Tigecycline Activity Tested Against Rarely Recovered Gram-positive Species

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ABSTRACT

Background: Very limited data is available on the antimicrobial susceptibility (S) of rarely occurring Gram-positive (GP) organisms; tigecycline (TIG) has demonstrated broad spectrum activity against GP pathogens, including many multidrug-resistant isolates. We assessed TIG activity and potency against GP clinical isolates collected from the SENTRY Antimicrobial Surveillance Program.

Methods: 1,714 clinically-significant isolates of GP (20 species) were collected from 174 hospitals in 34 countries over a 10 year period (2000-2009; North America [38.4%], Europe [38.4%], Latin America [12.8%] and Asia-Pacific region [10.3%]). Isolates were submitted to a reference monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) where species identifications were confirmed using standard algorithms and the automated Vitek 2 system (bioMérieux, Hazelwood, Missouri, USA). Where needed, 16S rRNA sequencing was also used for identification.

Results: Isolates were recovered mainly from bacteremias (57.1%) and skin/skin structure infections (16.9%). TIG was highly active against all species listed with MIC_{50} and MIC_{90} values ranging from ≤0.03 to 0.12 μg/ml and 0.06 to 0.25 μg/ml, respectively (Table). Highest TIG MIC observed was 1 μg/ml (only 2 strains) and >99% of strains had TIG MIC of ≤0.25 μg/ml. TIG was generally four- to 16-fold more potent than vancomycin (MIC_{50}, 0.25 – 1 μg/ml; except *Leuconostoc* spp. [>16 μg/ml]) or linezolid (MIC_{50}, 0.25 – 2 μg/ml).

	TIG MIC (μg/ml)			TIG MIC (μg/ml)	
Organism (no. tested)	50%	90%	Organism (no. tested)	50%	90%
Aerococcus viridans (28)	0.06	0.12	Group C streptococci (315)	≤0.03	0.12
Bacillus cereus (63)	0.12	0.25	Group F streptococci (61)	≤0.03	0.06
Corynebacterium amycolatum (11)	≤0.03	0.12	*Kocuria kristinae* (18)	0.06	0.25
C. jeikeium (42)	≤0.03	0.12	*Lactococcus garvieae* (24)	0.12	0.25
C. striatum (34)	≤0.03	0.06	*Leuconostoc* spp. (22)	≤0.03	0.06
C. urealyticum (11)	≤0.03	0.06	*Listeria monocytogenes* (96)	0.06	0.12
Enterococcus avium (234)	0.06	0.12	*Micrococcus luteus* (53)	0.06	0.25
E. durans (83)	0.06	0.25	*Rothia mucilaginosa* (10)	0.06	0.12
E. hirae (47)	0.06	0.12	*Staphylococcus lugdunensis* (221)	0.12	0.25
E. raffinosus (48)	0.06	0.12	*Streptococcus bovis* group (293)	≤0.03	0.06

Conclusions: TIG exhibited potent in vitro activity against many rarely isolated GP organisms for which there are very limited S data currently available to guide therapy. These results indicate that TIG may have a role in the treatment of infections caused by these species as guided by reference MIC test results.

INTRODUCTION

Very limited data is available on the antimicrobial susceptibility of rarely occurring Gram-positive organisms. These organisms are generally opportunists and rarely affect healthy persons, but may cause infections in immunocompromised hosts and those with severe underlying medical conditions. In addition, some of these bacterial species can contaminate the hospital environment and spread horizontally.

Given the compromised at-risk population, intrinsic resistance and that susceptibility testing methodologies are not well standardized for most of these organisms, appropriate broad-spectrum empiric therapy strategies are crucial. Tigecycline is approved in the United States (USA) and Europe for the treatment of complicated skin and skin structure infections (cSSSI) and intra-abdominal infections (IAI). Tigecycline possesses a proven broad-spectrum of activity against numerous bacterial pathogens, including aerobic and anaerobic species. In this study, we evaluated the activity and potency of tigecycline against a clinically-significant and worldwide collection of several infrequently recovered aerobic Gram-positive organisms.

