

In Vitro Activity of Tigecycline and Comparators Against Pathogens from Switzerland, Sweden and The Netherlands

#P1-014

S. Bouchillon¹, T. Stevens¹, J. Johnson¹, D. Hoban¹, B. Johnson¹, R. Badal¹, M. Dowzicky²

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

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

REVISED ABSTRACT

Background: Tigecycline (TIG), a new glycolycycline, 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 respective gram positive/negative species. Isolates were collected during 2004 to 2006. **Methods:** A total of 570 clinically significant isolates from Switzerland, Sweden and The Netherlands were analyzed in this survey. 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 guidelines. **Results:** Selected pathogens tested against tigecycline are shown in the table below:

	<i>E. coli</i> and <i>Klebsiella</i> spp. (n=148)		<i>Enterobacter</i> spp. (n=60)		<i>Acinetobacter</i> spp.* (n=37)		<i>P. aeruginosa</i> ** (n=62)	
	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀
Tigecycline	98.6	0.5	100	0.5	n/a	0.25	n/a	16
Amikacin	100	2	100	2	100	4	98.4	8
Cefepime	97.3	0.5	100	0.5	91.9	8	90.3	8
Ceftazidime	99.3	8	90	16	91.9	8	90.3	8
Imipenem	100	0.5	100	1	97.3	1	93.5	2
Levofloxacin	93.9	0.5	98.3	0.06	97.3	0.12	93.5	2
Minocycline	92.6	4	93.3	4	100	0.5	25.8	>16
PipTazo	96.6	2	95	8	97.3	4	95.8	8

	<i>S. aureus</i> (n=75)		<i>Enterococcus</i> spp. (n=48)		<i>S. pneumoniae</i> * (n=46)		<i>S. agalactiae</i> ** (n=30)	
	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀
Tigecycline	100	0.12	100	0.12	n/a	0.5	100	0.06
Levofloxacin	81.3	4	56.3	>32	100	1	96.7	1
Linezolid	100	2	100	2	100	1	100	1
Minocycline	100	0.25	50	8	n/a	4	n/a	8
Vancomycin	100	1	100	2	100	0.5	100	0.5

Conclusion: Overall, the pathogens analyzed from these three countries are still very susceptible to most broad spectrum antimicrobials. Tigecycline's MIC₉₀ of 0.5mcg/ml against gram-positive pathogens (including resistant phenotypes) and MIC₉₀ of 0.5mcg/ml against overall *Enterobacteriaceae* and *Acinetobacter* spp. validate the potent inhibitory activity of TIG against community/hospital pathogens isolated from Switzerland, Sweden, and The Netherlands.

INTRODUCTION

Tigecycline (formerly GAR-936) is a member of a new class of antimicrobial agents, the glycolycyclines. 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 four-fold better than vancomycin and daptomycin [1, 2]. The development of tigecycline is important in that it is 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].

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 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 pathogens collected in population centers in Switzerland, Sweden, and The Netherlands. This study is part of the larger ongoing global Tigecycline Evaluation and Surveillance Trials (T.E.S.T.) program.

RESULTS

The results are listed in the following tables.

