Antimicrobial Activity of Tigecycline and Comparators from Inpatient and Outpatient Pathogens in North America

M. Hackel[1], R. Badal[1], J. Johnson[1], D. Hoban[1], B. Johnson[1], S. Bouchillon[1], M. Dowzicky[2]

[1]International Health Management Associates, Schaumburg, IL, USA
[2]Wyeth Pharmaceuticals, Collegeville, PA, USA

IHMA, Inc.
2122 Palmer Dr.
Schaumburg, IL 60173
Tel: (847) 303-5003
Fax: (847) 303-5601
www.ihmainc.com

REVISED ABSTRACT

Background: Tigecycline, a new glycylcycline, has potent expanded broad spectrum activity against commonly encountered species responsible for community and hospital acquired infections. The T.E.S.T. program determined the in vitro activity of tigecycline compared to broad spectrum antimicrobials against gram negative and gram positive species collected from hospitals within North America throughout 2004-2006. **Methods:** A total of 21,792 clinical isolates were identified to the species level. Minimum Inhibitory Concentration (MICs) were determined by the local laboratory using supplied broth microdilution panels and interpreted according to CLSI guidelines. **Results:** Results are in the table as follows:

	ESBLs				*Acinetobacter* spp.			
	IP (n=258)		OP (n=29)		IP (n=1168)		OP (n=348)	
	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}
Tigecycline	93	2	83	4	NA	2	NA	1
Amikacin	88	32	97	16	82	32	88	32
Cefepime	50	>32	62	>32	45	>32	65	>32
Ceftazidime	7	>32	14	>32	46	>32	65	?8
Imipenem	86	8	100	0.5	87	8	91	4
Levofloxacin	20	>8	24	>8	48	>8	67	>8
Minocycline	67	>16	59	>16	88	8	92	≤0.5
PipTazo	52	>128	59	>128	56	>128	74	1

	S. aureus				*Enterococcus* spp.			
	IP (n=2289)		OP (n=711)		IP (n=1429)		OP (n=308)	
	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}
Tigecycline	99	0.25	99	0.12	99	0.12	99	0.12
Levofloxacin	47	>32	60	32	41	>32	47	>32
Linezolid	100	2	100	2	98	2	99	2
Minocycline	99	≤0.25	99	0.5	55	8	48	8
Vancomycin	100	1	100	1	76	>32	85	>32

Conclusion: Tigecycline's in vitro activity was comparable to or greater than most commonly prescribed antimicrobials. The presented data suggest that tigecycline may be an effective and reliable therapeutic option against pathogens in both inpatient and outpatient clinical settings.

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 restored 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 mcg/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 isolates collected in North America from in-patient and out-patient populations. 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, 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 hospitals within North America. Isolates were identified to the species level and tested at each site by the participating laboratory.
- Organism collection, transport, confirmation of organism identification, as well as development and management of a centralized database was 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 site 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., 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 recent US Food and Drug Administration packaging insert for tigecycline [9], where applicable.
- *Escherichia coli*, *Klebsiella pneumoniae*, and *Klebsiella oxytoca* were screened for ESBL activity when MIC results for ceftriaxone were >1mcg/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.
- 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; *Klebsiella pneumoniae* ATCC 700603; and *Pseudomonas aeruginosa* ATCC 27853. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI (2006) guidelines [8].