MATERIALS AND METHODS

Bacterial isolates. A total of 1,714 clinically-significant isolates of Gram-positive organisms (20 species) were collected from 174 hospitals in 34 countries as part of the SENTRY Antimicrobial Surveillance Program over a 10 year period (2000-2009). The isolates were collected from medical centers located in North America [38.4%], Europe [38.4%], Latin America [12.8%] and Asia-Pacific region [10.3%]). Isolates were submitted to a reference monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) where species identifications were confirmed using standard algorithms and the automated Vitek 2 system (bioMérieux, Hazelwood, Missouri, USA). Where needed, 16S rRNA sequencing was also used for identification.

Antimicrobial susceptibility testing. All isolates were tested for susceptibility by reference broth microdilution methods using the Clinical Laboratory Standards Institute recommendations (CLSI; M07-A8, 2009). Susceptibility testing was performed by using validated broth microdilution panels manufactured by TREK Diagnostics Systems/Sensititre (Cleveland, Ohio, USA). Validation of the minimum inhibitory concentration (MIC) values was performed by concurrent testing of CLSI-recommended (M100-S20, 2010) quality control (QC) strains: *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* ATCC 29213 and *Streptococcus pneumoniae* ATCC 49619.

Categorical interpretation of comparator MIC values was performed according to CLSI (M100-S20, 2010) and The European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria, where available. Tigecycline susceptible breakpoints approved by the USA Food and Drug Administration (FDA) and EUCAST were applied. MIC ranges for tigecycline and comparator agents tested against ATCC QC strains were those published in the CLSI M100-S20 (2010) document.

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RESULTS

- Isolates were recovered predominantly from bacteremia (57.1%) and SSSI (16.9%).
- Less frequently isolated species of *Streptococcus* (669 strains; 39.0% of total) *Enterococcus* (412 strains; 24.0%) and *Staphylococcus lugdunensis* (221 strains; 12.9%) represented the majority of isolates in this investigation (75.9%; **Table 1**).
- Overall, 99.3% of strains were inhibited at tigecycline MIC of ≤0.25 μg/ml. The highest tigecycline MIC value was only 1 μg/ml, which was observed in only two strains (0.11%), one *Aerococcus viridans* and one *Staphylococcus lugdunensis* (**Table 1**).
- Tigecycline was very active against organisms of various *Corynebacterium* species tested with MIC_{50} of ≤0.03 μg/ml and MIC_{90} varying from ≤0.03 to 0.12 μg/ml (**Tables 1 and 2**). Linezolid (MIC_{50}, 0.25 μg/ml and MIC_{90}, 0.25 - 0.5 μg/ml) and vancomycin (MIC_{50}, 0.25 - 0.5 μg/ml and MIC_{90}, 0.5 μg/ml) were also very active against *Corynebacterium* spp., but eight- to 16-fold less potent than tigecycline (**Table 2**).
- Tigecycline was also active against less commonly isolated *Enterococcus* species (other than *faecalis* and *faecium;* MIC_{50}, 0.06 μg/ml and MIC, 0.12 - 0.25 μg/ml). Overall, 99.0% of strains were inhibited at tigecycline MIC of ≤0.25 μg/ml (**Table 1**).

Table 1. MIC distribution of tigecycline tested against infrequently isolated Gram-positive clinical isolates collected as part of the SENTRY Antimicrobial Surveillance Program (2000-2009).

