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In vitro extracellular and intracellular activity of omadacycline against Staphylococcus aureus

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Background: Omadacycline (OMC) is the first aminomethylcycline in late stage clinical development for community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infection (ABSSSI) as once-daily oral and IV formulations. *In vitro* extracellular bacterial activities and intracellular activities using human monocytes against a variety of resistant *S. aureus* were investigated.

Materials/methods: The extracellular and intracellular activity of **OMC** was compared with that of tigecycline (TI), linezolid (LI), ceftaroline (CE), levofloxacin (LE), moxifloxacin (MO) and azithromycin (AZ) against a total of 2 ATCC methicillin-susceptible (MSSA) and 2 ATCC methicillin-resistant strains of *S. aureus*. The intracellular activity was determined by exposing human monocytes, TPH-1 cell line, infected with intracellular *S. aureus* at the 1, 2, 8 or 16XMIC of antibiotic for each strain during 24 hour exposure. The extracellular activity was performed using the same antibiotic concentration and time exposure against *S. aureus* growing in cell culture medium RPMI1640. Viable bacterial cells (CFU/mL) were enumerated for all groups at time zero, 2, 6 and 24h in triplicate using the Brain Heart Infusion agar.

Results: Against all tested strains of *S. aureus* ATCC (MSSA or MRSA) and after 24 hour of extracellular antibiotic, **OMC** exposure at 1 to 16XMIC reduced bacterial growth ≥99.9% and was as active as CE, LE and MO. **OMC** was more active than LI which reduced growth <99.9% to ≥99%, TI <99% to ≥90% and AZ <90%. Against all tested intracellular strains of *S. aureus* ATCC (MSSA or MRSA) and after 24 hour of antibiotic exposure, **OMC** exposure at 2 to 16XMIC reduced intracellular growth ≥99% and was as active as LE and MO. **OMC** was more active than TI and LI (intracellular growth reduction of <99% to ≥90%), CE and AZ (intracellular growth reduction <90%).

Conclusions: This data demonstrate good bactericidal activity and human monocytes penetration of **OMC** and suggest that **OMC** may have use in infections caused by MSSA or MRSA *S. aureus* and highlights the potential utility of this oral and IV agent for the treatment of ABSSSI or CABP.