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In vitro activity of omadacycline and comparators against Gram-negative bacterial isolates collected from patients in European medical centres (2016): results from the SENTRY antimicrobial surveillance programme

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Background: Omadacycline is a broad spectrum aminomethylcycline of the tetracycline family in late stage clinical development for community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections (intravenous and oral formulations). Omadacycline has shown potent *in vitro* activity against key bacterial pathogens including Gram-negative bacterial isolates expressing resistance to β-lactams, fluoroquinolones and/or common tetracycline resistance mechanisms. This study evaluated the *in vitro* antibacterial activity of omadacycline and comparators against Gram-negative bacterial isolates collected from patients in European medical centres that participated in the 2016 SENTRY surveillance program.

Material/methods: A total of 4,131 clinically significant Enterobacteriaceae, 195 *Haemophilus influenzae*, 105 *Moraxella catarrhalis* and 266 *Acinetobacter baumannii* representing multiple infection types were collected during 2016. One isolate/patient/infection episode was included. Species identification confirmation and antimicrobial susceptibility testing was performed in a central laboratory according to reference (CLSI) broth microdilution methodology and results interpreted per EUCAST/CLSI breakpoints.

Results: Gram-negative isolates were collected from blood stream infection (BSI; 29.9%), pneumonia in hospitalized patients (PIHP; 20.3%), urinary tract infection (UTI; 19.1%), skin and skin structure infection (SSSI; 15.4%), intra-abdominal infection (IAI; 9.3%), respiratory tract infection (RTI; 5.6%) and other infection types (0.4%). Against Enterobacteriaceae, omadacycline ($MIC_{50/90}$ 1/4 mg/L) was very active, inhibiting 90.7% of isolates at ≤4 mg/L; corresponding susceptibilities (EUCAST/CLSI) to ciprofloxacin, ceftazidime, piperacillin-tazobactam and tetracycline were 74.2%/76.1%, 77.5%/82.3%, 83.5%/87.6% and -/62.1%, respectively. Where treatment options may be limited, omadacycline remained active against resistant organisms/groups, including ESBL phenotype *Escherichia coli* ($MIC_{50/90}$ 1/2 mg/L) and *Klebsiella pneumoniae* ($MIC_{50/90}$ 2/8 mg/L; 84.6% inhibited at ≤4mg/L),

ceftazidime non-susceptible *Enterobacter cloacae* species complex ($MIC_{50/90}$ 2/4 mg/L) and *A. baumannii* ($MIC_{50/90}$ 2/8 mg/L; 74.8% inhibited at ≤4mg/L). *H. influenzae* and *M. catarrhalis* isolates were also very susceptible to omadacycline with $MIC_{50/90}$ values of 0.5/1 and 0.12/0.25 mg/L, respectively.

Conclusions: Omadacycline was very active against contemporary Gram-negative isolates from Europe, including resistant strains. Omadacycline inhibited ≥90% of Enterobacteriaceae, *A. baumannii*, *H. influenzae* and *M. catarrhalis* isolates at ≤4, 8, 1 and 0.25 mg/L, respectively. These data support further clinical investigation, especially where resistant pathogens may occur.

		Omadacycline MIC (mg/L)		**Tetracycline MIC (mg/L)**		
Organism	**# tested**	**MIC_{50}**	**MIC_{90}**	**MIC_{50}**	**MIC_{90}**	**%S EUCAST / CLSI**
Enterobacteriaceae	4,131	1	4	2	>16	-[a] / 62.1
Escherichia coli	1,972	0.5	2	2	>16	- / 61.7
E. coli (ESBL phenotype)	413	1	2	>16	>16	- / 37.8
Klebsiella pneumoniae	805	1	4	2	>16	- / 68.2
Enterobacter cloacae	325	1	4	2	>16	- / 85.2
A. baumannii	266	4	8	>16	>16	- / 17.6
H. influenzae	195	0.5	1	0.5	0.5	100.0 / 100.0
M. catarrhalis	105	0.12	0.25	0.25	0.5	100.0 / 100.0

[a] EUCAST breakpoints unavailable