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Updated Analysis of Oritavancin Activity against Gram-Positive Clinical Isolates Responsible for Bloodstream Infections in United States and European Hospitals (2014–2016)

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Amended Abstract

Background: Oritavancin has documented *in vitro* activity against gram-positive isolates. This study provides an updated analysis for oritavancin tested against organisms causing bloodstream infections (BSI) in US and European sites.

Methods: A total of 8,257 organisms recovered from BSI at 30 US and 34 Europe sites during the SENTRY Antimicrobial Surveillance Program (2014-2016) were included. Isolates were identified by standard biochemical algorithms and matrix-assisted laser desorption ionization-time of flight mass spectrometry. Susceptibility testing was performed by CLSI methods and MICs were interpreted per CLSI and/or EUCAST criteria.

Results: Oritavancin had similar MIC_{50} values (0.06 µg/mL) against *Staphylococcus aureus* and coagulase-negative-staphylococci, inhibiting ≥99.4% of these isolates at ≤0.12 µg/mL. Oritavancin MIC_{50} values were 8- to 32-fold lower than those for vancomycin, daptomycin, and ceftaroline against staphylococci. Oritavancin showed MIC results against vancomycin-susceptible *Enterococcus faecium* ($MIC_{50/90}$, 0.004/0.015 µg/mL) that were up to 4-fold lower than against vancomycin-susceptible *E. faecalis* ($MIC_{50/90}$, 0.015/0.03 µg/mL; 100.0% S). Oritavancin inhibited 98.3% of all enterococci, including vancomycin-resistant isolates at ≤0.12 µg/mL. Vancomycin, daptomycin, ampicillin, and linezolid ($MIC_{50/90}$, 1/1-2 µg/mL) were similarly active against *E. faecalis*, while daptomycin and linezolid had coverage (99.0–99.4% susceptible) against *E. faecium*. Overall, *Streptococcus pyogenes* and *S. agalactiae* were highly susceptible to all agents tested, except for erythromycin (55.4–88.8% susceptible) and tetracycline (18.5–81.9% susceptible), and also clindamycin against *S. agalactiae* (70.5% susceptible). Oritavancin was highly active ($MIC_{50/90}$, 0.015/0.12 µg/mL; 99.7% susceptible) against viridans group streptococci.

Conclusions: Oritavancin continues to show potent *in vitro* activity against gram-positive isolates recovered from blood in patients hospitalized in US and European sites. The data presented here warrant further investigations to determine whether oritavancin has a role for treating BSI, especially those caused by *E. faecium*.

Introduction

- Bloodstream infections (BSI) are associated with significant morbidity, mortality, and associated health care costs in hospitalized patients
- Aerobic gram-positive cocci, most notably *Staphylococcus aureus,* coagulase-negative staphylococci (CoNS), and enterococci are leading causes of BSI
- The high prevalence of *S. aureus* causing BSI is significant since methicillin-resistant *S. aureus* (MRSA) isolates are associated with a high crude mortality rate (22.5%), high costs, and an extended hospital stay
- In the last decade, emerging and rapidly disseminating community-associated MRSA (CA-MRSA) drastically changed the BSI epidemiology in the United States (US) and other regions, challenging empiric therapy
- Oritavancin was approved by the Food and Drug Administration (FDA; 2014) and by the European Medicines Agency (EMA; 2015) to treat adults with acute bacterial skin and skin structure infections
- Oritavancin demonstrates potent *in vitro* inhibitory activity against gram-positive organisms that pose treatment challenges in BSI, including MRSA and vancomycin-resistant enterococci (VRE)
- This study updates the *in vitro* activity of oritavancin against a contemporary collection of gram-positive clinical isolates responsible for BSI in the US and Europe

