# 470 Oritavancin Activity against Gram-positive Clinical Isolates Responsible for Documented Skin and Skin Structure Infections in USA and European Hospitals (2012-2013)

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## Amended Abstract

**Background:** Oritavancin was recently (August, 2014) approved in the USA for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive pathogens. Oritavancin activity was assessed against contemporary isolates causing SSSI.

**Methods:** 8,377 isolates from documented SSSI were collected from 27 sites in the USA and 34 sites in Europe, Israel and Turkey as part of the SENTRY Antimicrobial Surveillance Program (2012-2013). Bacteria were identified by standard algorithms and MALDI-TOF. Susceptibility testing was performed by CLSI methods (M07-A9); interpretation of MIC results used CLSI (2014) and EUCAST (2014) criteria.

**Results:** Oritavancin had $MIC_{50/90}$ values of 0.03/0.06 μg/ml against *S. aureus*, which were ≥8-fold lower than those obtained for vancomycin ($MIC_{50/90}$, 1/1 μg/ml), daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/ml) or linezolid ($MIC_{50/90}$, 1/1 μg/ml).

$MIC_{50/90}$ values against methicillin-susceptible (MSSA) and -resistant *S. aureus* (MRSA) were equivalent for these four agents.

Oritavancin $MIC_{50/90}$ values against coagulase-negative staphylococci (CoNS; $MIC_{50/90}$, 0.03/0.06 μg/ml) were ≥8-fold lower than comparators. VanA-phenotype *E. faecalis* had oritavancin MIC values ($MIC_{50/90}$, 0.25/0.5 μg/ml) 16-fold higher than those obtained for vancomycin-susceptible isolates ($MIC_{50/90}$, 0.015/0.03 μg/ml); nevertheless, oritavancin was ≥2-fold more active than daptomycin ($MIC_{50/90}$, 0.5/1 μg/ml) or linezolid ($MIC_{50/90}$, 1/1 μg/ml) against VanA *E. faecalis*.

Oritavancin ($MIC_{50/90}$, 0.004/0.008 μg/ml) had equivalent MIC values against VanB and vancomycin-susceptible *E. faecium* and higher MIC values ($MIC_{50/90}$, 0.03/0.12 μg/ml) against VanA strains. However, oritavancin MIC values against VanA *E. faecium* were 8- to -64 lower than active (100% susceptible) comparators (daptomycin, $MIC_{50/90}$, 2/4 μg/ml; and linezolid, $MIC_{50/90}$, 1/1 μg/ml).

Oritavancin had potent activity against *S. pyogenes* ($MIC_{50/90}$, 0.03/0.12 μg/ml), *S. agalactiae* ($MIC_{50/90}$, 0.03/0.06 μg/ml) and the *S. anginosus* group ($MIC_{50/90}$, 0.008/0.015 μg/ml), with slightly higher MIC results against *S. dysgalactiae* ($MIC_{50/90}$, 0.06/0.25 μg/ml).

**Conclusions**: Oritavancin had potent activity *in vitro* against this contemporary collection of Gram-positive isolates causing SSSI. These results benchmark oritavancin activity just prior to becoming clinically available.

## Introduction

ORBACTIV™ (oritavancin for injection) was recently (August, 2014) approved by the Food and Drug Administration (FDA) for the treatment of adults with acute bacterial skin and skin structure infections (ABSSSI) caused by designated Gram-positive bacteria. The approved oritavancin indication includes the following pathogens: *Staphylococcus aureus* (including methicillin-susceptible [MSSA] and -resistant [MRSA]), *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus* group, and vancomycin-susceptible *Enterococcus faecalis* isolates. In addition, oritavancin is under regulatory review by the European Medicines Agency (EMA) for the treatment of patients with complicated skin and soft-tissue infections.

