0	99.0	99.0	100.0				
MSSA (182)	CARTI	0	1	3	21	126	**28**	1	2						0.12	**0.25**
		0.0	0.5	2.2	13.7	83.0	**98.4**	98.9	100.0							
Staphylococcus lugdunensis (29)	SSSI	0	3	5	19	**2**									0.06	**0.06**
		0.0	10.3	27.6	93.1	**100.0**										
Streptococcus anginosus group (19)	SSSI	0	5	2	10	**2**									0.06	**0.12**
		0.0	26.3	36.8	89.5	**100.0**										
Streptococcus pyogenes (125)	SSSI			0	66	**56**	3								0.06	**0.12**
				0.0	52.8	**97.6**	100.0									
S. pyogenes macrolide-R (16)[a]	SSSI			0	5	9	**2**								0.12	**0.25**
				0.0	31.3	87.5	**100.0**									
S. pyogenes tetracycline-R (24)[a]	SSSI			0	5	16	**3**								0.12	**0.25**
				0.0	20.8	87.5	**100.0**									
Streptococcus pneumoniae (794)	RTI	0	6	96	456	**220**	16	1							0.06	**0.12**
		0.0	0.8	12.8	70.3	**98.0**	100.0									
S. pneumoniae penicillin-R (99)[a]	RTI			0	3	48	**43**	5							0.06	**0.12**
				0.0	3.0	51.5	**94.9**	100.0								
S. pneumoniae tetracycline-R (173)[a]	RTI	0	1	16	82	**64**	10								0.06	**0.12**
		0.0	0.6	9.8	57.2	**94.2**	100.0									
Enterococcus faecalis (101)	SSSI			0	1	44	42	**13**	1						0.12	**0.25**
				0.0	1.0	44.6	86.1	**99.0**	100.0							
E. faecium (39)	SSSI			0	3	20	12	**3**	1						0.06	**0.25**
				0.0	7.7	59.0	89.7	**97.4**	100.0							
E. faecium vancomycin-R (14)[a]	SSSI				0	8	4	**2**							0.06	**0.25**
					0.0	57.1	85.7	**100.0**								
Haemophilus influenzae (512)	RTI					0	7	17	268	**199**	26	1			0.5	**1**
						0.0	0.2	3.5	55.9	**94.7**	99.8	100.0				
H. parainfluenzae (9)	RTI							0	1	4	3	**1**			1	**—**
								0.0	11.1	55.6	88.9	**100.0**				
Moraxella catarrhalis (259)	RTI					0	160	**96**	3						≤0.12	**0.25**
						0.0	61.8	**98.8**	100.0							
Enterobacter cloacae (89)	SSSI							0	8	64	**10**	4	3		2	**4**
								0.0	9.0	80.9	**92.1**	96.6	100.0			
Klebsiella pneumoniae (141)	SSSI						0	7	55	42	22	**7**	7	1	2	**8**
							0.0	5.0	44.0	73.8	89.4	**94.3**	99.3	100.0		
Klebsiella pneumoniae (290)	RTI						0	9	83	115	43	**17**	21	2	2	**8**
							0.0	3.1	31.7	71.4	86.2	**92.1**	99.3	100.0		
Klebsiella pneumoniae (341)	UTI						0	11	161	118	**27**	12	10	2	1	**4**
							0.0	3.2	50.4	85.0	**93.0**	96.5	99.4	100.0		
Escherichia coli (314)	SSSI			0	1	0	4	126	122	**44**	14	2	1		1	**2**
				0.0	0.3	0.3	1.6	41.7	80.6	**94.6**	99.0	99.7	100.0			
E. coli (279)	RTI					0	1	115	111	**44**	6	1	1		0.5	**2**
						0.0	0.4	41.6	81.4	**97.1**	99.3	99.6	100.0			
E. coli (865)	UTI			0	2	0	20	395	318	**101**	23	6			1	**2**
				0.0	0.2	0.2	2.5	48.2	85.0	**96.6**	99.3	100.0				

SSSI, skin and skin structure infection; RTI, respiratory tract infection; UTI, urinary tract infection; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; R, resistant
MIC_{50}, MIC_{90} values are listed in **bold**.
Green, susceptible according to FDA breakpoint interpretive criteria for acute bacterial skin and skin structure infection or community-acquired bacterial pneumonia.
Yellow, intermediate according to FDA breakpoint interpretive criteria for acute bacterial skin and skin structure infection or community-acquired bacterial pneumonia.
Gray, resistant according to FDA breakpoint interpretive criteria for acute bacterial skin and skin structure infection or community-acquired bacterial pneumonia.
[a] CLSI (2019).