REFERENCES

1. Hoellman, D.B., et al., *Antipneumococcal activities of GAR-936 (a new glycylcycline) compared to those of nine other agents against penicillin-susceptible and -resistant pneumococci*. Antimicrob Agents Chemother, 2000. 44(4): p. 1085-8.
2. Labthavikul, P., P.J. Petersen, and P.A. Bradford, *In vitro activity of tigecycline against Staphylococcus epidermidis growing in an adherent-cell biofilm model*. Antimicrob Agents Chemother, 2003. 47(12): p. 3967-9.
3. Projan, S.J., *Preclinical pharmacology of GAR-936, a novel glycylcycline antibacterial agent. Pharmacotherapy, 2000*. 20(9 Pt 2): p. 219S-223S; discussion 224S-228S.
4. Gales, A.C. and R.N. Jones, *Antimicrobial activity and spectrum of the new glycylcycline, GAR-936 tested against 1,203 recent clinical bacterial isolates*. Diagn Microbiol Infect Dis, 2000. 36(1): p. 19-36.
5. Patel, R., et al., *In vitro activity of GAR-936 against vancomycin-resistant enterococci, methicillin-resistant Staphylococcus aureus and penicillin-resistant Streptococcus pneumoniae*. Diagn Microbiol Infect Dis, 2000. 38(3): p. 177-9.
6. Rupp, M.E. and P.D. Fey, *Extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae: considerations for diagnosis, prevention and drug treatment*. Drugs, 2003. 63(4): p. 353-65.
7. *CLSI, Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-Sixth Edition, in Document M7-A6. 2005*: Clinical Laboratory Standards Institute (CLSI), 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
8. *CLSI, Performance Standards for Antimicrobial Susceptibility Testing, in Document M100-S16. 2006*: Clinical Laboratory Standards Institute (CLSI), 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
9. Tygacil, *Product Insert. 2005*: Wyeth Pharmaceuticals, Inc., Philadelphia, PA, USA.

ACKNOWLEDGEMENTS

We gratefully acknowledge the contributions of the investigators, laboratory personnel and all members of the Tigecycline Evaluation Study Trials program group. This study was sponsored by a grant from Wyeth Pharmaceuticals.

RESULTS

The results are listed in the following Tables.

Table 1. In Vitro Activity of Tigecycline and Comparative Antimicrobial Agents Against Gram-Negative Clinical Pathogens Isolated from In-Patients and Out-Patients - North American Results.

