Poster P1579

Telavancin Activity Tested Against Gram-Positive Clinical Isolates From European Hospitals (2011–2013) Using A Revised Broth Microdilution Testing Method: Redefining the Baseline Activity for Telavancin

Rodrigo E. Mendes*, David J. Farrell, Jennifer M. Streit, Ronald N. Jones

JMI Laboratories, North Liberty, Iowa, USA

Contact information:
Rodrigo E. Mendes, PhD
JMI Laboratories
345 Beaver Kreek Ctr, Ste A
North Liberty, Iowa 52317 USA
Phone: 319-665-3370
Fax: 319-665-3371
E-mail: rodrigo-mendes@jmilabs.com

ABSTRACT

Objectives: To reassess the activity of telavancin when tested against clinical isolates recovered from hospitalised patients in European and adjacent countries. This revised method for telavancin utilises dimethyl sulphoxide as solvent and diluent for stock solution preparation and dilution, following the CLSI guidelines for water-insoluble agents, and incorporates polysorbate-80 (or Tween; 0.002%) in the test medium. Like other lipoglycopeptides, addition of P-80 was deemed necessary for more accurate and reproducible telavancin MIC determinations.

Methods: 11,601 consecutive, non-duplicate Gram-positive clinical isolates were collected from 36 centres in 18 countries. Isolates were submitted to a central monitoring laboratory and identification was performed by standard algorithms and MALDI-TOF, as needed. Susceptibility testing for comparator agents was performed by CLSI methods (M07-A9). Quality assurance applied MIC QC ranges from CLSI M100-S24. Interpretation of MIC results for telavancin used the updated US-FDA criteria, while comparator agents were guided by current EUCAST (2014) and CLSI (2014) breakpoint criteria.

Results: Isolates were recovered mostly from skin and soft-tissue (37%), bacteraemia (22%), and respiratory tract infections (24%). Telavancin ($MIC_{50/90}$, 0.03/0.06 mg/L) was equally potent when tested against methicillin-susceptible (MSSA) and -resistant *S. aureus* (MRSA). Telavancin was eight-fold more active than daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L) and 16- to 32-fold more active than linezolid ($MIC_{50/90}$, 1/1 mg/L) and vancomycin ($MIC_{50/90}$, 1/1 mg/L) against MRSA. *E. faecalis* were highly susceptible to telavancin ($MIC_{50/90}$, 0.12/0.12 mg/L) and were inhibited at ≤0.25 mg/L except for VanA-phenotype vancomycin-resistant isolates (ie, telavancin MIC, >1 mg/L). Telavancin was at least eight-fold more active than ampicillin ($MIC_{50/90}$, 1/2 mg/L), vancomycin ($MIC_{50/90}$, 1/2 mg/L), and daptomycin ($MIC_{50/90}$, 1/1 mg/L) against all *E. faecalis*. Telavancin ($MIC_{50/90}$, ≤0.015/0.03 mg/L) was active against vancomycin-susceptible *E. faecium*, while higher MIC values were obtained for VanA-phenotype strains, where daptomycin ($MIC_{50/90}$, 2/4 mg/L) and linezolid ($MIC_{50/90}$, 1/2 mg/L) remained more active. Telavancin (MIC_{50}, ≤0.015 mg/L) was very potent against *S. pneumoniae* with MIC_{50} values at least 32-fold lower than vancomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), levofloxacin ($MIC_{50/90}$, 1/1 mg/L), and linezolid ($MIC_{50/90}$, 1/1 mg/L), and 64-fold lower than penicillin ($MIC_{50/90}$, ≤0.06/2 mg/L). Telavancin showed similar MIC_{50} and MIC_{90} results against ß-haemolytic streptococci ($MIC_{50/90}$, ≤0.015/0.06 mg/L) and viridans group streptococci ($MIC_{50/90}$, ≤0.015/0.03 mg/L).

