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In vitro activity of omadacycline and comparators against staphylococci, streptococci and enterococci (including resistant organism subsets) from patients in European medical centres during 2016: results from the SENTRY antimicrobial surveillance programme

Michael Huband¹, Paul R. Rhomberg¹, Helio S. Sader¹, Jason Schuchert¹, Robert Flamm¹

¹*Jmi Laboratories*

Background: Omadacycline is a broad spectrum aminomethylcycline antibacterial in late stage clinical development for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP). Omadacycline has demonstrated potent *in vitro* activity against Gram-positive and -negative bacterial pathogens commonly associated with skin and skin structure infections (SSSI) and respiratory tract infections (RTI). In addition, omadacycline remains highly active against isolates expressing common tetracycline, penicillin, fluoroquinolone and macrolide resistance mechanisms. The *in vitro* susceptibility results for omadacycline and comparator agents tested against Gram-positive bacterial clinical isolates collected from patients in European medical centres participating in the SENTRY surveillance program during 2016 are presented.

Material/methods: A total of 4,296 clinically significant Gram-positive isolates that include 2,839 staphylococci, 1,003 streptococci and 454 enterococci representing multiple infection types were collected during 2016 and included only one isolate/patient/infection episode. A central monitoring laboratory confirmed isolate identifications using standard bacteriologic algorithms, matrix-assisted laser desorption/ionization (MALDI) mass spectrometry and/or molecular characterization. Susceptibility testing was performed according to reference (CLSI) broth microdilution methodology and results were interpreted per EUCAST breakpoints.

Results: Omadacycline demonstrated potent *in vitro* activity against *Staphylococcus aureus* (SA; n=2,345) with MIC_{50/90} values of 0.12/0.12 mg/L. Overall, methicillin resistance in SA (MRSA) was 21.3%. Omadacycline (MIC_{50/90} 0.12/0.25 mg/L) and tigecycline (MIC_{50/90} 0.12/0.12 mg/L; 100.0% susceptible) were the most potent antimicrobials tested against MRSA whereas susceptibility to clindamycin (77.0%), erythromycin (41.6%), levofloxacin (30.2%) and tetracycline (83.6%) were

compromised. Omadacycline was also highly active against coagulase-negative staphylococci (CoNS, n=494; MIC_{50/90} 0.12/0.5 mg/L) including methicillin-resistant strains (n=336; MIC_{50/90} 0.12/0.5 mg/L) where susceptibility to clindamycin (67.9%), erythromycin (20.2%), levofloxacin (28.3%) and tetracycline (75.9%) was also reduced.

Streptococci including *S. pneumoniae* (n=542; MIC_{50/90} 0.06/0.06 mg/L), β -haemolytic streptococci (n=345; MIC_{50/90} 0.06/0.12 mg/L) and viridans group streptococci (n=116; MIC_{50/90} 0.06/0.12 mg/L) were inhibited by low levels of omadacycline. Penicillin-resistance in *S. pneumoniae* (PRSP) was 10.7%. All PRSP isolates were inhibited by \leq 0.12 mg/L of omadacycline whereas resistance to ceftriaxone (10.3%), erythromycin (70.7%) and tetracycline (62.1%) was high. All β -haemolytic streptococci were susceptible to tigecycline, β -lactams, linezolid, daptomycin, and vancomycin; however, resistance to levofloxacin (95.7% susceptible), erythromycin (79.5% susceptible), clindamycin (89.6% susceptible) and tetracycline (57.3% susceptible) occurred.

Omadacycline exhibited potent *in vitro* activity against both *Enterococcus faecalis* (n=263; MIC_{50/90} 0.12/0.25 mg/L) and *E. faecium* (n=174; MIC_{50/90} 0.06/0.12 mg/L) that included vancomycin-resistant isolates. Vancomycin resistance rates were 0.4% and 16.1% against *E. faecalis* and *E. faecium*, respectively.

Conclusions: Omadacycline demonstrated potent *in vitro* antibacterial activity against Gram-positive bacterial pathogens commonly associated with SSSI and RTI infections including *S. aureus* (including MRSA), *S. pneumoniae* (including PRSP), β -haemolytic streptococci and enterococci (including vancomycin-resistant strains). These data support further omadacycline clinical evaluation studies, especially where these resistant pathogens are likely to occur.