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Evaluation of Tigecycline and Comparators in Nosocomial Pathogens from South America

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REVISED ABSTRACT

Background: One of the goals of surveillance studies is to identify and document patterns of bacterial resistance to help guide current therapy. The Tigecycline Evaluation Surveillance Trial (TEST) is an ongoing global study that can serve to help recognize current trends in resistance on many levels. This study reports on the susceptibility patterns of tigecycline and 13 antimicrobial agents against common nosocomial pathogens from 10 South American hospitals. **Methods:** 1,586 strains isolated were collected and identified from 2004-2006 at 10 investigative sites. MICs for each strain were determined per CLSI guidelines at each facility using custom broth microdilution panels. **Results:** Summary results for key pathogens are shown in the following table.

Organism (#)	Tigecycline MIC$_{50}$	Tigecycline MIC$_{90}$	% inhibited at MIC ≤0.25	0.5	1	2	4	8
Acinetobacter spp. (149)	0.5	1	26.2	70.5	94.6	100	-	-
E. faecalis/faecium (86)	0.06	0.25	100	-	-	-	-	-
VREs (7)	*	*	100	-	-	-	-	-
Enterobacteriaceae (730)	0.5	1	40.8	76	92.7	98.1	99.9	100
ESBLs (67)	0.5	2	26.9	61.2	82.1	94	100	-
P. aeruginosa (165)	8	>16	1.2	1.8	2.4	6.7	20	61.8
S. aureus (230)	0.12	0.25	92.6	100	-	-	-	-
MRSAs (104)	0.12	0.25	96.2	100	-	-	-	-

* No MIC$_{50}$ and MIC$_{90}$ calculated for strains with n<10

Conclusion: TIG was shown to be a broad spectrum antimicrobial with consistent activity against *Enterobacteriaceae* including ESBL phenotypes, *S. aureus* including MR strains and both VS and VR *Enterococcus spp*. TIG's wide spectrum of activity promises to provide enhanced antimicrobial coverage of serious nosocomial pathogens.

INTRODUCTION

Tigecycline (formerly GAR-936) is a member of a new class of antimicrobial agents, the glycylcyclines. This synthetic analogue of the tetracyclines exhibits significant antibacterial activity that is both bacteriostatic and, in certain instances, bactericidal with killing activity that is as much as fourfold better than vancomycin and daptomycin [1, 2]. The development of tigecycline is important in that tigecycline and other glycylcyclines are active against bacterial strains carrying either or both of the two major forms of tetracycline resistance: efflux and ribosomal protection. Certain substituents at the 9-position of the tetracycline molecule restore activity against bacteria harboring genes encoding either or both efflux and ribosomal protection. A single chemical modification of tigecycline overcomes the two molecularly distinct forms of resistance while maintaining activity against susceptible gram-positive, gram-negative, aerobic, and anaerobic bacteria [3]. Furthermore, resistance to tigecycline is difficult to produce even in the laboratory.

Previous studies have demonstrated excellent in vitro activity for tigecycline against clinical and laboratory strains of gram-positive and -negative bacteria with minimum inhibitory concentrations for the 90th percentile inhibited at or below 2 µg/ml, including difficult to treat methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), and extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae [4-6]. This study was undertaken to document the in vitro activity of tigecycline against significant numbers of clinical pathogens collected in 10 laboratories from South America. This study is part of the larger ongoing global Tigecycline Evaluation and Surveillance Trials (T.E.S.T.) program.

