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Activity of Telavancin against Gram-Positive Cocci from CANWARD 2007-2013 using Previously Established and Revised CLSI Guidelines

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ABSTRACT

Background: Telavancin (TLV) is a bactericidal lipoglycopeptide with activity against methicillin-resistant *Staphylococcus aureus* and other Gram-positive pathogens. The revised method for broth microdilution (BMD) susceptibility testing of TLV utilizes DMSO as solvent/diluent for stock solution preparation/dilution and incorporates 0.002% polysorbate-80 (P-80) in the BMD test medium. We evaluated the in vitro activity of TLV against Gram-positive cocci associated with infections in Canadian hospitals using previously established and revised methodology.

Methods: Between 2007 and 2013, more than 10,000 Gram-positive cocci were collected from tertiary-care medical centres across Canada as part of the ongoing national CANWARD surveillance study. Vancomycin-intermediate *S. aureus* (VISA) and vancomycin-resistant *S. aureus* (VRSA) isolates from the Network on Antimicrobial Resistance in *S. aureus* (NARSA) repository were also included in this comparison. TLV activity was assessed using the previously established BMD methodology for isolates collected from 2007-2012 and by the revised BMD method for 2013 isolates. Susceptibility testing of comparator agents was performed by broth microdilution following CLSI guidelines.

Results: The activity of TLV by both BMD methods and select comparators (vancomycin [VAN], daptomycin [DAP], linezolid [LZD]) against Gram-positive cocci is summarized below:

Organism, # (previous/revised BMD)	TLV, previous BMD MIC_{50}/MIC_{90}/Range	TLV, revised BMD MIC_{50}/MIC_{90}/Range	Comparators (MIC_{50}/MIC_{90})		
			VAN	DAP	LZD
MSSA (4734/630)	0.25/0.5/≤0.06-1	0.06/0.06/0.03-0.06	1/1	0.25/0.25	2/2
MRSA (1391/160)	0.25/0.5/≤0.06-1	0.06/0.06/0.03-0.06	1/1	0.25/0.25	2/2
HA-MRSA (936/92)	0.25/0.5/0.12-1	0.03/0.06/0.03-0.06	1/1	0.25/0.25	2/4
CA-MRSA (415/57)	0.25/0.5/≤0.06-1	0.06/0.06/0.03-0.06	1/1	0.25/0.25	2/2
MSSE (533/72)	0.25/0.5/≤0.06-1	0.12/0.25/0.06-0.25	1/2	0.12/0.25	0.5/1
MRSE (97/14)	0.25/0.25/≤0.06-1	0.06*/0.06-0.25	1/2	0.12/0.25	1/1
hVISA (10/10)	0.5*/0.25-1	0.12*/0.03-0.25	2*	0.5*	1*
VISA (11/11)	0.5*/0.25-1	0.25*/0.06-0.25	2*	0.5*	1*
VRSA (7/7)	4*/2-8	0.5*/0.25-1	32*	0.25*	2*

*Median MIC value. MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; HA-MRSA, healthcare-associated MRSA; CA-MRSA, community-associated MRSA; MSSE, methicillin-susceptible *S. epidermidis*; MRSE, methicillin-resistant *S. epidermidis*; hVISA, heterogeneous vancomycin-intermediate *S. aureus*.

Conclusions: With the revised BMD methodology, TLV MIC_{90}s were 8-fold lower than with the previously established method for *S. aureus* and at least 2-fold lower for *S. epidermidis*. The median TLV MIC was reduced 4-fold for hVISA, 2-fold for VISA and 8-fold for VRSA when tested with P-80. TLV demonstrates equal or greater potency in vitro than VAN, DAP and LZD against MSSA, MRSA (including CA-MRSA and HA-MRSA), MSSE and MRSE. TLV also exhibits excellent activity versus hVISA, VISA and VRSA.

BACKGROUND

Telavancin is a semisynthetic lipoglycopeptide with a dual mechanism of action against a broad spectrum of clinically relevant Gram-positive bacteria, including both susceptible and multidrug-resistant staphylococci and streptococci. The rapid bactericidal activity of telavancin is derived from its ability to inhibit synthesis of the bacterial cell wall as well as to disrupt bacterial membrane integrity and increase cell membrane permeability.