Oritavancin is a semisynthetic bactericidal lipoglycopeptide with potent *in vitro* activity against a broad spectrum of Gram-positive organisms. This activity originates from multiple mechanisms of action consisting of disruption of bacterial membrane integrity, and inhibition of transglycosylation and transpeptidation steps of cell wall synthesis. In this study, the *in vitro* activity of oritavancin and comparator agents was assessed against a recent collection of Gram-positive clinical isolates (2012 – 2013) responsible for SSSI collected from subjects in several medical centers located in the USA, Europe, Israel and Turkey.

## Methods

**Bacterial strain collection.** A total of 8,377 pathogens (6,132 *S. aureus*, 461 coagulase-negative staphylococci [CoNS], 674 enterococci and 1,110 streptococci) responsible for SSSI, per local guidelines, were included in the study. Isolates were collected from 27 sites in the USA and 34 sites in Europe, Israel and Turkey as part of the SENTRY Antimicrobial Surveillance Program (2012-2013). Selected isolates were submitted to the monitoring laboratory (JMI Laboratories; North Liberty, Iowa, USA). Isolates were primarily identified by the participating laboratory and identification confirmed by the reference monitoring laboratory (JMI Laboratories) by standard algorithms and supported by MALDI-TOF-MS (Bruker Daltonics, Bremen, Germany).

**Antimicrobial susceptibility test methods.** Isolates were tested for susceptibility by broth microdilution following the Clinical and Laboratory Standards Institute (CLSI) M07-A9 document. Testing was performed using panels manufactured by Thermo Fisher Scientific (Cleveland, Ohio, USA). These validated panels provide MIC results equivalent to the CLSI-approved broth microdilution method which includes 0.002% polysorbate-80 in the broth. Bacterial inoculum density was monitored by colony counts to assure an adequate number of cells for each testing event. Quality of the MIC values was assured by concurrent testing of CLSI-recommended quality control (QC) reference strains (*S. aureus* ATCC 29213, *E. faecalis* ATCC 29212 and *Streptococcus pneumoniae* ATCC 49619). All QC results were within published acceptable ranges (M100-S24).

MIC interpretations for oritavancin were based on breakpoint criteria available in the product package insert (2014), and are as follows: *S. aureus* at ≤0.12 μg/ml for susceptible; *E. faecalis* (vancomycin-susceptible) at ≤0.12 μg/ml for susceptible; *S. pyogenes*, *S. agalactiae*, *S. dysgalactiae* and *S. anginosus* group at ≤0.25 μg/ml for susceptible. MIC interpretations for comparators were based on the CLSI M100-S24 (2014) and European Committee on Antimicrobial Susceptibility Testing (EUCAST; 2014) breakpoint criteria, as available.

