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Telavancin activity against Gram-positive bacteria isolated from respiratory tract specimens of patients with nosocomial pneumonia

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Objectives: The antimicrobial activity of telavancin against 2279 clinical Gram-positive cocci obtained from patients with nosocomial pneumonia [NP; including those with ventilator-acquired pneumonia (VAP)] located in numerous medical centres worldwide was evaluated.

Methods: A contemporary collection of 2279 non-duplicate consecutive Gram-positive clinical isolates were submitted from 87 hospitals located in North America (913 isolates), Latin America (222 isolates), Europe (690 isolates), and the Asia-Pacific region (454 isolates) as part of the international telavancin surveillance programme for 2007–08. Isolates were tested for susceptibility by the reference broth microdilution method (with 2%–5% lysed horse blood added for testing of streptococci). Interpretive criteria were those from CLSI (M100-S20, 2010) except for telavancin, for which the susceptible breakpoints approved by the US FDA were applied.

Results: Telavancin was highly active against *Staphylococcus aureus* (MIC_{90}, 0.25 mg/L; 100% susceptible), coagulase-negative staphylococci (MIC_{90}, 0.25 mg/L), *Streptococcus pneumoniae* (MIC_{90}, 0.03 mg/L), viridans group streptococci (MIC_{90}, 0.06 mg/L; 100% susceptible), β-haemolytic streptococci (MIC_{90}, 0.06 mg/L; 100% susceptible) and vancomycin-susceptible enterococci (MIC_{90}, 0.5 mg/L; 100% susceptible). Telavancin inhibited all staphylococci at ≤0.5 mg/L. Among enterococci non-susceptible to vancomycin (all *Enterococcus faecium*), telavancin was active against isolates exhibiting a VanB phenotype (MIC, 0.06–0.12 mg/L), but less potent against VanA strains (MIC, ≥2 mg/L).

Conclusions: Telavancin demonstrated equal or greater potency than the comparators (vancomycin, teicoplanin, daptomycin, linezolid and quinupristin/dalfopristin) against Gram-positive pathogens implicated in NP. Telavancin showed elevated MIC values only against enterococcus isolates showing a VanA phenotype. The continued appearance of multidrug-resistant pathogens among Gram-positive isolates, mainly *S. aureus*, necessitates the introduction of new agents and longitudinal surveillance to monitor for the potential emergence of resistance.

Keywords: telavancin, lipoglycopeptides, nosocomial pneumonia

Introduction

Nosocomial pneumonia (NP) is currently the second most common nosocomial infection in the USA and is associated with high morbidity and mortality.[1–4] NP may be further delineated into hospital-acquired pneumonia (HAP; pneumonia that occurs 48 h or more after admission), ventilator-associated pneumonia (VAP; pneumonia that arises more than 48–72 h after endotracheal intubation) and healthcare-associated pneumonia [infections that occur prior to hospital admission in patients with specific risk factors (immunosuppression, recent hospitalization, residence in a nursing facility, dialysis requirement)].[1–3,5]

NP accounts for up to 25% of all intensive care unit (ICU) infections and for more than 50% of antibacterial agent prescriptions.[6] VAP occurs in 9%–27% of all intubated patients, and in some ICU patient populations nearly 90% of episodes of NP occur during mechanical ventilation.[1,7] The presence of NP increases hospital stay by an average of 7–9 days per patient and has been reported to produce an excess healthcare cost of more than $40000 per patient.[2] The increased or 'attributable' mortality related to NP has been estimated to be between 33% and 50% in several studies.[1,2]

A variety of infectious organisms can cause NP.[2] Although aerobic Gram-negative bacilli (e.g. *Pseudomonas aeruginosa*,

