

Revised Abstract

Background: Tigecycline is approved for use in United States for the treatment of complicated intra-abdominal, skin and soft tissue infections and community-acquired pneumonia. The Tigecycline Evaluation and Surveillance Trial (TEST) program is an ongoing global surveillance study. The current study reports trends in susceptibility of multiple pathogens from respiratory sources collected from 2004 – 2009 to tigecycline and comparator agents. **Methods:** A total of 2,259 clinical isolates from respiratory sources were collected from 539 cumulative investigative sites in the United States. Clinical isolates were identified to the species level at each participating site and confirmed by the central laboratory. Minimum Inhibitory Concentrations (MICs) were determined by the local laboratory using supplied broth microdilution panels and interpreted according to CLSI/FDA guidelines. **Results:** Summary data for tigecycline and key respiratory species by year are as follows:

Organism	Tigecycline MIC ₉₀ / %Susceptible/(N)		2008		2009	
	2004-2006	2007	2008	2009	2008	2009
<i>Acinetobacter</i> spp	1/na(57)	1/na(17)	1/na(11)	8/na(5)		
<i>Enterobacter</i> spp	4/100(80)	1/100(20)	1/100(17)	2/94.1(17)		
<i>H. influenzae</i>	0.25/100(443)	0.25/99.5(1394)	0.25/97.2(72)	0.25/100(38)		
<i>K. pneumoniae</i>	2/100(57)	1/96(25)	2/100(17)	1/100(10)		
<i>P. aeruginosa</i>	>16/na(165)	16/na(76)	16/na(29)	>16/na(14)		
<i>Serratia</i> spp	2/100(94)	2/100(32)	2/95(20)	4/57(17)		
<i>S. aureus</i>	0.25/100(113)	0.25/100(41)	0.25/100(13)	0.5/100(8)		
<i>S. pneumoniae</i>	0.25/83.2(370)	0.06/95.6(114)	0.06/90.9(44)	0.03/100(39)		

%S defined by FDA (Tygacil®, 2010) where available; na = breakpoints not defined.

Conclusions: The majority of isolates were susceptible to tigecycline in this study. High susceptibility rates were observed for all pathogens for which clinical breakpoints exist for tigecycline.

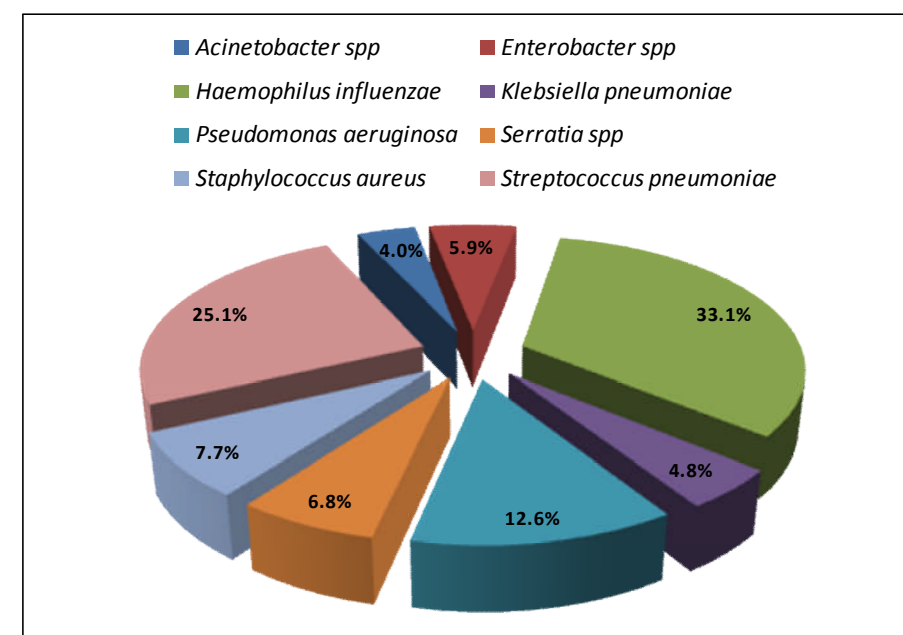
Introduction

Tigecycline is approved for use in United States for the treatment of complicated intra-abdominal, skin and soft tissue infections and bacterial community-acquired pneumonia (CAP). New guidelines for the management of in-patient and out-patient community-acquired pneumonia have recently been published [1]. This study describes the activity of tigecycline and comparators against multiple respiratory pathogens, including *S. pneumoniae*, an important etiologic agent that was added in 2009 to the FDA Tygacil® monograph for the treatment of CAP [2]. Trends in susceptibility are reported for pathogens collected from 2004 – 2009 to tigecycline and comparator agents in the United States as part of the larger ongoing global Tigecycline Evaluation and Surveillance Trial (TEST).