Figure 1 Incidence of bacterial pathogens by infection type from the omadacycline 2018 surveillance program

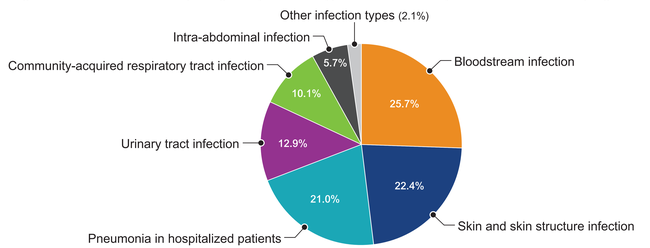

Table 2 Antimicrobial activity of omadacycline and comparators against bacterial isolates collected from all infection types in United States and European medical centers during 2018

Organism (no. tested)	Omadacycline		Tetracycline		Tigecycline		Levofloxacin	
	$MIC_{50/90}$	%S (FDA)	$MIC_{50/90}$	%S (CLSI)	$MIC_{50/90}$	%S (CLSI)	$MIC_{50/90}$	%S (CLSI)
Staphylococcus aureus (3,117)	0.12 **0.25**	98.7[a]	≤0.5 **≤0.5**	94.6	0.12 **0.12**	99.9	0.25 **>4**	74.0
MRSA (996)	0.12 **0.25**	96.3[a]	≤0.5 **2**	91.0	0.12 **0.12**	99.8	**4** **>4**	32.9
MSSA (2,121)	0.12 **0.25**	99.8[a]	≤0.5 **≤0.5**	96.3	0.12 **0.12**	100.0	0.25 **0.5**	93.3
S. lugdunensis (39)	0.06 **0.12**	97.4[b]	≤0.5 **≤0.5**	100.0	0.06 **0.06**	—	0.25 **0.5**	100.0
Streptococcus anginosus group (59)	0.06 **0.12**	100.0[c]	0.5 **>4**	75.9	0.03 **0.06**	100.0	0.5 **1**	100.0
S. pyogenes (283)	0.12 **0.12**	97.9[c]	0.25 **>4**	80.2	0.06 **0.06**	100.0	0.5 **1**	100.0
S. pyogenes macrolide-R (35)	0.12 **0.25**	85.7[a]	>4 **>4**	22.9	0.06 **0.12**	100.0	0.5 **1**	100.0
S. pyogenes tetracycline-R (53)	0.12 **0.25**	88.7[a]	>4 **>4**	0.0	0.06 **0.12**	100.0	0.5 **1**	100.0
Streptococcus pneumoniae (871)	0.06 **0.12**	98.0[a]	0.5 **>4**	79.0	0.06 **0.12**	89.4	1 **2**	98.5
S. pneumoniae penicillin-R (102)	0.06 **0.12**	95.1[a]	>4 **>4**	43.1	0.06 **0.12**	80.4	1 **2**	97.1
S. pneumoniae tetracycline-R (181)	0.06 **0.12**	94.5[a]	>4 **>4**	0	0.06 **0.12**	85.1	1 **2**	98.9
Enterococcus faecalis (473)	0.12 **0.25**	98.5[c]	>16 **>16**	27.7	0.12 **0.12**	99.6	1 **>4**	76.1
E. faecium (243)	0.06 **0.12**	98.8[c]	>16 **>16**	38.7	0.06 **0.12**	—	>4 **>4**	10.3
E. faecium vancomycin-R (93)	0.06 **0.12**	98.9[c]	>16 **>16**	21.5	0.06 **0.12**	—	>4 **>4**	0.0
Haemophilus influenzae (527)	0.5 **1**	99.8[d]	0.5 **1**	99.2	0.25 **0.25**	90.9	0.015 **0.03**	99.6
H. parainfluenzae (47)	1 **2**	93.6[b]	0.5 **1**	91.5	0.5 **0.5**	—	0.03 **0.06**	97.9
Moraxella catarrhalis (263)	≤0.12 **0.25**	—	0.25 **0.5**	99.2	0.06 **0.06**	—	0.03 **0.06**	100.0
Enterobacter cloacae species complex (413)	2 **4**	91.5[c]	2 **>16**	83.8	0.5 **1**	97.1	0.03 **1**	88.5
Klebsiella pneumoniae (1,180)	2 **8**	87.8[c]	2 **>16**	66.6	0.5 **1**	96.3	0.06 **32**	70.7
Escherichia coli (2,627)	1 **2**	99.3[a]	2 **>16**	65.6	0.25 **0.25**	100.0	0.03 **16**	70.9

MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; R, resistant
MIC_{50}, MIC_{90} values are listed in **bold**.
Green, susceptible according to CLSI or FDA breakpoint interpretive criteria.
Yellow, intermediate according to CLSI or FDA breakpoint interpretive criteria.
Gray, resistant according to CLSI or FDA breakpoint interpretive criteria.
[a] Omadacycline acute bacterial skin and skin structure infection breakpoints for *S. aureus* applied for comparison purposes.
[b] Omadacycline acute bacterial skin and skin structure infection breakpoints for *S. lugdunensis* applied for comparison purposes.
[c] Omadacycline acute bacterial skin and skin structure infection breakpoints for *S. anginosus* applied for comparison purposes.
[d] Omadacycline acute bacterial skin and skin structure infection breakpoints for *S. pyogenes* applied for comparison purposes.
[e] Omadacycline community-acquired bacterial pneumonia breakpoints for *S. pneumoniae* applied for comparison purposes.
[f] Omadacycline acute bacterial skin and skin structure infection breakpoints for *E. faecalis* applied for comparison purposes.
[g] Omadacycline acute bacterial skin and skin structure infection breakpoints for *E. faecalis* applied for comparison purposes.
[h] Omadacycline community-acquired bacterial pneumonia breakpoints for *Haemophilus* spp. applied for comparison purposes.
[i] Omadacycline acute bacterial skin and skin structure infection breakpoints for *E. cloacae* applied for comparison purposes.
[j] Omadacycline acute bacterial skin and skin structure infection and community-acquired bacterial pneumonia breakpoints for *K. pneumoniae* applied for comparison purposes.
[k] Omadacycline acute bacterial skin and skin structure infection and community-acquired bacterial pneumonia breakpoints for *K. pneumoniae* applied for comparison purposes.

CONCLUSIONS

- Omadacycline demonstrated potent activity against the Gram-positive and Gram-negative species assessed, including those with resistance to antimicrobials in the tetracycline class as well as other members of the macrolide, penicillin, and fluoroquinolone classes
  - Omadacycline was potent against *S. aureus*, including MRSA and MSSA
  - Omadacycline was highly active against penicillin-resistant, tetracycline-resistant, and macrolide-resistant *Streptococcus* spp.
  - Omadacycline exhibited potent activity against tetracycline-resistant *E. faecalis*
  - Omadacycline was highly active against tigecycline-resistant and β-lactamase-producing *Haemophilus* spp.
  - Omadacycline demonstrated good activity against *E. cloacae* and *K. pneumoniae*
- Results of this surveillance study support the continued use and development of omadacycline, especially in infections where resistant pathogens are likely to be encountered, including SSSI, CABP, and UTI

ACKNOWLEDGEMENTS

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

REFERENCES

Clinical and Laboratory Standards Institute (2018). *M07-A11. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard—eleventh edition.* Wayne, PA: CLSI.

Clinical and Laboratory Standards Institute (2019). *M100-S29. Performance standards for antimicrobial susceptibility testing: 29th informational supplement.* Wayne, PA: CLSI.

EUCAST (2019). Breakpoint tables for interpretation of MICs and zone diameters. Version 7.0, January 2017. Available at: http://www.eucast.org/clinical_breakpoints/. Accessed August 2019.

US Food and Drug Administration: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm575163.htm. Accessed August 2019.