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Assessment of Oritavancin Activity Tested against Gram-positive Bacteria from USA and European Medical Centers over a Three-year Period (2008 – 2010)

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Amended Abstract

Background: Oritavancin is under development for the treatment of acute bacterial skin and skin structure infections (Phase 3 trials). Oritavancin activity has been monitored over a three-year period as part of the SENTRY Antimicrobial Surveillance Program. The results obtained during this period are presented here.

Methods: Gram-positive isolates (28,664) were collected from USA (30 sites) and 14 European nations (38 sites), including Turkey and Israel. Identification was performed by standard algorithms and Vitek 2, when needed. Susceptibility testing (M07-A8) and interpretations (M100-S21) were performed by reference CLSI methods.

Results: Oritavancin exhibited potent activity against all staphylococcal species (**Table)**. Vancomycin, daptomycin and linezolid had good coverage against staphylococci. Oritavancin showed $MIC_{50/90}$ values eight-fold lower than daptomycin and 16- to 64-fold lower than vancomycin and linezolid against staphylococci. Against vancomycin-susceptible and Van-B type *E. faecalis*, oritavancin was 32- to 64-fold more active than ampicillin ($MIC_{50/90}$, ≤1/2 μg/mL; 100.0% susceptible), vancomycin, daptomycin and linezolid. Oritavancin was 2- to 4-fold more potent than ampicillin ($MIC_{50/90}$, ≤1/2 μg/mL; 100.0% susceptible), daptomycin and linezolid against VanA-type *E. faecalis*. Oritavancin, daptomycin, linezolid (**Table**) and quinupristin/dalfopristin ($MIC_{50/90}$, ≤0.5/1 μg/mL; 96.1% susceptible) had activity against VanA-type *E. faecium*. Oritavancin was ≥8-fold more active than comparators against multidrug-resistant (MDR) viridans group streptococci. Oritavancin ($MIC_{50/90}$, 0.06/0.12 μg/mL) and penicillin ($MIC_{50/90}$, 0.06/0.06 μg/mL) were similarly active against MDR β-hemolytic streptococci and ≥2-fold more potent (MIC_{90}) than comparators.

Conclusions: These three-year surveillance data show potent activity of oritavancin against Gram-positive pathogens, with equal or greater potency than comparators. These results provide a susceptibility benchmark for oritavancin and comparators against current Gram-positive pathogens as this drug enters late-stage clinical development.

Organism[a] (No. tested[b])	Oritavancin MIC μg/mL 50%	Oritavancin MIC μg/mL 90%	Vancomycin MIC μg/mL 50%	Vancomycin MIC μg/mL 90%	Vancomycin %S[c]	Daptomycin MIC μg/mL 50%	Daptomycin MIC μg/mL 90%	Daptomycin %S	Linezolid MIC μg/mL 50%	Linezolid MIC μg/mL 90%	Linezolid %S
MSSA (6,520)	0.03	0.06	1	1	100.0	0.25	0.5	100.0	1	2	100.0
MRSA (4,666)	0.03	0.06	1	1	100.0	0.25	0.5	99.9	1	2	99.9
CoNS (2,875)	0.03	0.06	1	2	100.0	0.25	0.5	99.8	1	1	99.2
VA-S EF (3,057)	0.015	0.03	1	2	100.0	1	2	>99.9	1	2	>99.9
VanA EF (66)	0.25	0.5	>16	>16	0.0	1	1	100.0	1	2	100.0
VanB EF(32)	0.015	0.03	>16	>16	0.0	1	2	100.0	1	1	100.0
VA-S EFM (777)	≤0.008	≤0.008	1	1	100.0	2	4	99.5	1	2	99.5
VanA EFM (998)	0.03	0.06	>16	>16	0.0	2	2	99.7	1	2	98.2
VanB EFM (56)	≤0.008	≤0.008	>16	>16	0.0	2	2	100.0	1	2	98.3
MDR VGS (32)	≤0.008	0.06	0.5	0.5	100.0	0.25	1	100.0	0.5	1	100.0
MDR BHS (215)	0.06	0.12	0.5	0.5	100.0	0.25	0.25	100.0	1	1	100.0

a. MSSA = methicillin-susceptible *S. aureus*; MRSA = methicillin-resistant *S. aureus*; CoNS = coagulase-negative staphylococci; VA-S = vancomycin-susceptible; VanA and VanB phenotypes were determined based on vancomycin and teicoplanin MIC results; MDR = multidrug-resistant (resistance to three to four classes of drugs); BHS = β-hemolytic streptococci; VGS = viridans group streptococci; EF = *E. faecalis*; EFM = *E. faecium*.