Acinetobacter spp. and Enterobacteriaceae) continue to be important, infections due to Gram-positive cocci such as *Staphylococcus aureus*, particularly methicillin (oxacillin)-resistant *S. aureus* (MRSA), have been rapidly emerging in the USA and elsewhere.[2,6,8] Notably, analysis of a large US inpatient database revealed that, among all pathogens associated with NP, *S. aureus* was the only pathogen associated with significantly increased mortality.[2] In contrast to *S. aureus*, Gram-positive respiratory tract commensals, such as viridans group streptococci (VGS), enterococci and coagulase-negative staphylococci (CoNS), are usually not considered causative agents in NP.[2,5] However, significant growth of these organisms from invasive bronchial specimens may be difficult to interpret, but they may produce infections in immunocompromised hosts and rarely in immunocompetent patients.[9] Moreover, *Streptococcus pneumoniae* is commonly responsible for community-acquired pneumonia, but usually this pathogen represents fewer than 10% of NP cases.[10]

Telavancin is an intravenous, semisynthetic, lipoglycopeptide that is broadly active against both aerobic and anaerobic Gram-positive bacteria, including streptococci, methicillin-susceptible *S. aureus* (MSSA), MRSA, and some vancomycin-resistant enterococci (VRE).[11–16] Against *S. aureus* with reduced susceptibility to glycopeptides, telavancin showed slightly elevated MIC values that were still below the approved breakpoint for susceptibility ($\leq$1 mg/L).[17–20] Telavancin is bactericidal by means of two mechanisms acting in concert: (i) interference with cell wall synthesis by potent binding to the cell wall precursor lipid II, thereby preventing polymerization (transglycosylation) and cross-linking (transpeptidation) events; and (ii) binding to lipid II and inserting a hydrophobic anchor into the bacterial lipid membrane, resulting in depolarization and disruption of the functional integrity of the membrane.[21,22]

In this report, we summarize the 2007–08 results of an international surveillance programme comparing the *in vitro* activity of telavancin and currently marketed glycopeptides with other antimicrobial agents against Gram-positive clinical isolates obtained from respiratory tract specimens from patients with NP. A total of 2279 bacterial strains were tested by reference CLSI methods with susceptibilities to comparator agents interpreted by CLSI breakpoint criteria.

Methods

Bacterial clinical isolates

A total of 2279 consecutive, non-duplicate Gram-positive clinical strains were collected and referred by 87 hospitals located in North America (913 strains), Latin America (222), Europe (690), and the Asia-Pacific region (APAC; 454) as part of the international telavancin surveillance programme for 2007–08. Isolates were obtained from patients with pneumonia considered to be clinically significant by local criteria and occurring more than 72 h after hospitalization. The bacterial collection included 1756 *S. aureus* (77.1% of total; 45% MRSA), 20 CoNS (0.9% of total; 95% oxacillin-resistant), 314 *S. pneumoniae* (13.7% of total; 47.1% penicillin-non-susceptible at $\geq$0.12 mg/L), 30 VGS (1.3% of total; 63.3% penicillin-non-susceptible), 61 β-haemolytic streptococci (BHS; 2.7% of total; 19.7% macrolide-resistant) and 98 enterococci (4.3% of total; 14.3% VRE).

Appropriate specimens included bronchoalveolar lavage, tracheal aspirates, protected brush and high-quality Gram stain screened sputums.[23] All isolates were shipped to the monitoring laboratories (JMI Laboratories, North Liberty, IA, USA and Women's and Children's Hospital, North Adelaide, South Australia) on charcoal transport swabs for confirmation of organism identification and reference susceptibility testing.[24] Identification was performed by using conventional algorithms and the Vitek® 2 Microbial Identification System (Biomérieux, Hazelwood, MO, USA), when necessary.