Conclusions: Telavancin exhibited potent activity *in vitro* when tested against this contemporary collection of Gram-positive clinical isolates using a revised broth microdilution method. VanA-phenotype enterococci were less susceptible to telavancin, a feature previously determined by the previously established susceptibility testing method. These study results redefine the benchmark for telavancin activity when tested against isolates from the European region.

INTRODUCTION

- Telavancin is a lipoglycopeptide antibiotic approved in the United States and Canada for the treatment of patients with complicated skin and skin structure infections due to susceptible Gram-positive pathogens, and in the United States and Europe for the treatment of hospital-acquired bacterial pneumonia, including ventilator-associated bacterial pneumonia (HABP/VABP) due to susceptible isolates of *Staphylococcus aureus* (methicillin-resistant strains [MRSA] only in Europe), when alternative medicines are unsuitable.[1,2]
- The broth microdilution (BMD) susceptibility testing for telavancin was initially established according to the Clinical and Laboratory Standards Institute (CLSI) recommendations described in the M100-S23 (2013) and previous standards documents.[3]
- These recommendations consisted of the use of dimethyl sulfoxide (DMSO) and water as solvent and diluent, respectively, for preparation of stock solution and dilution for manufacturing frozen-form BMD panels.[3]
- However, this reference method was revised and updated recommendations are described in the current M100-S24 document (2014), which consist of the use of DMSO as solvent and diluent, following the current CLSI guidelines for stock solution and dilution preparations of water-insoluble agents. Moreover, this revised method encompasses the addition of polysorbate-80 (P-80; 0.002%) to the test medium.[2,4]
- This revised reference method for telavancin resembles those utilised for other lipoglycopeptide agents, such as dalbavancin and oritavancin.[5,6]
- The susceptibility testing methods for these agents also incorporate P-80, which was shown to be essential for accurate minimum inhibitory concentration (MIC) determinations and improved test performance via minimising the drug-binding to plastic panels.[4,5,6]
- Consequently, the use of P-80 (to minimise plastic binding) and DMSO (to increase drug solubility) provided lower telavancin MIC results when compared with those obtained by the previously established CLSI BMD method.[5,6]
- Therefore, the objective of this investigation was to reassess the activity of telavancin when tested against a contemporary collection of isolates recovered from hospitalised patients in European and adjacent countries using the revised method.

MATERIALS AND METHODS

Bacterial strain collection

- A total of 11,601 consecutive, non-duplicate Gram-positive clinical isolates were included in this study, which were collected from 36 centres in 17 European countries (Belgium, Czech Republic, France, Germany, Greece, Hungary, Ireland, Italy, Poland, Portugal, Russia, Slovenia, Spain, Sweden, Turkey, United Kingdom, and Ukraine) and Israel.
- These isolates were recovered mostly from skin and soft-tissue infections (SSTI) (37%), bacteraemia (22%), and respiratory tract infections (24%) and submitted to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA), as part of the SENTRY Antimicrobial Surveillance Programme during 2011–2013.
- Isolates were initially identified by the participating laboratory and identification confirmed by the reference monitoring laboratory by standard algorithms and supported by Vitek® 2 (bioMérieux, Hazelwood, Missouri, USA), and more recently MALDI-TOF-MS (Bruker Daltonics, Bremen, Germany).

