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P1876 *In vitro* activity of omadacycline and comparators against Gram-positive and -negative clinical isolates collected in 2018 from patients in European medical centres: SENTRY surveillance program results

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Background: Omadacycline is new aminomethylcycline antibacterial that recently received US FDA approval for the treatment of acute bacterial skin and skin structure infections (ABSSSIs) and community-acquired bacterial pneumonia (CABP). Omadacycline is currently in a phase 2 clinical trial for the treatment of uncomplicated urinary tract infections (uUTIs). Bacterial isolates expressing common tetracycline, penicillin, fluoroquinolone, and macrolide resistance mechanisms remain susceptible to omadacycline.

Materials/methods: The *in vitro* activity of omadacycline was evaluated against bacterial isolates from patients in Europe (2018 SENTRY Antimicrobial Surveillance Program). Isolates including staphylococci (1,875), streptococci (683), enterococci (266), *Haemophilus* spp. (313), and Enterobacteriaceae (2,071) isolates were collected (multiple infection types) during 2018 (1 isolate/patient/infection episode). A central laboratory confirmed isolate identifications using standard bacteriologic algorithms, MALDI-TOF MS, and/or molecular characterization. Susceptibility testing was performed according to reference (CLSI) broth microdilution methodology; results were interpreted per FDA, CLSI (2018), and EUCAST (v 8.1) breakpoints.

Results: Omadacycline demonstrated potent activity against *Staphylococcus aureus* (SA) isolates, including methicillin-resistant SA (MRSA; $MIC_{50/90}$ 0.12/0.25) with ≥99.6% susceptible (S) (Table). Omadacycline was active against coagulase-negative staphylococci (CoNS; $MIC_{50/90}$ 0.12/0.5 mg/L; 94.1% inhibited at ≤0.5 mg/L), including MRCoNS ($MIC_{50/90}$ 0.12/0.5 mg/L). All (100.0%) *S. lugdunensis* isolates were susceptible to omadacycline ($MIC_{50/90}$, 0.06/0.12 mg/L). *Streptococcus pneumoniae* isolates were inhibited by low levels of omadacycline ($MIC_{50/90}$, 0.06/0.12 mg/L; 98.4%S) whereas susceptibility to tetracycline ($MIC_{50/90}$, 0.25/>4 mg/L; 84.7%/84.7%S [CLSI/EUCAST]) was reduced. All (100.0%) *S. anginosus* and *S. pyogenes* isolates were S to omadacycline; corresponding tetracycline susceptibilities were 58.8% (CLSI) and 89.1%/89.1% (CLSI/EUCAST), respectively. Omadacycline exhibited potent activity against *Enterococcus faecalis* ($MIC_{50/90}$ 0.12/0.25 mg/L; 99.2%S), including vancomycin-resistant isolates whereas S to tetracycline (24.1% S [CLSI]) was compromised. Susceptibility of *Enterobacter cloacae* and *Klebsiella pneumoniae* isolates to omadacycline were 82.1% and 85.0%, respectively; corresponding tetracycline susceptibilities were reduced (72.4% and 65.5%, respectively). Susceptibility of *Haemophilus* spp. isolates to omadacycline was 99.4%. A majority of *Klebsiella pneumoniae* isolates were inhibited by ≤4 mg/L of omadacycline ($MIC_{50/90}$, 2/8 mg/L; 85.0%S FDA]) whereas tetracycline S ($MIC_{50/90}$, 2/>16 mg/L; 65.0%S [CLSI]) was reduced.

Conclusions: Omadacycline demonstrated potent activity against recent European clinical isolates commonly associated with ABSSSI, CABP, and uUTI, including resistant isolates.

Organism	n	Omadacycline		Tetracycline	
		$MIC_{50/90}$ (mg/L)	FDA %S	$MIC_{50/90}$ (mg/L)	CLSI / EUCAST %S
Enterococcus faecalis	266	0.12/0.25	99.2[a]	>16/>16	24.1 / --
S. aureus	1,653	0.12/0.25	99.6[a]	≤0.5/≤0.5	94.3 / 94.1
MRSA	297	0.12/0.25	99.0[a]	≤0.5/>8	84.5 / 84.2
S. lugdunensis	25	0.06/0.12	100.0[a]	≤0.5/≤0.5	100.0 / 100.0
CoNS	222	0.12/0.5	--	≤0.5/8	86.0 / 78.4
Streptococcus anginosus	17	0.06/0.06	100.0[a]	0.5/>4	58.8 / --
S. pneumoniae	425	0.06/0.12	98.4[b]	0.25/>4	84.7 / 84.7
S. pyogenes	92	0.12/0.12	100.0[a]	0.25/4	89.1 / 89.1
β-haemolytic streptococci	241	0.12/0.25	--	0.5/>4	55.6/54.8
Enterobacter cloacae	145	2/8	82.1[a]	2/>16	72.4 / --
Escherichia coli	1,398	1/2	--	2/>16	65.2 / --
Haemophilus spp.[c]	313	0.5/1	99.4[b]	0.5/1	97.8 / 97.1
Klebsiella pneumoniae	528	2/8	85.0[a,b]	2/>16	65.5 / --

[a] ABSSSI breakpoints.
[b] CABP breakpoints.
[c] *H. influenzae* and *H. parainfluenzae*.