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**Paper Poster Session**
**Omadacycline in vitro and in vivo**

# Omadacycline activity tested against European bacterial isolates from a combined 2010-2011global surveillance programme

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**Background:** Omadacycline is a broad spectrum aminomethylcycline in late stage clinical development for the treatment of acute bacterial skin and skin structure infections and community-acquired pneumonia that is being evaluated as both oral and intravenous, once-daily formulations. It has excellent activity against Gram-positive and –negative pathogens including tetracycline resistant organisms. The results from testing omadacycline and comparator agents against clinical isolates collected during 2010-2011 from the European region of a global surveillance study are presented.

**Material/methods:** More than 20,000 Gram-positive and –negative isolates were selected from patients in 45 medical centers in 14 European countries and Israel. Only one isolate per infection episode per patient was included. A central monitoring laboratory confirmed isolate identity using standard bacteriologic algorithms, the VITEK 2 System, or molecular characterization if necessary. Antibacterial susceptibility testing was performed by broth microdilution per CLSI guidelines. EUCAST breakpoints were used to determine susceptibility rates.

**Results:** The omadacycline $MIC_{50/90}$ for all *Staphylococcus aureus* was 0.12/0.25 mg/L (Table). Against MRSA, omadacycline ($MIC_{90}$, 0.25 mg/L) and tigecycline ($MIC_{90}$, 0.25 mg/L; 100.0% susceptible) were the most potent antimicrobials tested while susceptibility to multiple agents including erythromycin (32.9%), clindamycin (67.7%), and levofloxacin (12.0%) were compromised. Omadacycline and tigecycline exhibited potent activity against *Enterococcus faecalis* and *E. faecium* ($MIC_{90}$ values at ≤0.25 mg/L). The $MIC_{50}$ and $MIC_{90}$ for omadacycline (0.06/0.06 mg/L) and tigecycline (≤0.03/0.06 mg/L) against *Streptococcus pneumoniae*, were the lowest among the agents tested and demonstrated activity against ceftriaxone and levofloxacin resistant isolates. Omadacycline and tigecycline MIC values for *S. pneumoniae* were 16-fold lower than ceftriaxone ($MIC_{90}$, 1 mg/L) and levofloxacin ($MIC_{90}$, 1 mg/L). Omadacycline was potent against the β-haemolytic streptococci, $MIC_{90}$ 0.12 mg/L. All β-haemolytic streptococci were susceptible to tigecycline, β-lactams, linezolid, daptomycin, and vancomycin, however resistance to levofloxacin (95.0% susceptible), erythromycin (81.4% susceptible), clindamycin (92.5% susceptible), tetracycline (45.7% susceptible) and doxycycline (49.5% susceptible) occurred. The $MIC_{50}$ and $MIC_{90}$ for omadacycline for the Enterobacteriaceae was 1 and 8 mg/L, respectively. Omadacycline was less potent against *Klebsiella pneumoniae* ($MIC_{50/90}$, 2/8 mg/L [86.8% inhibited at ≤4 mg/L]); ESBL-phenotype $MIC_{50/90}$, 2/8 mg/L [78.3% inhibited at ≤4 mg/L]) and more potent against *Escherichia coli* ($MIC_{50/90}$, 0.5/2 mg/L; ESBL-phenotype $MIC_{50/90}$, 1/4 mg/L [97.9% inhibited at ≤4 mg/L]).

**Conclusions:** Omadacycline was active against a broad spectrum of Gram-positive and –negative pathogens including MRSA, Enterococci, β-haemolytic streptococci, *S. pneumoniae* including MDR isolates, and Enterobacteriaceae. Further evaluation in clinical trials is warranted.

| Select organisms | n | Omadacycline MIC in mg/L: | |
|---|---|---|---|
| | | $MIC_{50}$ | $MIC_{90}$ |
| *S. aureus* | 5,533 | 0.12 | 0.25 |
| MRSA | 1,539 | 0.12 | 0.25 |
| Coagulase negative staphylococci | 1,256 | 0.12 | 1 |
| *E. faecalis* | 1,196 | 0.12 | 0.25 |
| *E. faecium* | 692 | 0.06 | 0.12 |
| *S. pneumoniae* | 2,233 | 0.06 | 0.06 |
| β-haemolytic streptococci | 1,313 | 0.06 | 0.12 |
| *E. coli* | 3,757 | 0.5 | 2 |
| *K. pneumoniae* | 1,250 | 2 | 8 |
| *Acinetobacter baumannii* | 502 | 2 | 4 |