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Gender Analysis of Global Pathogen Susceptibility (2004-2006): Tigecycline vs. Comparators in the TEST Study

S. Bouchillon[1], T. Stevens[1], J. Johnson[1], D. Hoban[1], B. Johnson[1], R. Badal[1], S. Lob[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 (TIG), a new glycylcycline, has been shown to have potent broad spectrum activity against most commonly encountered species responsible for community and hospital acquired infections. The T.E.S.T. program determined the in vitro activity of TIG and 10 comparators against gram positive/negative species. Isolates were collected from 205 hospital sites in 30 countries from 2004 to 2006. **Methods:** A total of 48,068 clinically significant isolates collected worldwide were analyzed in this survey. The isolates were identified to the species level at the participating sites and confirmed by the central laboratory. MICs were determined by each site using supplied broth microdilution panels and interpreted according to CLSI (formerly NCCLS) guidelines. **Results:** Selected pathogens tested against tigecycline are shown in the table below*:

		Tigecycline		
		N=	%S	MIC_{90}
Male	EcKpKo	5,720	97.6	1
	Acinetobacter spp.	1,906	na	1
	S. aureus	3,331	100	0.25
	Enterococcus spp.	1,942	100	0.12
	S. pneumoniae	1,883	na	0.25
	H. influenzae	1,738	na	0.5
Female	EcKpKo	7,143	98.2	1
	Acinetobacter spp.	1,416	na	1
	S. aureus	2,536	100	0.25
	Enterococcus spp.	1,969	100	0.12
	S. pneumoniae	1,366	na	0.25
	H. influenzae	1,293	na	0.5

* EcKpKo = *E. coli*, *K. pneumoniae* and *K. oxytoca*. na = breakpoints not available.

Conclusion: Tigecycline showed excellent inhibitory activity against all groups of pathogens regardless of gender group. Tigecycline MIC_{90} of 0.25 mcg/ml, 0.12 mcg/ml and 0.25 mcg/ml against *S. aureus*, *Enterococcus spp.*, and *S. pneumoniae*, respectively, and MIC_{90} of $\leq$2 mcg/ml and 1 mcg/ml against *Enterobacteriaceae* and *Acinetobacter spp.*, respectively, validate the potent inhibitory activity of TIG against community/hospital pathogens in both gender groups.

INTRODUCTION

Tigecycline is a novel antimicrobial with expanded broad-spectrum activity from a new class of compounds, the glycylcyclines. Tigecycline inhibits protein synthesis by binding to the 30S ribosomal subunit. Although it is perceived to be bacteriostatic, its anti-bacterial activity is significant and has shown some bactericidal activity against key targeted pathogens [1,2]. Tigecycline was developed to provide activity against tetracycline and multi-drug-resistant gram-positive pathogens and has demonstrated significant broad-spectrum activity against aerobic and anaerobic gram-positive and gram-negative microorganisms [2-4].

Tigecycline resistance is very infrequent and is also difficult to induce in the laboratory [5, 6] with a selection frequency observed at less than 10^{-9} [3, 5, 7]. With the exception of *P. aeruginosa*, tetracycline-resistant bacteria with either tetracycline efflux pumps or ribosomal protective features are sensitive to tigecycline [2-4, 7-11]. Tigecycline has been shown to be highly effective against multi-resistant *Acinetobacter spp.*, particularly *A. baumannii* that are commonly associated with serious nosocomial infections. Similar activity has been observed against *Enterobacteriaceae*, even extended-spectrum beta-lactamase (ESBL)- and AmpC-producing strains [10]. Tigecycline has demonstrated MIC_{90} values of <0.5 mcg/ml against methicillin-resistant *Staphylococcus aureus* (MRSA) and other gram-positive organisms [2, 4-6]. Tigecycline has shown potent activity against animal models infected with selected strains of multi-drug resistant *Enterococcus faecium* and *Enterococcus faecalis* [4, 5] with diverse genotypes van-A, -B and -C [6].

The T.E.S.T. program determined the in vitro activity of tigecycline compared to most commonly prescribed broad spectrum antimicrobials against gram-negative and gram-positive species collected from 205 hospitals globally from 2004 to 2006. This study was designed to compare the in vitro activity of tigecycline in isolates from female and male patients.