Prior to 2014, Clinical and Laboratory Standards Institute (CLSI) guidelines for broth microdilution susceptibility testing of telavancin recommended the use of dimethyl sulfoxide (DMSO) as solvent and water as diluent for drug stock solution preparation and dilution (M100-S23, CLSI 2013). Recently, the method for broth microdilution susceptibility testing of telavancin was revised to utilize DMSO as both solvent and diluent for stock solution preparation/dilution to increase drug solubility and, additionally, incorporates 0.002% polysorbate-80 (P-80) in the broth microdilution test medium to minimize binding of the drug to plastic panels (M100-S24, CLSI 2014).

The purpose of this study was to assess the activity of telavancin against Gram-positive cocci associated with infections in Canadian hospitals using previously established and revised CLSI broth microdilution methods.

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MATERIALS & METHODS

CANWARD Study Design

Between January 2007 and December 2013, 33,433 clinical isolates, including more than 10,000 Gram-positive cocci, were collected as part of the ongoing CANWARD study assessing pathogen prevalence and antibiotic resistance in Canadian hospitals. Isolates were received from tertiary-care medical centres (12 in 2007, 10 in 2008, 15 in 2009, 14 in 2010, 15 in 2011, 12 in 2012, 15 in 2013) that were geographically distributed in a population-based fashion in eight of the ten Canadian provinces. Annually, each study site was asked to submit clinical isolates (consecutive, one per patient per infection site) from inpatients and outpatients with respiratory, urine, wound and bloodstream infections. Isolates were collected from patients attending hospital clinics, emergency rooms, medical/surgical wards and intensive care units. All organisms were identified by the submitting centre and were deemed clinically significant using local site criteria.

Additional Test Isolates

Ten heterogeneous vancomycin-intermediate *S. aureus* (hVISA) identified as part of the CANWARD study, as well as 11 vancomycin-intermediate *S. aureus* (VISA) and 7 vancomycin-resistant *S. aureus* (VRSA) isolates from the Network on Antimicrobial Resistance in *S. aureus* (NARSA) repository were also included in this comparison.

Antimicrobial Susceptibility Testing

The *in vitro* activities of comparator agents, including cefazolin, ceftriaxone, clarithromycin, clindamycin, ciprofloxacin, daptomycin, doxycycline, ertapenem, levofloxacin, linezolid, meropenem, moxifloxacin, penicillin, piperacillin-tazobactam, tigecycline, trimethoprim-sulfamethoxazole and vancomycin, were determined by broth microdilution in accordance with CLSI guidelines (M7-A9, CLSI 2012). Telavancin susceptibility testing for isolates collected from 2007-2012 was performed by the previously established broth microdilution method in the absence of P-80 using Trek Sensititre dry-form panels. The revised telavancin broth microdilution method, which utilizes DMSO as both solvent and diluent for stock solution preparation/dilution and incorporates 0.002% P-80 in the test medium, was used to assess telavancin activity against isolates collected in 2013. MIC interpretive standards were defined according to CLSI breakpoints for comparator agents (M100-S24, CLSI 2014). The following interpretive breakpoints (FDA) were used with *S. aureus*: telavancin susceptible, ≤1 μg/ml for previous broth microdilution method results and ≤0.12 μg/ml for the current broth microdilution method; tigecycline susceptible, ≤0.5 μg/ml. With *S. pneumoniae*, an interpretive breakpoint (FDA) of ≤0.06 μg/ml was used for tigecycline susceptible. Tetracycline breakpoints were used to interpret *S. pneumoniae* doxycycline MIC values. For *S. pyogenes* and *S. agalactiae*, interpretive breakpoints (FDA) of ≤0.12 μg/ml and ≤0.25 μg/ml were used to define telavancin and tigecycline susceptibility, respectively.

CONCLUSIONS

With the revised broth microdilution methodology, telavancin MIC_{90}s were 8-fold lower than with the previously established method for methicillin-susceptible and methicillin-resistant *S. aureus*, including both community- and healthcare-associated MRSA strains. Telavancin was more active than the comparator agents vancomycin, daptomycin and linezolid against MSSA and MRSA.

The median telavancin MIC was reduced 4-fold for hVISA, 2-fold for VISA and 8-fold for VRSA when tested using the revised CLSI guidelines. As measured by the MIC, telavancin had superior activity to vancomycin, daptomycin and linezolid against hVISA and VISA strains. Against VRSA, telavancin was more active than vancomycin and linezolid.

Telavancin demonstrated greater potency *in vitro* than vancomycin and linezolid and comparable activity to daptomycin against methicillin-susceptible and methicillin-resistant *S. epidermidis*. The telavancin MIC_{90} for MSSE was 4-fold lower in the presence of P-80.