## Results

- Oritavancin showed modal MIC, $MIC_{50}$ and $MIC_{90}$ results of 0.03, 0.03 and 0.06 μg/ml against all *S. aureus*, and inhibited 99.1% of isolates at the FDA-breakpoint for susceptibility (i.e. ≤0.12 μg/ml; Table 1). Equivalent modal MIC, $MIC_{50}$, $MIC_{90}$ results were obtained against MRSA and methicillin-susceptible isolates, and coagulase-negative staphylococci.
- Based on $MIC_{50}$ values against *S. aureus* and the MRSA subset, oritavancin ($MIC_{50/90}$, 0.03/0.06 μg/ml) was eight-fold more potent than tetracycline ($MIC_{50/90}$, 0.25/0.25-1 μg/ml), daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/ml) and 16- to 32-fold lower than trimethoprim/sulfamethoxazole ($MIC_{50/90}$, ≤0.5/≤0.5 μg/ml), vancomycin ($MIC_{50/90}$, 1/1 μg/ml) and linezolid ($MIC_{50/90}$, 1/1 μg/ml; Table 2).
- All *S. aureus* isolates in this study were susceptible to vancomycin. Oritavancin exhibited modal MIC and $MIC_{50}$ results of 0.03 μg/ml against MRSA isolates displaying vancomycin MIC values at ≤1 μg/ml, and modal MIC and $MIC_{50}$ results of 0.06 μg/ml against MRSA isolates displaying vancomycin MIC values of 2 μg/ml (Table 1).
- Vancomycin-susceptible *E. faecalis* isolates were susceptible to oritavancin ($MIC_{50/90}$, 0.015/0.03 μg/ml; 100.0% susceptible; Tables 1 and 2). VanA-phenotype *E. faecalis* ($MIC_{50/90}$, 0.25/0.5 μg/ml) exhibited oritavancin MIC values 16-fold higher than the susceptible isolates ($MIC_{50/90}$, 0.015/0.03 μg/ml). However, all *E. faecalis*, including high-level vancomycin-resistant strains were inhibited by oritavancin at ≤0.5 μg/ml.
- Against vancomycin-susceptible *E. faecalis*, oritavancin ($MIC_{50/90}$, 0.015/0.03 μg/ml; 100.0% susceptible) was 32- to 64-fold more potent than active comparators, such as ampicillin ($MIC_{50/90}$, 1/2 μg/ml; 100.0% susceptible), vancomycin ($MIC_{50/90}$, 1/2 μg/ml; 100.0% susceptible), daptomycin ($MIC_{50/90}$, 1/2 μg/ml; 100.0% susceptible) and linezolid ($MIC_{50/90}$, 1/1 μg/ml; 100.0% susceptible; Table 2).
- Oritavancin ($MIC_{50/90}$, 0.004/0.008 μg/ml) demonstrated potent *in vitro* activity against vancomycin-susceptible and -resistant (VanB) *E. faecium* (Table 1). Oritavancin MIC values ($MIC_{50/90}$, 0.03/0.12 μg/ml) against vancomycin-resistant VanA-phenotype *E. faecium* were eight- to 16-fold higher than those obtained from the susceptible counterpart isolates; still inhibiting all VanA isolates at ≤0.25 μg/ml.
- Oritavancin was 128- to 512-fold more active *in vitro* than vancomycin ($MIC_{50/90}$, 1/1 μg/ml; 100.0% susceptible), daptomycin ($MIC_{50/90}$, 2/4 μg/ml; 100.0% susceptible) and linezolid ($MIC_{50/90}$, 1/1 μg/ml; 100.0% susceptible) against vancomycin-susceptible *E. faecium*.
- Oritavancin ($MIC_{50/90}$, 0.03/0.12 μg/ml; 98.1% susceptible), daptomycin ($MIC_{50/90}$, ≤0.06/≤0.06 μg/ml; 100.0% susceptible) and penicillin ($MIC_{50/90}$, ≤0.06/≤0.06 μg/ml; 100.0% susceptible) were the most active agents tested *in vitro* against *S. pyogenes*.
- Oritavancin ($MIC_{50/90}$, 0.03/0.06 μg/ml; 98.1% susceptible) and penicillin ($MIC_{50/90}$, ≤0.06/≤0.06 μg/ml; 100.0% susceptible) were the most active tested agents *in vitro* against *S. agalactiae* (Tables 1 and 2).
- Oritavancin ($MIC_{50/90}$, 0.06/0.25 μg/ml; 100.0% susceptible), penicillin ($MIC_{50/90}$, ≤0.06/≤0.06 μg/ml; 100.0% susceptible), vancomycin ($MIC_{50/90}$, 0.25/0.25 μg/ml; 100.0% susceptible), daptomycin ($MIC_{50/90}$, ≤0.06/0.12 μg/ml; 100.0% susceptible) and clindamycin ($MIC_{50/90}$, ≤0.25/≤0.25 μg/ml; 93.2% susceptible) were similarly active *in vitro* against *S. dysgalactiae* (Table 2).
- Isolates of the *S. anginosus* group were all susceptible *in vitro* to oritavancin ($MIC_{50/90}$, 0.008/0.015 μg/ml; 100.0% susceptible), against which the highest oritavancin MIC value was 0.03 μg/ml (Tables 1 and 2).