MATERIALS & METHODS

- For the T.E.S.T program all isolates were derived from blood, respiratory tract, urine (no more than 25% of all isolates), skin, wound, fluids, and few other defined sources. Only one isolate per patient was accepted.
- Clinical isolates (n=34,512) were collected from 2004 to 2006 at 205 testing sites in 30 countries.
- Custom broth microdilution panels were supplied by MicroScan (Dade Behring, West Sacramento, CA, USA) with the following antimicrobial agents and concentrations (expressed in mcg/ml): amoxicillin-clavulanic acid (0.12-32); piperacillin-tazobactam (0.06-128); levofloxacin (0.008-8); ceftriaxone (0.06-64); cefepime (0.5-32); ampicillin (0.5-32); amikacin (0.5-64); minocycline (0.5-16); ceftazidime (8-32); tigecycline (0.008-16); and imipenem (0.06-16).
- MIC interpretive criteria followed published guidelines established by the CLSI where applicable [12].
- MIC interpretive criteria for tigecycline followed published guidelines established by the FDA where applicable [13].
- Isolates were identified to genus and species by the local laboratory. Each site tested the isolates using broth microdilution.
- Quality control of broth microdilution panels followed manufacturer's and CLSI guidelines using the following ATCC strains: *Enterococcus faecalis* ATTC 29212; *Escherichia coli* ATCC 25922; *Klebsiella pneumoniae* ATCC 700603; *Haemophilus influenzae* ATCC 49247; *Haemophilus influenzae* ATCC 49766; *Staphylococcus aureus* ATCC 29213; *Streptococcus pneumoniae* ATCC 49619; and *Pseudomonas aeruginosa* ATCC 27853.
- The collection and transportation of organisms, confirmation of identification, and construction and management of a centralized database were conducted and coordinated by Laboratories International for Microbiology Studies (LIMS), a subsidiary of International Health Management Associates, Inc. (IHMA, Schaumburg, IL, USA).

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RESULTS

The results are listed in the following tables.

Table 1. *In vitro* activity of tigecycline and comparative agents against gram-negative isolates