		In-Patients			Out-Patients		
Organism (N)	Drug	MIC_{50}[a]	MIC_{90}	%Sus[b]	MIC_{50}	MIC_{90}	%Sus
E. coli, *K. pneumoniae*,	Tigecycline	0.25	1	97.3	0.25	0.5	97.8
K. oxytoca	Amikacin	2	4	98.7	2	4	99.7
In-Patient (n=4,314)	AmoxClav	4	32	79.3	4	16	83.6
Out-Patient (n=1,387)	Ampicillin	>32	>32	22.6	>32	>32	28.1
	Cefepime	≤0.5	2	95.9	≤0.5	≤0.5	98.7
	Ceftazidime	≤8	≤8	90.1	≤8	≤8	95.2
	Ceftriaxone	≤0.06	4	92	≤0.06	0.25	96.8
	Imipenem	0.25	0.5	99.2	0.25	0.5	99.9
	Levofloxacin	0.06	>8	81.6	0.03	8	86.1
	Minocycline	1	8	85.8	1	8	85.9
	PipTazo	1	8	92.7	1	4	96.6
All ESBLs[c]	Tigecycline	0.5	2	93	0.5	4	82.8
In-Patient (n=258)	Amikacin	8	32	88.4	4	16	96.6
Out-Patient (n=29)	AmoxClav	16	>32	25.6	32	>32	24.1
	Ampicillin	>32	>32	0.8	>32	>32	0
	Cefepime	16	>32	49.6	8	>32	62.1
	Ceftazidime	>32	>32	7.4	>32	>32	13.8
	Ceftriaxone	64	>64	24	32	>64	31
	Imipenem	0.5	8	86.4	0.25	0.5	100
	Levofloxacin	>8	>8	19.8	8	>8	24.1
	Minocycline	4	>16	67.4	4	>16	58.6
	PipTazo	16	>128	51.6	16	>128	58.6
E. aerogenes	Tigecycline	0.5	1	94.9	0.5	1	93.5
In-Patient (n=529)	Amikacin	2	4	99.1	2	4	99.4
Out-Patient (n=155)	AmoxClav	>32	>32	3.2	>32	>32	0.6
	Ampicillin	>32	>32	0	>32	>32	0
	Cefepime	≤0.5	1	98.1	≤0.5	1	97.4
	Ceftazidime	≤8	32	80	≤8	16	85.8
	Ceftriaxone	0.12	8	91.5	0.12	4	94.2
	Imipenem	1	1	100	1	2	100
	Levofloxacin	0.06	1	92.6	0.06	0.25	95.5
	Minocycline	2	8	89.4	2	4	91.6
	PipTazo	2	32	85.3	2	16	92.3
E. cloacae	Tigecycline	0.5	2	91.7	0.5	2	94
In-Patient (n=1,405)	Amikacin	2	4	99.3	2	2	99.5
Out-Patient (n=366)	AmoxClav	>32	>32	1.6	>32	>32	1.1
	Ampicillin	>32	>32	0	>32	>32	0
	Cefepime	≤0.5	4	95.3	≤0.5	2	97.3
	Ceftazidime	≤8	>32	68.9	≤8	32	84.4
	Ceftriaxone	0.25	64	73.2	0.25	16	86.6
	Imipenem	0.5	1	100	0.5	1	100
	Levofloxacin	0.03	4	89.6	0.03	2	92.1
	Minocycline	2	16	83	2	16	83.9
	PipTazo	2	64	77.9	2	32	89.6
E. coli	Tigecycline	0.12	0.25	99.5	0.12	0.25	99.5
In-Patient (n=2,131)	Amikacin	2	4	99.5	2	4	99.7
Out-Patient (n=793)	AmoxClav	4	32	74.4	4	16	78.4
	Ampicillin	>32	>32	45.8	32	>32	49.2
	Cefepime	≤0.5	≤0.5	97.3	≤0.5	≤0.5	99
	Ceftazidime	≤8	≤8	93.6	≤8	≤8	96.3
	Ceftriaxone	≤0.06	1	93.9	≤0.06	0.12	97.4
	Imipenem	0.25	0.5	100	0.25	0.5	100
	Levofloxacin	0.03	>8	75.4	0.03	>8	80.2
	Minocycline	1	8	86	1	8	86.3
	PipTazo	1	4	95.9	1	4	97.5
E. coli, ESBL[c]	Tigecycline	0.25	0.5	100	-	-	100
