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In Vitro Activity of Tigecycline Against Pathogens Isolated from Most Common Body Sites – Eastern European Data T.E.S.T. Program 2008

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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 respective gram-positive/negative species. For the overall T.E.S.T. program isolates were collected from 205 hospital sites in 30 countries from 2004 to 2008. **Methods**: In this survey, clinically significant isolates from 8 East European testing sites (Poland, Hungary, Croatia, Czech Republic, Lithuania, Slovak Republic Slovenia, and Latvia) were analyzed. 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 EUCAST guidelines. **Results**: TIG activity against selected pathogens and body sites are shown in the table below*:

	Blood			Respiratory			Urinary tract		
	n	%S[a]	MIC_{90a}[a]	n	%S[a]	MIC_{90}[a]	n	%S[a]	MIC_{90}[a]
EcKpKo	208	93.8	1	199	97.0	0.5	203	96.1	0.5
Enterobacter spp.	56	66.1	2	145	92.4	1	51	76.5	2
Acinetobacter spp.	45	na	1	107	na	1	22	na	2
S. aureus	129	100	0.25	115	100	0.25	13	100	0.25
Enterococcus spp.	69	100	0.12	13	100	0.25	83	100	0.25
S. pneumoniae	32	na	0.06	119	na	0.12	0		
H. influenzae	3	na	-	209	na	0.5	0		

* na = breakpoints not available.
[a] No MIC_{90} calculated if n<10; %S may not be statistically significant when n's are small.

Conclusions: Tigecycline showed excellent inhibitory activity against all groups of pathogens regardless of isolation site. Tigecycline MIC_{90} of ≤1mg/L against gram-positive pathogens (including resistant phenotypes) and MIC_{90} of ≤2mg/L against *Enterobacteriaceae* and *Acinetobacter* spp. validate the potent inhibitory activity of TIG against Eastern European community/hospital pathogens.

Introduction

Tigecycline is a member of a new class of antimicrobial agents, the glycylcyclines. This synthetic analogue of the tetracyclines exhibits 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.

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 mg/L, including difficult to treat methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and extended-spectrum beta-lactamase (ESBL) producing *Enterobacteriaceae* [3-5]. This study was undertaken to document the *in vitro* activity of tigecycline against significant numbers of clinical pathogens collected in Eastern European laboratories. This study is part of the larger ongoing global Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) program with isolates collected from 1016 testing sites in 53countries from 2004 to 2008.

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 to 2008 from study centers in Poland, Slovak Republic, Slovenia, Croatia, Czech Republic, Lithuania Hungary and Latvia. 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 [6]. 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 mg/L): 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 [6], the US Food and Drug Administration package insert for tigecycline [7], where applicable and EUCAST(8).
- *Escherichia coli*, *Klebsiella pneumoniae*, and *Klebsiella oxytoca* were screened for ESBL activity when MIC results for ceftriaxone were >1 mg/L using broth microdilution panels. ESBL activity was confirmed using the CLSI (2009) phenotypic confirmatory disk test (Oxoid, Ogdensburg, NY, USA) on Mueller-Hinton agar (Remel Inc., Lenexa, KS, USA) according to CLSI (2009) 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; *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. *K. pneumoniae* ATCC 700603 was used for ESBL confirmation by the reference lab. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI (2009) guidelines [6].

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Results

The results are listed in the following tables.

Table 1. *In vitro* activity of tigecycline and comparative agents against 540 blood culture isolates.