Susceptibility test methods

All strains were tested by the broth microdilution method[24] using commercial validated panels (Trek Diagnostics, Cleveland, OH, USA) in cation-adjusted Mueller-Hinton broth (with 2%–5% lysed horse blood added for testing of streptococci). Telavancin and the comparator antimicrobial agents were obtained from the respective manufacturers. For enterococci, the VanA phenotype was characterized by non-susceptibility to vancomycin and teicoplanin, while isolates with a VanB phenotype were those non-susceptible to vancomycin but susceptible to teicoplanin according to CLSI criteria.[25] Interpretation of comparator MIC results was in accordance with published CLSI criteria.[25] Telavancin-susceptible breakpoints for *S. aureus* ($\leq$1 mg/L), BHS and VGS ($\leq$0.12 mg/L) and vancomycin-susceptible enterococci (VSE) ($\leq$1 mg/L) were those recently approved by the US FDA.[18] Quality control strains used included *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212 and *S. pneumoniae* ATCC 49619.[25]

Results

Bacterial clinical isolates

S. aureus was the predominant Gram-positive respiratory tract pathogen in all four monitored regions, ranging from 46.3% of strains in the APAC region to 91.9% in North America. The lowest frequency of MRSA (28.9% of *S. aureus*) was observed in Europe and the highest (60.1%) in Latin America. *S. pneumoniae* accounted for fewer than 10% of Gram-positive respiratory tract strains in all regions with the exception of the APAC region (43.4%). This region also had the highest rate of penicillin-non-susceptible pneumococci (38.1% resistant and 12.2% intermediate). The remaining Gram-positive respiratory tract pathogens each accounted for less than 5% of the total number of isolates from any given region with the exception of *Enterococcus* spp., which accounted for 9.3% of European strains. The highest frequency of VRE (all *E. faecium*) was detected among *Enterococcus* spp. from North America (38.5%).

Telavancin spectrum of activity

Telavancin had potent activity against staphylococcal, streptococcal and enterococcal isolates (Table 1). Telavancin inhibited all *S. pneumoniae*, VGS (100% susceptible) and BHS (100% susceptible) at $\leq$0.12 mg/L, all *S. aureus* (100% susceptible) and CoNS at $\leq$0.5 mg/L and all vancomycin-susceptible enterococci at $\leq$1 mg/L (100% susceptible). Among *E. faecium* non-susceptible to vancomycin, six isolates showed a VanA phenotype, while 10 strains displayed a VanB phenotype. Isolates with the VanA phenotype exhibited telavancin MIC values $\geq$2 mg/L, whereas VanB-type isolates were inhibited by lower concentrations of telavancin with MIC values at $\leq$0.12 mg/L ($MIC_{50/90}$, 0.06/0.12 mg/L; Table 1). Oxacillin resistance among staphylococci and penicillin-non-susceptibility among streptococci had no effect on telavancin potency (MIC_{90}) compared with the respective susceptible populations. There was no geographic variation in the potency of telavancin against isolates of *S. aureus* or other pathogens (data not shown).

Table 1. Antimicrobial activity of telavancin against six organism species/groups with resistant subsets from patients with nosocomial pneumonia, 2007–08

	MIC (mg/L)		Cumulative % inhibited at a telavancin MIC (mg/L) of							
Organism (no. tested)	50%	90%	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2
Staphylococcus aureus (1756)	0.12	0.25	0.0	0.5	7.1	65.4	98.3	100	—	—
oxacillin-susceptible (966)	0.12	0.25	0.0	0.8	8.6	72.4	99.2	100	—	—
oxacillin-resistant (790)	0.12	0.25	0.0	0.1	5.2	57.0	97.3	100	—	—
CoNS (20)	0.12	0.25	10.0	10.0	15.0	65.0	95.0	100	—	—
Streptococcus pneumoniae (314)	≤0.015	0.03	70.1	96.5	100	—	—	—	—	—
penicillin-susceptible (166)	≤0.015	0.03	66.9	94.0	100	—	—	—	—	—
penicillin-intermediate (40)	≤0.015	0.03	75.0	100	—	—	—	—	—	—
penicillin-resistant (108)	≤0.015	0.03	73.1	99.1	100	—	—	—	—	—
VGS (30)	0.03	0.06	16.7	60.0	93.3	100	—	—	—	—
penicillin-susceptible (11)	0.03	0.06	27.3	72.7	100	—	—	—	—	—
penicillin-non-susceptible (19)	0.03	0.12	10.5	52.6	89.5	100	—	—	—	—
BHS (61)	0.03	0.06	27.9	72.1	95.1	100	—	—	—	—
Enterococcus spp. (98)	0.25	0.5	1.0	17.3	29.6	49.0	69.4	92.9	93.9	94.9
vancomycin-susceptible (82)	0.25	0.5	1.2	17.1	25.6	46.3	70.7	98.8	100	—
VanA phenotype (6)[a]	>2	—	0.0	0.0	0.0	0.0	0.0	0.0	0.0	16.7
VanB phenotype (10)[a]	0.06	0.12	0.0	30.0	80.0	100	—	—	—	—