		Male				MIC (mcg/ml)		Female				MIC (mcg/ml)	
Organism Name	Drug	n	%SUS [a]	%INT	%RES	MIC_{50}	MIC_{90}	n	%SUS [a]	%INT	%RES	MIC_{50}	MIC_{90}
E. coli [b]	Tigecycline	2,636	100	0	0	0.12	0.25	3,990	100	0	0	0.12	0.25
	Amikacin	2,636	98.6	0.7	0.7	2	4	3,990	99.5	0.4	0.2	2	4
	AmoxClav	2,636	71.3	14.9	13.8	8	32	3,990	75.7	14	10.3	4	32
	Ampicillin	2,636	41.6	0.9	57.5	>32	>32	3,990	45	0.8	54.2	>32	>32
	Cefepime	2,636	94.1	1.3	4.6	≤0.5	2	3,990	96.3	0.9	2.8	≤0.5	≤0.5
	Ceftazidime	2,636	92.6	2.4	4.9	≤8	≤8	3,990	94.8	2	3.2	≤8	≤8
	Ceftriaxone	2,636	90.5	1.9	7.6	≤0.06	8	3,990	93.5	1.8	4.7	≤0.06	0.5
	Imipenem	2,495	100	0	0	0.25	0.5	3,827	100	0	0	0.25	0.5
	Levofloxacin	2,636	71.7	3.3	25	0.03	>8	3,990	77.3	2.2	20.5	0.03	>8
	Meropenem	141	100	0	0	≤0.06	0.25	163	100	0	0	≤0.06	0.12
	Minocycline	2,636	84.3	8.4	7.2	1	8	3,990	84.4	9.1	6.5	1	8
	PipTazo	2,636	94.5	2.6	2.9	1	8	3,990	96.3	1.9	1.9	1	4
K pneumoniae [c]	Tigecycline	2,415	94.5	4.4	1.1	0.5	2	2,624	95.5	3.3	1.2	0.5	2
	Amikacin	2,415	96.6	1.5	1.9	2	8	2,624	97.6	1.2	1.2	2	4
	AmoxClav	2,415	76.3	8.7	15	2	32	2,624	81.4	7.5	11.1	2	32
	Ampicillin	2,415	0	13.3	86.7	>32	>32	2,624	0	17.4	82.6	>32	>32
	Cefepime	2,415	89.9	2.6	7.5	≤0.5	16	2,624	92.7	2.1	5.2	≤0.5	4
	Ceftazidime	2,415	82	1.9	16.1	≤8	>32	2,624	86.5	2.2	11.3	≤8	32
	Ceftriaxone	2,415	83.1	5	11.8	≤0.06	64	2,624	88.5	3.2	8.4	≤0.06	32
	Imipenem	2,292	99.6	0.1	0.3	0.25	0.5	2,476	99.8	0.2	0	0.25	0.5
	Levofloxacin	2,415	85.2	2.6	12.3	0.06	8	2,624	88.5	2	9.5	0.06	4
	Meropenem	123	100	0	0	≤0.06	0.25	148	100	0	0	≤0.06	0.25
	Minocycline	2,415	79.2	7.9	12.9	2	16	2,624	83.9	6.7	9.4	2	8
	PipTazo	2,415	86.5	3.7	9.8	2	64	2,624	89.9	3.2	6.8	2	32
K. oxytoca [d]	Tigecycline	669	99.1	0.9	0	0.25	1	529	97.9	2.1	0	0.25	1
	Amikacin	669	99	0.4	0.6	2	4	529	99.6	0	0.4	2	4
	AmoxClav	669	82.5	6.4	11.1	2	32	529	85.1	5.5	9.5	2	16
	Ampicillin	669	0	11.2	88.8	>32	>32	529	0	10.4	89.6	>32	>32
	Cefepime	669	96.7	1.2	2.1	≤0.5	2	529	97.9	0.9	1.1	≤0.5	1
	Ceftazidime	669	93.9	1.3	4.8	≤8	≤8	529	93.4	1.9	4.7	≤8	≤8
	Ceftriaxone	669	92.5	4	3.4	≤0.06	8	529	93.8	3.6	2.6	≤0.06	8
	Imipenem	632	100	0	0	0.25	0.5	497	100	0	0	0.25	0.5
	Levofloxacin	669	95.1	2.4	2.5	0.03	1	529	93.4	1.7	4.9	0.03	1
	Meropenem	37	100	0	0	≤0.06	0.5	32	100	0	0	≤0.06	0.12
	Minocycline	669	94.2	4.5	1.3	1	4	529	92.4	4.5	3	1	4
	PipTazo	669	87.6	1.6	10.8	1	128	529	88.1	2.1	9.8	1	64
ESBL-producers	Tigecycline	549	95.3	3.5	1.3	0.5	2	445	93.9	4.5	1.6	0.5	2
	Amikacin	549	87.6	6.2	6.2	4	32	445	89.2	6.1	4.7	4	32
	AmoxClav	549	26	29.7	44.3	16	>32	445	24.9	33.3	41.8	16	>32
	Ampicillin	549	0.5	0.4	99.1	>32	>32	445	0.9	0.2	98.9	>32	>32
	Cefepime	549	48.1	9.5	42.4	16	>32	445	44.7	11.7	43.6	16	>32
	Ceftazidime	549	21.9	10.6	67.6	>32	>32	445	20.7	14.2	65.2	32	>32
	Ceftriaxone	549	18.6	19.3	62.1	>64	>64	445	20.2	17.1	62.7	>64	>64
	Imipenem	533	98.7	0.2	1.1	0.5	1	435	98.9	0.9	0.2	0.5	1
	Levofloxacin	549	37.2	6.9	55.9	8	>8	445	31.2	8.3	60.4	8	>8
	Meropenem	16	100	0	0	≤0.06	0.5	10	100	0	0	≤0.06	0.25
	Minocycline	549	65.9	12.6	21.5	4	>16	445	64.3	13.3	22.5	4	>16
	PipTazo	549	61	13.3	25.7	8	>128	445	61.1	11.9	27	8	>128
Enterobacter spp.	Tigecycline	3,249	94.5	4.2	1.4	0.5	2	2,558	93.9	4	2.1	0.5	2
	Amikacin	3,249	98.7	0.4	0.9	2	4	2,558	98.3	0.9	0.8	2	4