**Table 1. Antimicrobial activity *in vitro* and MIC distribution for oritavancin against a contemporary (2012 – 2013) collection of clinical isolates causing SSSI.**

| Organism[a] (no. tested) | MIC (μg/ml) | | Number (cumulative %) inhibited at oritavancin MIC (μg/ml)[b] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 50% | 90% | ≤0.002 | 0.004 | 0.008 | 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 |
| ***S. aureus* (6,132)** | 0.03 | 0.06 | 13 (0.2) | 7 (0.3) | 155 (2.9) | 1599 (28.9) | **2568 (70.8)** | 1393 (93.5) | 343 (99.1) | 53 (>99.9) | 1 (100.0) |
| MSSA (3,780) | 0.03 | 0.06 | 11 (0.3) | 6 (0.4) | 105 (3.2) | 991 (29.4) | **1586 (71.4)** | 859 (94.1) | 198 (99.4) | 23 (>99.9) | 1 (100.0) |
| MRSA (2,352) | 0.03 | 0.06 | 2 (0.1) | 1 (0.1) | 50 (2.3) | 608 (28.1) | **982 (69.9)** | 534 (92.6) | 145 (98.7) | 30 (100.0) | |
| Vancomycin MIC, ≤1 μg/ml (2,316) | 0.03 | 0.06 | 2 (0.1) | 1 (0.1) | 50 (2.3) | 607 (28.5) | **974 (70.6)** | 516 (92.8) | 138 (98.8) | 28 (100.0) | |
| Vancomycin MIC, 2 μg/ml (36) | 0.06 | 0.12 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (2.8) | 8 (25.0) | **18 (75.0)** | 7 (94.4) | 2 (100.0) | |
| **CoNS (461)** | 0.03 | 0.06 | 6 (1.3) | 34 (8.7) | 95 (29.3) | 66 (43.6) | **135 (72.9)** | 105 (95.7) | 19 (99.8) | 1 (100.0) | |
| ***E. faecalis* (426)** | 0.015 | 0.03 | 0 (0.0) | 9 (2.1) | 102 (26.1) | **194 (71.6)** | 79 (90.1) | 23 (95.5) | 11 (98.1) | 5 (99.3) | 3 (100.0) |
| Vancomycin-susceptible (413) | 0.015 | 0.03 | 0 (0.0) | 9 (2.2) | 102 (26.9) | **192 (73.4)** | 79 (92.5) | 22 (97.8) | 9 (100.0) | | |
| VanA (10) | 0.25 | 0.5 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (20.0) | **5 (70.0)** | 3 (100.0) |
| ***E. faecium* (248)** | 0.008 | 0.06 | 20 (8.1) | **67 (35.1)** | 61 (59.7) | 34 (73.4) | 26 (83.9) | 26 (94.4) | 12 (99.2) | 2 (100.0) | |
| Vancomycin-susceptible (111) | 0.004 | 0.008 | 16 (14.4) | **58 (66.7)** | 37 (100.0) | | | | | | |
| VanA (123) | 0.03 | 0.12 | 1 (0.8) | 1 (1.6) | 22 (19.5) | **33 (46.3)** | 26 (67.5) | 26 (88.6) | 12 (98.4) | 2 (100.0) | |
| VanB (14) | 0.004 | 0.008 | 3 (21.4) | **8 (78.6)** | 2 (92.9) | 1 (100.0) | | | | | |
| **BHS (885)** | 0.03 | 0.12 | 15 (1.7) | 7 (2.5) | 117 (15.7) | **236 (42.4)** | 215 (66.7) | 115 (79.7) | 89 (90.0) | 68 (97.4) | 22 (99.9)[c] |
| *S. pyogenes* (469) | 0.03 | 0.12 | 11 (2.3) | 4 (3.2) | 72 (18.6) | **120 (44.1)** | 102 (65.9) | 61 (78.9) | 55 (90.6) | 35 (98.1) | 8 (99.8)[c] |
| *S. agalactiae* (269) | 0.03 | 0.06 | 1 (0.4) | 0 (0.4) | 35 (13.4) | **96 (49.1)** | 90 (82.5) | 25 (91.8) | 12 (96.3) | 5 (98.1) | 5 (100.0) |
| *S. dysgalactiae* (73) | 0.06 | 0.25 | 0 (0.0) | 0 (0.0) | 6 (8.2) | 11 (23.3) | 9 (35.6) | **18 (60.3)** | 12 (76.7) | 17 (100.0) | |
| **VGS (225)** | 0.008 | 0.015 | 46 (20.4) | 26 (32.0) | **90 (72.0)** | 42 (90.7) | 7 (93.8) | 11 (98.7) | 3 (100.0) | | |
| *S. anginosus* group (135) | 0.008 | 0.015 | 37 (27.4) | 17 (40.0) | **62 (85.9)** | 18 (99.3) | 1 (100.0) | | | | |