CoNS, coagulase-negative staphylococci; VGS, viridans group streptococci; BHS, β-haemolytic streptococci.
[a]All *E. faecium*.

In vitro activity of telavancin and comparator agents

The telavancin MIC_{90} values for MSSA, MRSA and CoNS were 2- to 32-fold lower than those of vancomycin, teicoplanin, daptomycin, linezolid and quinupristin/dalfopristin (Table 2). Among the staphylococci tested, there were 60 *S. aureus* and 13 CoNS isolates for which vancomycin MIC values were 2 mg/L. Linezolid MIC values were ≥4 mg/L for five isolates of *S. aureus* (four were MRSA); the telavancin MIC results for all of these strains were ≤0.5 mg/L. Levofloxacin, erythromycin, clindamycin and gentamicin all exhibited very limited activity against MRSA and CoNS. Modest anti-staphylococcal activity was also observed for tetracycline and trimethoprim/sulfamethoxazole (82.4% and 88.3% of MRSA were susceptible, respectively).

Among all agents tested, telavancin had the greatest potency against *S. pneumoniae*, with an MIC_{90} of 0.03 mg/L, regardless of resistance to penicillin or other agents. Notably, 6.5% of penicillin-resistant pneumococci were resistant to levofloxacin and none was non-susceptible to linezolid. Among the VGS and BHS, 50.0% and 19.7%, respectively, were resistant to erythromycin. Telavancin demonstrated potent activity against these organisms (MIC_{90}, 0.06 mg/L for both groups), unaffected by their susceptibility to erythromycin. Telavancin had MIC values ranging from ≤0.015 to 1 mg/L against VSE and it was 4- to 8-fold more potent than all of the comparators.

Discussion

As noted previously,[2,3,10,26] *S. aureus* was the dominant Gram-positive pathogen in all geographic regions, although the frequency of occurrence and resistance to methicillin (oxacillin) did vary considerably. Telavancin exhibited potent activity against all *S. aureus* (100% susceptible) and CoNS irrespective of resistance to other classes of antimicrobial agents. Although 99%–100% of MRSA were susceptible to vancomycin, teicoplanin, daptomycin, linezolid and quinupristin/dalfopristin according to CLSI interpretive criteria, telavancin was generally 2- to 8-fold more potent than these currently used agents against this important multidrug-resistant pathogen. Whereas glycopeptide-non-susceptible strains of *S. aureus* were not detected in this survey, it is notable that the vancomycin MIC was 2 mg/L for 60 isolates (3.4% of total). Although such strains are considered susceptible, it is now apparent that elevated vancomycin MIC results, defined as 1.5–2 mg/L, are an independent predictor of poor response to vancomycin therapy for MRSA infection, even when vancomycin trough levels >15 mg/L are achieved.[3,27–29] One MRSA isolate showed a resistant phenotype to linezolid (MIC, 8 mg/L; Table 2). An additional four isolates (three MRSA) showed elevated MIC results of 4 mg/L for linezolid. The telavancin MIC values for all five of these isolates were ≤0.5 mg/L.