Materials and Methods

Bacterial strain collection

- A total of 8,257 gram-positive isolates deemed responsible for BSI were collected from 30 medical centers in the US, 34 centers in Europe (14 countries), including 1 site in Israel, 3 centers in Russia, and 2 centers in Turkey
- Isolates were submitted to the monitoring laboratory (JMI Laboratories; North Liberty, Iowa, USA) as part of the SENTRY Antimicrobial Surveillance Program for 2014–2016
- Isolates were initially identified by the participating laboratory and identification was confirmed by the reference monitoring laboratory through standard algorithms and supported by matrix-assisted laser desorption ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany), as necessary

Antimicrobial susceptibility test methods

- Isolates were tested for susceptibility by reference broth microdilution, following the Clinical and Laboratory Standards Institute (CLSI) M07-A10 document, which includes supplementation with 0.002% polysorbate-80 for oritavancin
- Bacterial inoculum density was monitored by colony counts to assure adequate cell numbers for each testing event
- MIC values were validated by concurrently testing CLSI-recommended quality control (QC) reference strains (*S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, and *Streptococcus pneumoniae* ATCC 49619) – All QC results were within published acceptable ranges (M100-S27)
- MIC interpretations were based on CLSI (2017) and EUCAST (2017) breakpoint criteria, as available

Results

- Overall, oritavancin showed an MIC_{50} of 0.015 µg/mL and an MIC_{90} of 0.06 µg/mL when tested against *S. aureus* in aggregate, and against MSSA or MRSA, regardless of geographic region (Tables 1 and 2). At least 99.6% of *S. aureus* isolates were susceptible to oritavancin (Table 3), independent of region and methicillin susceptible/resistant phenotype
- When tested against MRSA, oritavancin ($MIC_{50/90}$, 0.015/0.06 µg/mL; 99.6% susceptible [CLSI and EUCAST]) and minocycline ($MIC_{50/90}$, ≤0.06/0.12µg/mL) had the lowest MIC_{50} and MIC_{90} results, which were at least 2-fold lower than daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL), ceftaroline ($MIC_{50/90}$, 0.5/1 µg/mL), and vancomycin ($MIC_{50/90}$, 0.5/1 µg/mL; Table 3)
- Comparator agents ceftaroline, linezolid, minocycline, teicoplanin, tetracycline, trimethoprim-sulfamethoxazole, daptomycin, and vancomycin were also active (90.2–100.0% susceptible) against MRSA isolates from EU and the US (Table 3)
- Oritavancin MIC_{90} values (0.06 µg/mL) were at least 8-fold lower than those of comparator agents when tested against CoNS from the US and European regions
- Oritavancin ($MIC_{50/90}$, 0.015/0.03 µg/mL) was equally potent when tested against vancomycin-susceptible *E. faecalis* from EU and the US, inhibiting 100.0% of strains at the FDA susceptibility breakpoint ≤0.12 µg/mL for vancomycin-susceptible *E. faecalis*) (Tables 1 and 2)
- A high number of *E. faecalis* isolates from both regions were susceptible (97.7−100.0%) to ampicillin, daptomycin, vancomycin, teicoplanin, and linezolid (Table 3)
- Oritavancin MIC results against vancomycin-susceptible *Enterococcus faecium* ($MIC_{50/90}$, 0.004/0.015 µg/mL) were 2- to 4-fold lower than against vancomycin-susceptible *E. faecalis* ($MIC_{50/90}$, 0.015/0.03 µg/mL; 100.0% susceptible; Tables 1 and 2)
- Oritavancin ($MIC_{50/90}$, 0.03 µg/mL) demonstrated an MIC_{50} value against VanA-producing *E. faecium* 8-fold higher than that observed for vancomycin-susceptible isolates ($MIC_{50/90}$, 0.004/0.015 µg/mL); however, all isolates were inhibited at 0.25 µg/mL (Tables 1 and 2)
- Vancomycin, daptomycin, ampicillin, and linezolid ($MIC_{50/90}$, 1/1-2 µg/mL) were similarly active against *E. faecalis*, while daptomycin and linezolid had coverage (99.0–99.4% susceptible) against *E. faecium* (Table 3)
- Oritavancin MIC_{50} results from both regions were 0.03 µg/mL for *S. agalactiae*, 0.03–0.06 µg/mL for *S. pyogenes*, and 0.12 µg/mL for *S. dysgalactiae* (Tables 1 and 2)
- In general, oritavancin (97.6% susceptible) and most comparator agents tested against β-hemolytic streptococcal species were active (>90% susceptible) *in vitro*, except for erythromycin, clindamycin, and tetracycline (Tables 1, 2 and 3)
- Oritavancin ($MIC_{50/90}$, 0.015/0.12 µg/mL) and ceftaroline ($MIC_{50/90}$, 0.015/0.12 µg/mL) demonstrated the lowest MIC_{50} and MIC_{90} results when tested against viridans group streptococci (Tables 1 and 2), and 99.7% of VGS in both geographic regions were susceptible to oritavancin (Table 3)