Antimicrobial susceptibility test methods

- Isolates were tested for susceptibility by BMD following the CLSI M07-A9 document.[7]
- Testing was performed using validated dry-form panels manufactured by ThermoFisher Scientific (Cleveland, Ohio, USA). These panels were previously developed and shown to provide MIC results equivalent to the Food and Drug Administration (FDA) and CLSI-approved revised BMD method (supplemented with 0.002% P-80) described above.[2,4]
- Bacterial inoculum density was monitored by colony counts to ensure an adequate number of cells for each testing event.
- Validation of the MIC values was performed by concurrent testing of CLSI-recommended quality control (QC) reference strains (*S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, and *Streptococcus pneumoniae* ATCC 49619).[4]
- Telavancin MIC ranges when tested against ATCC strains were those established during a QC study conducted according to the CLSI M23-A3 (2008) guideline document using the revised BMD method.[4]
- The MIC QC ranges for telavancin are available in the current M100-S24 document, as follows: *S. aureus* ATCC 29213 (0.03–0.12 mg/L); *E. faecalis* ATCC 29212 (0.03–0.12 mg/L); and *S. pneumoniae* ATCC 49619 (0.004–0.015 mg/L).[2,4]
- All QC results were within published acceptable CLSI ranges.
- MIC interpretations for telavancin were based on the FDA-approved breakpoint criteria appropriate for the revised BMD method, which are currently available in the updated product package insert (2014), and were as follows: *S. aureus* at ≤0.12 mg/L for susceptible; *E. faecalis* (vancomycin-susceptible) at ≤0.25 mg/L for susceptible; *Streptococcus pyogenes* and *Streptococcus agalactiae* at ≤0.12 mg/L for susceptible; and *Streptococcus anginosus* group at ≤0.06 mg/L for susceptible.[1]
- The CLSI M100-S24 (2014) and European Committee on Antimicrobial Susceptibility Testing (EUCAST; 2014) breakpoint criteria was applied for comparator agents, as available.[4,8]

Table 1. Antimicrobial activity and MIC distribution for telavancin when tested against 11,601 contemporary (2011–2013) clinical isolates from European and adjacent countries, as part of the international telavancin surveillance programme

Organism[a] (no. tested)	MIC (mg/L) 50%	MIC (mg/L) 90%	Number (cumulative %) inhibited at telavancin MIC (mg/L)[b] ≤0.015	0.03	0.06	0.12	0.25	0.5	1	>1
MSSA (4108)	0.03	0.06	157 (3.8)	**2514 (65.0)**	1430 (99.8)	7 (100.0)				
MRSA (1207)	0.03	0.06	37 (3.1)	**770 (66.9)**	395 (99.6)	5 (100.0)				
CoNS (1071)	0.06	0.06	169 (15.8)	341 (47.6)	**543 (98.3)**	16 (100.0)				
E. faecalis (991)	0.12	0.12	5 (0.5)	25 (3.0)	284 (31.7)	**657 (98.0)**	11 (99.1)	0 (99.1)	0 (99.1)	9[c] (100.0)
VAN-S *E. faecium* (428)	≤0.015	0.03	**270 (63.1)**	136 (94.9)	20 (99.5)	2 (100.0)				
VanA *E. faecium* (232)	1	>1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (4.7)	71 (35.3)	**112 (83.6)**	38 (100.0)
S. pneumoniae (2064)	≤0.015	≤0.015	**2027 (98.2)**	36 (100.0)	1 (100.0)					
VGS[d] (487)	≤0.015	0.03	**266 (54.6)**	198 (95.3)	23 (100.0)					
S. anginosus group[e] (153)	≤0.015	0.03	**85 (55.6)**	63 (96.7)	5 (100.0)					
BHS[f] (953)	≤0.015	0.06	**562 (59.0)**	282 (88.6)	90 (98.0)	19 (100.0)				
S. pyogenes (377)	≤0.015	0.03	**326 (86.5)**	39 (96.8)	11 (99.7)	1 (100.0)				
S. agalactiae (338)	0.03	0.06	70 (20.7)	**192 (77.5)**	59 (95.0)	17 (100.0)				

