Tigecycline Activity Against *Staphylococcus aureus*, Including Vancomycin-Intermediate and -Resistant Isolates

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Background: Antimicrobial activity of tigecycline tested against *S. aureus* strains with decreased susceptibility to vancomycin, including vancomycin-intermediate *S. aureus* (VISA), hetero-resistant VISA (hVISA) and vancomycin-resistant *S. aureus* (VRSA) was studied. Tigecycline, a first-in-class glycylcycline, was recently approved by the US-FDA for use in complicated skin and skin structure and intra-abdominal infections.
Methods: 105 well-characterized strains with decreased susceptibility to vancomycin (81 hVISA, 19 VISA, and 5 VRSA, as well as a large surveillance collection (2000-2004) of wild-type (WT) *S. aureus*, were susceptibility tested by the CLSI broth microdilution method against vancomycin, tigecycline (with fresh media) and comparators. Breakpoint criteria were those of the US-FDA (tigecycline) or CLSI.
Results: MIC results for the subsets of *S. aureus* are summarized in the Table.

	Tigecycline (mg/L)			
Organism (no. tested)	MIC_{50}	MIC_{90}	Range	%S
WT-*S. aureus* (19,539)	0.12	0.25	<=0.016 - 1	99.5
Oxacillin-S (12,283)	0.12	0.25	<= 0.016 - 1	99.8
Oxacillin-R (7,256)	0.12	0.5	<= 0.016 - 1	99.0
VISA (19)	0.25	1	0.06 - 1	89.5
hVISA (81)	0.12	0.25	0.06 - 0.5	100.0
VRSA (5)	0.12	-	0.06 - 0.5	100.0

While MRSA was common in surveillance studies (37.1%), vancomycin non-susceptibility was not. Among 6 isolates with vancomycin MICs of 4 mg/L, five had tigecycline values of <= 0.5 and one at 1 mg/L. Tigecycline provides near-complete coverage of this species (MIC_{90}, 0.25 mg/L; 99.5% susceptible); only linezolid, vancomycin and Synercid had marginally higher susceptibility rates (100, 100 and 99.8%, respectively). Among VISA, hVISA and VRSA isolates, tigecycline was uniformly active, with MIC_{50} and MIC_{90} values of 0.06 to 0.25, and 0.25 to 1 mg/L (98.1% susceptible), respectively. Against 5 VRSA (NARSA), tigecycline MICs were consistent with WT-*S. aureus* (MIC_{50}, 0.12 mg/L), indicating lack of cross-resistance.
Conclusions: Tigecycline was found to be highly active against all WT *S. aureus* tested, including a large MRSA subset. Among strains with decreased susceptibility to vancomycin, no cross-resistance with tigecycline was observed. All VISA, hVISA and VRSA strains remained susceptible to tigecycline. The broad-spectrum of activity and potency exhibited by tigecycline against clinically-significant Gram-positive and -negative pathogens, supports its continued application for indicated infections, including those caused by recently emerging, highly resistant, staphylococci.

Key words: Tigecycline, vancomycin, vancomycin-intermediate *Staphylococcus aureus*, vancomycin-resistant *Staphylococcus aureus*
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