Results

Table 1. Antimicrobial activity of oritavancin tested against the main organisms and organism groups of isolates from US medical centers

Organism/organism group (no. of isolates)	No. of isolates at MIC (µg/mL; cumulative %)												
	≤0.0005	0.001	0.002	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	MIC_{50}	MIC_{90}
S. aureus (1,864)	2 0.1	0 0.1	0 0.1	3 0.3	136 7.6	1,043 63.5	461 88.3	184 98.1	32 99.8	3 100.0		0.015	0.06
Methicillin-susceptible (1,068)	1 0.1	0 0.1	0 0.1	2 0.3	75 7.3	594 62.9	269 88.1	110 98.4	17 100.0			0.015	0.06
Methicillin-resistant (796)	1 0.1	0 0.1	0 0.1	1 0.3	61 7.9	449 64.3	192 88.4	74 97.7	15 99.6	3 100.0		0.015	0.06
CoNS (699)			1 0.1	15 2.3	79 13.6	114 29.9	74 40.5	287 71.0	161 94.0	38 99.4	4 100.0	0.03	0.06
Methicillin-susceptible (232)			1 0.4	10 4.7	48 25.4	46 45.3	26 56.5	86 82.3	35 97.4	6 100.0		0.03	0.06
Methicillin-resistant (467)				5 1.1	31 7.7	68 22.3	48 65.3	201 92.3	126 99.1	32 100.0	4 100.0	0.03	0.06
E. faecalis (400)			1 0.2	16 4.2	130 36.8	174 80.2	46 91.8	15 95.5	11 98.2	5 99.5	2 100.0	0.015	0.03
Vancomycin-susceptible (384)			1 0.3	16 4.4	129 38.0	171 82.6	46 94.5	15 98.4	6 100.0			0.015	0.03
VanA (13)						1 7.7	0 7.7	0 7.7	5 46.2	5 84.6	2 100.0	0.25	0.5
VanB (3)					1 33.3	2 100.0						0.015	
E. faecium (256)		1 0.4	9 3.9	50 23.4	29 34.8	54 55.9	51 75.8	37 90.2	21 98.4	4 100.0		0.015	0.06
Vancomycin-susceptible (85)			1 1.2	48 68.2	12 82.4	13 97.6	2 100.0					0.004	0.015
VanA (165)				1 0.6	13 8.5	40 32.7	49 62.4	37 84.8	21 97.6	4 100.0		0.03	0.12
VanB (6)				1 16.7	4 83.3	1 100.0						0.008	
S. pyogenes (145)			2 1.4	2 2.8	14 12.4	23 28.3	32 50.3	30 71.0	23 86.9	17 98.6	2 100.0	0.03	0.25
S. agalactiae (245)			1 0.4	2 1.2	14 6.9	50 27.3	85 62.0	58 85.7	26 96.3	9 100.0		0.03	0.12
S. dysgalactiae (82)			1 1.2	0 1.2	5 7.3	4 12.2	11 25.6	12 40.2	19 63.4	21 89.0	9 100.0	0.12	0.5
VGS (252)	9 3.6	6 6.0	15 11.9	41 28.2	48 47.2	44 64.7	36 79.0	22 87.7	21 96.0	9 99.6	1 100.0	0.015	0.12
S. anginosus group (38)	3 7.9	1 10.5	2 15.8	4 26.3	11 55.3	9 78.9	7 97.4	0 97.4	1 100.0			0.008	0.03