[a]MSSA = methicillin-susceptible *S. aureus*; MRSA = methicillin-resistant *S. aureus*; CoNS = coagulase-negative staphylococci (60% of *S. epidermidis*); VAN-S = vancomycin-susceptible; VanA = vancomycin and teicoplanin MIC values of >4 and >8 mg/L, respectively; VGS = viridans group streptococci; BHS = ß-haemolytic streptococci.
[b]Modal MIC values are shown in bold.
[c]All VanA-phenotype.
[d]Includes *S. anginosus* (91 strains), *S. anginosus* group (17 strains), *S. australis* (one strain), *S. bovis* (six strains), *S. bovis* group (11 strains), *S. constellatus* (38 strains), *S. cristatus* (three strains), *S. gallolyticus* (six strains), *S. gordonii* (three strains), *S. infantis* (two strains), *S. intermedius* (seven strains), *S. milleri* (four strains), *S. mitis/oralis* (50 strains), *S. mitis* (23 strains), *S. mitis* group (24 strains), *S. mutans* (two strains), *S. oralis* (64 strains), *S. parasanguinis* (22 strains), *S. salivarius* (26 strains), *S. sanguinis* (30 strains), *S. suis* (one strain), *S. vestibularis* (two strains), unspecified *Streptococcus* (54 strains).
[e]Includes *S. anginosus* (91 strains), *S. anginosus* group (17 strains), *S. constellatus* (38 strains), and *S. intermedius* (seven strains).
[f]Includes *S. agalactiae* (124 strains), *S. dysgalactiae* (91 strains), *S. equi* (one strain), *S. equisimilis* (three strains), *S. pyogenes* (145 strains), Group A *Streptococcus* (*S. pyogenes*) (232 strains), Group B *Streptococcus* (*S. agalactiae*; 214 strains), Group C *Streptococcus* (43 strains), Group F *Streptococcus* (three strains), Group G *Streptococcus* (96 strains), and unspecified ß-haemolytic streptococci (one strain).

RESULTS

- Telavancin ($MIC_{50/90}$, 0.03/0.06 mg/L) was equally potent when tested against methicillin-susceptible *S. aureus* (MSSA) and MRSA (**Table 1**). These telavancin MIC_{50} and MIC_{90} results were eight-fold lower than daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), and 16- to 32-fold lower than linezolid ($MIC_{50/90}$, 1/1 mg/L) and vancomycin ($MIC_{50/90}$, 1/1 mg/L) against MRSA (**Table 2**).
- The majority of coagulase-negative staphylococci (73.4%) were methicillin-resistant, and telavancin ($MIC_{50/90}$, 0.06/0.06 mg/L) showed MIC results eight- to 32-fold more potent than vancomycin ($MIC_{50/90}$, 1/2 mg/L) or linezolid ($MIC_{50/90}$, 0.5/1 mg/L), and four- to eight-fold more potent than daptomycin ($MIC_{90/90}$, 0.25/0.5 mg/L; **Tables 1** and **2**).
- All *E. faecalis* were inhibited by telavancin at the breakpoint for susceptibility (ie, ≤0.25 mg/L), except for nine vancomycin-resistant (VanA phenotype) clinical isolates (**Table 1**).
- Telavancin ($MIC_{50/90}$, 0.12/0.12 mg/L) was at least eight-fold more active than ampicillin ($MIC_{50/90}$, 1/2 mg/L), vancomycin ($MIC_{50/90}$, 1/2 mg/L), and daptomycin ($MIC_{50/90}$, 1/1 mg/L) when tested against vancomycin-susceptible *E. faecalis* (**Table 2**).
- The MIC_{50} and MIC_{90} results (≤0.015 and 0.03 mg/L, respectively) obtained for telavancin against vancomycin-susceptible *E. faecium* were at least four-fold lower than those from vancomycin-susceptible *E. faecalis* ($MIC_{50/90}$, 0.12/0.12 mg/L; **Table 2**).
- Telavancin ($MIC_{50/90}$, ≤0.015/0.03 mg/L) was very active against vancomycin-susceptible *E. faecium*, while higher MIC results were obtained for VanA-phenotype strains (**Table 1**), where daptomycin ($MIC_{50/90}$, 2/4 mg/L) and linezolid ($MIC_{50/90}$, 1/2 mg/L) remained more active (data not shown).
- Telavancin (MIC_{50}, ≤0.015 mg/L) was very potent against *S. pneumoniae*, with MIC_{90} values at least 32-fold lower than vancomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), levofloxacin ($MIC_{50/90}$, 1/1 mg/L), and linezolid ($MIC_{50/90}$, 1/1 mg/L), and 128-fold lower than penicillin ($MIC_{50/90}$, ≤0.06/2 mg/L; **Tables 1** and **2**).
- Viridans group streptococci had low MIC results for telavancin ($MIC_{50/90}$, ≤0.015/0.03 mg/L), including when tested against the subset of *S. anginosus* group ($MIC_{50/90}$, ≤0.015/0.03 mg/L; **Table 1**). Moreover, telavancin demonstrated MIC_{90} values at least 32-fold more potent than the comparator agents (**Table 2**).
- When tested against *S. pyogenes* ($MIC_{50/90}$, ≤0.015/0.03 mg/L), telavancin MIC results were slightly lower (≤two-fold) than those obtained for *S. agalactiae* ($MIC_{50/90}$, 0.03/0.06 mg/L; **Table 1**). In addition, telavancin and penicillin were the most potent agents overall tested against ß-haemolytic streptococci (**Table 2**).