MATERIALS & METHODS

- All isolates were derived from blood, respiratory tract, urine (no more than 25% of all isolates), skin, wound, body fluids, and other defined sources. Only one isolate per patient was accepted into the study. Clinical isolates were collected and tested between 2004 and 2006 from 10 study centers in South America. Isolates were identified to the species level and tested at each site by the participating laboratory.
- Organism collection, transport, confirmation of organism identification, and development and management of a centralized database, were coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of medical history, antimicrobial use, age, or gender. All sites identified each study isolate utilizing local laboratory criteria.
- Minimum inhibitory concentrations (MICs) were determined by the CLSI recommended broth microdilution testing method [7]. Tigecycline was supplied by Wyeth Pharmaceuticals (Collegeville, PA, USA). All other agents were supplied by the panel manufacturer, MicroScan (Dade Behring Inc., West Sacramento, CA, USA). The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mcg/ml): amikacin (0.5-64); amoxicillin/clavulanic acid (0.12/0.06-32/16); ampicillin (0.5-32, gram-negative panel, and 0.06-16, gram-positive panel); cefepime (0.5-32); ceftriaxone (0.06-64); ceftazidime (8-32); imipenem (0.06-16); linezolid (0.5-8); levofloxacin (0.008-8); minocycline (0.5-16); tigecycline (0.008-16); penicillin (0.06-8); piperacillin/tazobactam (0.06/4-128/4), and vancomycin (0.12-32). MIC interpretive criteria followed published guidelines established by the Clinical and Laboratory Standards Institute [8] and the recent US Food and Drug Administration package insert for tigecycline [9], where applicable.
- *Escherichia coli*, *Klebsiella pneumoniae* and *Klebsiella oxytoca* were screened for ESBL activity when MIC results for ceftriaxone were >1 mcg/ml using broth microdilution panels. ESBL activity was confirmed using the CLSI (2006) phenotypic confirmatory disk test (Oxoid, Ogdensburg, NY, USA) on Mueller-Hinton agar (Remel Inc., Lenexa, KS, USA) according to CLSI (2006) guidelines. ESBL presence was confirmed by testing the following antibiotic disks: cefotaxime (30-mcg), cefotaxime/clavulanic acid (30/10-mcg), ceftazidime (30-mcg), and ceftazidime/clavulanic acid (30/10-mcg). Antimicrobial disks were manufactured by Oxoid, Inc. (Ogdensburg, NY, USA). Mueller-Hinton agar used in testing was manufactured by Remel, Inc. (Lenexa, KS, USA). An organism was interpreted as containing an ESBL if there was an increase of >5 mm in the inhibition zone of the combination disk when compared to that of the cephalosporin alone. *K. pneumoniae* ATCC 700603 was used to QC the ESBL confirmation tests.
- Quality controls (QC) were performed by each testing site on each day of testing using the corresponding ATCC control strains: *E. coli* ATCC 25922; *E. coli* ATCC 35218; *H. influenzae* ATCC 49766; *H. influenzae* ATCC 49247; *S. aureus* ATCC 29213; *Pseudomonas aeruginosa* ATCC 27853; *Enterococcus faecalis* ATCC 29212 and *S. pneumoniae* ATCC 49619. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI (2006) guidelines [8].

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RESULTS

Table 1. In vitro activity of tigecycline and comparative agents against 730 strains of *Enterobacteriaceae* .