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci; VanA, vancomycin- and teicoplanin-resistant isolates (vancomycin MIC, >4 µg/mL and teicoplanin MIC, >8 µg/mL); VanB, vancomycin-resistant and teicoplanin-susceptible isolates (vancomycin MIC, >4 µg/mL and teicoplanin MIC, ≤8 µg/mL); VGS, viridans group streptococci

Table 2. Antimicrobial activity of oritavancin tested against the main organisms and organism groups of isolates from European medical centers

Organism/organism group (no. of isolates)	No. of isolates at MIC (µg/mL; cumulative %)												
	≤0.0005	0.001	0.002	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	MIC_{50}	MIC_{90}
S. aureus (2,013)					106 5.3	1,049 57.4	632 88.8	162 96.8	62 99.9	2 100.0		0.015	0.06
Methicillin-susceptible (1,465)					78 5.3	745 56.2	472 88.4	119 96.5	51 100.0			0.015	0.06
Methicillin-resistant (548)					28 5.1	304 60.6	160 89.8	43 97.6	11 99.6	2 100.0		0.015	0.06
CoNS (740)				13 1.8	82 12.8	136 31.2	272 68.0	191 93.8	42 99.5	4 100.0		0.03	0.06
Methicillin-susceptible (194)				5 2.6	51 29.4	58 58.8	43 80.9	31 96.9	5 99.5	1 100.0		0.015	0.06
Methicillin-resistant (546)				8 1.5	31 7.1	78 21.4	229 63.4	160 92.7	37 99.5	3 100.0		0.03	0.06
E. faecalis (458)				27 5.9	136 35.6	182 75.3	69 90.4	29 96.7	11 99.3	3 100.0		0.015	0.03
Vancomycin-susceptible (454)				27 5.9	136 35.9	182 76.0	69 91.2	29 97.6	11 100.0			0.015	0.03
VanA (4)									1 25.0	3 100.0		0.25	
E. faecium (365)	1 0.3	5 1.6	49 15.1	177 63.6	59 79.7	36 89.6	22 95.6	11 98.6	4 99.7	1 100.0		0.004	0.03
Vancomycin-susceptible (296)	1 0.3	5 2.0	42 16.2	174 75.0	41 88.9	27 98.0	6 100.0					0.004	0.015
VanA (55)				2 3.6	13 27.3	9 43.6	4 70.9	11 90.9	4 98.2	1 100.0		0.03	0.06
VanB (14)			7 50.0	0 57.1	5 92.9	0 92.9	1 100.0					0.002	0.008
S. pyogenes (133)				2 1.5	4 4.5	21 20.3	31 43.6	30 66.2	24 84.2	19 98.5	2 100.0	0.06	0.25
S. agalactiae (138)					11 8.0	27 27.5	60 71.0	26 89.9	8 95.7	5 99.3	1 100.0	0.03	0.12
S. dysgalactiae (82)					1 1.2	4 4.9	12 19.5	17 40.2	19 63.4	24 92.7	6 100.0	0.12	0.25
VGS (385)	9 2.3	6 3.9	30 11.7	42 22.6	70 40.0	64 57.4	61 73.2	46 85.2	31 93.2	25 99.7	1 100.0	0.015	0.12
S. anginosus group (61)	6 9.8	2 13.1	11 31.1	8 44.3	18 73.8	11 91.8	5 100.0					0.008	0.015

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci; VanA, vancomycin- and teicoplanin-resistant isolates (vancomycin MIC, >4 µg/mL and teicoplanin MIC, >8 µg/mL); VanB, vancomycin-resistant and teicoplanin-susceptible isolates (vancomycin MIC, >4 µg/mL and teicoplanin MIC, ≤8 µg/mL); VGS, viridans group streptococci