For *Streptococcus* species, including *S. pneumoniae*, *S. pyogenes* and *S. agalactiae*, telavancin MIC_{90}s were 4-fold lower when tested with P-80. Telavancin had comparable activity to penicillin and superior activity to vancomycin and linezolid against *S. pyogenes* and *S. agalactiae,* and was the most potent agent tested against *S. pneumoniae*.

The addition of 0.002% polysorbate-80 during broth microdilution susceptibility testing of telavancin significantly reduced the telavancin MICs and MIC_{90}s for all organisms tested and is required to accurately reflect the *in vitro* potency of this drug.

RESULTS

Table 1. Activity of telavancin and comparators against Gram-positive cocci

Organism (n), Antibiotic	% of Isolates per Category S	I	R	MIC (μg/mL) 50%	90%	Range
S. aureus						
MSSA (4734)						
Telavancin[a]	**100**			**0.25**	**0.5**	**≤0.06 - 1**
Telavancin[a] +P80 (632)	**99.7**		**0.3**	**0.06**	**0.06**	**0.015 - 0.25**
Vancomycin	100			1	1	≤0.25 - 2
Cefazolin	100			≤0.5	1	≤0.5 - 32
Clarithromycin	74.9	0.2	24.9	0.25	>16	≤0.25 - >16
Clindamycin	92.8	0.3	6.9	≤0.25	≤0.25	≤0.25 - >8
Daptomycin	100			0.25	0.25	≤0.06 - 1
Levofloxacin	90.1	0.3	9.6	0.25	1	≤0.06 - >32
Linezolid	100			2	2	≤0.12 - 4
Meropenem	100			0.12	0.25	≤0.12 - 4
Moxifloxacin	90.1	0.6	9.3	≤0.06	0.5	≤0.06 - >16
Pip-Tazo	99.9		0.1	≤1	≤1	≤1 - 32
Tigecycline[a]	99.9		0.1	0.12	0.25	≤0.03 - 1
TMP/SMX	99.4		0.6	≤0.12	≤0.12	≤0.12 - >8
MRSA (1391)						
Telavancin[a]	**100**			**0.25**	**0.5**	**≤0.06 - 1**
Telavancin[a] +P80 (159)	**100**			**0.06**	**0.06**	**0.03 - 0.12**
Vancomycin	99.9	0.1		1	1	≤0.25 - 4
Cefazolin			100[b]	64	>128	1 - >128
Clarithromycin	13.0	0.1	86.9	>16	> 16	≤0.25 - >16
Clindamycin	50.0	0.1	49.9	0.5	> 8	≤0.25 - >8
Daptomycin	100			0.25	0.25	0.06 - 1
Levofloxacin	14.1		85.9	>32	>32	0.12 - >32
Linezolid	100			2	2	≤0.12 - 4
Meropenem			100[b]	8	32	0.12 - >32
Moxifloxacin	15.5	2.2	82.3	8	>16	≤0.06 - >16
Pip-Tazo			100[b]	32	128	≤1 - 512
Tigecycline[a]	99.6		0.4	0.25	0.5	0.06 - 2
TMP/SMX	92.5		7.5	≤0.12	≤0.12	≤0.12 - >8
CA-MRSA (415)						
Telavancin[a]	**100**			**0.25**	**0.5**	**0.12 - 1**
Telavancin[a] +P80 (57)	**100**			**0.06**	**0.06**	**0.03 - 0.12**
Vancomycin	100			1	1	0.5 - 2
Cefazolin			100[b]	16	64	1 - >128
Clarithromycin	26.0	0.2	73.8	>16	>16	≤0.25 - >16
Clindamycin	86.9		13.1	≤0.25	>8	≤0.25 - >8
Daptomycin	100			0.25	0.25	0.12 - 1
Levofloxacin	40.0		60.0	4	8	0.12 - 32
Linezolid	100			2	2	1 - 4
Meropenem			100[b]	2	4	0.12 - 32
Moxifloxacin	35.8	6.7	57.5	2	2	≤0.06 - 16
Pip-Tazo			100[b]	16	32	2 - 128
Tigecycline[a]	100			0.25	0.25	0.06 - 0.5
TMP/SMX	100			≤0.12	≤0.12	≤0.12 - 2
HA-MRSA (936)						