In-Patient (n=54)	Amikacin	4	16	100	-	-	100
Out-Patient (n=9)[d]	AmoxClav	16	32	20.4	-	-	11.1
	Ampicillin	>32	>32	3.7	-	-	0
	Cefepime	32	>32	33.3	-	-	33.3
	Ceftazidime	32	>32	20.4	-	-	11.1
	Ceftriaxone	>64	>64	20.4	-	-	22.2
	Imipenem	0.25	0.5	98.1	-	-	100
	Levofloxacin	>8	>8	9.3	-	-	11.1
	Minocycline	2	>16	72.2	-	-	66.7
	PipTazo	4	64	85.2	-	-	66.7
H. influenzae	Tigecycline[d]	0.12	0.5	na	0.12	0.25	na
In-Patient (n=845)	Amikacin	4	8	na	8	8	na
Out-Patient (n=459)	AmoxClav	0.5	1	99.9	0.5	1	99.8
	Ampicillin	≤0.5	32	74	≤0.5	>32	67.1
	Cefepime	≤0.5	≤0.5	98.7	≤0.5	≤0.5	98.5
	Ceftazidime	≤8	≤8	0	≤8	≤8	0
	Ceftriaxone	≤0.06	≤0.06	99.9	≤0.06	≤0.06	99.8
	Imipenem	0.5	1	100	0.5	1	100
	Levofloxacin	0.015	0.03	100	0.015	0.015	100
	Minocycline	≤0.5	1	na	≤0.5	1	na
	PipTazo	≤0.06	≤0.06	100	≤0.06	≤0.06	99.8
Beta-lactamase Negative	Tigecycline[d]	0.12	0.5	na	0.12	0.25	na
H. influenzae	Amikacin	4	8	na	8	8	na
In-Patient (n=630)	AmoxClav	0.25	1	100	0.25	1	100
Out-Patient (n=314)	Ampicillin	≤0.5	≤0.5	99.2	≤0.5	1	98.1
	Cefepime	≤0.5	≤0.5	99.2	≤0.5	≤0.5	97.8
	Ceftazidime	≤8	≤8	0	≤8	≤8	0
	Ceftriaxone	≤0.06	≤0.06	100	≤0.06	≤0.06	99.7
	Imipenem	0.5	1	100	0.5	1	100
	Levofloxacin	0.015	0.03	100	0.015	0.015	100
	Minocycline	≤0.5	1	na	≤0.5	1	na
	PipTazo	≤0.06	≤0.06	100	≤0.06	≤0.06	100
Beta-lactamase Positive	Tigecycline[d]	0.12	0.25	na	0.12	0.5	na
H. influenzae	Amikacin	4	8	na	8	8	na
In-Patient (n=215)	AmoxClav	1	2	99.5	1	2	99.3
Out-Patient (n=145)	Ampicillin	32	>32	0	32	>32	0
	Cefepime	≤0.5	≤0.5	97.2	≤0.5	≤0.5	100
	Ceftazidime	≤8	≤8	0	≤8	≤8	0
	Ceftriaxone	≤0.06	≤0.06	99.5	≤0.06	≤0.06	100
	Imipenem	0.5	1	100	0.5	1	100
	Levofloxacin	0.015	0.03	100	0.015	0.03	100
	Minocycline	≤0.5	1	na	≤0.5	2	na
	PipTazo	≤0.06	≤0.06	100	≤0.06	≤0.06	99.3
K. oxytoca	Tigecycline	0.25	1	98.6	0.25	1	98
In-Patient (n=360)	Amikacin	2	4	99.4	2	4	100
Out-Patient (n=99)	AmoxClav	2	16	85.6	2	8	92.9
	Ampicillin	>32	>32	0.3	>32	>32	0
	Cefepime	≤0.5	1	98.9	≤0.5	≤0.5	99
	Ceftazidime	≤8	≤8	93.6	≤8	≤8	97
	Ceftriaxone	≤0.06	2	95	≤0.06	0.25	98
	Imipenem	0.5	0.5	100	0.5	0.5	100
	Levofloxacin	0.03	0.5	95.6	0.03	0.5	96
	Minocycline	1	4	93.9	1	2	96
	PipTazo	1	16	90	1	4	94.9
K. oxytoca, ESBL[c]	Tigecycline	1	2	91.7	-	-	100
In-Patient (n=12)	Amikacin	1	8	100	-	-	100
Out-Patient (n=1)[e]	AmoxClav	8	16	83.3	-	-	0
	Ampicillin	>32	>32	0	-	-	0