Organism Name	Drug	%SUS[a]	%INT	%RES	MIC (mcg/ml) MIC$_{50}$	MIC$_{90}$	MIC range (mcg/ml) Low	High
All *Enterobacteriaceae* (n=730)	Tigecycline	98.1	1.8	0.1	0.5	1	≤0.008	8
	Amikacin	90.3	5.3	4.4	2	16	≤0.5	>64
	AmoxClav	37	8.4	54.7	32	>32	0.25	>32
	Ampicillin	10.7	4.7	84.7	>32	>32	≤0.5	>32
	Cefepime	75.3	5.3	19.3	≤0.5	>32	≤0.5	>32
	Ceftazidime	71.6	5.8	22.6	≤8	>32	≤8	>32
	Ceftriaxone	67.5	4.1	28.4	0.12	>64	≤0.06	>64
	Imipenem	100	0	0	0.5	1	0.12	4
	Levofloxacin	74.8	4.2	21	0.06	>8	≤0.008	>8
	Minocycline	83	8.5	8.5	2	8	≤0.5	>16
	PipTazo	74.7	11.6	13.7	2	128	0.12	>128
E. coli (n=219)	Tigecycline	100	0	0	0.12	0.25	≤0.008	1
	Amikacin	97.7	0.9	1.4	2	8	≤0.5	>64
	AmoxClav	68.9	15.5	15.5	8	32	0.25	>32
	Ampicillin	35.6	0.5	63.9	>32	>32	≤0.5	>32
	Cefepime	89	2.7	8.2	≤0.5	16	≤0.5	>32
	Ceftazidime	90	4.1	5.9	≤8	16	≤8	>32
	Ceftriaxone	84.5	0.5	15.1	≤0.06	>64	≤0.06	>64
	Imipenem	100	0	0	0.5	0.5	0.12	4
	Levofloxacin	70.3	5	24.7	0.03	>8	≤0.008	>8
	Minocycline	79	11.9	9.1	1	8	≤0.5	>16
	PipTazo	92.7	4.1	3.2	1	16	0.12	>128
K. pneumoniae (n=179)	Tigecycline	96.6	2.8	0.6	0.5	2	0.12	8
	Amikacin	91.6	3.4	5	2	16	≤0.5	>64
	AmoxClav	43	8.4	48.6	16	>32	0.5	>32
	Ampicillin	0	8.9	91.1	>32	>32	16	>32
	Cefepime	57	6.1	36.9	1	>32	≤0.5	>32
	Ceftazidime	57.5	7.3	35.2	≤8	>32	≤8	>32
	Ceftriaxone	51.4	5	43.6	1	>64	≤0.06	>64
	Imipenem	100	0	0	0.5	0.5	0.25	2
	Levofloxacin	64.8	3.9	31.3	0.25	>8	≤0.008	>8
	Minocycline	81.6	7.8	10.6	2	16	≤0.5	>16
	PipTazo	55.3	14.5	30.2	4	>128	0.25	>128
K. oxytoca (n=21)	Tigecycline	100	0	0	0.25	0.5	0.12	0.5
	Amikacin	95.2	4.8	0	2	16	1	32
	AmoxClav	81	4.8	14.3	4	32	1	32
	Ampicillin	0	9.5	90.5	>32	>32	16	>32
	Cefepime	95.2	4.8	0	≤0.5	8	≤0.5	16
	Ceftazidime	85.7	0	14.3	≤8	32	≤8	>32
	Ceftriaxone	76.2	4.8	19	≤0.06	64	≤0.06	>64
	Imipenem	100	0	0	0.5	0.5	0.25	0.5
	Levofloxacin	100	0	0	0.06	1	0.015	1
	Minocycline	100	0	0	2	2	≤0.5	4
	PipTazo	90.5	4.8	4.8	1	4	0.5	>128
All ESBL producers (n=67)	Tigecycline	94	6	0	0.5	2	0.12	4
	Amikacin	86.6	10.4	3	8	32	1	>64
	AmoxClav	7.5	17.9	74.6	32	>32	2	>32
	Ampicillin	0	0	100	>32	>32	>32	>32
	Cefepime	19.4	10.4	70.1	>32	>32	1	>32
	Ceftazidime	19.4	14.9	65.7	32	>32	≤8	>32
	Ceftriaxone	4.5	10.4	85.1	>64	>64	2	>64
	Imipenem	100	0	0	0.5	0.5	0.25	2
	Levofloxacin	49.3	4.5	46.3	4	>8	0.03	>8
	Minocycline	71.6	17.9	10.4	2	16	≤0.5	>16
	PipTazo	38.8	19.4	41.8	64	>128	1	>128
E. aerogenes (n=22)	Tigecycline	100	0	0	0.5	1	0.25	2
	Amikacin	81.8	4.5	13.6	2	64	1	>64
	AmoxClav	4.5	0	95.5	>32	>32	8	>32
	Ampicillin	0	4.5	95.5	>32	>32	16	>32
	Cefepime	72.7	4.5	22.7	≤0.5	32	≤0.5	>32
	Ceftazidime	63.6	9.1	27.3	≤8	>32	≤8	>32
	Ceftriaxone	68.2	4.5	27.3	1	>64	≤0.06	>64
	Imipenem	100	0	0	1	1	0.5	4
	Levofloxacin	77.3	18.2	4.5	0.06	4	0.03	>8
	Minocycline	90.9	0	9.1	2	4	≤0.5	>16
	PipTazo	68.2	22.7	9.1	4	64	0.5	128
E. cloacae (n=122)	Tigecycline	95.1	4.9	0	0.5	2	0.12	4
	Amikacin	90.2	7.4	2.5	2	16	≤0.5	>64
	AmoxClav	0.8	0	99.2	>32	>32	2	>32
	Ampicillin	0	7.4	92.6	>32	>32	16	>32
	Cefepime	77.9	9	13.1	≤0.5	32	≤0.5	>32
	Ceftazidime	63.1	3.3	33.6	≤8	>32	≤8	>32
	Ceftriaxone	61.5	9.8	28.7	0.5	>64	≤0.06	>64
	Imipenem	100	0	0	0.5	1	0.25	4
	Levofloxacin	83.6	3.3	13.1	0.03	>8	≤0.008	>8
	Minocycline	82.8	5.7	11.5	4	16	≤0.5	>16
	PipTazo	73.8	13.1	13.1	2	128	0.12	>128
S. marcescens (n=64)	Tigecycline	98.4	1.6	0	1	2	0.5	4
	Amikacin	82.8	17.2	0	4	32	1	32
	AmoxClav	3.1	3.1	93.8	>32	>32	8	>32
	Ampicillin	0	4.7	95.3	>32	>32	16	>32
	Cefepime	79.7	6.3	14.1	≤0.5	>32	≤0.5	>32
	Ceftazidime	79.7	10.9	9.4	≤8	16	≤8	>32
	Ceftriaxone	79.7	0	20.3	0.25	>64	≤0.06	>64
	Imipenem	100	0	0	0.5	2	0.5	4
	Levofloxacin	92.2	3.1	4.7	0.12	2	0.015	>8
	Minocycline	90.6	7.8	1.6	4	4	1	16
	PipTazo	81.3	10.9	7.8	1	64	0.5	>128