Table 3. Activity of oritavancin and comparator antimicrobial agents when tested against 2014-2016 gram-positive isolates

Organism group (no. tested) Antimicrobial agent	2014-2016			
	Percentage susceptible[a]		$MIC_{50/90}$ (µg/mL)	MIC Range (µg/mL)
	CLSI	EUCAST		
MSSA (2,533)				
Oritavancin	100.0	100.0	0.015 / 0.06	≤0.0005 — 0.12
Ceftaroline	100.0	100.0	0.25 / 0.25	≤0.06 — 0.5
Clindamycin	97.2	96.9	≤0.25 / ≤0.25	≤0.25 — >2
Daptomycin	>99.9	>99.9	0.25 / 0.5	≤0.12 — 4
Erythromycin	78.1	78.8	0.25 / >8	≤0.12 — >8
Levofloxacin	91.9	91.9	0.25 / 0.5	≤0.12 — >4
Linezolid	100.0	100.0	1 / 1	≤0.12 — 2
Minocycline	99.5	99.1	≤0.06 / 0.12	≤0.06 — >8
Teicoplanin	100.0	99.8	≤2 / ≤2	≤2 — 4
Tetracycline	96.3	95.3	≤0.5 / ≤0.5	≤0.5 — >8
Trimethoprim-sulfamethoxazole	99.6	99.6	≤0.5 / ≤0.5	≤0.5 — >4
Vancomycin	100.0	100.0	0.5 / 1	0.25 — 2
MRSA (1,344)				
Oritavancin	99.6	99.6	0.015 / 0.06	≤0.0005 — 0.25
Ceftaroline	94.3	94.3	0.5 / 1	0.25 — 2
Clindamycin	71.8	71.7	≤0.25 / >2	≤0.25 — >2
Daptomycin	99.7	99.7	0.25 / 0.5	≤0.12 — 2
Erythromycin	21.7	22.5	>8 / >8	≤0.12 — >8
Levofloxacin	22.2	22.2	>4 / >4	≤0.12 — >4
Linezolid	100.0	100.0	1 / 1	≤0.12 — 2
Minocycline	98.8	97.4	≤0.06 / 0.12	≤0.06 — >8
Teicoplanin	100.0	99.7	≤2 / ≤2	≤2 — 8
Tetracycline	92.1	90.2	≤0.5 / 1	≤0.5 — >8
Trimethoprim-sulfamethoxazole	96.4	96.4	≤0.5 / ≤0.5	≤0.5 — >4
Vancomycin	100.0	100.0	0.5 / 1	≤0.12 — 2
CoNS[b] (1,439)				
Oritavancin			0.03 / 0.06	0.002 — 0.25
Ceftaroline			0.25 / 0.5	≤0.06 — 4
Clindamycin	71.1	70.2	≤0.25 / >2	≤0.25 — >2
Daptomycin	99.9	99.9	0.5 / 0.5	≤0.12 — 2
Erythromycin	34.7	35.4	>8 / >8	≤0.12 — >8
Levofloxacin	46.0	46.0	2 / >4	≤0.12 — >4
Linezolid	98.7	98.7	0.5 / 1	≤0.12 — >8
Oxacillin	29.6	30.2	>2 / >2	≤0.25 — >2
Teicoplanin	99.2	90.9	≤2 / 4	≤2 — >16
Tetracycline	84.4	80.5	≤0.5 / >8	≤0.5 — >8
Trimethoprim-sulfamethoxazole	67.1	67.1	≤0.5 / >4	≤0.5 — >4
Vancomycin	100.0	100.0	1 / 2	≤0.12 — 4
E. faecalis (858)				
Oritavancin	98.8[c]		0.015 / 0.03	0.002 — 0.5
Ampicillin	100.0	100.0	1 / 2	≤0.5 — 4
Daptomycin	100.0		1 / 1	≤0.25 — 4
Erythromycin	8.9		>16 / >16	≤0.12 — >16
Levofloxacin	68.6[d]	69.5[d]	1 / >4	≤0.5 — >4
Linezolid	99.9	100.0	1 / 2	≤0.25 — 4
Teicoplanin	98.0	98.0	≤2 / ≤2	≤2 — >16
Tetracycline	23.6		>8 / >8	≤1 — >8
Vancomycin	97.7	97.7	1 / 2	≤0.5 — >16
E. faecium (621)				
Oritavancin			0.008 / 0.06	≤0.0005 — 0.25
Ampicillin	10.6	10.1	>8 / >8	≤0.5 — >8
Daptomycin	99.4		2 / 2	≤0.25 — >8
Erythromycin	4.2		>16 / >16	≤0.12 — >16
Levofloxacin	8.2[d]	12.2[d]	>4 / >4	≤0.5 — >4
Linezolid	99.0	99.4	1 / 2	≤0.25 — 8
Teicoplanin	64.6	63.4	≤2 / >16	≤2 — >16
Tetracycline	39.9		>8 / >8	≤1 — >8
Vancomycin	61.4	61.4	1 / >16	≤0.5 — >16