b. Table does not display all Gram-positive clinical isolates tested during the study period.

c. %S = percentage susceptible (CLSI, M100-S21).

Introduction

Acute bacterial skin and skin structure infections (ABSSSI) involve deeper skin or soft tissue structures. These infections usually require rapid and intensive antimicrobial intervention to minimize tissue damage and prevent further spread of infection. *Staphylococcus aureus* remains the leading etiology, followed by β-hemolytic streptococci (BHS). The proportion of ABSSSI caused by methicillin-resistant *S. aureus* (MRSA) has increased significantly in the USA in the last decade. MRSA currently accounts for 50 to 60% of all ABSSSI seen in USA emergency departments, and for 50% of surgical site infections.

Oritavancin is being developed for the treatment of ABSSSI (Phase 3 trials). It has demonstrated broad *in vitro* activity against Gram-positive pathogens, including MRSA, and *S. aureus* strains with reduced susceptibility to vancomycin. In addition, oritavancin possesses intracellular activity against pathogens sequestered in neutrophils and macrophages. As oritavancin enters late-stage clinical development, its activity has been monitored over a three-year period, as part of the SENTRY Antimicrobial Surveillance Program. The results obtained during this time period are presented here.

Methods

Bacterial strain collection. Gram-positive clinical isolates (28,664) were collected from 30 medical institutions in the USA and 38 centers in 14 European countries, including Turkey and Israel. Isolates were submitted to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) following established protocols as part of the SENTRY Antimicrobial Surveillance Program. Isolates included were: *S. aureus* (16,624), coagulase-negative staphylococci (CoNS; 3,054), *Enterococcus faecalis* (3,447), *Enterococcus faecium* (1,988), viridans group streptococci (VGS; 938) and BHS (2,613). Bacterial species identification was performed by using an automated system (Vitek®2; bioMérieux, Hazelwood, Missouri, USA) or conventional biochemical algorithms, as required.

Antimicrobial susceptibility test methods. Isolates were tested for susceptibility by broth microdilution methods following the Clinical and Laboratory Standards Institute (CLSI; M07-A8, 2009) recommendations. Susceptibility testing was performed in cation-adjusted Mueller-Hinton broth (CA-MHB) using dry-form panels (TREK Diagnostic Systems, Cleveland, Ohio, USA). These panels provide results equivalent to the CLSI-approved broth microdilution method supplemented with 0.002% polysorbate-80. CA-MHB was supplemented with 2.5–5% lysed horse blood for testing of streptococci.

Quality assurance was performed by concurrent testing of CLSI-recommended (M100-S21, 2011) strains: *E. faecalis* ATCC 29212, *S. aureus* ATCC 29213 and *Streptococcus pneumoniae* ATCC 49619. Interpretation of comparator MIC results was in accordance with published CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST, 2011) criteria.