					MIC (mg/L)		MIC range (mg/L)	
Organism Name	Drug	%SUS[a]	%INT	%RES	MIC_{50}	MIC_{90}	Low	High
E. coli (n=108)	Tigecycline	100.0	0.0	0.0	0.12	0.25	0.06	1
	Amikacin	100.0	0.0	0.0	2	4	≤0.5	8
	AmoxClav	46.3	19.4	34.3	8	32	2	>32
	Ampicillin	39.8	3.7	56.5	>32	>32	≤0.5	>32
	Cefepime	94.4	1.9	3.7	≤0.5	≤0.5	≤0.5	>32
	Ceftazidime	0.0	99.1	0.9	≤8	≤8	≤8	>32
	Ceftriaxone	94.4	0.0	5.6	≤0.06	0.12	≤0.06	>64
	Levofloxacin	75.0	0.9	24.1	0.03	8	≤0.008	>8
	Meropenem	100.0	0.0	0.0	≤0.06	≤0.06	≤0.06	0.5
	Minocycline	77.8	10.2	12.0	1	16	≤0.5	>16
	PipTazo	95.4	1.9	2.8	1	4	0.12	>128
***Klebsiella* spp.** (n=101)	Tigecycline	87.1	9.9	3.0	0.5	2	0.06	8
	Amikacin	93.1	0.0	6.9	2	8	≤0.5	>64
	AmoxClav	52.5	3.0	44.6	4	32	0.5	>32
	Ampicillin	0.0	0.0	100.0	>32	>32	16	>32
	Cefepime	67.3	5.0	27.7	≤0.5	>32	≤0.5	>32
	Ceftazidime	0.0	71.3	28.7	≤8	>32	≤8	>32
	Ceftriaxone	63.4	2.0	34.7	0.12	>64	≤0.06	>64
	Levofloxacin	71.3	1.0	27.7	0.06	>8	0.015	>8
	Meropenem	100.0	0.0	0.0	≤0.06	0.12	≤0.06	2
	Minocycline	79.2	5.9	14.9	2	>16	≤0.5	>16
	PipTazo	74.3	5.9	19.8	2	128	0.25	>128
Enterobacter spp. (n=56)	Tigecycline	66.1	25.0	8.9	0.5	2	0.12	8
	Amikacin	87.5	3.6	8.9	2	16	≤0.5	>64
	AmoxClav	1.8	0.0	98.2	>32	>32	2	>32
	Ampicillin	0.0	0.0	100.0	>32	>32	16	>32
	Cefepime	55.4	35.7	8.9	≤0.5	8	≤0.5	>32
	Ceftazidime	0.0	50.0	50.0	≤8	>32	≤8	>32
	Ceftriaxone	42.9	1.8	55.4	8	>64	≤0.06	>64
	Levofloxacin	71.4	1.8	26.8	0.06	>8	0.015	>8
	Meropenem	100.0	0.0	0.0	0.12	0.5	≤0.06	2
	Minocycline	58.9	19.6	21.4	4	>16	1	>16
	PipTazo	53.6	0.0	46.4	8	>128	0.25	>128
***Acinetobacter* spp.** (n=45)	Tigecycline	na	na	na	0.5	1	0.03	2
	Amikacin	37.8	2.2	60.0	32	>64	1	>64
	AmoxClav	na	na	na	>32	>32	0.5	>32