Organism group (no. tested) Antimicrobial agent	2014-2016			
	Percentage susceptible[a]		$MIC_{50/90}$ (µg/mL)	MIC Range (µg/mL)
	CLSI	EUCAST		
S. pyogenes (278)				
Oritavancin	98.6	98.6	0.06 / 0.25	0.002 — 0.5
Ceftaroline	100.0	100.0	≤0.008 / ≤0.008	≤0.008
Clindamycin	96.4	97.1	≤0.25 / ≤0.25	≤0.25 — >2
Daptomycin	100.0	100.0	≤0.06 / 0.12	≤0.06 — 0.5
Erythromycin	88.8	88.8	≤0.12 / 1	≤0.12 — >4
Levofloxacin	100.0	100.0	0.5 / 1	0.12 — 2
Linezolid	100.0	100.0	1 / 1	0.5 — 2
Penicillin	100.0	100.0	≤0.06 / ≤0.06	≤0.06
Teicoplanin		100.0	≤2 / ≤2	≤2
Tetracycline	81.9	81.5	≤0.5 / >8	≤0.5 — >8
Trimethoprim-sulfamethoxazole			≤0.5 / ≤0.5	≤0.5 — 4
Vancomycin	100.0	100.0	0.25 / 0.5	≤0.06 — 0.5
S. agalactiae (383)				
Oritavancin	99.7	99.7	0.03 / 0.12	0.002 — 0.5
Ceftaroline	100.0	100.0	0.015 / 0.015	≤0.008 — 0.03
Clindamycin	70.5	71.3	≤0.25 / >2	≤0.25 — >2
Daptomycin	100.0	100.0	0.25 / 0.5	≤0.06 — 1
Erythromycin	55.4	55.4	≤0.12 / >4	≤0.12 — >4
Levofloxacin	99.7	99.7	0.5 / 1	0.12 — >4
Linezolid	100.0	100.0	1 / 1	0.25 — 2
Penicillin	100.0	100.0	≤0.06 / ≤0.06	≤0.06 — 0.12
Teicoplanin		100.0	≤2 / ≤2	≤2
Tetracycline	18.5	18.5	>8 / >8	≤0.5 — >8
Trimethoprim-sulfamethoxazole		99.5	≤0.5 / ≤0.5	≤0.5 — >4
Vancomycin	100.0	100.0	0.5 / 0.5	0.12 — 0.5
S. dysgalactiae (164)				
Oritavancin	90.9	90.9	0.12 / 0.25	0.002 — 0.5
Ceftaroline	100.0	100.0	≤0.008 / 0.015	≤0.008 — 0.03
Clindamycin	89.6	90.9	≤0.25 / 0.5	≤0.25 — >2
Daptomycin	100.0	100.0	≤0.06 / 0.12	≤0.06 — 0.25
Erythromycin	76.8	76.8	≤0.12 / >4	≤0.12 — >4
Levofloxacin	98.2	98.2	0.5 / 1	≤0.12 — >4
Linezolid	100.0	100.0	1 / 1	0.5 — 2
Penicillin	100.0	100.0	≤0.06 / ≤0.06	≤0.06 — 0.12
Teicoplanin		100.0	≤2 / ≤2	≤2
Tetracycline	64.0	64.0	≤0.5 / >8	≤0.5 — >8
Trimethoprim-sulfamethoxazole			≤0.5 / ≤0.5	≤0.5 — >4
Vancomycin	100.0	100.0	0.25 / 0.25	0.12 — 0.5
VGS[e] (637)				
Oritavancin	99.7[f]	99.7[f]	0.015 / 0.12	≤0.0005 — 0.5
Ceftaroline			0.015 / 0.12	≤0.008 — >1
Clindamycin	87.3	88.5	≤0.25 / >2	≤0.25 — >2
Daptomycin	99.8		0.25 / 1	≤0.06 — >2
Erythromycin	50.9		≤0.12 / >4	≤0.12 — >4
Levofloxacin	92.5		1 / 2	≤0.12 — >4
Linezolid	100.0		0.5 / 1	≤0.12 — 2
Penicillin	69.7	77.2	≤0.06 / 2	≤0.06 — >4
Teicoplanin		100.0	≤2 / ≤2	≤2
Tetracycline	65.8		≤0.5 / >8	≤0.5 — >8
Trimethoprim-sulfamethoxazole			≤0.5 / 4	≤0.5 — >4
Vancomycin	100.0	100.0	0.5 / 0.5	≤0.12 — 1