Resistance to penicillin and the macrolides was common among isolates of *S. pneumoniae* and VGS from all regions. Although *S. pneumoniae* was the second most common Gram-positive respiratory tract isolate in all four regions, it was more prominent in the APAC region (43.4% of all isolates) than in the other three regions (5.0%–8.3%; data not shown). Whereas *S. pneumoniae* is a well-known cause of community-acquired pneumonia (CAP), it is also observed as a cause of early-onset HAP (within the first 4 days of hospitalization) and is an uncommon cause of late-onset (5 days or more) infection.[1,2] Telavancin

Table 2. Antimicrobial activity of telavancin and comparator antimicrobial agents against 2279 isolates of Gram-positive cocci from patients with nosocomial pneumonia, 2007–08

	MIC (mg/L)[a]			Percentage by category[b]	
Organism (no. tested)/agent	range	50%	90%	susceptible	resistant
Staphylococcus aureus (1756)					
telavancin	0.03–0.5	0.12	0.25	100	—
oxacillin	≤0.25 to >2	0.5	>2	55.0	45.0
vancomycin	≤0.12–2	1	1	100	0.0
teicoplanin	≤2–4	≤2	≤2	100	0.0
daptomycin	≤0.06–1	0.25	0.5	100	—
linezolid	0.25–8	1	2	99.9	0.1
quinupristin/dalfopristin	≤0.25 to >2	0.5	0.5	99.5	0.1
levofloxacin	≤0.5 to >4	≤0.5	>4	55.5	44.0
erythromycin	≤0.25 to >2	>2	>2	43.3	56.2
clindamycin	≤0.25 to >2	≤0.25	>2	71.0	28.8
gentamicin	≤2 to >8	≤2	>8	84.8	14.6
tetracycline	≤2 to >8	≤2	8	89.6	9.9
trimethoprim/sulfamethoxazole	≤0.5 to >2	≤0.5	≤0.5	94.1	5.9
oxacillin-susceptible (966)					
telavancin	0.03–0.5	0.12	0.25	100	—
vancomycin	≤0.12–2	1	1	100	0.0
teicoplanin	≤2	≤2	≤2	100	0.0
daptomycin	≤0.06–1	0.25	0.5	100	—
linezolid	0.5–4	2	2	100	0.0
quinupristin/dalfopristin	≤0.25–2	≤0.25	0.5	99.7	0.0
levofloxacin	≤0.5 to >4	≤0.5	≤0.5	91.6	8.0
erythromycin	≤0.25 to >2	≤0.25	>2	72.6	26.9
clindamycin	≤0.25 to >2	≤0.25	≤0.25	94.8	5.0
gentamicin	≤2 to >8	≤2	≤2	97.3	2.5
tetracycline	≤2 to >8	≤2	≤2	95.5	3.6
trimethoprim/sulfamethoxazole	≤0.5 to >2	≤0.5	≤0.5	98.9	1.1
oxacillin-resistant (790)					
telavancin	0.03–0.5	0.12	0.25	100	—
vancomycin	0.25–2	1	1	100	0.0
teicoplanin	≤2–4	≤2	≤2	100	0.0
daptomycin	0.12–1	0.25	0.5	100	—
linezolid	0.25–8	1	2	99.9	0.1
quinupristin/dalfopristin	≤0.25 to >2	0.5	1	99.4	0.3
levofloxacin	≤0.5 to >4	>4	>4	11.4	88.1
erythromycin	≤0.25 to >2	>2	>2	7.6	92.0
clindamycin	0.25 to >2	>2	>2	41.9	57.8
gentamicin	≤2 to >8	≤2	>8	69.5	29.4
tetracycline	≤2 to >8	≤2	>8	82.4	17.6
trimethoprim/sulfamethoxazole	≤0.5 to >2	≤0.5	>2	88.3	11.7
CoNS (20)					
telavancin	≤0.015–0.5	0.12	0.25	—	—
oxacillin	≤0.25 to >2	>2	>2	5.0	95.0
vancomycin	0.25–2	2	2	100	0.0
teicoplanin	≤2–8	4	8	100	0.0
daptomycin	≤0.06–2	0.5	1	95.0	—
linezolid	0.25–2	1	1	100	0.0
quinupristin/dalfopristin	≤0.025–2	≤0.25	1	95.0	0.0
levofloxacin	≤0.5 to >4	4	>4	35.0	65.0