CONCLUSIONS

- Telavancin exhibited *in vitro* potencies greater than comparator agents when tested against contemporary Gram-positive clinical isolates using a revised CLSI BMD method. VanA-phenotype enterococci were less susceptible to telavancin, a feature also well documented by the previously established reference BMD susceptibility testing method.[9]
- The telavancin *in vitro* results described here are now comparable to those reported for other lipoglycopeptide molecules (dalbavancin and oritavancin), for which results have been generated with similar susceptibility testing method containing P-80 in the test media to minimise drug-binding to plastics in BMD panels.[5,10]
- This study documents telavancin MIC results that are lower than those previously reported using the previous BMD method, which markedly underestimated the *in vitro* drug potency.[9] These results redefine the benchmark for telavancin activity when tested against isolates from the European region as the revised BMD method supersedes the previous testing methodology worldwide.

REFERENCES

1. European Medicines Agency. Vibativ (telavancin). Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001240/human_med_001467.jsp&mid=WC0b01ac058001d124. Accessed 2 April 2014.
2. VIBATIV® Package Insert (2014). Available at: http://www.vibativ.com. Accessed 2 April 2014.
3. Clinical and Laboratory Standards Institute (2013). *Performance standards for antimicrobial susceptibility testing; 23rd Informational Supplement M100-S23*. Wayne, PA, USA.
4. Clinical and Laboratory Standards Institute (2014). *Performance standards for antimicrobial susceptibility testing; 24th Informational Supplement M100-S24*. Wayne, PA, USA.
5. Arhin F et al. *Antimicrob Agents Chemother* 2008;52:1597–1603.
6. Rennie RP et al. *J Clin Microbiol* 2007;45:3151–3154.
7. Clinical and Laboratory Standards Institute (2012). *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; Approved Standard M07-A9: Ninth edition*. Wayne, PA, USA.
8. European Committee on Antimicrobial Susceptibility Testing (2014). Breakpoint tables for interpretation of MICs and zone diameters. Version 4.0, January 2014. Available at: http://www.eucast.org/clinical_breakpoints/. Accessed January 1, 2014.
9. Mendes RE et al. *Diagn Microbiol Infect Dis* 2012;72:113–117.
10. Jones RN et al. *Diagn Microbiol Infect Dis* 2012;76:122–123.

Table 2. Antimicrobial activity of telavancin and comparator agents tested against Gram-positive clinical isolates from European and adjacent countries, as part of the 2011–2013 international telavancin surveillance programme