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

Organism Name	Drug	%SUS ^a	%INT	%RES	MIC (mcg/ml)	
					MIC ₅₀	MIC ₉₀
<i>E. coli</i> (n=73)	Tigecycline	100	0	0	0.12	0.12
	Amikacin	100	0	0	2	4
	AmoxClav	89	8.2	2.7	4	16
	Ampicillin	58.9	0	41.1	4	>32
	Cefepime	95.9	1.4	2.7	≤0.5	≤0.5
	Ceftazidime	98.6	1.4	0	≤8	≤8
	Ceftriaxone	94.5	0	5.5	≤0.06	0.12
	Imipenem	100	0	0	0.25	0.25
	Levofloxacin	87.7	6.8	5.5	0.03	4
	Minocycline	91.8	6.8	1.4	1	4
<i>K. pneumoniae</i> (n=42)	PipTazo	97.3	2.7	0	0.5	2
	Tigecycline	95.2	2.4	2.4	0.25	0.5
	Amikacin	100	0	0	1	2
	AmoxClav	97.6	2.4	0	2	8
	Ampicillin	0	33.3	66.7	32	>32
	Cefepime	100	0	0	≤0.5	≤0.5
	Ceftazidime	100	0	0	≤8	≤8
	Ceftriaxone	100	0	0	≤0.06	≤0.06
	Imipenem	100	0	0	0.25	0.5
	Levofloxacin	100	0	0	0.03	0.25
<i>K. oxytoca</i> (n=33)	Minocycline	88.1	0	11.9	1	16
	PipTazo	97.6	0	2.4	1	2
	Tigecycline	100	0	0	0.25	0.5
	Amikacin	100	0	0	1	2
	AmoxClav	100	0	0	2	4
	Ampicillin	0	21.2	78.8	>32	>32
	Cefepime	97	3	0	≤0.5	≤0.5
	Ceftazidime	100	0	0	≤8	≤8
	Ceftriaxone	97	0	3	≤0.06	0.25
	Imipenem	100	0	0	0.25	0.5
<i>E. aerogenes</i> (n=17)	Levofloxacin	100	0	0	0.03	0.06
	Minocycline	100	0	0	1	2
	PipTazo	93.9	6.1	0	1	4
	Tigecycline	100	0	0	0.25	0.5
	Amikacin	100	0	0	2	2
	AmoxClav	0	0	100	>32	>32
	Ampicillin	0	0	100	>32	>32
	Cefepime	100	0	0	≤0.5	≤0.5
	Ceftazidime	100	0	0	≤8	≤8
	Ceftriaxone	100	0	0	≤0.06	0.5
<i>E. cloacae</i> (n=40)	Imipenem	100	0	0	1	1
	Levofloxacin	100	0	0	0.03	0.06
	Minocycline	100	0	0	2	2
	PipTazo	100	0	0	2	8
	Tigecycline	100	0	0	0.5	1
	Amikacin	100	0	0	2	2
	AmoxClav	2.5	2.5	95	>32	>32
	Ampicillin	0	5	95	>32	>32
	Cefepime	100	0	0	≤0.5	2
	Ceftazidime	85	2.5	12.5	≤8	32
<i>S. marcescens</i> (n=26)	Ceftriaxone	87.5	7.5	5	0.25	16
	Imipenem	100	0	0	0.5	0.5
	Levofloxacin	100	0	0	0.03	0.06
	Minocycline	92.5	0	7.5	2	4
	PipTazo	92.5	2.5	5	1	8
	Tigecycline	100	0	0	0.5	1
	Amikacin	100	0	0	2	2
	AmoxClav	0	0	100	>32	>32
	Ampicillin	0	0	100	>32	>32
	Cefepime	100	0	0	≤0.5	≤0.5
<i>P. aeruginosa</i> (n=62)	Ceftazidime	100	0	0	≤8	≤8
	Ceftriaxone	96.2	3.8	0	0.12	1
	Imipenem	100	0	0	0.5	1
	Levofloxacin	96.2	0	3.8	0.06	0.12
	Minocycline	100	0	0	2	4
	PipTazo	97.3	0	2.7	≤0.06	4
	Tigecycline	na	na	na	8	16
	Amikacin	98.4	1.6	0	2	8
	Cefepime	90.3	6.5	3.2	2	8
	Ceftazidime	90.3	1.6	8.1	≤8	≤8
<i>S. marcescens</i> (n=26)	Ceftriaxone	29	6.5	64.5	>64	>64
	Imipenem	93.5	6.5	0	1	2
	Levofloxacin	93.5	4.8	1.6	0.5	2
	Minocycline	25.8	27.4	46.8	8	>16
	PipTazo	98.9	0	3.2	2	8
	Tigecycline	na	na	na	8	16
	Amikacin	98.4	1.6	0	2	8
	Cefepime	90.3	6.5	3.2	2	8
	Ceftazidime	90.3	1.6	8.1	≤8	≤8