Continued

Table 2. *Continued*

Organism (no. tested)/agent	MIC (mg/L)[a]			Percentage by category[b]	
	range	50%	90%	susceptible	resistant
erythromycin	≤0.25 to >2	>2	>2	25.0	75.0
clindamycin	≤0.25 to >2	1	>2	45.0	50.0
gentamicin	≤2 to >8	>8	>8	45.5	54.5
tetracycline	≤2 to >8	≤2	>8	75.0	25.0
trimethoprim/sulfamethoxazole	≤0.5 to >2	1	>2	72.7	27.3
Streptococcus pneumoniae (314)					
telavancin	≤0.015–0.06	≤0.015	0.03	—	—
penicillin[c]	≤0.015–16	0.03	4	84.1	3.2
penicillin[d]	≤0.015–16	0.03	4	52.9	34.4
vancomycin	≤0.12–0.5	0.5	0.5	100	—
linezolid	0.25–2	1	1	100	—
quinupristin/dalfopristin	≤0.25–2	0.5	1	99.7	0.0
levofloxacin	≤0.5 to >4	1	1	96.5	2.9
erythromycin	≤0.25 to >2	≤0.25	>2	56.4	43.0
clindamycin	≤0.25 to >2	≤0.25	>2	73.9	25.5
tetracycline	≤2 to >8	≤2	>8	64.6	34.7
penicillin-susceptible (166)					
telavancin	≤0.015–006	≤0.015	0.03	—	—
penicillin[c]	≤0.015–0.06	≤0.015	0.03	100	0.0
penicillin[d]	≤0.015–0.06	≤0.015	0.03	100	0.0
vancomycin	≤0.012–0.5	0.25	0.5	100	—
linezolid	0.25–2	1	1	100	—
quinupristin/dalfopristin	≤0.25–2	0.5	1	99.4	0.0
levofloxacin	≤0.5 to >4	1	1	97.6	1.2
erythromycin	≤0.25 to >2	≤0.25	>2	81.3	18.1
clindamycin	≤0.25 to >2	≤0.25	≤0.25	93.4	6.6
tetracycline	≤2 to >8	≤2	>8	88.6	10.8
penicillin-intermediate (40)					
telavancin	≤0.015–0.03	≤0.015	0.03	—	—
penicillin[c]	0.12–1	0.25	1	100	0.0
penicillin[d]	0.12–1	0.25	1	0.0	0.0
vancomycin	0.25–0.05	0.25	0.5	100	—
linezolid	0.25–2	1	1	100	—
quinupristin/dalfopristin	≤0.25–1	0.5	1	100	0.0
levofloxacin	≤0.5–2	1	1	100	0.0
erythromycin	≤0.25 to >2	2	>2	47.5	52.5
clindamycin	≤0.25 to >2	≤0.25	>2	77.5	22.5
tetracycline	≤2 to >8	≤2	>8	62.5	35.0
penicillin-resistant (108)					
telavancin	≤0.015–0.06	≤0.015	0.03	—	—
penicillin[c]	2–16	2	4	53.7	9.3
penicillin[d]	2–16	2	4	0.0	100
vancomycin	≤0.12–0.5	0.5	0.5	100	—
linezolid	0.5–2	1	1	100	—
quinupristin/dalfopristin	≤0.25–1	0.5	1	100	0.0
levofloxacin	≤0.5 to >4	1	2	93.5	6.5
erythromycin	≤0.25 to >2	>2	>2	21.3	77.8
clindamycin	≤0.25 to >2	>2	>2	42.6	55.6
tetracycline	≤2 to >8	>8	>8	28.7	71.3