Telavancin[a]	**100**			**0.25**	**0.5**	**≤0.06 - 1**
Telavancin[a] +P80 (91)	**100**			**0.06**	**0.06**	**0.03 - 0.12**
Vancomycin	99.9	0.1		1	1	≤0.25 - 4
Cefazolin			100[b]	128	>128	1 - >128
Clarithromycin	4.9		95.1	>16	>16	≤0.25 - >16
Clindamycin	32.1	0.1	67.8	>8	>8	≤0.25 - >8
Daptomycin	100			0.25	0.25	0.06 - 1
Levofloxacin	2.9		97.1	>32	>32	0.12 - >32
Linezolid	100			2	4	≤0.12 - 4
Meropenem			100[b]	8	>32	0.25 - >32
Moxifloxacin	3.5	0.2	96.3	8	>16	≤0.06 - >16
Pip-Tazo			100[b]	64	128	≤1 - 512
Tigecycline[a]	99.4		0.6	0.25	0.5	0.06 - 2
TMP/SMX	88.9		11.1	≤0.12	8	≤0.12 - >8
S. aureus						
CANWARD hVISA (10)						
Telavancin[a]	**100**			**0.5***	**-**	**0.12 - 1**
Telavancin[a] +P80 (10)	**90.0**		**10.0**	**0.12***	**-**	**0.03 - 0.25**
Vancomycin	100			2*	-	1 - 2
Cefazolin			100[b]	>128*	-	1 - >128
Clarithromycin			100	>32	-	>32
Clindamycin	20.0		80.0	>8*	-	≤0.12 - >8
Daptomycin	90.0		10.0	0.25*	-	0.25 - 2
Levofloxacin	10.0		90.0	>32*	-	0.25 - >32
Linezolid	100			1*	-	0.5 - 2
Meropenem			100[b]	>32*	-	0.5 - >32
Moxifloxacin	10.0		90.0	8*	-	≤0.06 - >16
Pip-Tazo			100[b]	128*	-	8 - 512
Tigecycline[a]	100			0.12*	-	0.06 - 0.25
TMP/SMX	100			≤0.12*	-	≤0.12
NARSA VISA (11)						
Telavancin[a]	**100**			**0.5***	**-**	**0.25 - 1**
Telavancin[a] +P80 (11)	**36.4**		**63.6**	**0.25***	**-**	**0.06 - 0.25**
Vancomycin	81.8	18.2		2*	-	1 - 4
Cefazolin			100[b]	64*	-	4 - >128
Clarithromycin	91.9		90.9	>32*	-	0.12 - >32
Clindamycin	91.9		90.9	>8*	-	≤0.12 - >8
Daptomycin	100			0.5*	-	≤0.25 - 1
Levofloxacin			100	32*	-	16 - >32
Linezolid	100			1*	-	1 - 2
Meropenem			100[b]	8*	-	1 - >32
Moxifloxacin			100	4*	-	2 - 8
Pip-Tazo			100[b]	128*	-	32 - 256
Tigecycline[a]	100			0.25*	-	0.12 - 0.5
TMP/SMX	72.7		27.3	0.25*	-	≤0.12 - >8
NARSA VRSA (7)						
Telavancin[a]			**100**	**4***	**-**	**2 - 8**
Telavancin[a] +P80 (7)			**100**	**0.5***	**-**	**0.25 - 1**
Vancomycin			100	32*	-	16 - >32
Cefazolin			100[b]	>128*	-	≤0.5 - >128
Clarithromycin			100	>32*	-	>32
Clindamycin			100	>8*	-	>8
Daptomycin	100			0.25*	-	0.12 - 0.25
Levofloxacin			100	32*	-	16 - >32
Linezolid	100			2*	-	1 - 2
Meropenem			100[b]	16*	-	0.12 - >32
Moxifloxacin			100	4*	-	4 - >16
Pip-Tazo			100[b]	64*	-	≤1 - 64
Tigecycline[a]	100			0.12*	-	0.12 - 0.5
TMP/SMX	100			≤0.12*	-	≤0.12 - 2
***S. epidermidis*, MSSE (533)**						
Telavancin	**No BP**			**0.25**	**0.5**	**≤0.06 - 1**
Telavancin +P80 (72)	**No BP**			**0.06**	**0.12**	**0.03 - 0.25**
Vancomycin	100			1	2	≤0.25 - 4
Cefazolin	100			1	4	≤0.5 - 8
Clarithromycin	34.2	1.3	64.5	>16	>16	≤0.25 - >16
Clindamycin	62.2	0.9	36.9	≤0.25	>8	≤0.25 - >8
Daptomycin	100			0.12	0.25	≤0.06 - 1
Levofloxacin	51.9	1.1	47.0	0.25	>32	0.12 - >32
Linezolid	100			0.5	1	≤0.12 - 4