Materials & Methods

- Clinical isolates:** Isolates were identified to the species level and MICs determined at each participating laboratory. All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of medical history, antimicrobial use, age, or gender. Sites identified each study isolate utilizing local laboratory criteria. All 2,259 respiratory isolates were collected from outpatients during the period 2004 - 2009 and from 539 cumulative sites in the U.S.
- Susceptibility testing:** Minimum inhibitory concentrations (MICs) were determined using broth microdilution panels manufactured by MicroScan (Siemens Medical Solutions Diagnostics, West Sacramento, CA, USA) or Trek Diagnostics (TREK Diagnostic Systems, Cleveland, OH, USA), following manufacturer and Clinical and Laboratory Standards Institute (CLSI) instructions for broth microdilution testing [3]. Susceptibility was determined using clinical breakpoints published by the CLSI [4] and the FDA (tigecycline) [2].
- Quality Control:** Quality controls (QC) were performed by each testing site on each day of testing using appropriate ATCC control strains. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI (2011) guidelines [4].

Figure 1. Distribution of 2,259 community-acquired pneumococcal isolates from the United States, 2004-2009.



References

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Results

Table 1. *In vitro* activity of tigecycline and comparators against respiratory isolates from 2004-2006 in the United States.^a

Drugs	N	Tigecycline		Amikacin		AmoxClav		Ampicillin		Cefepime		Ceftriaxone		Levofloxacin		Linezolid		Meropenem		Minocycline		Penicillin		Pip-tazo		Vancomycin		
		MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	
<i>Acinetobacter</i> spp	57	1	na	64	95.0	>32	na	>32	na	>32	70.6	>64	60.0	>8	75.0	na	na	8	100	na	na	128	82.4	na	na	na	na	
<i>Enterobacter</i> spp	80	4	100	4	100	>32	8.6	>32	na	4	100	64	91.4	0.5	97.1	na	na	8	91.4	na	na	128	100	na	na	na	na	
<i>H. influenzae</i>	443	0.25	100	8	na	2	100	>32	74.7	<=0.5	100	<=0.06	100	0.03	100	na	na	1	na	na	na	<=0.06	100	na	na	na	na	
beta-lactamase negative	317	0.25	100	8	na	1	100	1	99.2	<=0.5	100	<=0.06	100	0.03	100	na	na	1	na	na	na	<=0.06	100	na	na	na	na	
beta-lactamase positive	126	0.25	100	8	na	2	100	>32	0	<=0.5	100	<=0.06	100	0.015	100	na	na	1	na	na	na	<=0.06	100	na	na	na	na	
<i>Klebsiella pneumoniae</i>	57	2	100	32	100	8	100	>32	8.3	16	100	32	91.7	>8	100	na	na	16	91.7	na	na	32	100	na	na	na	na	
ESBL	8	--	8.8	--	8.8	--	8.8	--	0.8	--	8.8	--	0.8	--	8.8	na	na	--	8.8	na	na	--	8.8	na	na	na	na	
non ESBL	49	2	100	4	100	4	100	>32	9.1	<=0.5	100	0.5	100	0.25	100	na	na	16	90.9	na	na	4	100	na	na	na	na	
<i>P. aeruginosa</i>	165	>16	na	32	100	>32	na	>32	na	16	90.5	>64	42.9	>8	73.8	na	na	>16	na	na	na	32	100	na	na	na	na	na
<i>Serratia</i> spp	94	2	100	8	100	>32	2.9	>32	2.8	1	100	4	91.7	1	100	na	na	4	100	na	na	4	100	na	na	na	na	na
<i>S. aureus</i>	113	0.25	100	na	na	>8	75.0	>16	23.4	na	na	>64	75.0	>32	71.4	4	100	1	100	>8	21.3	16	75.0	1	100	na	na	na
MRSA	43	0.5	100	na	na	>8	0	>16	0	na	na	>64	0	>32	31.3	4	100	1	100	>8	0	>16	0	2	100	na	na	na
MSSA	70	0.25	100	na	na	2	100	>16	40.7	na	na	8	100	2	90.9	4	100	0.5	100	>8	37.0	2	100	1	100	na	na	na
<i>S. pneumoniae</i>	370	0.25	83.2	na	na	4	93.4	8	na	na	1	100	1	100	1	100	4	na	2	54.8	4	na	0.5	100	na	na	na	na
penicillin resistant	112	0.25	82.3	na	na	2	100	2	na	na	na	0.5	100	1	97.6	1	100	8	na	1	0	2	na	0.5	100	na	na	na
penicillin intermediate	64	0.25	81.6	na	na	8	57.9	8	na	na	na	2	100	1	100	1	100	4	na	4	0	4	na	0.5	100	na	na	na
penicillin sensitive	194	0.25	84.8	na	na	<=0.03	100	<=0.06	na	na	na	0.06	100	1	100	1	100	2	na	<=0.06	100	<=0.25	na	0.5	100	na	na	na