[a] Interpretive criteria as defined by CLSI, M100-S16 (2006), where available; tigecycline susceptibility breakpoints are according to FDA package insert (Tygacil®, 2005), where applicable [9].

Table 2. In vitro activity of tigecycline and comparative agents against *Acinetobacter spp* . and *P. aeruginosa* .

Organism Name	Drug	%SUS[a]	%INT	%RES	MIC (mcg/ml) MIC$_{50}$	MIC$_{90}$	MIC range (mcg/ml) Low	High
Acinetobacter spp. (n=149)	Tigecycline	na	na	na	0.5	1	≤0.008	2
	Amikacin	19.5	18.8	61.7	64	>64	1	>64
	Cefepime	13.4	23.5	63.1	32	>32	≤0.5	>32
	Ceftazidime	6	6	87.9	>32	>32	≤8	>32
	Ceftriaxone	1.3	4.7	94	>64	>64	8	>64
	Imipenem	51.7	6.7	41.6	4	>16	0.25	>16
	Levofloxacin	6.7	28.2	65.1	8	>8	0.03	>8
	Minocycline	100	0	0	≤0.5	2	≤0.5	4
	PipTazo	10.1	30.2	59.7	128	>128	≤0.06	>128
P. aeruginosa (n=165)	Tigecycline	na	na	na	8	>16	0.12	>16
	Amikacin	67.3	15.8	17	8	64	≤0.5	>64
	Cefepime	54.5	23.6	21.8	8	32	≤0.5	>32
	Ceftazidime	58.2	11.5	30.3	≤8	>32	≤8	>32
	Ceftriaxone	20	21.8	58.2	64	>64	0.5	>64
	Imipenem	67.7	21.3	11	1	16	0.25	>16
	Levofloxacin	45.5	3.6	50.9	8	>8	0.06	>8
	Minocycline	3	20	77	>16	>16	≤0.5	>16
	PipTazo	85.5	0	14.5	16	128	≤0.06	>128

[a] Interpretive criteria as defined by CLSI, M100-S16 (2006), where available; tigecycline susceptible breakpoint is according to FDA package insert (2005), where applicable [9]; na = not available - breakpoints are not yet established against this species.

Table 3. In vitro activity of tigecycline and comparative agents against gram-positive pathogens.