	AmoxClav	3,249	2.2	1.8	96	>32	>32	2,558	2.6	1.9	95.5	>32	>32
	Ampicillin	3,249	0	4.6	95.4	>32	>32	2,558	0	5.7	94.3	>32	>32
	Cefepime	3,249	93.5	2.5	4	≤0.5	8	2,558	94.7	1.8	3.5	≤0.5	4
	Ceftazidime	3,249	69.7	5.7	24.6	≤8	>32	2,558	72.4	5.6	22	≤8	>32
	Ceftriaxone	3,249	75.8	10.2	14	0.25	64	2,558	77.2	9.2	13.6	0.25	64
	Imipenem	3,047	100	0	0	0.5	1	2,391	100	0	0	0.5	1
	Levofloxacin	3,249	88.5	3.2	8.3	0.06	4	2,558	89.4	1.9	8.7	0.06	4
	Meropenem	202	100	0	0	≤0.06	0.5	167	100	0	0	≤0.06	0.5
	Minocycline	3,249	84.5	7.7	7.8	2	8	2,558	83.9	7.2	8.8	2	8
	PipTazo	3,249	79	12	9	2	64	2,558	80.9	10.8	8.2	2	64
Serratia spp.	Tigecycline	1,462	96.6	2.7	0.8	1	2	951	97	2.5	0.5	1	2
	Amikacin	1,462	97.9	1.3	0.8	2	4	951	98.2	0.8	0.9	2	4
	AmoxClav	1,462	1.8	1.6	96.5	>32	>32	951	1.8	2.6	95.6	>32	>32
	Ampicillin	1,462	0.7	4.9	94.4	>32	>32	951	0.8	6.4	92.7	>32	>32
	Cefepime	1,462	97.1	0.6	2.3	≤0.5	1	951	96.7	1.1	2.2	≤0.5	1
	Ceftazidime	1,462	93.2	1.6	5.2	≤8	≤8	951	92.2	2.1	5.7	≤8	≤8
	Ceftriaxone	1,462	91.3	4.4	4.2	0.25	8	951	92.4	3.5	4.1	0.25	4
	Imipenem	1,379	100	0	0	0.5	1	883	100	0	0	0.5	1
	Levofloxacin	1,462	94.9	2.1	3	0.12	1	951	95.2	2.1	2.7	0.12	1
	Meropenem	83	100	0	0	≤0.06	0.12	68	100	0	0	0.12	1
	Minocycline	1,462	89.9	7.5	2.6	2	8	951	90.6	6.7	2.6	2	4
	PipTazo	1,462	94.4	3.7	1.9	1	8	951	96.2	2.3	1.5	1	8
Acinetobacter spp.	Tigecycline	1,906	na	na	na	0.25	1	1,416	na	na	na	0.25	1
	Amikacin	1,906	76.6	7.5	15.9	4	64	1,416	81.1	6.5	12.4	4	64
	AmoxClav	1,906	na	na	na	32	>32	1,416	na	na	na	32	>32
	Ampicillin	1,906	na	na	na	>32	>32	1,416	na	na	na	32	>32
	Cefepime	1,906	49.9	15.8	34.3	16	>32	1,416	53.6	13.6	32.8	8	>32
	Ceftazidime	1,906	47.8	6.6	45.6	16	>32	1,416	54	6.7	39.3	≤8	>32
	Ceftriaxone	1,906	32	21.9	46.1	32	>64	1,416	35.7	24.9	39.5	16	>64
	Imipenem	1,855	84.4	1.8	13.9	0.5	16	1,377	88.6	1.5	9.9	0.5	8
	Levofloxacin	1,906	50.3	9.8	39.9	2	>8	1,416	56	7.8	36.2	0.5	>8
	Meropenem	51	96.1	0	3.9	1	2	39	94.9	2.6	2.6	1	4
	Minocycline	1,906	90.6	6.9	2.5	≤0.5	4	1,416	91	6.5	2.5	≤0.5	4
	PipTazo	1,906	56.4	15.7	27.9	8	>128	1,416	63.1	14.5	22.5	4	>128
H. influenzae [e]	Tigecycline	1,738	na	na	na	0.12	0.5	1,293	na	na	na	0.12	0.5
	AmoxClav	1,738	99.8	0	0.2	0.5	1	1,293	99.6	0	0.4	0.5	1
	Ampicillin	1,738	77.8	2	20.3	≤0.5	32	1,293	74.5	2.2	23.4	≤0.5	>32
	Cefepime	1,738	99.2	0	0.8	≤0.5	≤0.5	1,293	99.4	0	0.6	≤0.5	≤0.5
	Ceftriaxone	1,738	99.9	0	0.1	≤0.06	≤0.06	1,293	99.9	0	0.1	≤0.06	≤0.06
	Imipenem	1,619	100	0	0	0.5	1	1,215	100	0	0	0.5	1
	Levofloxacin	1,738	100	0	0	0.015	0.03	1,293	100	0	0	0.015	0.03
	Meropenem	119	100	0	0	≤0.06	0.25	78	100	0	0	≤0.06	0.25
	PipTazo	1,738	99.9	0	0.1	≤0.06	≤0.06	1,293	99.8	0	0.2	≤0.06	≤0.06
H. influenzae beta-lactamase positive	Tigecycline	371	na	na	na	0.12	0.5	313	na	na	na	0.12	0.5
	AmoxClav	371	98.9	0	1.1	1	2	313	98.4	0	1.6	1	2
	Ampicillin	371	0	5.1	94.9	32	>32	313	0	3.5	96.5	32	>32
	Cefepime	371	98.4	0	1.6	≤0.5	≤0.5	313	98.7	0	1.3	≤0.5	≤0.5
	Ceftriaxone	371	99.7	0	0.3	≤0.06	≤0.06	313	99.7	0	0.3	≤0.06	≤0.06
	Imipenem	346	100	0	0	0.5	1	284	100	0	0	0.5	1
	Levofloxacin	371	100	0	0	0.015	0.03	313	100	0	0	0.015	0.03
	Meropenem	25	100	0	0	≤0.06	0.12	29	100	0	0	≤0.06	0.25
	PipTazo	371	99.5	0	0.5	≤0.06	≤0.06	313	99.4	0	0.6	≤0.06	≤0.06