Organism[a] (no. tested)/ Antimicrobial agent	MIC (mg/L) Range	50%	90%	%Susceptible/%Intermediate/Resistant[b] CLSI	EUCAST
MRSA (1207)				100.0 / -/ -	
Telavancin	≤0.015–0.12	0.03	0.06		100.0 / 0.0 / 0.0
Vancomycin	0.25–2	1	1	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Daptomycin	0.12–2	0.25	0.5	99.8 / - / -	99.8 / 0.0 / 0.2
Linezolid	≤0.12–8	1	1	99.8 / 0.0 / 0.2	99.8 / 0.0 / 0.2
Levofloxacin	≤0.12–>4	>4	>4	11.7 / 1.0 / 87.3	11.7 / 1.0 / 87.3
Erythromycin	≤0.12–>16	>16	>16	31.4 / 4.3 / 64.3	32.0 / 1.3 / 66.7
Clindamycin	≤0.25–>2	≤0.25	>2	72.8 / 0.3 / 26.9	72.5 / 0.3 / 27.2
Gentamicin	≤1–>8	≤1	>8	87.3 / 0.4 / 12.3	86.3 / 0.0 / 13.7
Tetracycline	≤0.25–>8	≤0.25	8	89.6 / 1.0 / 9.4	89.2 / 0.1 / 10.7
Trimethoprim/ sulfamethoxazole	≤0.5–>4	≤0.5	≤0.5	99.2 / 0.0 / 0.8	99.2 / 0.2 / 0.6
CoNS (1071)					
Telavancin	≤0.015–0.12	0.06	0.06	- / - / -	- / - / -
Oxacillin	≤0.25–>2	>2	>2	26.6 / 0.0 / 73.4	26.6 / 0.0 / 73.4
Vancomycin	≤0.12–4	1	2	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Daptomycin	≤0.06–2	0.25	0.5	99.8 / - / -	99.8 / 0.0 / 0.2
Linezolid	0.25–>8	0.5	1	99.5 / 0.0 / 0.5	99.5 / 0.0 / 0.5
Levofloxacin	≤0.12–>4	0.5	>4	51.9 / 3.5 / 44.6	51.9 / 3.5 / 44.6
Erythromycin	≤0.12–>16	>16	>16	39.6 / 0.5 / 59.9	39.7 / 0.2 / 60.1
Clindamycin	≤0.25–>2	≤0.25	>2	75.4 / 0.6 / 24.0	73.3 / 2.0 / 24.7
Gentamicin	≤1–>8	≤1	>8	61.0 / 5.9 / 33.1	57.4 / 0.0 / 42.6
Tetracycline	≤0.25–>8	0.5	>8	81.7 / 1.4 / 16.9	71.8 / 7.8 / 20.4
Trimethoprim/ sulfamethoxazole	≤0.5–>4	≤0.5	>4	66.9 / 0.0 / 33.1	66.9 / 15.5 / 17.6
Vancomycin-susceptible *E. faecalis* (979)					
Telavancin	≤0.015–0.25	0.12	0.12		100.0 / - / -
Ampicillin	≤0.25–4	1	2	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Vancomycin	0.25–4	1	2	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Daptomycin	≤0.06–2	1	1	100.0 / - / -	- / - / -
Linezolid	0.25–4	1	2	99.8 / 0.2 / 0.0	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12–>4	1	>4	70.8 / 0.4 / 28.8	- / - / -
Tetracycline	≤0.25–>8	>8	>8	22.8 / 0.1 / 77.1	- / - / -
Vancomycin-susceptible *E. faecium* (428)					
Telavancin	≤0.015–0.12	≤0.015	0.03	- / - / -	- / - / -
Ampicillin	0.5–>8	>8	>8	9.1 / 0.0 / 90.9	8.2 / 0.9 / 90.9
Vancomycin	0.5–4	1	1	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Daptomycin	≤0.06–4	2	4	100.0 / - / -	- / - / -
Linezolid	0.25–8	1	1	99.8 / 0.0 / 0.2	99.8 / 0.0 / 0.2
Levofloxacin	0.5–>4	>4	>4	7.0 / 4.9 / 88.1	- / - / -
Tetracycline	≤0.25–>8	0.5	>8	55.7 / 1.2 / 43.1	- / - / -
S. pneumoniae (2064)					
Telavancin	≤0.015–0.06	≤0.015	≤0.015	- / - / -	- / - / -
Penicillin	≤0.06–>8	≤0.06	2	93.9 / 5.2 / 0.9[d]	- / -