Organism Name	Drug	%SUS[a]	%INT	%RES	MIC (mcg/ml) MIC$_{50}$	MIC$_{90}$	MIC range (mcg/ml) Low	High
S. aureus (n=230)	Tigecycline	100	0	0	0.12	0.25	0.03	0.5
	AmoxClav	59.6	0	40.4	1	>8	0.06	>8
	Ampicillin	6.5	0	93.5	16	>16	≤0.06	>16
	Ceftriaxone	56.5	3.9	39.6	4	>64	1	>64
	Imipenem	63	3.9	33	0.25	>16	≤0.12	>16
	Levofloxacin	58.3	5.7	36.1	0.25	8	≤0.06	32
	Linezolid	100	0	0	2	2	≤0.5	4
	Minocycline	98.7	1.3	0	≤0.25	1	≤0.25	8
	Penicillin	5.7	0	94.3	>8	>8	≤0.06	>8
	PipTazo	59.6	0	40.4	1	>16	≤0.25	>16
	Vancomycin	100	0	0	0.5	1	0.25	2
S. aureus (MRSA) (n=104)	Tigecycline	100	0	0	0.12	0.25	0.06	0.5
	AmoxClav	10.6	0	89.4	>8	>8	1	>8
	Ampicillin	0	0	100	>16	>16	2	>16
	Ceftriaxone	3.8	8.7	87.5	>64	>64	4	>64
	Imipenem	19.2	7.7	73.1	>16	>16	≤0.12	>16
	Levofloxacin	12.5	10.6	76.9	4	16	0.12	32
	Linezolid	100	0	0	2	2	≤0.5	4
	Minocycline	98.1	1.9	0	≤0.25	4	≤0.25	8
	Penicillin	0	0	100	>8	>8	4	>8
	PipTazo	10.6	0	89.4	>16	>16	1	>16
	Vancomycin	100	0	0	1	1	0.5	2
E. faecalis[b] (n=74)	Tigecycline	100	0	0	0.12	0.25	0.03	0.25
	Ampicillin	100	0	0	1	2	0.12	4
	Levofloxacin	78.4	0	21.6	1	32	0.25	>32
	Linezolid	89.2	10.8	0	2	4	1	4
	Minocycline	55.4	29.7	14.9	4	>8	≤0.25	>8
	Penicillin	100	0	0	2	8	0.5	8
	Vancomycin	97.3	0	2.7	1	2	0.25	>32
E. faecium[b] (n=12)	Tigecycline	100	0	0	0.03	0.06	0.03	0.12
	Ampicillin	33.3	0	66.7	>16	>16	0.25	>16
	Levofloxacin	33.3	8.3	58.3	32	>32	1	>32
	Linezolid	91.7	8.3	0	2	2	1	4
	Minocycline	83.3	0	16.7	≤0.25	>8	≤0.25	>8
	Penicillin	33.3	0	66.7	>8	>8	1	>8
	Vancomycin	58.3	0	41.7	1	>32	0.5	>32
All VREsc (n=7)	Tigecycline	-	-	-	-	-	0.03	0.25
	Ampicillin	-	-	-	-	-	2	>16
	Levofloxacin	-	-	-	-	-	16	>32
	Linezolid	-	-	-	-	-	1	2
	Minocycline	-	-	-	-	-	≤0.25	>8
	Penicillin	-	-	-	-	-	8	>8
	Vancomycin	-	-	-	-	-	>32	>32

[a] Interpretive criteria as defined by CLSI, M100-S16 (2006), where available; tigecycline susceptible breakpoint is according to FDA package insert (2005), where available [9].

[b] FDA susceptible breakpoint of 0.25 µg/ml for vancomycin-susceptible E. faecalis was used for all enterococci for comparative purposes only.