	No. of strains (cumulative %) inhibited at tigecycline MIC (μg/ml) value of:					
Organism (no. tested)	**≤0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**
Aerococcus viridans (28)	12 (42.9)	5 (60.7)	9 (92.9)	1 (96.4)	0 (96.4)	1 (100.0)
Bacillus cereus (63)	18 (28.6)	13 (49.2)	21 (82.5)	11 (100.0)	-	-
Corynebacterium amycolatum (11)	7 (63.6)	2 (81.8)	2 (100.0)	-	-	-
C. jeikeium (42)	26 (61.9)	7 (78.6)	6 (92.9)	2 (97.6)	1 (100.0)	-
C. striatum (34)	21 (61.8)	10 (91.2)	2 (97.1)	1 (100.0)	-	-
C. urealyticum (11)	10 (90.9)	1 (100.0)	-	-	-	-
Enterococcus avium (234)	70 (25.9)	78 (63.3)	68 (92.3)	15 (98.7)	3 (100.0)	-
E. durans (83)	24 (28.9)	27 (61.5)	21 (86.8)	10 (98.8)	1 (100.0)	-
E. hirae (47)	9 (19.2)	15 (51.1)	19 (91.5)	4 (100.0)	-	-
E. raffinosus (48)	11 (22.9)	23 (70.8)	11 (93.8)	3 (100.0)	-	-
Group C *Streptococcus* (315)	188 (59.7)	89 (87.9)	28 (96.8)	10 (100.0)	-	-
Group F *Streptococcus* (61)	53 (86.9)	5 (95.1)	3 (100.0)	-	-	-
Kocuria kristinae (18)	4 (22.2)	7 (61.1)	5 (88.9)	2 (100.0)	-	-
Lactococcus garvieae (24)	6 (25.0)	5 (45.8)	4 (62.5)	8 (95.8)	1 (100.0)	-
Leuconostoc spp. (22)	19 (86.4)	3 (100.0)	-	-	-	-
Listeria monocytogenes (96)	5 (5.2)	58 (65.6)	29 (95.8)	3 (99.0)	1 (100.0)	-
Micrococcus luteus (53)	5 (9.4)	22 (50.9)	19 (86.8)	7 (100.0)	-	-
Rothia mucilaginosa (10)	3 (30.0)	4 (100.0)	-	-	-	-
Staphylococcus lugdunensis (221)	43 (19.5)	106 (48.0)	83 (85.5)	27 (97.7)	4 (99.5)	1 (100.0)
Streptococcus bovis (293)	165 (56.3)	102 (91.1)	26 (100.0)	-	-	-

- Tigecycline was generally eight-fold more active than vancomycin (MIC_{50}, 0.5 - 1 μg/ml and MIC_{90}, 1 - >16 μg/ml) and 16-fold more active than linezolid (MIC_{50}, 1 - 2 μg/ml and MIC_{90}, 2 μg/ml; **Tables 1 and 2**).
- Less frequently recovered β-haemolytic streptococci (Groups C and F; MIC_{50}, ≤0.03 μg/ml and MIC_{90}, 0.06 – 0.12 μg/ml) and *Streptococcus bovis* (MIC_{50} and MIC_{90}, 0.06 μg/ml) were very susceptible to tigecycline. Tigecycline activity was comparable to that of penicillin (MIC_{50}, ≤0.015 - 0.06 μg/ml and MIC_{90}, 0.03 - 0.06 μg/ml) when testing these organisms (**Tables 1 and 2**).
- Tigecycline was the most active agent tested against *Kocuria kristinae* (an aerobic Gram-positive species closely related to *Micrococcus*; MIC_{50}, 0.06 μg/ml and MIC_{90}, 0.25 μg/ml) and *Lactococcus garvieae* (MIC_{50}, 0.12 μg/ml and MIC_{90}, 0.25 μg/ml; **Table 2**).
- *Leuconostoc* spp. (MIC_{50}, ≤0.03 μg/ml and MIC_{90}, 0.06 μg/ml), *Listeria monocytogenes* (MIC_{50}, 0.06 μg/ml and MIC_{90}, 0.12 μg/ml), *Micrococcus* spp. (MIC_{50}, 0.06 μg/ml and MIC_{90}, 0.25 μg/ml) and *Rothia mucilaginosa* (MIC_{50}, 0.06 μg/ml and MIC_{90}, 0.12 μg/ml) were highly susceptible to tigecycline (**Tables 1 and 2**).
- Against *Staphylococcus lugdunensis* (78.7% oxacillin-resistant), tigecycline (MIC_{50}, 0.12 μg/ml and MIC_{90}, 0.25 μg/ml) was four- to eight-fold more active than linezolid (MIC_{50}, 0.5 μg/ml and MIC_{90}, 1 μg/ml) or vancomycin (MIC_{50} and MIC_{90}, 1 μg/ml). Furthermore, 99.5% of strains were inhibited at tigecycline concentration of ≤0.5 μg/ml, the susceptible breakpoint established by the USA-FDA for *S. aureus* and by the EUCAST for *S. aureus* and coagulase-negative staphylococci (**Tables 1 and 2**).