	Cefepime	2	8	91.7	-	-	100
	Ceftazidime	>32	>32	8.3	-	-	0
	Ceftriaxone	8	32	50	-	-	100
	Imipenem	0.5	0.5	100	-	-	100
	Levofloxacin	1	4	75	-	-	0
	Minocycline	4	8	66.7	-	-	100
	PipTazo	4	>128	83.3	-	-	100
K. pneumoniae	Tigecycline	0.5	2	94.5	0.5	1	94.9
In-Patient (n=1,823)	Amikacin	2	4	97.8	2	2	99.6
Out-Patient (n=495)	AmoxClav	2	32	83.7	2	16	89.9
	Ampicillin	>32	>32	0	>32	>32	0
	Cefepime	≤0.5	4	93.6	≤0.5	≤0.5	98.2
	Ceftazidime	≤8	>32	85.5	≤8	≤8	92.9
	Ceftriaxone	≤0.06	16	89.1	≤0.06	0.25	95.6
	Imipenem	0.5	0.5	98.1	0.25	0.5	99.8
	Levofloxacin	0.06	8	86.1	0.06	1	93.5
	Minocycline	2	8	84	2	16	83.2
	PipTazo	2	32	89.6	2	8	95.6
K. pneumoniae, ESBL	Tigecycline	1	2	91.1	1	4	73.7
In-Patient (n=192)	Amikacin	8	32	84.4	4	16	94.7
Out-Patient (n=20)	AmoxClav	32	>32	23.4	16	>32	31.6
	Ampicillin	>32	>32	0	>32	>32	0
	Cefepime	8	>32	51.6	4	>32	73.7
	Ceftazidime	>32	>32	3.6	>32	>32	15.8
	Ceftriaxone	64	>64	23.4	32	>64	31.6
	Imipenem	0.5	8	82.3	0.25	0.5	100
	Levofloxacin	>8	>8	19.3	8	>8	31.6
	Minocycline	4	>16	66.1	4	>16	52.6
	PipTazo	128	>128	40.1	16	>128	52.6
S. marcescens	Tigecycline	1	2	96.5	1	2	97.8
In-Patient (n=805)	Amikacin	2	4	99.6	2	4	100
Out-Patient (n=229)	AmoxClav	>32	>32	0.9	>32	>32	0.4
	Ampicillin	>32	>32	0	>32	>32	0
	Cefepime	≤0.5	1	97.8	≤0.5	1	98.7
	Ceftazidime	≤8	≤8	93.8	≤8	≤8	94.8
	Ceftriaxone	0.25	4	94.7	0.25	8	92.6
	Imipenem	0.5	1	100	0.5	2	100
	Levofloxacin	0.12	1	94.8	0.12	1	96.1
	Minocycline	2	4	90.6	2	4	91.7
	PipTazo	1	8	96.4	1	8	96.5
Acinetobacter spp.	Tigecycline	0.5	2	na	0.25	1	na
In-Patient (n=1,168)	Amikacin	4	32	81.8	4	32	88.2
Out-Patient (n=348)	AmoxClav	32	>32	na	16	>32	na
	Ampicillin	>32	>32	na	16	>32	na
	Cefepime	16	>32	45.2	4	>32	65.2
	Ceftazidime	16	>32	45.8	≤8	>32	65.2
	Ceftriaxone	32	>64	28.3	16	>64	47.1
	Imipenem	0.5	8	87	0.5	4	90.8
	Levofloxacin	4	>8	47.7	0.25	>8	66.7
	Minocycline	≤0.5	8	88.4	≤0.5	4	91.7
	PipTazo	8	>128	56.3	1	128	74.1
P. aeruginosa	Tigecycline	8	>16	na	8	>16	na
In-Patient (n=1,859)	Amikacin	4	8	97.3	4	8	97.1
Out-Patient (n=420)	AmoxClav	>32	>32	na	>32	>32	na
	Ampicillin	>32	>32	na	>32	>32	na
	Cefepime	4	32	75.7	4	16	87.9
	Ceftazidime	≤8	32	80.1	≤8	≤8	91.4
	Ceftriaxone	64	>64	15.8	32	>64	23.8
	Imipenem	1	8	82.8	1	8	88.6
	Levofloxacin	1	>8	62.6	1	>8	71.2
	Minocycline	>16	>16	4.2	>16	>16	4.3
	PipTazo	4	128	88.1	4	32	95.5