na = breakpoints not available.
[a] Interpretive criteria as defined by CLSI, M100-S16 (2006) [12], where available; tigecycline susceptibility breakpoints are according to FDA package insert (Tygacil®, 2005), where available [13].
[b] Isolates from male patients include 174 ESBL-producing strains; isolates from female patients include 149 ESBL-producing strains.
[c] Isolates from male patients include 347 ESBL-producing strains; isolates from female patients include 278 ESBL-producing strains.
[d] Isolates from male patients include 28 ESBL-producing strains; isolates from female patients include 18 ESBL-producing strains
[e] Isolates from male patients include 371 ß-lactamase positive strains; isolates from female patients include 313 ß-lactamase positive strains.

Table 2. *In vitro* activity of tigecycline and comparative agents against gram-positive isolates

		Male				MIC (mcg/ml)		Female				MIC (mcg/ml)	
Organism Name	Drug	n	%SUS [a]	%INT	%RES	MIC_{50}	MIC_{90}	n	%SUS [a]	%INT	%RES	MIC_{50}	MIC_{90}
S. aureus [b]	AmoxClav	3,331	66	0	34	2	>8	2,536	67.2	0	32.8	1	>8
	Ampicillin	3,331	10.3	0	89.7	16	>16	2,536	11.6	0	88.4	16	>16
	Ceftriaxone	3,331	58.8	20.2	21	4	>64	2,536	59.6	20.5	19.9	4	>64
	Imipenem	3,217	87.2	1.6	11.2	0.25	16	2,440	89.4	1.9	8.6	0.25	8
	Levofloxacin	3,331	61.1	2.7	36.2	0.25	32	2,536	62.2	2.2	35.6	0.25	32
	Linezolid	3,331	100	0	0	2	2	2,536	100	0	0	2	2
	Meropenem	114	95.6	0.9	3.5	0.25	2	96	92.7	1	6.3	0.25	4
	Minocycline	3,331	98.5	1.4	0.1	≤0.25	0.5	2,536	98.7	1.2	0.1	≤0.25	0.5
	Penicillin	3,331	8.7	0	91.3	>8	>8	2,536	10.3	0	89.7	>8	>8
	PipTazo	3,331	69.8	0	30.2	1	>16	2,536	71.1	0	28.9	1	>16
	Vancomycin	3,331	100	0	0	0.5	1	2,536	100	0	0	0.5	1
S. aureus (MRSA)	Tigecycline	1,532	100	0	0	0.12	0.25	1,131	100	0	0	0.12	0.25
	AmoxClav	1,532	26.1	0	73.9	8	>8	1,131	26.4	0	73.6	8	>8
	Ampicillin	1,532	0	0	100	>16	>16	1,131	0	0	100	>16	>16
	Ceftriaxone	1,532	11.4	43	45.6	32	>64	1,131	10	45.4	44.7	32	>64
	Imipenem	1,489	72.3	3.6	24.2	0.5	>16	1,093	76.4	4.3	19.3	0.5	>16
	Levofloxacin	1,532	19.3	3.2	77.5	8	>32	1,131	19.6	3.2	77.2	8	>32
	Linezolid	1,532	100	0	0	2	2	1,131	100	0	0	2	2
	Meropenem	43	88.4	2.3	9.3	1	8	38	81.6	2.6	15.8	2	16
	Minocycline	1,532	97.2	2.6	0.2	≤0.25	2	1,131	98.1	1.9	0.1	≤0.25	1
	Penicillin	1,532	0	0	100	>8	>8	1,131	0	0	100	>8	>8
	PipTazo	1,532	34.4	0	65.6	16	>16	1,131	35.3	0	64.7	16	>16
	Vancomycin	1,532	100	0	0	1	1	1,131	100	0	0	1	1
Enterococcus spp. [c]	Tigecycline	1,942	100	0	0	0.06	0.12	1,969	100	0	0	0.06	0.12
	Ampicillin	1,942	75.3	0	24.7	1	>16	1,969	78.7	0	21.3	1	>16
	Levofloxacin	1,942	46.8	1.2	52	16	>32	1,969	50.5	1.4	48.1	2	>32