Continued

Table 2. *Continued*

Organism (no. tested)/agent	MIC (mg/L)[a]			Percentage by category[b]	
	range	50%	90%	susceptible	resistant
VGS (30)					
telavancin	≤0.015–0.12	0.03	0.06	100	—
penicillin	≤0.015–16	0.25	4	36.7	26.7
vancomycin	0.25–1	0.5	1	100	—
teicoplanin	≤2	≤2	≤2	—	—
daptomycin	≤0.06–1	0.25	1	100	—
linezolid	0.12–2	1	1	100	—
quinupristin/dalfopristin	≤0.25–2	0.5	1	96.7	0.0
levofloxacin	≤0.5 to >4	1	2	90.0	10.0
erythromycin	≤0.25 to >2	≤0.25	>2	50.0	50.0
clindamycin	≤0.25 to >2	≤0.25	>2	70.0	30.0
tetracycline	≤2 to >8	≤2	>8	50.0	46.7
penicillin-susceptible (11)					
telavancin	≤0.015–0.06	0.03	0.06	100	—
penicillin	≤0.015–0.06	0.03	0.06	100	0.0
vancomycin	0.5–1	0.5	1	100	—
daptomycin	≤0.06–1	0.25	0.5	100	—
linezolid	0.12–1	1	1	100	—
quinupristin/dalfopristin	≤0.25–2	0.5	1	90.9	0.0
levofloxacin	≤0.5–1	≤0.5	1	100	0.0
erythromycin	≤0.25 to >2	≤0.25	≤0.25	90.9	9.1
clindamycin	≤0.25 to >2	≤0.25	≤0.25	90.9	9.1
tetracycline	≤2 to >8	≤2	>8	72.7	18.2
penicillin-non-susceptible (19)					
telavancin	≤0.015–0.12	0.3	0.12	100	—
penicillin	0.25–16	1	8	0.0	42.1
vancomycin	0.25–1	0.5	1	100	—
daptomycin	0.12–1	0.25	1	100	—
linezolid	0.25–2	1	1	100	—
quinupristin/dalfopristin	≤0.25–1	1	1	100	0.0
levofloxacin	≤0.5 to >4	1	>4	84.2	15.8
erythromycin	≤0.25 to >2	>2	>2	26.3	73.7
clindamycin	≤0.25 to >2	≤0.25	>2	57.9	42.1
tetracycline	≤2 to >8	>8	>8	36.8	63.2
BHS (61)					
telavancin	≤0.15–0.12	0.03	0.06	100	—
penicillin	≤0.015–0.06	≤0.015	0.06	100	—
vancomycin	≤0.12–1	0.5	0.5	100	—
daptomycin	≤0.06–0.25	≤0.06	0.12	100	—
linezolid	0.25–2	1	1	100	—
quinupristin/dalfopristin	≤0.25–0.5	≤0.25	≤0.25	100	0.0
levofloxacin	≤0.05>4	≤0.5	1	98.4	1.6
erythromycin	≤0.25 to >2	≤0.25	>2	80.3	19.7
clindamycin	≤0.25 to >2	≤0.25	≤0.25	93.4	6.6
tetracycline	≤2 to >8	≤2	>8	77.0	21.3
Enterococcus spp. (98)					
telavancin	≤0.015 to >2	0.25	0.5	—	—
ampicillin	≤1 to >16	2	>16	59.2	40.8
vancomycin	0.5 to >16	1	>16	83.7	14.3