[a] MIC in mcg/mL
[b] Interpretive criteria as defined by CLSI, M100-S15 (2005), where available; Tigecycline susceptible breakpoint is according to FDA package insert (2005), where available [9]; na = not available.
[c] Extended Spectrum Beta-Lactamase producing strains
[d] Sample sizes <20 were not analyzed for $MIC_{50/90}$.

Table 2. In Vitro Activity of Tigecycline and Comparative Antimicrobial Agents Against Gram-Positive Clinical Pathogens Isolated from In-Patients and Out-Patients - North American Results.

		In-Patients			Out-Patients		
Organism (N)	Drug	MIC_{50}[a]	MIC_{90}	%Sus[b]	MIC_{50}	MIC_{90}	%Sus
E. faecalis	Tigecycline	0.06	0.12	99.7	0.12	0.12	99.2
In-Patient (n=941)	AmoxClav	0.5	1	na	0.5	1	na
Out-Patient (n=246)	Ampicillin	1	1	100	1	1	100
	Ceftriaxone	>64	>64	na	>64	>64	na
	Imipenem	1	1	na	1	1	na
	Levofloxacin	1	>32	54.1	1	>32	55.7
	Linezolid	2	2	98.8	2	2	98.8
	Minocycline	8	8	46.9	8	8	42.7
	Penicillin	2	4	100	2	4	100
	PipTazo	2	4	na	2	4	na
	Vancomycin	1	2	95	1	2	96.7
Vancomycin	Tigecycline	0.06	0.12	100	-	-	100
Resistant,	AmoxClav	0.5	1	na	-	-	na
E. faecalis	Ampicillin	1	2	100	-	-	100
In-Patient (n=41)	Ceftriaxone	>64	>64	na	-	-	na
Out-Patient (n=6)[c]	Imipenem	1	2	na	-	-	na
	Levofloxacin	32	>32	4.9	-	-	0
	Linezolid	1	2	100	-	-	100
	Minocycline	4	8	56.1	-	-	50
	Penicillin	2	4	100	-	-	100
	PipTazo	2	4	na	-	-	na
	Vancomycin	>32	>32	0	-	-	0
E. faecium	Tigecycline	0.06	0.12	99.8	0.06	0.12	100
In-Patient (n=432)	AmoxClav	>8	>8	na	>8	>8	na
Out-Patient (n=55)	Ampicillin	>16	>16	14.4	>16	>16	9.1
	Ceftriaxone	>64	>64	na	>64	>64	na
	Imipenem	>16	>16	na	>16	>16	na
	Levofloxacin	>32	>32	9	>32	>32	3.6
	Linezolid	2	2	97.7	2	2	98.2
	Minocycline	≤0.25	8	73.4	≤0.25	8	72.7
	Penicillin	>8	>8	13.2	>8	>8	7.3
	PipTazo	>16	>16	na	>16	>16	na
	Vancomycin	>32	>32	34.5	>32	>32	34.5
Vancomycin	Tigecycline	0.06	0.12	100	0.03	0.12	100
Resistant,	AmoxClav	>8	>8	na	>8	>8	na
E. faecium	Ampicillin	>16	>16	2.5	>16	>16	5.6
In-Patient (n=278)	Ceftriaxone	>64	>64	na	>64	>64	na
Out-Patient (n=36)	Imipenem	>16	>16	na	>16	>16	na
	Levofloxacin	>32	>32	0.4	>32	>32	0
	Linezolid	2	2	97.5	2	2	97.2
	Minocycline	≤0.25	8	71.9	≤0.25	8	72.2
	Penicillin	>8	>8	1.4	>8	>8	2.8
	PipTazo	>16	>16	na	>16	>16	na
	Vancomycin	>32	>32	0	>32	>32	0
S. aureus	Tigecycline	0.12	0.25	99.1	0.12	0.12	99.3
In-Patient (n=2,289)	AmoxClav	4	>8	61.9	2	>8	66.5
Out-Patient (n=711)	Ampicillin	16	>16	8.5	16	>16	9.3
	Ceftriaxone	16	>64	48.8	8	>64	54
	Imipenem	0.25	4	90.2	0.25	1	94.9
	Levofloxacin	4	>32	47.2	0.25	32	59.9
	Linezolid	2	2	100	2	2	100
	Minocycline	≤0.25	≤0.25	99.4	≤0.25	0.5	99.3
	Penicillin	>8	>8	7.2	>8	>8	7.7
	PipTazo	4	>16	66.8	2	>16	70.3
	Vancomycin	0.5	1	100	0.5	1	100
S. aureus, MSSA	Tigecycline	0.12	0.12	99.3	0.12	0.12	98.9
In-Patient (n=1,022)	AmoxClav	0.5	2	99	1	2	99.4
Out-Patient (n=359)	Ampicillin	4	>16	19	4	>16	18.4
	Ceftriaxone	4	4	96.1	4	4	96.7
	Imipenem	≤0.12	0.5	99.3	≤0.12	0.25	99.7