Results-1

- Oritavancin ($MIC_{50/90}$, 0.03/0.06 μg/mL) was very active against staphylococci, inhibiting all *S. aureus* and CoNS isolates at ≤0.5 and ≤0.25 μg/mL, respectively (**Table 1**).
- Vancomycin, teicoplanin, daptomycin and linezolid also demonstrated antimicrobial activity when tested against MRSA (≥99.9% susceptible) or the entire population of CoNS isolates (≥97.5% susceptible; CLSI criteria; **Table 2**).
- Oritavancin (MIC_{90}, 0.06 μg/mL) was eight-fold more potent than daptomycin (MIC_{90}, 0.5 μg/mL) and 16- to 32-fold more potent than vancomycin (MIC_{90}, 1 – 2 μg/mL) or linezolid (MIC_{90}, 1 – 2 μg/mL) when tested against MRSA or CoNS (**Table 2**).
- Overall, vancomycin-susceptible and VanB-type *E. faecalis* isolates were very susceptible to oritavancin ($MIC_{50/90}$, 0.015/0.03 μg/mL; **Table 1**). Higher (16-fold) oritavancin MIC results ($MIC_{50/90}$, 0.25/0.5 μg/mL) were observed for VanA-type *E. faecalis* strains.
- While ampicillin (MIC_{90}, 2 μg/mL), daptomycin (MIC_{90}, 1 – 2 μg/mL) and linezolid (MIC_{90}, 1 – 2 μg/mL) were active against all *E. faecalis* isolates, oritavancin demonstrated MIC results two- to 64-fold lower than these comparators (**Table 2**).
- Oritavancin inhibited all vancomycin-susceptible and -resistant (VanB-type) *E. faecium* strains at ≤0.03 μg/mL (**Table 1**). VanA-type *E. faecium* isolates were inhibited by oritavancin at ≤0.5 μg/mL.
- Daptomycin ($MIC_{50/90}$, 2/2 μg/mL; ≥99.7% susceptible) and linezolid ($MIC_{50/90}$, 1/2 μg/mL; ≥98.2% susceptible) showed similar activity when tested against vancomycin-resistant *E. faecium* (**Table 2**). Oritavancin exhibited ≥32-fold greater activity than these comparator agents.
- Multidrug-resistant (MDR; resistant to three or four classes of drugs) clinical isolates of VGS and BHS isolates were equally susceptible to oritavancin when compared with the respective susceptible counterpart strains (**Tables 1 and 2**).
- Oritavancin ($MIC_{50/90}$, ≤0.008/0.06 μg/mL) demonstrated MIC_{90} results eight- to 16-fold lower than vancomycin ($MIC_{50/90}$, 0.5/0.5 μg/mL), daptomycin ($MIC_{50/90}$, 0.25/1 μg/mL) and linezolid ($MIC_{50/90}$, 0.5/1 μg/mL; **Table 2**) against MDR VGS.
- Penicillin (MIC_{90}, 0.06 μg/mL) and oritavancin (MIC_{90}, 0.12 μg/mL) were the most active compounds tested against susceptible and MDR subsets of BHS. These two agents were two- to 16-fold more active than levofloxacin, vancomycin, daptomycin and linezolid when tested against these two subsets (**Table 2**) .

Results-2

Table 1. MIC distribution of oritavancin tested against Gram-positive species/groups and resistant subsets submitted as part of the 2008 – 2010 international oritavancin surveillance program.