a. MSSA = methicillin-susceptible *S. aureus*; MRSA = methicillin-resistant *S. aureus*; CoNS = coagulase-negative staphylococci; VanA = vancomycin and teicoplanin MIC values of >4 and >8 μg/ml, respectively; VanB = vancomycin and teicoplanin MIC values of >4 and ≤8 μg/ml, respectively; BHS = β-hemolytic streptococci; VGS = viridans group streptococci.
b. Modal MIC values are shown in bold.
c. One isolate displayed a MIC of 1 μg/ml.

**Table 2. Antimicrobial activity of oritavancin and comparator agents *in vitro* against a contemporary (2012 – 2013) collection of clinical isolates responsible for SSSI.**

| Organism[a] (no. tested) Antimicrobial agent | MIC (mg/ml) | | % Susceptible/ %Intermediate/%Resistant[b] | |
|---|---|---|---|---|
| | 50% | 90% | CLSI | EUCAST |
| ***S. aureus* (6,132)** | | | | |
| Oritavancin | 0.03 | 0.06 | 99.1 / - / - | - / - / - |
| Oxacillin | 0.5 | >2 | 61.6 / 0.0 / 38.4 | 61.6 / 0.0 / 38.4 |
| Vancomycin | 1 | 1 | 100.0 / 0.0 / 0.0 | 100.0 / 0.0 / 0.0 |
| Erythromycin | 0.25 | >16 | 52.7 / 2.2 / 45.1 | 53.0 / 0.6 / 46.4 |
| Clindamycin | ≤0.25 | >2 | 89.4 / 0.1 / 10.5 | 89.0 / 0.4 / 10.6 |
| Tetracycline | 0.25 | 0.25 | 93.8 / 0.6 / 5.6 | 93.2 / 0.3 / 6.5 |
| Levofloxacin | 0.25 | >4 | 69.9 / 1.2 / 28.9 | 69.9 / 1.2 / 28.9 |
| Daptomycin | 0.25 | 0.5 | 99.9 / - / - | 99.9 / 0.0 / 0.1 |
| Linezolid | 1 | 1 | >99.9 / 0.0 / <0.1 | >99.9 / 0.0 / <0.1 |
| TMP/SMXd | ≤0.5 | ≤0.5 | 99.2 / 0.0 / 0.8 | 99.2 / 0.1 / 0.7 |
| MRSA (2,352) | | | | |
| Oritavancin | 0.03 | 0.06 | 98.7 / - / - | - / - / - |
| Vancomycin | 1 | 1 | 100.0 / 0.0 / 0.0 | 100.0 / 0.0 / 0.0 |
| Erythromycin | >16 | >16 | 16.5 / 1.9 / 81.6 | 16.9 / 0.4 / 82.7 |
| Clindamycin | ≤0.25 | >2 | 78.3 / 0.1 / 21.6 | 77.8 / 0.5 / 21.7 |
| Tetracycline | 0.25 | 1 | 91.6 / 0.7 / 7.7 | 90.6 / 0.7 / 8.7 |
| Levofloxacin | 4 | >4 | 34.6 / 1.5 / 63.9 | 34.6 / 1.5 / 63.9 |
| Daptomycin | 0.25 | 0.5 | 99.8 / - / - | 99.8 / 0.0 / 0.2 |
| Linezolid | 1 | 1 | 98.9 / 0.0 / 0.1 | 99.9 / 0.0 / 0.1 |
| TMP/SMX | ≤0.5 | ≤0.5 | 98.5 / 0.0 / 1.5 | 98.5 / 0.1 / 1.4 |
| **Vancomycin-susceptible *E. faecalis* (426)** | | | | |
| Oritavancin | 0.015 | 0.03 | 100.0 / - / - | - / - / - |
| Ampicillin | 1 | 2 | 100.0 / 0.0 / 0.0 | 100.0 / 0.0 / 0.0 |
| Vancomycin | 1 | 2 | 100.0 / 0.0 / 0.0 | 100.0 / 0.0 / 0.0 |
| Erythromycin | >16 | >16 | 8.5 / 37.0 / 54.5 | - / - / - |
| Tetracycline | >32 | >32 | 20.6 / 0.5 / 78.9 | - / - / - |
| Levofloxacin | 1 | >4 | 72.1 / 0.5 / 27.4 | 72.6 / 0.0 / 27.4 |
| Daptomycin | 1 | 2 | 100.0 / - / - | - / - / - |
| Linezolid | 1 | 1 | 100.0 / 0.0 / 0.0 | 100.0 / 0.0 / 0.0 |
| **Vancomycin-susceptible *E. faecium* (248)** | | | | |
| Oritavancin | 0.004 | 0.008 | - / - / - | - / - / - |
| Ampicillin | >8 | >8 | 12.6 / 0.0 / 87.4 | 11.7 / 0.9 / 87.4 |
| Vancomycin | 1 | 1 | 100.0 / 0.0 / 0.0 | 100.0 / 0.0 / 0.0 |
| Erythromycin | >16 | >16 | 5.4 / 9.9 / 84.7 | - / - / - |
| Tetracycline | 0.5 | >32 | 52.7 / 0.9 / 46.4 | - / - / - |
| Levofloxacin | >4 | >4 | 7.2 / 6.3 / 86.5 | 13.5 / 0.0 / 86.5 |
| Daptomycin | 2 | 4 | 100.0 / - / - | - / - / - |
| Linezolid | 1 | 1 | 100.0 / 0.0 / 0.0 | 100.0 / 0.0 / 0.0 |