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
<i>Acinetobacter</i> spp. (n=37)	Tigecycline	na	na	na	0.06	0.25
	Amikacin	100	0	0	1	4
	Cefepime	91.9	8.1	0	2	8
	Ceftazidime	91.9	2.7	5.4	≤8	≤8
	Ceftriaxone	78.4	18.9	2.7	4	16
	Imipenem	97.3	0	2.7	0.25	1
	Levofloxacin	97.3	2.7	0	0.06	0.12
	Minocycline	100	0	0	≤0.5	≤0.5
	PipTazo	97.3	0	2.7	≤0.06	4
	Tigecycline	na	na	na	8	16
<i>P. aeruginosa</i> (n=62)	Amikacin	98.4	1.6	0	2	8
	Cefepime	90.3	6.5	3.2	2	8
	Ceftazidime	90.3	1.6	8.1	≤8	≤8
	Ceftriaxone	29	6.5	64.5	>64	>64
	Imipenem	93.5	6.5	0	1	2
	Levofloxacin	93.5	4.8	1.6	0.5	2
	Minocycline	25.8	27.4	46.8	8	>16
	PipTazo	98.9	0	3.2	2	8
	Tigecycline	na	na	na	8	16
	Amikacin	98.4	1.6	0	2	8

^aInterpretive criteria as defined by CLSI M100-S16 (2006), where available; Tigecycline susceptible breakpoint is according to FDA package insert (Tygicel® 2005), where applicable [9]; na = not available; MIC₉₀ = 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	
<i>S. aureus</i> (n=75)	Tigecycline	100	0	0	0.12	0.12	
	AmoxClav	88	0	12	0.5	8	
	Ampicillin	24	0	76	2	>16	
	Ceftriaxone	86.7	1.3	12	2	>64	
	Imipenem	89.3	0	10.7	0.25	16	
	Levofloxacin	81.3	0	18.7	0.12	4	
	Linezolid	100	0	0	2	2	
	Minocycline	100	0	0	≤0.25	≤0.25	
	Penicillin	17.3	0	82.7	4	>8	
	PipTazo	89.3	0	10.7	0.5	>16	
<i>S. aureus</i> (MR) (n=12)	Vancomycin	100	0	0	0.5	1	
	Tigecycline	100	0	0	0.12	0.25	
	AmoxClav	25	0	75	>8	>8	
	Ampicillin	0	0	100	>16	>16	
	Ceftriaxone	16.7	8.3	75	>64	>64	
	Imipenem	33.3	0	66.7	>16	>16	
	Levofloxacin	16.7	0	83.3	4	16	
	Linezolid	100	0	0	2	2	
	Minocycline	100	0	0	≤0.25	≤0.25	
	Penicillin	0	0	100	>8	>8	
<i>Enterococcus</i> spp. ^b (n=48)	PipTazo	33.3	0	66.7	>16	>16	
	Vancomycin	100	0	0	1	1	
	Tigecycline	100	0	0	0.06	0.12	
	Ampicillin	81.3	0	18.8	1	>16	
	Levofloxacin	56.3	2.1	41.7	1	>32	
	Linezolid	100	0	0	1	2	
	Minocycline	50	41.7	8.3	4	8	
	Penicillin	81.3	0	18.8	4	>8	
	Vancomycin	100	0	0	1	2	
	<i>E. faecalis</i> ^b (n=37)	Tigecycline	100	0	0	0.12	0.12
Ampicillin		100	0	0	1	2	
Levofloxacin		67.6	0	32.4	1	32	
Linezolid		100	0	0	1	2	
Minocycline		43.2	48.6	8.1	8	8	
Penicillin		100	0	0	2	8	
Vancomycin		100	0	0	1	2	
<i>E. faecium</i> ^b (n=11)		Tigecycline	100	0	0	0.03	0.12
		Ampicillin	18.2	0	81.8	>16	>16
		Levofloxacin	18.2	9.1	72.7	32	>32
	Linezolid	100	0	0	1	2	
	Minocycline	72.7	18.2	9.1	≤0.25	8	
	Penicillin	18.2					