Organism (number tested)	MIC (μg/mL) 50%	MIC (μg/mL) 90%	Number (cumulative %) inhibited at each oritavancin MIC (μg/mL)[a] ≤0.008	0.015	0.03	0.06	0.12	0.25	0.5	1
S. aureus (16,624)	0.03	0.06	667(4.0)	5434(36.7)	**7846(83.9)**	2301(97.7)	327(99.7)	48(>99.9)	1(100.0)	–
Oxacillin-susceptible (9,789)	0.03	0.06	431(4.4)	3269(37.8)	**4571(84.5)**	1310(97.9)	181(99.7)	27(100.0)	–	–
Oxacillin-resistant (6,835)	0.03	0.06	236(3.5)	2165(35.1)	**3275(83.0)**	991(97.5)	146(99.7)	21(>99.9)	1(100.0)	–
CoNS (3,054)	0.03	0.06	557(18.2)	575(37.1)	**1236(77.5)**	588(96.8)	83(99.5)	15(100.0)	–	–
Oxacillin-susceptible (771)	0.015	0.06	205(26.6)	186(50.7)	**262(84.7)**	105(98.3)	13(100.0)	–	–	–
Oxacillin-resistant (2,283)	0.03	0.06	352(15.4)	389(32.5)	**974(75.1)**	483(96.3)	70(99.3)	15(100.0)	–	–
E. faecalis (3,447)	0.015	0.03	1008(29.2)	**1519(73.3)**	685(93.2)	142(97.3)	28(98.1)	41(99.3)	21(99.9)	3(100.0)
Vancomycin-susceptible (3,336)	0.015	0.03	999(30.0)	**1497(74.8)**	678(95.1)	136(99.2)	20(99.8)	5(99.9)	1(100.0)	–
VanB (34)	0.015	0.03	8(23.5)	**18(76.5)**	5(91.2)	2(97.1)	0(97.1)	1(100.0)	–	–
VanA (77)	0.25	0.5	1(1.3)	4(6.5)	2(9.1)	4(14.3)	8(24.7)	**35(70.1)**	20(96.1)	3(100.0)
E. faecium (1,988)	≤0.008	0.06	**1021(51.4)**	155(59.2)	361(77.3)	338(94.3)	96(99.1)	14(99.9)	3(100.0)	–
Vancomycin-susceptible (855)	≤0.008	≤0.008	**836(97.8)**	15(99.5)	4(100.0)	–	–	–	–	–
VanB (59)	≤0.008	≤0.008	**58(98.3)**	0(98.3)	1(100.0)	–	–	–	–	–
VanA (1,074)	0.03	0.06	127(11.8)	140(24.9)	**356(58.0)**	338(90.0)	96(98.4)	14(99.7)	3(100.0)	–
Viridans group streptococci (938)	≤0.008	0.03	**616(65.7)**	121(78.6)	101(90.0)	63(96.1)	32(99.5)	4(99.9)	1(100.0)	–
Susceptible-group (818)	≤0.008	0.03	**549(67.1)**	95(78.7)	89(90.0)	51(95.8)	29(99.4)	4(99.9)	1(100.0)	–
MDR (120)	≤0.008	0.06	**67(55.8)**	26(77.5)	12(87.5)	12(97.5)	3(100.0)	–	–	–
β-hemolytic streptococci (2,613)	0.06	0.12	297(11.4)	354(24.9)	636(49.3)	**697(75.9)**	426(92.2)	177(99.0)	25(99.9)	1(100.0)
Susceptible-group (2,360)	0.03	0.12	280(11.9)	320(25.4)	572(50.0)	**620(75.9)**	383(92.2)	161(99.0)	23(99.9)	1(100.0)
MDR (253)	0.06	0.12	17(6.7)	34(20.2)	64(45.5)	**77(75.9)**	43(92.9)	16(99.2)	2(100.0)	–

CoNS = coagulase-negative staphylococci. The VanA phenotype was characterized by non-susceptibility to vancomycin (MIC, ≥8 μg/mL) and teicoplanin (MIC, ≥16 μg/mL), while VanB was based on non-susceptibility to vancomycin (MIC, ≥8 μg/mL) and susceptibility to teicoplanin (≤8 μg/mL), according to CLSI criteria. MDR, multidrug-resistant (resistance to three to four classes of drugs).

a. Modal MIC results are in bold.

Table 2. Antimicrobial activity of oritavancin and comparator agents tested against Gram-positive species/groups and resistant subsets submitted as part of the 2008 – 2010 international oritavancin surveillance program.