	Ampicillin	na	na	na	>32	>32	1	>32
	Cefepime	35.6	35.6	28.9	16	32	≤0.5	>32
	Ceftazidime	22.2	8.9	68.9	>32	>32	≤8	>32
	Ceftriaxone	11.1	8.9	80.0	>64	>64	1	>64
	Levofloxacin	22.2	24.4	53.3	4	8	0.06	8
	Meropenem	57.9	28.9	13.2	1	16	≤0.06	>16
	Minocycline	97.8	2.2	0.0	≤0.5	2	≤0.5	8
	PipTazo	28.9	26.7	44.4	64	>128	≤0.06	>128
S. aureus (n=129)	Tigecycline	100.0	0.0	0.0	0.12	0.25	0.03	0.5
	AmoxClav	79.8	0.0	20.2	1	>8	0.06	>8
	Ampicillin	48.8	0.0	51.2	4	>16	≤0.06	>16
	Ceftriaxone	79.1	0.0	20.9	2	>64	0.5	>64
	Levofloxacin	79.1	2.3	18.6	0.25	4	≤0.06	32
	Linezolid	100.0	0.0	0.0	2	2	≤0.5	4
	Meropenem	77.1	0.0	22.9	≤0.12	>16	≤0.12	>16
	Minocycline	94.6	3.9	1.6	≤0.25	0.5	≤0.25	4
	Penicillin	17.8	0.0	82.2	8	>8	≤0.06	>8
	PipTazo	82.2	0.0	17.8	1	>16	≤0.25	>16
	Vancomycin	100.0	0.0	0.0	1	1	0.25	2
***Enterococcus* spp.** (n=69)	Tigecycline	100.0	0.0	0.0	0.12	0.12	≤0.008	0.25
	Ampicillin	75.4	0.0	24.6	1	>16	≤0.06	>16
	Levofloxacin	43.5	0.0	56.5	2	>32	0.12	>32
	Linezolid	100.0	0.0	0.0	2	2	≤0.5	4
	Minocycline	60.9	21.7	17.4	4	>8	≤0.25	>8
	Penicillin	73.9	0.0	26.1	2	>8	0.12	>8
	Vancomycin	97.1	0.0	2.9	1	2	0.25	>32
S. pneumoniae[c] (n=32)	Tigecycline	na	na	na	0.03	0.06	0.015	0.12
	AmoxClav	100.0	0.0	0.0	≤0.03	≤0.03	≤0.03	2
	Azithromycin	83.3	0.0	16.7	0.12	64	≤0.03	64
	Ceftriaxone	96.9	3.1	0.0	≤0.03	0.06	≤0.03	2
	Clarithromycin	83.3	0.0	16.7	0.03	32	≤0.015	64
	Clindamycin	91.7	0.0	8.3	0.06	0.25	≤0.015	64
	Levofloxacin	100.0	0.0	0.0	0.5	1	0.12	1
	Linezolid	100.0	0.0	0.0	≤0.5	1	≤0.5	1
	Meropenem	100.0	0.0	0.0	≤0.12	≤0.12	≤0.12	1
	Minocycline	90.6	0.0	9.4	≤0.25	0.5	≤0.25	8
	Penicillin	81.3	18.8	0.0	≤0.06	0.5	≤0.06	2
	Vancomycin	100.0	0.0	0.0	0.25	0.5	≤0.12	0.5