Meropenem	80.3	11.4	8.3	1	8	≤0.12 - 32
Moxifloxacin	53.5	7.5	39.0	0.12	16	≤0.06 - >16
Pip-Tazo	98.5		1.5	≤1	4	≤1 - 64
Tigecycline	No BP			0.12	0.5	≤0.03 - 1
TMP/SMX	65.8		34.2	≤0.12	8	≤0.12 - 8
***S. epidermidis*, MRSE (97)**						
Telavancin	**No BP**			**0.25**	**0.5**	**≤0.06 - 1**
Telavancin +P80 (4)	**No BP**			**0.06***	**-**	**0.06 - 0.25**
Vancomycin	100			1	2	≤0.25 - 2
Cefazolin			100	128	>128	32 - >128
Clarithromycin	14.4		85.6	>16	>16	≤0.25 - >16
Clindamycin	16.5		83.5	>8	>8	≤0.25 - >8
Daptomycin	100			0.12	0.25	≤0.06 - 0.5
Levofloxacin	2.2	2.2	95.6	>32	>32	1 - >32
Linezolid	100			1	1	≤0.12 - 1
Meropenem	1.0	2.1	96.9	32	32	4 - >32
Moxifloxacin	3.1	2	94.9	>16	>16	≤0.06 - >16
Pip-Tazo	7.3		92.7	32	64	≤1 - 128
Tigecycline	No BP			0.12	0.25	0.06 - 0.5
TMP/SMX	19.6		80.4	4	8	≤0.12 - >8
***S. pneumoniae* (1931)**						
Telavancin	**No BP**			**≤0.06**	**≤0.06**	**≤0.06 - 0.12**
Telavancin +P80 (188)	**No BP**			**0.008**	**0.015**	**0.004 - 0.03**
Vancomycin	100			≤0.25	0.25	≤0.25 - 1
Ceftriaxone	99.3	0.5	0.2	≤0.12	≤0.12	≤0.12 - 4
Clarithromycin	80.0	3.5	16.5	≤0.03	4	≤0.03 - >32
Clindamycin	93.0	0.5	6.5	≤0.12	≤0.12	≤0.12 - >8
Doxycycline[c]	93.2	3.0	3.8	≤0.25	1	≤0.25 - >16
Levofloxacin	99.0	0.2	0.8	1	1	≤0.06 - 32
Linezolid	100			0.5	1	≤0.12 - 2
Meropenem	95.5	2.8	1.7	≤0.06	≤0.06	≤0.06 - 2
Penicillin	82.0	13.5	4.5	≤0.03	0.25	≤0.03 - >8
Tigecycline[a]	99.7		0.3	0.03	0.06	≤0.03 - 0.25
TMP/SMX	85.1	6.4	8.5	≤0.12	2	≤0.12 - >8
***S. pyogenes* (427)**						
Telavancin	**98.6**		**1.4**	**0.06**	**0.12**	**≤0.06 - 0.25**
Telavancin +P80 (51)	**100**			**0.03**	**0.03**	**0.015 - 0.06**
Vancomycin	100			0.5	0.5	≤0.25 - 1
Ceftriaxone	100			≤0.12	≤0.12	≤0.12 - 0.25
Clarithromycin	88.1	2.6	9.4	≤0.03	0.5	≤0.03 - >32
Clindamycin	98.4		1.6	≤0.12	≤0.12	≤0.12 - >8
Doxycycline	No BP			≤0.25	1	≤0.25 - 16
Levofloxacin	99.8	0.2		0.5	1	≤0.06 - 4
Linezolid	100			1	1	≤0.12 - 2
Meropenem	100			≤0.06	≤0.06	≤0.06 - 0.12
Penicillin	100			≤0.03	≤0.03	≤0.03 - 0.12
Tigecycline[a]	100			0.03	0.06	≤0.03 - 0.25
TMP/SMX	No BP			≤0.12	≤0.12	≤0.12 - 8
***S. agalactiae* (181)**						
Telavancin	**89.5**		**10.5**	**≤0.06**	**0.25**	**≤0.06 - 0.5**
Telavancin +P80 (63)	**100**			**0.03**	**0.06**	**0.03 - 0.06**
Vancomycin	100			0.5	0.5	≤0.25 - 0.5
Ceftriaxone	100			≤0.12	≤0.12	≤0.12 - 0.25
Clarithromycin	70.7	5.0	24.3	0.5	32	0.5 - >32
Clindamycin	82.9	1.1	16.0	≤0.12	>8	≤0.12 - >8
Doxycycline	No BP			8	16	≤0.25 - >16
Levofloxacin	97.2		2.8	1	1	0.25 - >32
Linezolid	100			1	2	≤0.12 - 2
Meropenem	100			≤0.06	≤0.06	≤0.06 - ≤0.06
Penicillin	99.5		0.6	0.06	0.12	≤0.03 - 0.25
Tigecycline[a]	100			0.06	0.06	≤0.03 - 0.12
TMP/SMX	No BP			≤0.12	≤0.12	≤0.12 - 1