Organism[a] (no. tested)/agent	Range	MIC (μg/mL) 50%	MIC (μg/mL) 90%	% Susc./Resistant[b] CLSI	% Susc./Resistant[b] EUCAST
MSSA (9,789)					
Oritavancin	≤0.008 – 0.25	0.03	0.06	– / –	– / –
Vancomycin	≤0.12 – 2	1	1	100.0 / 0.0	100.0 / 0.0
Teicoplanin	≤2 – 8	≤2	≤2	100.0 / 0.0	99.8 / 0.2
Daptomycin	≤0.06 – 1	0.25	0.5	100.0 / –	100.0 / 0.0
Linezolid	≤0.12 – 2	1	2	100.0 / 0.0	100.0 / 0.0
Erythromycin	≤0.25 – >2	≤0.25	>2	75.3 / 23.3	75.8 / 23.7
Clindamycin	≤0.25 – >2	≤0.25	≤0.25	95.9 / 3.8	95.5 / 4.1
Tetracycline	≤2 – >8	≤2	≤2	95.3 / 4.0	94.7 / 5.1
Levofloxacin	≤0.5 – >4	≤0.5	≤0.5	91.4 / 7.9	91.4 / 7.9
TMP/SMX	≤0.5 – >2	≤0.5	≤0.5	99.2 / 0.8	99.2 / 0.8
MRSA (6,835)					
Oritavancin	≤0.008 – 0.5	0.03	0.06	– / –	– / –
Vancomycin	0.25 – 2	1	1	100.0 / 0.0	100.0 / 0.0
Teicoplanin	≤2 – 8	≤2	≤2	100.0 / 0.0	99.3 / 0.7
Daptomycin	≤0.06 – 4	0.25	0.5	99.9 / –	99.9 / 0.1
Linezolid	≤0.12 – >8	1	2	99.9 / 0.1	99.9 / 0.1
Erythromycin	≤0.25 – >2	>2	>2	14.7 / 84.6	15.0 / 84.8
Clindamycin	≤0.25 – >2	≤0.25	>2	65.6 / 34.1	65.0 / 34.4
Tetracycline	≤2 – >8	≤2	≤2	92.2 / 7.2	90.3 / 8.6
Levofloxacin	≤0.5 – >4	>4	>4	24.3 / 74.6	24.3 / 74.6
TMP/SMX	≤0.5 – >2	≤0.5	≤0.5	98.1 / 1.9	98.1 / 1.8
CoNS (3,054)					
Oritavancin	≤0.008 – 0.25	0.03	0.06	– / –	– / –
Oxacillin	≤0.25 – >2	>2	>2	25.2 / 74.8	25.2 / 74.8
Vancomycin	≤0.12 – 4	1	2	100.0 / 0.0	99.2 / 0.8
Teicoplanin	≤2 – >8	≤2	8	97.5 / 0.4	89.2 / 10.8
Daptomycin	≤0.06 – 4	0.25	0.5	99.8 / –	99.8 / 0.2
Linezolid	≤0.12 – >8	1	1	99.2 / 0.8	99.2 / 0.8
Erythromycin	≤0.25 – >2	>2	>2	35.7 / 63.5	35.9 / 63.7
Clindamycin	≤0.25 – >2	≤0.25	>2	69.0 / 29.4	66.9 / 31.0
Tetracycline	≤2 – >8	≤2	>8	86.2 / 12.6	79.8 / 16.7
Levofloxacin	≤0.5 – >4	>4	>4	44.0 / 53.4	44.0 / 53.4
TMP/SMX	≤0.5 – >2	≤0.5	>2	61.2 / 38.8	61.2 / 34.8
Vancomycin-susceptible *E. faecalis* (3,336)					
Oritavancin	≤0.008 – 0.5	0.015	0.03	– / –	– / –
Ampicillin	≤1 – 8	≤1	2	100.0 / 0.0	99.8 / 0.0
Vancomycin	0.25 – 4	1	2	100.0 / 0.0	100.0 / 0.0
Daptomycin	≤0.06 – 8	1	2	>99.9 / –	– / –
Linezolid	0.12 – >8	1	2	>99.9 / <0.1	>99.9 / <0.1
Teicoplanin	≤2 – 8	≤2	≤2	100.0 / 0.0	99.9 / 0.1
Tetracycline	≤2 – >8	>8	>8	24.8 / 75.1	– / –
Levofloxacin	≤0.5 – >4	1	>4	69.2 / 30.3	– / –
Q/D	≤0.5 – >2	>2	>2	0.8 / 95.4	0.8 / 91.0
VanA-*E. faecalis* (77)					
Oritavancin	≤0.004 – 1	0.25	0.5	– / –	– / –
Ampicillin	≤1 – 4	≤1	2	100.0 / 0.0	100.0 / 0.0
Vancomycin	>16	>16	>16	0.0 / 100.0	0.0 / 100.0