	Levofloxacin	0.12	4	84.2	0.12	2	88.3
	Linezolid	2	2	100	2	2	100
	Minocycline	≤0.25	≤0.25	99.5	≤0.25	0.5	98.9
	Penicillin	8	>8	16.1	8	>8	15.3
	PipTazo	0.5	2	99.6	1	1	99.4
	Vancomycin	0.5	1	100	0.5	1	100
S. aureus, MRSA	Tigecycline	0.12	0.25	99	0.12	0.25	99.7
In-Patient (n=1,267)	AmoxClav	8	>8	32	8	>8	33
Out-Patient (n=352)	Ampicillin	>16	>16	0	>16	>16	0
	Ceftriaxone	32	>64	10.7	16	>64	10.5
	Imipenem	0.5	16	82.9	0.5	4	90.1
	Levofloxacin	16	>32	17.3	4	>32	31
	Linezolid	2	2	100	2	2	100
	Minocycline	≤0.25	0.5	99.4	≤0.25	0.5	99.7
	Penicillin	>8	>8	0	>8	>8	0
	PipTazo	16	>16	40.4	16	>16	40.6
	Vancomycin	1	1	100	0.5	1	100
S. agalactiae	Tigecycline	0.03	0.12	100	0.03	0.12	100
In-Patient (n=584)	AmoxClav	0.06	0.12	na	0.06	0.12	na
Out-Patient (n=475)	Ampicillin	0.12	0.12	100	0.12	0.12	100
	Ceftriaxone	0.06	0.12	100	0.06	0.12	100
	Imipenem	≤0.12	0.25	na	≤0.12	0.25	na
	Levofloxacin	0.5	1	98.6	0.5	1	97.7
	Linezolid	1	1	100	1	1	100
	Minocycline	8	>8	na	8	>8	na
	Penicillin	≤0.06	0.12	100	≤0.06	0.12	100
	PipTazo	≤0.25	≤0.25	na	≤0.25	≤0.25	na
	Vancomycin	0.5	0.5	100	0.5	0.5	100
S. pneumoniae	Tigecycline[d]	0.03	0.5	na	0.03	0.5	na
In-Patient (n=1,054)	AmoxClav	≤0.03	2	93.6	≤0.03	2	93
Out-Patient (n=560)	Ampicillin	≤0.06	2	na	≤0.06	4	na
	Ceftriaxone	≤0.03	1	97.2	≤0.03	1	97.3
	Imipenem	≤0.12	0.5	60.5	≤0.12	0.5	61
	Levofloxacin	0.5	1	99.9	0.5	1	99.6
	Linezolid	≤0.5	1	100	≤0.5	1	100
	Minocycline	≤0.25	4	na	≤0.25	4	na
	Penicillin	≤0.06	2	58.2	≤0.06	2	57.3
	PipTazo	≤0.25	2	na	≤0.25	2	na
	Vancomycin	0.25	0.5	100	0.25	0.5	100
Penicillin	Tigecycline	0.03	0.5	na	0.03	0.5	na
Susceptible,	AmoxClav	≤0.03	≤0.03	100	≤0.03	≤0.03	100
S. pneumoniae	Ampicillin	≤0.06	≤0.06	na	≤0.06	≤0.06	na
In-Patient (n=613)	Ceftriaxone	≤0.03	≤0.03	100	≤0.03	0.06	100
Out-Patient (n=321)	Imipenem	≤0.12	0.25	85.6	≤0.12	0.25	84.4
	Levofloxacin	0.5	1	99.8	0.5	1	100
	Linezolid	≤0.5	1	100	≤0.5	1	100
	Minocycline	≤0.25	0.5	na	≤0.25	0.5	na
	Penicillin	≤0.06	≤0.06	100	≤0.06	≤0.06	100
	PipTazo	≤0.25	≤0.25	na	≤0.25	≤0.25	na
	Vancomycin	0.25	0.5	100	0.25	0.5	100
Penicillin	Tigecycline	0.03	0.5	na	0.03	0.5	na
Intermediate,	AmoxClav	0.12	1	99	0.12	1	98.7
S. pneumoniae	Ampicillin	0.25	2	na	0.25	2	na
In-Patient (n=309)	Ceftriaxone	0.12	0.5	98.7	0.12	0.5	99.4
Out-Patient (n=156)	Imipenem	0.25	0.5	36.6	0.25	0.5	44.5
	Levofloxacin	0.5	1	100	0.5	1	99.4
	Linezolid	≤0.5	1	100	≤0.5	1	100
	Minocycline	≤0.25	8	na	≤0.25	8	na
	Penicillin	0.25	1	0	0.25	1	0
	PipTazo	≤0.25	2	na	≤0.25	2	na
	Vancomycin	0.25	0.5	100	0.25	0.5	100
Penicillin Resistant	Tigecycline	0.03	0.5	na	0.03	0.5	na
S. pneumoniae	AmoxClav	2	8	51.5	2	8	55.4
In-Patient (n=132)	Ampicillin	4	8	na	4	8	na
Out-Patient (n=83)	Ceftriaxone	1	4	81.1	1	2	83.1
	Imipenem	0.5	1	0	0.5	1	0
	Levofloxacin	0.5	1	100	1	1	98.8
	Linezolid	≤0.5	1	100	≤0.5	1	100
	Minocycline	2	4	na	2	4	na
	Penicillin	2	4	0	2	4	0
	PipTazo	2	4	na	4	4	na
	Vancomycin	0.25	0.5	100	0.25	0.5	100