CONCLUSIONS

- Tigecycline showed potent in vitro activity against many rarely recovered Gram-positive organisms for which there are very limited contemporary susceptibility data available to guide therapy.
- The results of this study indicated that tigecycline may have an important role in the treatment of infections caused by these species as guided by reference MIC test results.

Table 2. Activity of Tigecycline and comparator antimicrobial agents when tested against uncommonly isolates species.

Antimicrobial agent (no. tested)	MIC_{50}	MIC_{90}	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
Aerococcus viridans (28)					
Tigecycline	0.06	0.12	≤0.03 – 1	- / -	- / -
Cefepime	1	>16	≤0.12 – >16	- / -	- / -
Clindamycin	≤0.25	>2	≤0.25 – >2	- / -	- / -
Erythromycin	>2	>2	≤0.25 – >2	- / -	- / -
Levofloxacin	1	>4	≤0.5 – >4	- / -	- / -
Linezolid	1	2	0.5 – 2	- / -	- / -
Penicillin	0.25	>32	≤0.015 - >32	- / -	- / -
Vancomycin	0.25	0.5	≤0.12 – 0.5	- / -	- / -
Bacillus cereus (63)					
Tigecycline	0.12	0.25	≤0.03 – 0.25	- / -	- / -
Oxacillin	>2	>2	0.5 – >2	- / -	- / -
Cefepime	>16	>16	16 – >16	- / -	- / -
Clindamycin	0.5	1	≤0.25 – >2	- / -	- / -
Erythromycin	≤0.25	2	≤0.25 – >2	- / -	- / -
Imipenem	≤0.5	4	≤0.5 – 8	- / -	- / -
Levofloxacin	≤0.5	≤0.5	≤0.5 – >4	- / -	- / -
Linezolid	1	1	0.25 – 1	- / -	- / -
Penicillin	>32	>32	1 - >32	- / -	- / -
Vancomycin	1	2	≤0.12 – 2	- / -	- / -
Corynebacterium amycolatum (11)					
Tigecycline	≤0.03	0.12	≤0.03 – 0.12	- / -	- / -
Cefepime	1	>16	≤0.12 – >16	- / -	- / -
Clindamycin	>2	>2	≤0.25 – >2	- / -	- / -
Gentamicin	≤2	4	≤2 – >8	- / -	- / -
Imipenem	0.25	>8	≤0.12 – >8	- / -	- / -
Levofloxacin	4	>4	≤0.5 – >4	- / -	- / -
Linezolid	0.25	0.25	0.12 – 0.25	- / -	- / -
Penicillin	2	>32	≤0.015 - >32	- / -	- / -
Vancomycin	0.25	0.5	0.25 – 0.5	- / -	- / -
Corynebacterium jeikeium (42)					
Tigecycline	≤0.03	0.12	≤0.03 – 0.5	- / -	- / -
Cefepime	>16	>16	≤0.12 – >16	- / -	- / -
Clindamycin	>2	>2	≤0.25 – >2	- / -	- / -
Gentamicin	4	>8	≤2 – >8	- / -	- / -
Imipenem	>8	>8	≤0.5 – >8	- / -	- / -
Levofloxacin	>4	>4	≤0.5 – >4	- / -	- / -
Linezolid	0.25	0.5	≤0.06 – 1	- / -	- / -
Penicillin	>32	>32	0.03 ->32	- / -	- / -
Vancomycin	0.5	0.5	≤0.12 – 2	- / -	- / -
Corynebacterium striatum (34)					
Tigecycline	≤0.03	0.06	≤0.03 – 0.25	- / -	- / -
Cefepime	2	8	≤0.12 – >16	- / -	- / -
Clindamycin	>2	>2	≤0.25 – >2	- / -	- / -
Gentamicin	≤2	8	≤2 – >8	- / -	- / -