Teicoplanin	>8	>8	>8	0.0 / 98.7	0.0 / 100.0
Daptomycin	≤0.06 – 2	1	1	100.0 / –	– / –
Linezolid	0.5 – 2	1	2	100.0 / 0.0	100.0 / 0.0
Tetracycline	≤2 – >8	>8	>8	6.5 / 93.5	– / –
Levofloxacin	1 – >4	>4	>4	5.2 / 94.8	– / –
Q/D	2 – >2	>2	>2	0.0 / 98.7	0.0 / 97.4
VanB-*E. faecalis* (34)					
Oritavancin	≤0.008 – 0.25	0.015	0.03	– / –	– / –
Ampicillin	≤1 – 4	≤1	2	100.0 / 0.0	100.0 / 0.0
Vancomycin	8 – >16	>16	>16	0.0 / 82.4	0.0 / 100.0
Teicoplanin	≤2 – 8	≤2	4	100.0 / 0.0	85.3 / 14.7
Daptomycin	≤0.06 – 2	1	2	100.0 / –	– / –
Linezolid	0.5 – 2	1	1	100.0 / 0.0	100.0 / 0.0
Tetracycline	≤2 – >8	>8	>8	32.4 / 67.6	– / –
Levofloxacin	1 – >4	>4	>4	8.8 / 91.2	– / –
Q/D	>2	>2	>2	0.0 / 100.0	0.0 / 100.0
Vancomycin-susceptible *E. faecium* (855)					
Oritavancin	≤0.008 – 0.03	≤0.008	≤0.008	– / –	– / –
Ampicillin	≤1 – >8	>8	>8	14.2 / 85.8	13.6 / 85.8
Vancomycin	0.25 – 4	1	1	100.0 / 0.0	100.0 / 0.0
Teicoplanin	≤2 – 4	≤2	≤2	100.0 / 0.0	99.5 / 0.5
Daptomycin	≤0.06 – >8	2	4	99.5 / –	– / –
Linezolid	0.5 – >8	1	2	99.5 / 0.5	99.5 / 0.5
Tetracycline	≤2 – >8	≤2	>8	59.1 / 40.5	– / –
Levofloxacin	≤0.5 – >4	>4	>4	14.7 / 78.8	– / –
Q/D	≤0.5 – >2	1	>2	70.1 / 18.6	70.1 / 15.1
VanA-*E. faecium* (1,074)					
Oritavancin	≤0.008 – 0.5	0.03	0.06	– / –	– / –
Vancomycin	>16	>16	>16	0.0 / 100.0	0.0 / 100.0
Teicoplanin	>8	>8	>8	0.0 / 96.1	0.0 / 100.0
Daptomycin	≤0.06 – 8	2	2	99.7 / –	– / –
Linezolid	0.5 – >8	1	2	98.2 / 1.4	98.6 / 1.4
Tetracycline	≤2 – >8	>8	>8	46.8 / 52.3	– / –
Levofloxacin	1 – >4	>4	>4	1.7 / 98.1	– / –
Q/D	≤0.5 – >2	≤0.5	1	96.1 / 1.1	96.1 / 0.8
VanB-*E. faecium* (59)					
Oritavancin	≤0.008 – 0.03	≤0.008	≤0.008	– / –	– / –
Ampicillin	≤1 – >8	>8	>8	1.7 / 98.3	1.7 / 98.3
Vancomycin	8 – >16	>16	>16	0.0 / 79.7	0.0 / 100.0
Teicoplanin	≤2 – 8	≤2	8	100.0 / 0.0	72.9 / 27.1
Daptomycin	≤0.06 – 4	2	2	100.0 / –	– / –
Linezolid	0.5 – 4	1	2	98.3 / 0.0	100.0 / 0.0
Tetracycline	≤2 – >8	≤2	>8	62.7 / 37.3	– / –
Levofloxacin	1 – >4	>4	>4	11.9 / 86.4	– / –
Q/D	≤0.5 – >2	≤0.5	>2	83.1 / 16.9	83.1 / 16.9
Non-MDR VGS (818)					
Oritavancin	≤0.008 – 0.5	≤0.008	0.03	– / –	– / –
Penicillin	≤0.03 – >4	0.06	1	76.9 / 3.1	85.2 / 3.1
Vancomycin	≤0.12 – 1	0.5	1	100.0 / –	100.0 / 0.0
Teicoplanin	≤2 – 4	≤2	≤2	– / –	99.8 / 0.2
Daptomycin	≤0.06 – 2	0.25	0.5	99.4 / –	– / –
Linezolid	≤0.12 – 2	1	1	100.0 / –	– / –
Erythromycin	≤0.25 – >2	≤0.25	>2	58.3 / 38.3	– / –
Clindamycin	≤0.25 – >2	≤0.25	≤0.25	98.5 / 1.2	98.8 / 1.2