na = breakpoints not available.
[a] Interpretive criteria as defined by CLSI, M100-S19 (2009), where available; tigecycline susceptibility breakpoints are according to FDA package insert (Tygacil®, 2005), where available [7] or EUCAST[8]

Table 2. *In vitro* activity of tigecycline and comparative agents against 292 urinary tract isolates.

					MIC (mg/L)		MIC range (mg/L)	
Organism Name	Drug	%SUS[a]	%INT	%RES	MIC_{50}	MIC_{90}	Low	High
E. coli (n=131)	Tigecycline	100.0	0.0	0.0	0.12	0.25	≤0.008	1
	Amikacin	98.5	1.5	0.0	2	4	≤0.5	16
	AmoxClav	56.5	23.7	19.8	4	16	1	>32
	Ampicillin	45.8	1.5	52.7	32	>32	≤0.5	>32
	Cefepime	95.4	3.1	1.5	≤0.5	≤0.5	≤0.5	>32
	Ceftazidime	0.0	98.5	1.5	≤8	≤8	≤8	>32
	Ceftriaxone	97.7	0.0	2.3	≤0.06	0.12	≤0.06	>64
	Levofloxacin	81.7	0.0	18.3	0.03	8	≤0.008	>8
	Meropenem	100.0	0.0	0.0	≤0.06	≤0.06	≤0.06	0.12
	Minocycline	79.4	11.5	9.2	1	8	≤0.5	>16
	PipTazo	93.9	1.5	4.6	1	4	0.12	128
***Klebsiella* spp.** (n=75)	Tigecycline	88.0	8.0	4.0	0.5	2	0.06	8
	Amikacin	80.0	14.7	5.3	2	16	≤0.5	>64
	AmoxClav	53.3	6.7	40.0	4	>32	1	>32
	Ampicillin	1.3	0.0	98.7	>32	>32	1	>32
	Cefepime	62.7	16.0	21.3	≤0.5	>32	≤0.5	>32
	Ceftazidime	0.0	72.0	28.0	≤8	>32	≤8	>32
	Ceftriaxone	58.7	2.7	38.7	0.12	>64	≤0.06	>64
	Levofloxacin	74.7	0.0	25.3	0.06	8	≤0.008	>8
	Meropenem	97.9	2.1	0.0	≤0.06	0.25	≤0.06	4
	Minocycline	72.0	13.3	14.7	2	16	≤0.5	>16
	PipTazo	69.3	4.0	26.7	2	>128	0.12	>128
Enterobacter spp. (n=51)	Tigecycline	76.5	13.7	9.8	0.5	2	0.12	4
	Amikacin	82.4	3.9	13.7	2	32	≤0.5	>64
	AmoxClav	3.9	0.0	96.1	>32	>32	1	>32
	Ampicillin	0.0	0.0	100.0	>32	>32	16	>32
	Cefepime	54.9	15.7	29.4	1	32	≤0.5	>32
	Ceftazidime	0.0	66.7	33.3	≤8	>32	≤8	>32
	Ceftriaxone	37.3	9.8	52.9	4	>64	≤0.06	>64
	Levofloxacin	58.8	2.0	39.2	0.12	>8	0.015	>8
	Meropenem	100.0	0.0	0.0	≤0.06	0.25	≤0.06	1
	Minocycline	68.6	9.8	21.6	2	16	≤0.5	>16
	PipTazo	54.9	5.9	39.2	8	>128	0.25	>128
***Acinetobacter* spp.** (n=22)	Tigecycline	na	na	na	0.25	2	0.06	2
	Amikacin	77.3	0.0	22.7	2	>64	≤0.5	>64
	AmoxClav	na	na	na	32	>32	0.25	>32
	Ampicillin	na	na	na	>32	>32	≤0.5	>32
	Cefepime	50.0	4.5	45.5	8	>32	≤0.5	>32
	Ceftazidime	50.0	0.0	50.0	≤8	>32	≤8	>32
	Ceftriaxone	40.9	4.5	54.5	64	>64	0.12	>64
	Levofloxacin	40.9	9.1	50.0	2	>8	0.015	>8
	Meropenem	76.5	11.8	11.8	1	16	≤0.06	>16
	Minocycline	95.5	4.5	0.0	≤0.5	4	≤0.5	8
	PipTazo	54.5	4.5	40.9	2	>128	≤0.06	>128
S. aureus (n=13)	Tigecycline	100.0	0.0	0.0	0.12	0.25	0.06	0.25
	AmoxClav	92.3	0.0	7.7	0.5	1	0.12	4
	Ampicillin	61.5	0.0	38.5	4	16	≤0.06	16
	Ceftriaxone	92.3	0.0	7.7	2	4	0.12	16
	Levofloxacin	92.3	0.0	7.7	0.12	0.25	≤0.06	32
	Linezolid	100.0	0.0	0.0	2	2	1	2
	Meropenem	83.3	0.0	16.7	≤0.12	1	≤0.12	1
	Minocycline	100.0	0.0	0.0	≤0.25	0.5	≤0.25	0.5
	Penicillin	15.4	0.0	84.6	4	>8	≤0.06	>8
	PipTazo	92.3	0.0	7.7	1	1	0.5	4
	Vancomycin	100.0	0.0	0.0	0.5	1	0.5	1
***Enterococcus* spp.** (n=83)	Tigecycline	100.0	0.0	0.0	0.12	0.25	0.03	0.25
	Ampicillin	80.7	1.2	18.1	1	>16	0.25	>16
	Levofloxacin	50.6	0.0	49.4	1	>32	0.25	>32
	Linezolid	100.0	0.0	0.0	2	2	≤0.5	2
	Minocycline	45.8	27.7	26.5	8	>8	≤0.25	>8
	Penicillin	79.5	0.0	20.5	4	>8	0.5	>8
	Vancomycin	95.2	0.0	4.8	1	2	0.25	>32

na = breakpoints not available.
[a] Interpretive criteria as defined by CLSI, M100-S19 (2009), where available; tigecycline susceptibility breakpoints are according to FDA package insert (Tygacil®, 2005), where available [7] or EUCAST[8].

Table 3. *In vitro* activity of tigecycline and comparative agents against 941 respiratory isolates.