Imipenem	≤0.5	4	≤0.5 – >8	- / -	- / -
Levofloxacin	>4	>4	≤0.5 – >4	- / -	- / -
Linezolid	0.25	0.25	≤0.06 – 0.5	- / -	- / -
Penicillin	1	16	0.12 - >32	- / -	- / -
Vancomycin	0.25	0.5	≤0.12 – 0.5	- / -	- / -
Corynebacterium urealyticum (11)					
Tigecycline	≤0.03	≤0.03	≤0.03 – 0.06	- / -	- / -
Cefepime	>16	>16	0.25 – >16	- / -	- / -
Clindamycin	>2	>2	≤0.25 – >2	- / -	- / -
Imipenem	>8	>8	≤0.12 – >8	- / -	- / -
Levofloxacin	>4	>4	4 – >4	- / -	- / -
Linezolid	0.25	0.25	≤0.06 – 0.5	- / -	- / -
Penicillin	>32	>32	1 - >32	- / -	- / -
Vancomycin	0.5	0.5	0.25 – 0.5	- / -	- / -
Enterococcus avium (234)					
Tigecycline	0.06	0.12	≤0.03 – 0.5	98.7 / - [b]	98.7 / 0.0
Ampicillin	≤2	16	≤2 – >16	80.8 / 19.2	78.2 / 19.2
Levofloxacin	2	4	≤0.5 – >4	86.3 / 8.1	- / -
Linezolid	1	2	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Quinupristin/dalfopristin	2	>2	≤0.25 – >2	20.2 / 22.7	20.2 / 22.3
Teicoplanin	≤2	≤2	≤2 – >16	98.7 / 0.9	98.7 / 1.3
Vancomycin	0.5	1	≤0.12 – >16	98.3 / 1.7	98.3 / 1.7
Enterococcus durans (83)					
Tigecycline	0.06	0.25	≤0.03 – 0.5	98.8 / - [b]	98.8 / 0.0
Ampicillin	≤2	>16	≤2 – >16	72.3 / 27.7	69.9 / 27.7
Cefepime	>16	>16	≤0.12 – >16	- / -	- / -
Levofloxacin	1	>4	≤0.5 – >4	67.5 / 25.3	- / -
Linezolid	1	2	0.25 – 2	100.0 / 0.0	100.0 / 0.0
Quinupristin/dalfopristin	1	>2	≤0.25 – >2	51.8 / 24.1	51.8 / 24.1
Teicoplanin	≤2	≤2	≤2 – >16	94.0 / 6.0	94.0 / 6.0
Vancomycin	0.5	1	0.25 – >16	94.0 / 6.0	94.0 / 6.0
Enterococcus hirae (47)					
Tigecycline	0.06	0.12	≤0.03 – 0.25	100.0 / - [b]	100.0 / 0.0
Ampicillin	≤1	16	≤1 – >16	89.1 / 10.9	89.1 / 10.9
Levofloxacin	≤0.5	2	≤0.5 – >4	91.3 / 8.7	0.0 / -
Linezolid	1	2	1 – >2	100.0 / 0.0	100.0 / 0.0
Quinupristin/dalfopristin	2	>2	≤0.25 – >2	23.4 / 12.8	23.4 / 12.8
Teicoplanin	≤2	≤2	≤2 – >16	95.7 / 4.3	95.7 / 4.3
Vancomycin	0.5	1	0.25 – >16	95.7 / 4.3	95.7 / 4.3
Enterococcus raffinosus (48)					
Tigecycline	0.06	0.12	≤0.03 – 0.25	100.0 / - [b]	100.0 / 0.0
Ampicillin	16	>16	≤1 – >16	25.0 / 75.0	20.8 / 75.0
Levofloxacin	4	>4	≤0.5 – >4	45.8 / 37.5	- / -
Linezolid	1	2	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Quinupristin/dalfopristin	2	>2	≤0.25 – >2	10.4 / 43.8	10.4 / 43.8
Teicoplanin	≤2	16	≤2 – >16	87.5 / 2.1	87.5 / 12.5
Vancomycin	1	>16	0.25 – >16	87.5 / 12.5	87.5 / 12.5
Group C *Streptococcus* (315)					
Tigecycline	≤0.03	0.12	≤0.03 – 0.25	100.0 / - [b]	100.0 / 0.0
Penicillin	≤0.015	0.03	≤0.015 – 0.12	100.0 / -	100.0 / 0.0