Peniicillin	≤0.06–>8	≤0.06	2	67.9 / 14.6 / 17.5[e]	67.9 / 26.0 / 6.1
Vancomycin	≤0.12–1	0.25	0.5	100.0 / - / -	100.0 / 0.0 / 0.0
Linezolid	≤0.12–2	1	1	100.0 / - / -	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12–>4	1	1	98.3 / 0.2 / 1.5	98.3 / 0.0 / 1.7
Erythromycin	≤0.12–>16	≤0.12	>16	67.0 / 0.5 / 32.5	67.0 / 0.5 / 32.5
Clindamycin	≤0.25–>2	≤0.25	>2	76.5 / 0.4 / 23.1	76.9 / 0.0 / 23.1
Tetracycline	≤0.25–>8	≤0.25	>8	72.7 / 0.5 / 26.8	72.7 / 0.5 / 26.8
VGS (487)					
Telavancin	≤0.015–0.06	≤0.015	0.03		100.0 / - / -
Peniicilin	≤0.06–>8	≤0.06	1	73.5 / 21.4 / 5.1	81.5 / 13.4 / 5.1
Vancomycin	0.25–1	0.5	1	100.0 / - / -	100.0 / 0.0 / 0.0
Daptomycin	≤0.06–4	0.25	1	99.4 / - / -	- / - / -
Linezolid	≤0.12–2	1	1	100.0 / - / -	- / - / -
Levofloxacin	≤0.12–>4	1	2	97.3 / 0.4 / 2.3	- / - / -
Erythromycin	≤0.12–>16	≤0.12	>16	56.1 / 2.0 / 41.9	- / - / -
Clindamycin	≤0.25–>2	≤0.25	>2	84.8 / 0.4 / 14.8	85.2 / 0.0 / 14.8
Tetracycline	≤0.25–>8	0.5	>8	65.6 / 2.2 / 32.2	- / - / -
BHS (953)					
Telavancin	≤0.015–0.12	≤0.015	0.06		100.0 / - / -
Peniicilin	≤0.06–0.12	≤0.06	≤0.06	100.0 / - / -	100.0 / 0.0 / 0.0
Vancomycin	≤0.12–1	0.25	0.5	100.0 / - / -	100.0 / 0.0 / 0.0
Daptomycin	≤0.06–0.5	≤0.06	0.25	100.0 / - / -	100.0 / 0.0 / 0.0
Linezolid	0.25–1	1	1	100.0 / - / -	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12–>4	0.5	1	99.2 / 0.0 / 0.8	94.7 / 4.5 / 0.8
Erythromycin	≤0.12–>16	≤0.12	8	80.4 / 0.8 / 18.8	80.4 / 0.8 / 18.8
Clindamycin	≤0.25–>2	≤0.25	≤0.25	90.2 / 0.5 / 9.3	90.7 / 0.0 / 9.3
Tetracycline	≤0.25–>8	0.5	>8	55.1 / 2.5 / 42.4	53.5 / 1.6 / 44.9

[a]MRSA = methicillin-resistant *S. aureus*; CoNS = coagulase-negative staphylococci; VGS = viridans group streptococci; BHS = ß-haemolytic streptococci.
[b]Breakpoint criteria for telavancin according to the updated package insert, as available. Breakpoint for VGS was that from *S. anginosus* group (≤0.06 mg/L for susceptible); while the interpretive criteria for *S. pyogenes* and *S. agalactiae* (≤0.12 mg/L for susceptible) was applied for BHS. Breakpoint criteria for comparator agents were those from CLSI (M100-S24, 2014) and EUCAST (2014), as available.
[c]Breakpoint not available.
[d]Susceptibility breakpoints for parenteral penicillin (nonmeningitis).
[e]Susceptibility breakpoints for oral penicillin.

Presented at the 24th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID); May 10–13, 2014; Barcelona, Spain.

The research and publication process was supported by Theravance, Inc. Poster production support was coordinated by Suzanne Douthwaite, a medical writer at Envision Scientific Solutions, funded by Theravance, Inc.