					MIC (mg/L)		MIC range (mg/L)	
Organism Name	Drug	%SUS[a]	%INT	%RES	MIC_{50}	MIC_{90}	Low	High
E. coli (n=75)	Tigecycline	100.0	0.0	0.0	0.12	0.5	0.03	1
	Amikacin	93.3	2.7	4.0	2	8	≤0.5	>64
	AmoxClav	49.3	17.3	33.3	8	32	1	>32
	Ampicillin	45.3	2.7	52.0	>32	>32	≤0.5	>32
	Cefepime	89.3	2.7	8.0	≤0.5	2	≤0.5	>32
	Ceftazidime	0.0	90.7	9.3	≤8	≤8	≤8	>32
	Ceftriaxone	89.3	0.0	10.7	≤0.06	16	≤0.06	>64
	Levofloxacin	80.0	1.3	18.7	0.03	>8	≤0.008	>8
	Meropenem	98.4	1.6	0.0	≤0.06	0.12	≤0.06	8
	Minocycline	81.3	9.3	9.3	1	8	≤0.5	>16
	PipTazo	88.0	1.3	10.7	1	32	≤0.06	>128
***Klebsiella* spp.** (n=133)	Tigecycline	93.2	5.3	1.5	0.5	1	0.06	4
	Amikacin	94.0	3.0	3.0	2	8	≤0.5	>64
	AmoxClav	67.7	5.3	27.1	2	32	0.5	>32
	Ampicillin	0.0	0.8	99.2	>32	>32	8	>32
	Cefepime	76.7	9.0	14.3	≤0.5	32	≤0.5	>32
	Ceftazidime	0.0	82.7	17.3	≤8	32	≤8	>32
	Ceftriaxone	75.2	2.3	22.6	≤0.06	>64	≤0.06	>64
	Levofloxacin	85.7	2.3	12.0	0.06	4	≤0.008	>8
	Meropenem	100.0	0.0	0.0	≤0.06	0.12	≤0.06	2
	Minocycline	87.2	7.5	5.3	2	8	≤0.5	>16
	PipTazo	85.7	3.8	10.5	2	32	0.12	>128
All ESBL producers (n=25)	Tigecycline	88.0	8.0	4.0	0.5	2	0.06	4
	Amikacin	68.0	12.0	20.0	8	>64	1	>64
	AmoxClav	0.0	12.0	88.0	32	>32	8	>32
	Ampicillin	0.0	0.0	100.0	>32	>32	>32	>32
	Cefepime	4.0	32.0	64.0	>32	>32	1	>32
	Ceftazidime	0.0	32.0	68.0	32	>32	≤8	>32
	Ceftriaxone	4.0	4.0	92.0	>64	>64	0.5	>64
	Levofloxacin	40.0	8.0	52.0	4	>8	0.015	>8
	Meropenem	100.0	0.0	0.0	≤0.06	1	≤0.06	2
	Minocycline	56.0	8.0	36.0	4	>16	≤0.5	>16
	PipTazo	48.0	8.0	44.0	16	>128	1	>128
Enterobacter spp. (n=145)	Tigecycline	92.4	5.5	2.1	0.5	1	0.06	4
	Amikacin	94.5	0.7	4.8	2	4	≤0.5	>64
	AmoxClav	0.7	0.7	98.6	>32	>32	2	>32
	Ampicillin	0.7	0.0	99.3	>32	>32	4	>32
	Cefepime	77.2	17.9	4.8	≤0.5	4	≤0.5	>32
	Ceftazidime	0.0	73.8	26.2	≤8	>32	≤8	>32
	Ceftriaxone	64.8	3.4	31.7	0.5	64	≤0.06	>64
	Levofloxacin	89.7	1.4	9.0	0.06	2	0.015	>8
	Meropenem	98.2	1.8	0.0	≤0.06	0.25	≤0.06	4
	Minocycline	82.8	9.0	8.3	2	8	≤0.5	>16
	PipTazo	76.6	4.1	19.3	2	64	≤0.06	>128
***Acinetobacter* spp.** (n=107)	Tigecycline	na	na	na	0.5	1	0.015	16
	Amikacin	65.4	2.8	31.8	4	>64	≤0.5	>64
	AmoxClav	na	na	na	>32	>32	1	>32
	Ampicillin	na	na	na	>32	>32	1	>32
	Cefepime	40.2	15.0	44.9	16	>32	≤0.5	>32
	Ceftazidime	29.0	11.2	59.8	32	>32	≤8	>32
	Ceftriaxone	17.8	14.0	68.2	>64	>64	1	>64
	Levofloxacin	30.8	10.3	58.9	4	>8	0.03	>8
	Meropenem	64.7	16.2	19.1	2	16	≤0.06	>16
	Minocycline	96.3	1.9	1.9	1	4	≤0.5	>16
	PipTazo	43.0	10.3	46.7	64	>128	≤0.06	>128
S. aureus (n=115)	Tigecycline	100.0	0.0	0.0	0.12	0.25	0.03	0.5
	AmoxClav	82.6	0.0	17.4	1	>8	0.06	>8
	Ampicillin	47.8	0.0	52.2	8	>16	≤0.06	>16
	Ceftriaxone	76.5	0.0	23.5	4	>64	0.5	>64