Cefepime	≤0.12	0.25	≤0.12 – 1	99.7 / -	100.0 / 0.0
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	93.0 / 5.4	94.6 / 5.4
Erythromycin	≤0.25	2	≤0.25 – >2	83.2 / 15.9	83.2 / 15.9
Levofloxacin	≤0.5	1	≤0.5 – >4	98.7 / 1.0	96.5 / 1.3
Linezolid	1	1	≤0.06 – 2	100.0 / -	100.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 1	100.0 / -	100.0 / 0.0
Group F *Streptococcus* (61)					
Tigecycline	≤0.03	0.06	≤0.03 – 0.12	100.0 / - [b]	100.0 / 0.0
Penicillin	0.06	0.25	≤0.03 – 0.25	- / -	- / -
Cefepime	0.5	0.5	≤0.12 – 1	98.4 / -	- / -
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	90.2 / 9.8	90.2 / 9.8
Erythromycin	≤0.25	2	≤0.25 – >2	82.0 / 16.4	82.0 / 16.4
Levofloxacin	≤0.5	1	≤0.5 – >4	96.7 / 3.3	96.7 / 3.3
Linezolid	1	1	0.12 – 1	100.0 / -	100.0 / 0.0
Vancomycin	1	1	0.25 – 1	100.0 / -	100.0 / 0.0
Kocuria kristinae (18)					
Tigecycline	0.06	0.25	≤0.03 – 0.25	- / -	- / -
Cefepime	4	>16	1 – >16	- / -	- / -
Clindamycin	>2	>2	≤0.25 – >2	- / -	- / -
Gentamicin	4	>8	≤2 – >8	- / -	- / -
Imipenem	≤0.5	>8	≤0.5 – >8	- / -	- / -
Levofloxacin	>4	>4	≤0.5 – >4	- / -	- / -
Linezolid	0.25	1	0.12 – 1	- / -	- / -
Penicillin	2	>32	0.06 - >32	- / -	- / -
Vancomycin	0.5	1	0.25 – 2	- / -	- / -
Lactococcus garvieae (24)					
Tigecycline	0.12	0.25	≤0.03 – 0.5	- / -	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1 – 2	- / -	- / -
Cefepime	0.25	16	≤0.12 – >16	- / -	- / -
Clindamycin	>2	>2	≤0.25 – >2	- / -	- / -
Erythromycin	≤0.25	≤0.25	≤0.25 – >2	- / -	- / -
Gentamicin	≤2	4	≤2 – 8	- / -	- / -
Imipenem	≤0.12	1	≤0.12 – 2	- / -	- / -
Levofloxacin	1	1	≤0.5 – >4	- / -	- / -
Linezolid	1	2	0.5 – 2	- / -	- / -
Penicillin	1	1	≤0.015 - 2	- / -	- / -
Vancomycin	0.5	1	0.25 – >16	- / -	- / -
Leuconostoc spp. (22)					
Tigecycline	≤0.03	0.06	≤0.03 – 0.06	- / -	- / -
Amoxicillin/clavulanate	≤1	4	≤1 – 8	- / -	- / -
Cefepime	2	>16	0.5 – >16	- / -	- / -
Clindamycin	≤0.25	≤0.25	≤0.25 – 1	- / -	- / -
Erythromycin	≤0.25	≤0.25	≤0.25	- / -	- / -
Gentamicin	≤2	≤2	≤2	- / -	- / -
Imipenem	2	4	≤0.12 – 8	- / -	- / -
Levofloxacin	1	2	≤0.5 – 4	- / -	- / -
Linezolid	2	2	1 – 2	- / -	- / -
Penicillin	0.25	0.5	0.12 - 1	- / -	- / -
Vancomycin	>16	>16	>16	- / -	- / -
Listeria monocytogenes (96)					
Tigecycline	0.06	0.12	≤0.03 – 0.5	- / -	- / -
Amoxicillin/clavulanate	≤2	≤2	≤2	- / -	- / -
Cefepime	>16	>16	8 – >16	- / -	- / -
Clindamycin	2	2	≤0.25 – >2	- / -	- / -
Erythromycin	≤0.25	≤0.25	≤0.25 – 0.5	- / -	- / -
