Activity of Oritavancin and Comparator Agents against Multidrug-resistant Staphylococcal and Streptococcal Isolates Responsible for Documented Infections in European Hospitals (2011-2013)

**Introduction**

The use of β-lactam antibiotics to empirically treat skin and soft-tissue infections (SSTIs) in many regions of the world has been compromised by the widespread isolation of community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA). Vancomycin remains the first-line antimicrobial therapy for infections caused by MRSA. Recent studies have correlated increased vancomycin MIC values with adverse clinical outcomes. However, this study identified the same high vancomycin MIC results as predictors for poor outcomes even among patients receiving a directed therapy for treating a methicillin-resistant S. aureus infection.

Oritavancin is a semisynthetic bactericidal lipoglycopeptide currently under regulatory review by the U.S. Food and Drug Administration for the treatment of patients with acute bacterial SSTIs. This study was performed to determine the activity of oritavancin against multidrug-resistant (MDR) staphylococcal and streptococcal pathogens recovered from European medical centres as part of the SENTRY Antimicrobial Surveillance Programme for 2011-2013.

**Materials and Methods**

**Bacterial strain collection.** A total of 9,039 isolates recovered from clinical specimens in hospitalised patients with documented infections in Europe (30 sites in 14 countries) and Israel (one site) were included. Selected isolates were submitted to the monitoring laboratory (JMI Laboratories; North Liberty, IA, USA) via the SENTRY Antimicrobial Surveillance Programme. Isolates were primarily identified by the participating laboratory; their identity was confirmed by the reference monitoring laboratory (JMI Laboratories) by standard algorithms and Vitek® 2 (bioMérieux, Hazelwood, MO, USA) and supported by VITEK-TDF-MOS (Bruker Daltonics, Bremen, Germany).

**Antimicrobial susceptibility test methods.** Isolates were susceptible for broth microdilution testing according to the Clinical and Laboratory Standards Institute (CLSI) M07-A9 document. Bacterial inoculum density was monitored by colony counts to assure that the inoculum used for each testing event. Validation of the MIC values was performed by concurrent testing of CLSI-recommended quality control (QC) strains against the modern ATCC 29213, Enterococcus faecalis ATCC 29212 and Staphylococcus pneumoniae ATCC 49619. All QC results were within acceptable ranges (M100-S24). MIC interpretations were based on the CLSI M100-S24 (2014) and European Committee on Antimicrobial Susceptibility Testing (EUCAST, 2014) breakpoint criteria, as available. Staphylocccal and streptococcal non-susceptible (based on CLSI criteria) were defined as MDR.

**Results**

**Introduction.** A total of 584 (9.4%) of S. aureus isolates met the criteria for MDR and non-MDR isolates were mostly (99.3%) methicillin-resistant (MRSA) and demonstrated elevated resistance rates (33.1 – 100% MIC50/90) for erythromycin, clindamycin, tetracycline and levofloxacin (Table). Oritavancin exhibited MIC50 results of 0.03 mg/L when tested against MDR CoNS showing equivalent MIC50 and MIC90 results when tested against MDR (data not shown).

**Materials and Methods.** Only 6.3% of β-haemolytic streptococci had a MDR phenotype, which was mostly due to non-susceptible to erythromycin, clindamycin and tetracycline. These MDR β-haemolytic streptococcal isolates had low MIC values to oritavancin (MIC0.03/0.12 mg/L), which was equivalent to that obtained against the non-MDR group (MIC0.03/0.06 mg/L).

**Activity of Oritavancin.** Oritavancin (MIC0.03/0.12 mg/L) and penicillin (MIC0.05/0.06 mg/L; 100% susceptible) were most active against β-haemolytic streptococci.

**Activity of Oritavancin.** Oritavancin (MIC0.015/0.06 mg/L) at 16-fold lower than those obtained for the comparator agents demonstrating in vitro activity (≥24) against the patient population of Viridans group streptococci (Table).

**Conclusions.** Oritavancin demonstrated potent in vitro activity against this contemporary challenge collection of MDR and non-MDR clinical isolates from Europe and Israel. Higher (2-fold) oritavancin MIC values were noted against S. aureus with borderline susceptibility to vancomycin (MIC2 ± 0.5 mg/L). However, oritavancin inhibited all tested strains at 0.5 mg/L.

**The in vitro activity presented for oritavancin was uniformly greater than those obtained for the comparator agents tested. These results warrant further investigation to determine the potential of oritavancin for treating infections caused by MDR Gram-positive isolates.

**References.**


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