| Organism[a] (no. tested) Antimicrobial agent | MIC (mg/ml) | | % Susceptible/ %Intermediate/%Resistant[b] | |
|---|---|---|---|---|
| | 50% | 90% | CLSI | EUCAST |
| ***S. pyogenes* (469)** | | | | |
| Oritavancin | 0.03 | 0.12 | 98.1 / - / - | - / - / - |
| Penicillin | ≤0.06 | ≤0.06 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Vancomycin | 0.25 | 0.5 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Erythromycin | ≤0.12 | 1 | 88.0 / 0.4 / 11.6 | 88.0 / 0.4 / 11.6 |
| Clindamycin | ≤0.25 | ≤0.25 | 96.4 / 0.0 / 3.6 | 96.4 / 0.0 / 3.6 |
| Tetracycline | 0.25 | 32 | 81.9 / 0.8 / 17.3 | 81.6 / 0.3 / 18.1 |
| Levofloxacin | 0.5 | 1 | 100.0 / 0.0 / 0.0 | 94.2 / 5.8 / 0.0 |
| Daptomycin | ≤0.06 | ≤0.06 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Linezolid | 1 | 1 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| TMP/SMX | ≤0.5 | ≤0.5 | - / - / - | 98.1 / 0.4 / 1.5 |
| ***S. agalactiae* (269)** | | | | |
| Oritavancin | 0.03 | 0.06 | 98.1 / - / - | - / - / - |
| Penicillin | ≤0.06 | ≤0.06 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Vancomycin | 0.5 | 0.5 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Erythromycin | ≤0.12 | >16 | 52.6 / 2.6 / 44.8 | 52.6 / 2.6 / 44.8 |
| Clindamycin | ≤0.25 | >2 | 72.1 / 0.8 / 27.1 | 72.9 / 0.0 / 27.1 |
| Tetracycline | 32 | >32 | 17.3 / 1.5 / 81.2 | 16.5 / 0.8 / 82.7 |
| Levofloxacin | 0.5 | 1 | 98.1 / 0.8 / 1.1 | 95.9 / 2.2 / 1.9 |
| Daptomycin | 0.25 | 0.25 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Linezolid | 1 | 1 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| TMP/SMX | ≤0.5 | ≤0.5 | - / - / - | 99.6 / 0.0 / 0.4 |
| ***S. dysgalactiae* (73)** | | | | |
| Oritavancin | 0.06 | 0.25 | 100.0 / - / - | - / - / - |
| Penicillin | ≤0.06 | ≤0.06 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Vancomycin | 0.25 | 0.25 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Erythromycin | ≤0.12 | 16 | 72.6 / 0.0 / 27.4 | 72.6 / 0.0 / 27.4 |
| Clindamycin | ≤0.25 | ≤0.25 | 93.2 / 0.0 / 6.8 | 93.2 / 0.0 / 6.8 |
| Tetracycline | 0.25 | 32 | 61.1 / 7.0 / 31.9 | 56.9 / 4.2 / 38.9 |
| Levofloxacin | 0.5 | 1 | 98.6 / 0.0 / 1.4 | 94.5 / 4.1 / 1.4 |