Gentamicin	≤2	≤2	≤2 – 8	- / -	- / -
Imipenem	≤0.5	≤0.5	≤0.5	- / -	- / -
Levofloxacin	1	1	≤0.5 – 1	- / -	- / -
Linezolid	2	2	0.5 – 2	- / -	- / -
Penicillin	0.5	0.5	≤0.015 - 2	- / -	- / -
Vancomycin	1	1	0.5 – 1	- / -	- / -
Micrococcus luteus (53)					
Tigecycline	0.06	0.25	≤0.03 – 0.25	- / -	- / -
Oxacillin	1	2	≤0.25 – >2	- / -	- / -
Amox/clav	≤1	≤1	≤1 – 4	- / -	- / -
Cefepime	0.25	4	≤0.12 – 8	- / -	- / -
Clindamycin	≤0.25	0.5	≤0.25 – 2	- / -	- / -
Erythromycin	≤0.25	≤0.25	≤0.25 – >2	- / -	- / -
Gentamicin	≤2	≤2	≤2	- / -	- / -
Imipenem	≤0.12	≤0.12	≤0.12 – 1	- / -	- / -
Levofloxacin	≤0.5	>4	≤0.5 – >4	- / -	- / -
Linezolid	0.5	0.5	0.25 – 0.5	- / -	- / -
Vancomycin	0.5	1	0.5 – 1	- / -	- / -
Rothia mucilaginosa (10)					
Tigecycline	0.06	0.12	≤0.03 – 0.12	- / -	- / -
Amox/clav	≤1	≤1	≤1 – 4	- / -	- / -
Cefepime	0.25	4	≤0.12 – 8	- / -	- / -
Clindamycin	≤0.25	0.5	≤0.25 – 2	- / -	- / -
Erythromycin	≤0.25	≤0.25	≤0.25 – >2	- / -	- / -
Gentamicin	≤2	≤2	≤2	- / -	- / -
Imipenem	≤0.12	≤0.12	≤0.12 – 1	- / -	- / -
Levofloxacin	≤0.5	>4	≤0.5 – >4	- / -	- / -
Linezolid	0.5	0.5	0.25 – 0.5	- / -	- / -
Penicillin	≤0.015	0.25	≤0.015 - 1	- / -	- / -
Vancomycin	0.5	1	0.5 – 1	- / -	- / -
Staphylococcus lugdunensis (221)					
Tigecycline	0.12	0.25	≤0.03 – 1	- / -	99.5 / 0.5
Oxacillin	0.5	2	≤0.25 – >2	21.3 / 78.7	21.3 / 78.7
Cefepime	2	4	0.25 – >16	95.5 / 3.6	- / -
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	92.8 / 6.8	92.8 / 7.2
Erythromycin	≤0.25	>2	≤0.25 – >2	79.2 / 19.9	80.1 / 19.9
Gentamicin	≤2	≤2	≤2 – >8	95.0 / 3.6	91.9 / 8.1
Imipenem	≤0.5	≤0.5	≤0.5 – >8	96.8 / 3.2	- / -
Levofloxacin	≤0.5	≤0.5	≤0.5 – >4	92.8 / 6.3	92.8 / 6.3
Linezolid	0.5	1	0.25 – 2	100.0 / 0.0	100.0 / 0.0
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Streptococcus bovis (293)					
Tigecycline	0.06	0.06	≤0.03 – 0.12	100.0 / - [b]	- / -
Penicillin	0.06	0.06	≤0.015 – 8	99.0 / 0.3	99.0 / 0.3
Cefepime	≤0.12	≤0.12	≤0.12 – 2	99.7 / 0.0	98.6 / 1.4
Clindamycin	≤0.25	>2	≤0.25 – >2	79.2 / 20.1	79.9 / 20.1
Erythromycin	≤0.25	>2	≤0.25 – >2	57.7 / 42.0	- / -
Imipenem	≤0.5	≤0.5	≤0.5 – 2	- / -	100.0 / 0.0
Levofloxacin	1	2	≤0.5 – >4	93.9 / 4.8	- / -
Linezolid	1	1	≤0.06 – 2	100.0 / -	100.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 1	100.0 / -	100.0 / 0.0

a. Criteria as published by the CLSI [2010] and EUCAST [2009].
b. US-FDA breakpoints were applied [Tygacil Product Insert, 2009].