	Linezolid	1,942	97.4	2.6	0	2	2	1,969	97.8	2.2	0	2	2
	Minocycline	1,942	53.5	35.8	10.7	4	>8	1,969	52.1	37.1	10.8	4	>8
	Penicillin	1,942	75	0	25	2	>8	1,969	77.8	0	22.2	2	>8
	Vancomycin	1,942	82.9	0.4	16.7	1	>32	1,969	82.9	0.8	16.3	1	>32
Enterococcus spp. (VRE)	Tigecycline	316	100	0	0	0.06	0.12	312	100	0	0	0.06	0.12
	Ampicillin	316	14.2	0	85.8	>16	>16	312	19.9	0	80.1	>16	>16
	Levofloxacin	316	1.6	0	98.4	>32	>32	312	1	0.3	98.7	>32	>32
	Linezolid	316	96.2	3.8	0	2	2	312	97.8	2.2	0	2	2
	Minocycline	316	72.2	20.3	7.6	≤0.25	8	312	71.8	21.8	6.4	0.5	8
	Penicillin	316	13.9	0	86.1	>8	>8	312	18.3	0	81.7	>8	>8
	Vancomycin	316	0	0	100	>32	>32	312	0	0	100	>32	>32
S. agalactiae	Tigecycline	740	100	0	0	0.03	0.12	1,590	100	0	0	0.03	0.12
	Ampicillin	740	100	0	0	0.12	0.12	1,590	100	0	0	0.12	0.12
	Ceftriaxone	740	100	0	0	0.06	0.12	1,590	100	0	0	0.06	0.12
	Levofloxacin	740	99.2	0.8	0	0.5	1	1,590	99.8	0.2	0	0.5	1
	Linezolid	740	100	0	0	1	1	1,590	100	0	0	1	1
	Penicillin	740	100	0	0	≤0.06	0.12	1,590	100	0	0	≤0.06	0.12
	Vancomycin	740	100	0	0	0.5	0.5	1,590	100	0	0	0.5	0.5
S. pneumoniae [d]	Tigecycline	1,883	na	na	na	0.03	0.25	1,366	na	na	na	0.03	0.25
	AmoxClav	1,883	95.8	2.7	1.5	≤0.03	1	1,366	95.8	2.8	1.5	≤0.03	1
	Ceftriaxone	1,883	98.2	1.1	0.7	≤0.03	1	1,366	98.2	1	0.7	≤0.03	0.5
	Imipenem	1,720	73.8	23.5	2.6	≤0.12	0.5	1,239	75.5	22	2.5	≤0.12	0.5
	Levofloxacin	1,883	99.8	0.2	0	0.5	1	1,366	99.8	0.2	0	0.5	1
	Linezolid	1,883	100	0	0	≤0.5	1	1,366	100	0	0	≤0.5	1
	Meropenem	163	96.3	2.5	1.2	≤0.12	≤0.12	127	100	0	0	≤0.12	≤0.12
	Penicillin	1,883	62.8	27.5	9.8	≤0.06	1	1,366	64.3	26.6	9	≤0.06	1
	Vancomycin	1,883	100	0	0	0.25	0.5	1,366	100	0	0	0.25	0.5
S. pneumoniae (PISP)	Tigecycline	517	na	na	na	0.03	0.25	364	na	na	na	0.03	0.25
	AmoxClav	517	99	1	0	0.12	1	364	99.5	0.3	0.3	0.12	1
	Ceftriaxone	517	99	0.8	0.2	0.12	0.5	364	98.6	1.4	0	0.12	0.5
	Imipenem	474	42.8	54.6	2.5	0.25	0.5	327	43.7	54.1	2.1	0.25	0.5
	Levofloxacin	517	99.8	0.2	0	0.5	1	364	99.5	0.5	0	0.5	1
	Linezolid	517	100	0	0	≤0.5	1	364	100	0	0	≤0.5	1
	Meropenem	43	100	0	0	≤0.12	0.25	37	100	0	0	≤0.12	0.25
	Penicillin	517	0	100	0	0.25	1	364	0	100	0	0.25	1
	Vancomycin	517	100	0	0	0.25	0.5	364	100	0	0	0.25	0.5
S. pneumoniae [e] (PRSP)	Tigecycline	184	na	na	na	0.03	0.25	123	na	na	na	0.03	0.25
	AmoxClav	184	59.2	25	15.8	2	8	123	54.5	30.1	15.4	2	8
	Ceftriaxone	184	84.2	8.7	7.1	1	2	123	84.6	7.3	8.1	1	2
	Imipenem	178	0	81.5	18.5	0.5	1	123	3.3	77.2	19.5	0.5	1
	Levofloxacin	184	98.9	1.1	0	1	1	123	100	0	0	0.5	1
	Linezolid	184	100	0	0	≤0.5	1	123	100	0	0	≤0.5	1
	Meropenem	6	0	66.7	33.3	-	-	0					
	Penicillin	184	0	0	100	2	4	123	0	0	100	2	4
	Vancomycin	184	100	0	0	0.25	0.5	123	100	0	0	0.25	0.5