Continued

Table 2. *Continued*

Organism (no. tested)/agent	MIC (mg/L)[a]			Percentage by category[b]	
	range	50%	90%	susceptible	resistant
teicoplanin	≤2 to >16	≤2	≤2	93.9	5.1
daptomycin	0.12–4	1	2	100	—
linezolid	0.5–2	1	2	100	0.0
quinupristin/dalfopristin	≤0.25 to >2	>2	>2	26.5	67.3
levofloxacin	≤0.5 to >4	>4	>4	34.7	63.3
gentamicin (HL)	≤500 to >1000	1000	>1000	48.0	52.0
streptomycin (HL)	≤1000 to >2000	≤1000	>2000	53.1	46.9
tetracycline	≤2 to >8	>8	>8	39.8	59.2
vancomycin-susceptible (82)					
telavancin	≤0.015–1	0.25	0.5	—	—
ampicillin	≤1 to >16	2	>16	70.7	29.3
vancomycin	0.5–4	1	2	100	0.0
teicoplanin	≤2	≤2	≤2	100	0.0
daptomycin	0.12–4	1	2	100	—
linezolid	0.5–2	1	2	100	0.0
quinupristin/dalfopristin	≤0.25 to >2	>2	>2	14.6	78.0
levofloxacin	≤0.5 to >4	>4	>4	41.5	56.1
gentamicin (HL)	≤500 to >1000	1000	>1000	46.3	53.7
streptomycin (HL)	≤1000 to >2000	≤1000	>2000	52.4	47.6
tetracycline	≤2 to >8	>8	>8	35.4	63.4
vancomycin-resistant (16)					
telavancin	0.03 to >2	0.06	>2	—	—
ampicillin	>16	>16	>16	0.0	100
vancomycin	16 to >16	>16	>16	0.0	87.5
teicoplanin	≤2 to >16	≤2	>16	62.5	31.3
daptomycin	1–4	2	2	100	—
linezolid	1–2	1	2	100	0.0
quinupristin/dalfopristin	0.5 to >2	1	>2	87.5	12.5
levofloxacin	>4	>4	>4	0.0	100
gentamicin (HL)	≤500 to >1000	≤500	>1000	56.3	43.8
streptomycin (HL)	≤1000 to >2000	≤1000	>2000	56.3	43.8
tetracycline	≤2 to >8	≤2	>8	62.5	37.5

CoNS, coagulase-negative staphylococci; VGS, viridans group streptococci; BHS, β-haemolytic streptococci; HL, high-level aminoglycoside resistance.
[a]50% and 90%, MIC encompassing 50% and 90% of isolates tested, respectively.
[b]Interpretation criteria as published by the CLSI.[25] Telavancin-susceptible breakpoints for *S. aureus* (≤1 mg/L), BHS and VGS (≤0.12 mg/L) and vancomycin-susceptible enterococci (≤1 mg/L) were those recently approved by the US FDA.[18] Dashes indicate no available CLSI interpretive criteria.
[c]Criteria as published by the CLSI[25] for 'penicillin parenteral (non-meningitis)'.
[d]Criteria as published by the CLSI[25] for 'penicillin (oral penicillin V)'.

demonstrated very potent activity against *S. pneumoniae*, VGS and BHS, with all isolates inhibited at ≤0.12 mg/L. It was 32-fold more potent than linezolid against penicillin-non-susceptible *S. pneumoniae* isolates.

Telavancin had MIC_{90} values that were 4-fold lower than those of vancomycin, teicoplanin, daptomycin, linezolid and quinupristin/dalfopristin against VSE isolates, but was less potent than daptomycin and linezolid against vancomycin-non-susceptible enterococci. Among these isolates, telavancin was highly active against all VanB isolates (MIC, ≤0.12 mg/L), and it was only adversely affected when tested against strains exhibiting a VanA phenotype (MIC, ≥2 mg/L).

In summary, this report confirms the potency and spectrum of telavancin against Gram-positive NP pathogens collected from four broad geographic regions between 2007 and 2008. In particular, we have demonstrated the superior *in vitro* potency of this agent compared with currently marketed antistaphylococcal agents against more than 1700 *S. aureus* clinical isolates from five continents. These data, in addition to recent clinical trial results in the treatment of NP, support telavancin as a potential therapeutic option for serious infections.[30] Continued surveillance to monitor telavancin activity, especially against staphylococci, will be critical in assessing the long-term utility of this promising new agent.

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