[a] MIC in mcg/mL
[b] Interpretive criteria as defined by CLSI, M100-S16 (2006), where available; Tigecycline susceptible breakpoint is according to FDA package insert (2005), where available [9]; Tigecycline FDA breakpoints (susceptible ≤0.25 mcg/mL) for enterococci are approved for vancomycin-susceptible *E. faecalis*, only; this criteria is applied to all enterococci for comparison purposes only. na = not available.
[c] MIC_{50} and MIC_{90} values not calculated for species or phenotypic groups with n < 10. Species with aggregate n's < 20 are not shown.

CONCLUSIONS

- There were no demonstrable changes in MIC_{90} values for tigecycline against either In-Patient or Out-Patient strains of *Enterobacteriaceae, S. aureus, Acinetobacter* spp., *H. influenzae*, *Streptococcus* spp, or *Enterococcus* spp.
- Tigecycline demonstrated excellent activity against all ESBL producers.
- The frequency of ESBL producing *Enterobacteriaceae* was slightly higher in In-Patient isolates (6%) than Out-Patients isolates (2.1%).
- Penicillin non-susceptible rates for *S. pneumoniae* were similar for In-Patient (41.8%) vs Out-Patient (42.7%) strains.
- The frequency of MRSA was similar between both In-Patient (55.4%) and Out-Patient (49.5%) populations.
- With MIC_{90} values of 0.25 mcg/ml against MRSA, Tigecycline demonstrated in vitro activity comparable to commonly prescribed antimicrobial agents, linezolid and vancomycin, currently used for the treatment of serious staphylococcal infections without regard to isolate source.
- Tigecycline presented an MIC_{90} of 0.12 mcg/ml against *Enterococcus* spp. regardless of susceptibility to vancomycin.
- Tigecycline demonstrated excellent inhibitory activity against *Acinetobacter* spp. with the lowest MIC_{90} of 2 mcg/ml for In-Patients and 1 mcg/ml for Out-Patients.
- Tigecycline demonstrated excellent inhibitory activity against *H. influenzae* regardless of beta-lactamase production.
- The in vitro activity of tigecycline in this study suggests that tigecycline is a suitable antimicrobial agent for consideration as empiric treatment of some of the most commonly encountered hospital and community acquired pathogens, as well as many of the difficult to treat resistant phenotypes.