na = breakpoints not available.
[a] Interpretive criteria as defined by CLSI, M100-S16 (2006) [12], where available; tigecycline susceptibility breakpoints are according to FDA package insert (Tygacil®, 2005), where available [13].
[b] Isolates from male patients include 1,532 MRSA strains, Isolates from female patients include 1,131 MRSA strains.
[c] Isolates from male patients include 41 vancomycin-resistant *E. faecalis* and 275 vancomycin-resistant *E. faecium* strains; isolates from female patients include 51 vancomycin-resistant *E. faecalis* and 261 vancomycin-resistant *E. faecium* strains.
[d] Isolates from male patients include 517 penicillin-intermediate (PISP) and 184 penicillin-resistant (PRSP) strains, isolates from female patients include 364 PISP and 123 PRSP strains.
[e] No MIC_{50} and MIC_{90} calculated if n<10; % SUS, % INT, % RES may not be statistically significant when n's are small.

Figure 1: In vitro activity of tigecycline against 2,636 *E. coli*, 2,415 *K. pneumoniae*, and 669 *K. oxytoca* from male patients; and 3,990 *E. coli*, 2,624 *K. pneumoniae*, and 529 *K. oxytoca* from female patients.

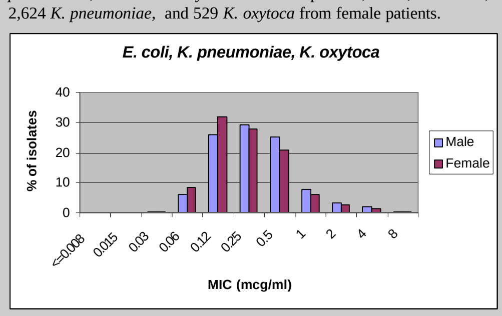


Figure 2: In vitro activity of tigecycline against 1,906 *Acinetobacter spp.* from male patients, and 1,416 *Acinetobacter spp.* from female patients.

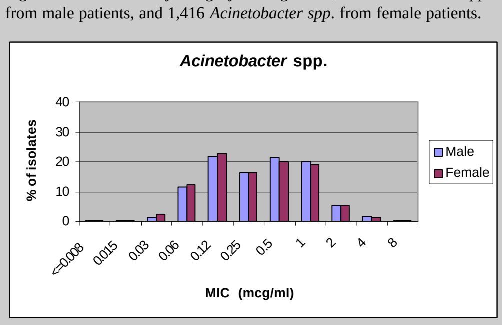


Figure 3: In vitro activity of tigecycline against 3,331 *S. aureus* (including 1,532 MRSA) from male patients, and 2,536 *S. aureus* (including 1,131 MRSA) from female patients.