| Daptomycin | ≤0.06 | 0.12 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Linezolid | 1 | 1 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| TMP/SMX | ≤0.5 | ≤0.5 | - / - / - | 97.3 / 0.0 / 2.7 |
| ***S. anginosus* group (135)** | | | | |
| Oritavancin | 0.008 | 0.015 | 100.0 / - / - | - / - / - |
| Penicillin | ≤0.06 | ≤0.06 | 96.3 / 3.7 / 0.0 | 99.3 / 0.7 / 0.0 |
| Vancomycin | 0.5 | 1 | 100.0 / - / - | 100.0 / 0.0 / 0.0 |
| Erythromycin | ≤0.12 | 2 | 81.3 / 1.5 / 17.2 | - / - / - |
| Clindamycin | ≤0.25 | ≤0.25 | 91.9 / 0.0 / 8.1 | 91.9 / 0.0 / 8.1 |
| Tetracycline | 0.5 | 32 | 69.2 / 3.7 / 27.1 | - / - / - |
| Levofloxacin | 0.5 | 1 | 98.5 / 0.8 / 0.7 | - / - / - |
| Daptomycin | 0.25 | 0.5 | 100.0 / - / - | - / - / - |
| Linezolid | 1 | 1 | 100.0 / - / - | - / - / - |
| TMP/SMX | ≤0.5 | ≤0.5 | - / - / - | - / - / - |

a. MRSA = methicillin-resistant *S. aureus*.
b. MIC interpretations for oritavancin were based on breakpoint criteria available in the product package insert (2014). Breakpoint criteria for comparator agents were those from CLSI (M100-S24, 2014) and/or EUCAST (2014), as available.
c. Breakpoint not available.
d. Trimethoprim/sulfamethoxazole.

## Conclusions

- This study evaluated the *in vitro* activity of oritavancin and comparators against a recent collection of Gram-positive clinical isolates implicated in SSSI, including MRSA in the USA, Europe, Israel and Turkey.
- Overall, the *in vitro* activity of oritavancin was greater than that of tested comparators, except against *S. dysgalactiae* isolates, for which comparable activity was noted for oritavancin, penicillin and daptomycin.
- According to the recently-approved FDA breakpoints, 98.1 - 100.0% of indicated pathogens were susceptible to oritavancin.
- The data presented here provide baseline oritavancin MIC results against clinical isolates collected in 2012-2013, just prior to oritavancin regulatory approval in 2014. Oritavancin represents the most recent addition to the anti-Gram-positive armamentarium.

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## References

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