Tetracycline	≤2 – >8	≤2	>8	72.1 / 23.8	– / –
Levofloxacin	≤0.5 – >4	1	2	96.2 / 3.1	– / –
MDR VGS (120)					
Oritavancin	≤0.008 – 0.12	≤0.008	0.06	– / –	– / –
Penicillin	≤0.03 – >4	0.12	>4	51.7 / 15.8	63.3 / 15.8
Vancomycin	0.25 – 1	0.5	0.5	100.0 / –	100.0 / 0.0
Teicoplanin	≤2 – 4	≤2	≤2	– / –	99.2 / 0.8
Daptomycin	≤0.06 – 1	0.25	1	100.0 / –	– / –
Linezolid	0.12 – 1	0.5	1	100.0 / –	– / –
Erythromycin	0.5 – >2	>2	>2	0.0 / 99.2	0.0 / 99.2
Clindamycin	≤0.25 – >2	>2	>2	1.2 / 97.2	2.8 / 97.2
Tetracycline	≤2 – >8	>8	>8	0.4 / 98.4	0.4 / 99.6
Levofloxacin	≤0.5 – >4	≤0.5	1	96.4 / 3.6	94.1 / 3.6
MDR BHS (253)					
Oritavancin	≤0.008 – 0.5	0.06	0.12	– / –	– / –
Penicillin	≤0.03 – 0.12	0.06	0.06	100.0 / –	100.0 / 0.0
Vancomycin	0.25 – 1	0.5	0.5	100.0 / –	100.0 / 0.0
Teicoplanin	≤2	≤2	≤2	– / –	100.0 / 0.0
Daptomycin	≤0.06 – 0.5	0.25	0.25	100.0 / –	100.0 / 0.0
Linezolid	0.25 – 1	1	1	100.0 / –	100.0 / 0.0
Erythromycin	0.5 – >2	>2	>2	0.0 / 99.2	0.0 / 99.2
Clindamycin	≤0.25 – >2	>2	>2	1.2 / 97.2	2.8 / 97.2
Tetracycline	≤2 – >8	>8	>8	0.4 / 98.4	0.4 / 99.6
Levofloxacin	≤0.5 – >4	≤0.5	1	96.4 / 3.6	94.1 / 3.6

a. MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci; TMP/SMX, Trimethoprim/sulfamethoxazole; Q/D, Quinupristin/dalfopristin. The VanA phenotype was characterized by non-susceptibility to vancomycin (MIC, ≥8 μg/mL) and teicoplanin (MIC, ≥16 μg/mL), while VanB was based on non-susceptibility to vancomycin (MIC, ≥8 μg/mL) and susceptibility to teicoplanin (≤8 μg/mL), according to CLSI criteria. MDR, multidrug-resistant (resistance to three to four classes of drugs).

b. Criteria for susceptibility as published by the CLSI (M100-S21, 2011) and EUCAST (2011) recommendations.

c. –, no breakpoint available.

Conclusions

- Oritavancin demonstrated antimicrobial activity greater than comparators when tested against staphylococci, enterococci and VGS isolates. Similar potencies were observed for oritavancin and penicillin when tested against BHS.
- Higher oritavancin MIC results were observed against VanA-type VRE isolates. Yet, oritavancin inhibited all tested enterococcal strains at clinically achievable concentrations (≤0.5 μg/mL).
- These three-year surveillance data provide a susceptibility benchmark for oritavancin against current Gram-positive pathogens as this drug enters late-stage clinical development.

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