[a] Interpretive breakpoints defined by FDA; [b] Based on oxacillin susceptibility; [c] Tetracycline breakpoints used to interpret MIC values; No BP, no breakpoints defined; S, susceptible; I, intermediate; R, resistant; *, median MIC value.
MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; CA-MRSA, community-associated methicillin-resistant *S. aureus*; HA-MRSA, healthcare-associated methicillin-resistant *S. aureus*; hVISA, heterogeneous vancomycin-intermediate *S. aureus*; VISA, vancomycin-intermediate *S. aureus*; VRSA, vancomycin-resistant *S. aureus*; MSSE, methicillin-susceptible *S. epidermidis*; MRSE, methicillin-resistant *S. epidermidis*.

Table 2. MIC distribution for telavancin, when tested with and without P-80, against Gram-positive cocci

Organism (no. tested)	Number (cumulative percentage) inhibited at telavancin MIC (μg/mL) [without P-80/with P-80]								
	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	>2
Methicillin-susceptible *S. aureus* (3729/632)			- / 1 (0.2)	- / 168 (26.7)	21 (0.6) / 432 (95.1)	1255 (34.2) / 29 (99.7)	1563 (76.1) / 2 (100)	789 (97.3) / -	101 (100) / -
Methicillin-resistant *S. aureus* (1087/159)				- / 39 (24.5)	1 (0.1) / 112 (95.0)	308 (28.4) / 8 (100)	440 (68.9) / -	301 (96.6) / -	37 (100) / -
Community-associated MRSA (349/57)				- / 14 (24.6)	- / 41 (96.5)	101 (28.9) / 2 (100)	143 (69.9) / -	95 (97.1) / -	10 (100) / -
Healthcare-associated MRSA (703/91)				- / 21 (23.1)	1 (0.1) / 64 (93.4)	196 (28.0) / 6 (100)	284 (68.4) / -	196 (96.3) / -	26 (100) / -
Methicillin-susceptible *S. epidermidis* (424/72)				- / 1 (1.4)	36 (8.5) / 44 (62.5)	157 (45.5) / 25 (97.2)	160 (83.3) / 2 (100)	64 (98.3) / -	7 (100) / -
Methicillin-resistant *S. epidermidis* (79/4)					3 (3.8) / 3 (75.0)	33 (45.6) / 0 (75.0)	34 (88.6) / 1 (100)	6 (96.2) / -	3 (100) / -
CANWARD hVISA (10/10)				- / 1 (10.0)	- / 1 (20.0)	1 (10.0) / 7 (90.0)	3 (40.0) / 1 (100)	4 (80.0) / -	2 (100) / -
NARSA VISA (11/11)					- / 1 (9.1)	- / 3 (36.4)	4 (36.4) / 7 (100)	2 (54.5) / -	5 (100) / -
NARSA VRSA (7/7)							- / 2 (28.6)	- / 3 (71.4)	- / 2 (100) 7 (100) / -
S. pneumoniae (1862/188)	- / 12 (6.4)	- / 146 (84.0)	- / 29 (99.5)	- / 1 (100)	1858 (99.8) / -	4 (100) / -			
S. pyogenes (427/51)			- / 4 (7.8)	- / 43 (92.2)	373 (87.4) / 4 (100)	48 (98.6) / -	6 (100) / -		
S. agalactiae (181/63)				- / 55 (87.3)	125 (69.1) / 8 (100)	37 (89.5) / -	16 (98.3) / -	3 (100) / -	