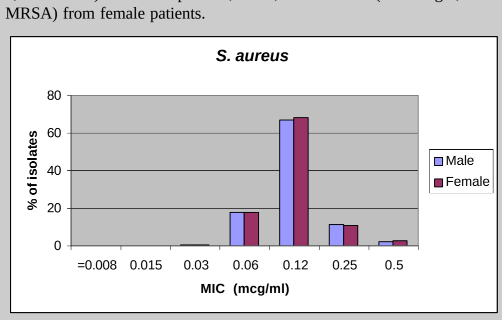


Figure 4: In vitro activity of tigecycline against 1,942 *Enterococcus spp.* (including 316 VRE) from male patients, and 1,969 *Enterococcus spp.* (including 312 VRE) from female patients.

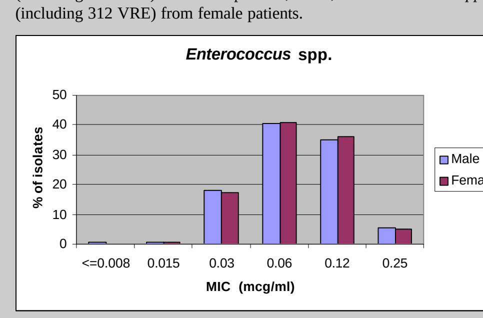


Figure 5: In vitro activity of tigecycline against 1,883 *S. pneumoniae* strains (including 517 penicillin-intermediate (PISP) and 184 penicillin-resistant (PRSP) strains) from male patients, and 1,366 *S. pneumoniae* strains (including 364 PISP and 123 PRSP strains) from female patients.

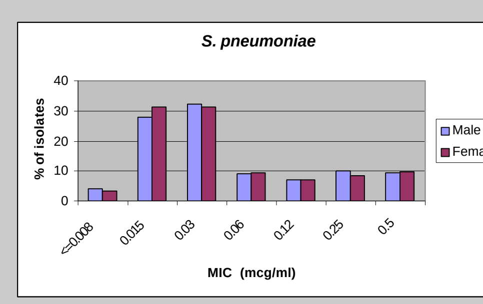
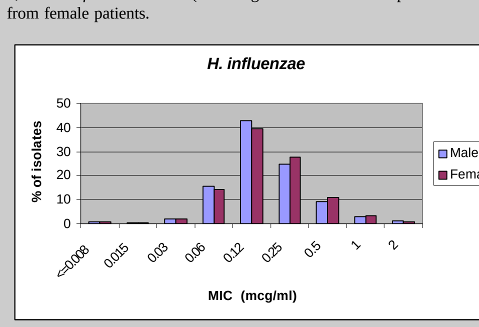


Figure 6: In vitro activity of tigecycline against 1,738 *H. influenzae* strains (including 371 beta-lactamase positive strains) from male patients, and 1,293 *H. influenzae* strains (including 313 beta-lactamase positive strains) from female patients.



CONCLUSIONS

- When comparing isolates from male and female patients, tigecycline MIC_{50} and MIC_{90} were the same in all species tested. For most other study antimicrobials the difference in $MIC_{50/90}$ between isolates from male and female patients was also only one doubling dilution.
- Tigecycline MIC_{90} of 0.25 mcg/ml, 0.12 mcg/ml and 0.25 mcg/ml against *S. aureus*, *Enterococcus spp.*, and S. pneumoniae, respectively, and MIC_{90} of < 2 mcg/ml and 1 mcg/ml against *Enterobacteriaceae* and *Acinetobacter spp.*, respectively, validate the potent inhibitory activity of TIG against community/hospital pathogens in both gender groups.
- Tigecycline's inhibitory activity against all *Enterobacteriaceae*, including ESBL-producers, was comparable to imipenem.
- Tigecycline's inhibitory activity (% susceptible) was similar to linezolid and vancomycin against *S. aureus* (including MRSA) and *S. agalactiae*. Against *S. pneumoniae*, tigecycline's MIC_{90} value was similar to linezolid and vancomycin.
- Against *Enterococcus spp.* (including VRE), tigecycline's activity (% susceptible) was similar to linezolid and superior to vancomycin.
- Tigecycline showed excellent inhibitory activity against all groups of study pathogens regardless of patient gender.