[a] Criteria as published by CLSI [2017] and EUCAST [2017].

[b] Organisms include: *Staphylococcus arlettae* (1), *S. auricularis* (5), *S. capitis* (97), *S. caprae* (7), *S. camosus* (2), *S. cohnii* (6), *S. condimenti* (1), *S. epidermidis* (876), *S. haemolyticus* (147), *S. hominis* (206), *S. lugdunensis* (28), *S. pasteuri* (4), *S. pettenkoferi* (15), *S. saprophyticus* (12), *S. schleiferi* (2), *S. simulans* (3), *S. warneri* (28).

[c] Breakpoint approved for vancomycin-susceptible *E. faecalis* applied to all isolates. All vancomycin-susceptible isolates were susceptible to oritavancin

[d] Uncomplicated UTI only

[e] Organisms include: *Streptococcus anginosus* (69), *S. anginosus* group (16), *S. australis* (8), *S. bovis* group (6), *S. constellatus* (10), *S. criatatus* (4), *S. equinus* (2), *S. gallolyticus* (57), *S. gordonii* (20), *S. infantarius* (1), *S. infantis* (6), *S. intermedius* (4), *S. lutetiensis* (10), *S. massiliensis* (1), *S. mitis* (11), *S. mitis* group (99), *S. mitioricola* (75), *S. mutans* (9), *S. oralis* (71), *S. parasanguinis* (51), *S. salivarius* (30), *S. salivarius* group (23), *S. salivarius/vestibularis* (4), *S. sanguinis* (38), *S. vestibularis* (8)

[f] Breakpoint for *S. anginosus* group applied to all viridans group streptococci

Conclusions

- Oritavancin exhibited potent *in vitro* activity against gram-positive clinical isolates responsible for BSI in US and EU hospitals
- Equivalent potency results were observed for oritavancin when tested against selected isolates in aggregate and resistant subsets from EU and the US
- Overall, oritavancin demonstrated greater *in vitro* potency than comparator agents against *S. aureus, E. faecalis*, and *E. faecium* clinical isolates
- The data presented here warrant further investigations to determine whether oritavancin has a role for treating BSI, especially those caused by *S. aureus* and *E. faecium*

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