[c] No % SUS, % INT, % RES, MIC50, and MIC90 calculated for strains with n<10

Table 4. *In vitro* activity of tigecycline against selected pathogens: frequency distribution (n) and cumulative percent inhibited (%) at each MIC (mcg/ml)

Organism name n %	≤0.008	0.015	0.03	≤0.06	0.06	≤0.12	0.12	≤0.25	0.25	≤0.5	0.5	1	2	4	≤8	8	>8	16	>16
Acinetobacter spp. (n=149)	1 0.7				4 3.4		3 5.4		31 26.2		66 70.5	36 94.6	8 100						
E. faecalis/E. faecium (n=86)			12 14		33 52.3		25 81.4		16 100										
All VREs (n=7)			4 57.1		1 71.4		1 85.7		1 100										
Enterobacteriaceae (n=730)	1 0.1				23 3.3		109 18.2		165 40.8		257 76	122 92.7	39 98.1	13 99.9		1 100			
All ESBLs (n=67)							4 6		14 26.9		23 61.2	14 82.1	8 94	4 100					
P. aeruginosa (n=165)							1 0.6		1 1.2		1 1.8	1 2.4	7 6.7	22 20		69 61.8		44 88.5	19 100
S. aureus (n=230)			1 0.4		49 21.7		121 74.3		42 92.6		17 100								
S. aureus (MRSA) (n=104)					20 19.2		53 70.2		27 96.2		4 100								

Table 5. *In vitro* activity of tigecycline and comparators against *Enterobacteriaceae* (n=730): frequency distribution (n) and cumulative percent inhibited (%) at each MIC (mcg/ml).

MIC n %	≤0.008	0.015	0.03	≤0.06	0.06	0.12	0.25	≤0.5	0.5	1	2	4	≤8	8	>8	16	>16	32	>32	64	>64	128	>128
Tigecycline	1 0.1				23 3.3	109 18.2	165 40.8		257 76	122 92.7	39 98.1	13 99.9		1 100									
Amikacin								17 2.3		179 26.8	245 60.4	91 72.9		79 83.7		48 90.3		39 95.6		8 96.7	24 100		
AmoxClav							1 0.1		10 1.5	8 2.6	115 18.4	64 27.1		72 37		61 45.3		115 61.1	284 100				
Ampicillin								3 0.4		8 1.5	42 7.3	22 10.3		3 10.7		34 15.3		81 26.4	537 100				
Cefepime								462 63.3		25 66.7	14 68.6	19 71.2		30 75.3		39 80.7		37 85.8	104 100				
Ceftazidime													523 71.6			42 77.4		37 82.5	128 100				
Ceftriaxone				282 38.6		98 52.1	43 57.9		23 61.1	12 62.7	16 64.9	8 66		11 67.5		13 69.3		17 71.6		28 75.5	179 100		
Imipenem						4 0.6	135 19.2		490 86.8	72 96.7	20 99.4	4 100											
Levofloxacin	13 1.8	58 9.7	226 40.7		83 52.1	43 57.9	36 62.9		41 68.5	32 72.9	14 74.8	31 79		44 85.1	109 100								
Minocycline								70 9.6		143 29.2	233 61.1	160 83		62 91.5		38 96.7	24 100						
PipTazo						2 0.3	20 3		89 15.2	246 48.9	97 62.2	41 67.8		20 70.5		30 74.7		36 79.6		49 86.3		46 92.6	54 100

Table 6. *In vitro* activity of tigecycline and comparators against Acinetobacter spp. (n=149): frequency distribution (n) and cumulative percent inhibited (%) at each MIC (mcg/ml).

MIC n %	≤0.008	0.03	≤0.06	0.06	0.12	0.25	≤0.5	0.5	1	2	4	≤8	8	>8	16	>16	32	>32	64	>64	128	>128
Tigecycline	1 0.7			4 3.4	3 5.4	31 26.2		66 70.5	36 94.6	8 100												
Amikacin									2 1.3	5 4.7	4 7.4		7 12.1		11 19.5		28 38.3		41 65.8	51 100		
Cefepime							1 0.7			2 2	4 4.7		13 13.4		35 36.9		47 68.5	47 100				
Ceftazidime												9 6			9 12.1		11 19.5	120 100				
Ceftriaxone													2 1.3		4 4		3 6		16 16.8	124 100		
Imipenem						3 2		26 19.5	35 43	8 48.3	5 51.7		10 58.4		26 75.8	36 100						
Levofloxacin		1 0.7		1 1.3	1 2	2 3.4		1 4	2 5.4	2 6.7	42 34.9		55 71.8	42 100								
Minocycline							113 75.8		21 89.9	14 99.3	1 100											
PipTazo			6 4			2 5.4		1 6			1 6.7		1 7.4		4 10.1		20 23.5		25 40.3		20 53.7	69 100

Table 7. *In vitro* activity of tigecycline and comparators against *S. aureus* (n=230): frequency distribution (n) and cumulative percent inhibited (%) at each MIC (mcg/ml).