	Levofloxacin	79.1	0.9	20.0	0.25	4	≤0.06	16
	Linezolid	100.0	0.0	0.0	2	2	≤0.5	4
	Meropenem	72.6	0.0	27.4	≤0.12	>16	≤0.12	>16
	Minocycline	92.2	1.7	6.1	≤0.25	0.5	≤0.25	>8
	Penicillin	16.5	0.0	83.5	>8	>8	≤0.06	>8
	PipTazo	81.7	0.0	18.3	1	>16	≤0.25	>16
	Vancomycin	100.0	0.0	0.0	1	1	0.25	2
***Enterococcus* spp.**[c] (n=13)	Tigecycline	100.0	0.0	0.0	0.12	0.25	0.06	0.25
	Ampicillin	84.6	0.0	15.4	1	>16	0.5	>16
	Levofloxacin	38.5	0.0	61.5	32	>32	0.5	>32
	Linezolid	100.0	0.0	0.0	2	2	1	2
	Minocycline	46.2	30.8	23.1	8	>8	≤0.25	>8
	Penicillin	84.6	0.0	15.4	4	>8	2	>8
	Vancomycin	92.3	0.0	7.7	1	4	0.5	>32
S. pneumoniae (n=119)	Tigecycline	na	na	na	0.03	0.12	0.015	0.12
	AmoxClav	100.0	0.0	0.0	≤0.03	1	≤0.03	2
	Azithromycin	79.3	0.0	20.7	0.12	>64	≤0.03	>64
	Ceftriaxone	92.4	7.6	0.0	≤0.03	0.5	≤0.03	2
	Clarithromycin	79.3	0.0	20.7	0.03	64	≤0.015	>64
	Clindamycin	85.9	0.0	14.1	0.06	32	≤0.015	>64
	Levofloxacin	100.0	0.0	0.0	0.5	1	0.12	2
	Linezolid	100.0	0.0	0.0	≤0.5	1	≤0.5	1
	Meropenem	100.0	0.0	0.0	≤0.12	0.25	≤0.12	1
	Minocycline	78.2	3.4	18.5	≤0.25	8	≤0.25	>8
	Penicillin	73.1	24.4	2.5	≤0.06	2	≤0.06	4
	Vancomycin	100.0	0.0	0.0	0.25	0.5	≤0.12	1
H. influenzae (n=209)	Tigecycline	na	na	na	0.25	0.5	≤0.008	0.5
	AmoxClav	95.7	0.0	4.3	0.5	1	≤0.12	8
	Ampicillin	92.3	0.0	7.7	≤0.5	1	≤0.5	>32
	Cefepime	97.6	0.0	2.4	≤0.5	≤0.5	≤0.5	4
	Ceftriaxone	99.0	0.0	1.0	≤0.06	≤0.06	≤0.06	1
	Levofloxacin	100.0	0.0	0.0	0.015	0.03	≤0.008	1
	Meropenem	100.0	0.0	0.0	≤0.06	0.12	≤0.06	0.25
	PipTazo	100.0	0.0	0.0	≤0.06	≤0.06	≤0.06	0.25

na = breakpoints not available.
[a] Interpretive criteria as defined by CLSI, M100-S19 (2009), where available; tigecycline susceptibility breakpoints are according to FDA package insert (Tygacil®, 2005), where available [7] or EUCAST[8].

Conclusions

- Tigecycline's MIC_{90} of ≤0.25mg/L against *S. aureus* (including MRSA) and *Enterococcus* spp. (including VRE strains) and was the lowest of all antimicrobials evaluated in this study.
- Tigecycline inhibited all *Enterobacteriaceae* at MICs of ≤8 mg/L with an MIC_{90} of 0.25-2mg/L.
- Tigecycline inhibited all *Acinetobacter* spp. at MICs of ≤2 mg/L with an MIC_{90} of ≤1mg/L. This potent inhibitory activity was only matched by minocycline. All other antimicrobials tested showed higher MICs.
- Tigecycline demonstrated excellent inhibitory activity against *S. pneumoniae* and *H. influenzae*, without regard to susceptibility to penicillin or β-lactamase production.
- The *in vitro* activity of tigecycline in this study validates its potent inhibitory activity against Eastern European community/hospital pathogens.