MIC n %	0.03	≤0.06	0.06	≤0.12	0.12	≤0.25	0.25	≤0.5	0.5	1	2	4	8	>8	16	>16	32	64	>64
Tigecycline	1 0.4		49 21.7		121 74.3		42 92.6		17 100										
AmoxClav			1 0.4		7 3.5		15 10		28 22.2	69 52.2	12 57.4	5 59.6	5 61.7	88 100					
Ampicillin		3 1.3			10 5.7		2 6.5		7 9.6	10 13.9	28 26.1	20 34.8	20 43.5		21 52.6	109 100			
Ceftriaxone										3 1.3	43 20	80 54.8	4 56.5		8 60		1 60.4	5 62.6	86 100
Imipenem				100 43.5			29 56.1		11 60.9	2 61.7	3 63		9 67		15 73.5	61 100			
Levofloxacin		23 10			69 40		33 54.3		7 57.4	2 58.3	13 63.9	56 88.3	16 95.2		8 98.7		3 100		
Linezolid								6 2.6		66 31.3	142 93	16 100							
Minocycline						173 75.2			32 89.1	5 91.3	3 92.6	14 98.7	3 100						
Penicillin		11 4.8			2 5.7		3 7		6 9.6	3 10.9	16 17.8	24 28.3	18 36.1	147 100					
PipTazo						5 2.2			51 24.3	62 51.3	6 53.9	10 58.3	3 59.6		6 62.2	87 100			
Vancomycin							2 0.9		115 50.9	107 97.4	6 100								

CONCLUSIONS

- Tigecycline inhibited 98.1% of *Enterobacteriaceae* at MICs the enteric susceptible breakpoint of 2 mcg/ml.
- Tigecycline's MIC$_{90}$ of 1 mcg/ml vs. *Enterobacteriaceae* was equivalent to imipenem and 8 to 128-fold lower than other beta-lactams, beta-lactam/beta-lactamase inhibitor combinations, levofloxacin, minocycline, and amikacin.
- Tigecycline was the second most effective agent tested vs. 67 ESBL-producing *E. coli* and *Klebsiella spp*., inhibiting 94.0% at 2 mcg/ml; only imipenem was more effective (100% inhibited). The two strains not susceptible to tigecycline had MICs of 4, categorized as intermediate. Of the other agents tested, only amikacin had a reasonable degree of activity (86.6%) against the ESBL-producing strains.
- Against 149 *Acinetobacter spp*., only tigecycline and minocycline had significant activity (MIC$_{90}$s of 1 mcg/ml and 2 mcg/ml, respectively); levofloxacin, imipenem, cefepime, ceftazidime and ceftriaxone had MIC$_{90}$s of >8, >16, >32, >32, or >64, respectively. Furthermore, except for imipenem (MIC$_{50}$=4), all drugs other than tigecycline and minocycline had MIC$_{50}$s in their resistant ranges.
- The *P. aeruginosa* isolates in this study were generally non-susceptible to most of the agents evaluated; other than pip/tazo (85.5% inhibited), no other drug inhibited more than 67.7% of the strains. Tigecycline and minocycline, like all tetracyclines, exhibited low activity against *P. aeruginosa*.
- 100% of *S. aureus* (including 104 MRSA) were susceptible to tigecycline, linezolid, and vancomycin, and 98.7% to minocycline.
- The in vitro activity of tigecycline in this study suggests that it is a promising compound for the treatment of serious infections caused by nosocomial pathogens, especially since such strains are typically resistant to many other antimicrobials.