^aInterpretive criteria defined in CLSI document M100-S21 (2011), where available. Tigecycline breakpoints are defined by FDA (Tygacil®, 2010). na = no breakpoints and/or interpretive criteria unavailable. -- = For n<10, MIC₉₀ and %S are not shown; susceptibility is reported as n S / n total. Meropenem was not included for testing by the investigators during 2004-2006.

Table 3. *In vitro* activity of tigecycline and comparators against respiratory isolates from 2008 in the United States.^a

Drugs	N	Tigecycline		Amikacin		AmoxClav		Ampicillin		Cefepime		Ceftriaxone		Levofloxacin		Linezolid		Meropenem		Minocycline		Penicillin		Pip-tazo		Vancomycin	
		MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S
<i>Acinetobacter</i> spp	11	1	na	2	100	32	na	>32	na	8	90.9	32	81.8	0.25	90.9	na	na	1	100	4	90.9	na	na	16	90.9	na	na
<i>Enterobacter</i> spp	17	1	100	4	100	>32	0	>32	0	1	100	8	64.7	2	100	na	na	0.12	100	16	82.4	na	na	16	94.1	na	na
<i>H. influenzae</i>	72	0.25	97.2	8	na	2	100	>32	73.6	<=0.5	100	<=0.06	100	0.03	100	na	na	0.12	100	2	na	na	<=0.06	100	na	na	na
beta-lactamase negative	54	0.25	100	8	na	1	100	1	98.2	<=0.5	100	<=0.06	100	0.03	100	na	na	0.12	100	2	na	na	<=0.06	100	na	na	na
beta-lactamase positive	18	0.5	88.9	8	na	4	100	>32	0	<=0.5	100	<=0.06	100	0.03	100	na	na	0.12	100	2	na	na	<=0.06	100	na	na	na
<i>Klebsiella pneumoniae</i>	17	2	100	8	94.1	32	88.2	>32	0	1	94.1	4	88.2	4	88.2	na	na	0.12	94.1	8	70.6	na	na	16	94.1	na	na
ESBL	2	0.5	100	64	50.0	>32	0	>32	0	32	50.0	>64	0	>8	50.0	na	na	16	50.0	8	50.0	na	na	>128	50.0	na	na
non ESBL	15	2	100	4	100	4	100	>32	0	<=0.5	100	0.12	100	0.5	93.3	na	na	0.12	100	8	73.3	na	na	8	100	na	na
<i>P. aeruginosa</i>	29	16	na	16	93.1	>32	na	>32	na	16	86.2	>64	31.0	8	72.4	na	na	4	93.1	>16	na	na	128	86.2	na	na	na
<i>Serratia</i> spp	20	2	95.0	4	100	>32	0	>32	0	1	100	2	85.0	0.5	100	na	na	0.12	100	8	60.0	na	na	8	95.0	na	na
<i>S. aureus</i>	13	0.25	100	na	na	>8	69.2	>16	15.4	na	na	>64	69.2	16	53.9	2	100	4	69.2	0.5	100	>8	15.4	>16	69.2	1	100
MRSA	4	0.25	100	na	na	>8	0	>16	0	na	na	>64	0	32	0	4	100	8	0	<=0.25	100	>8	0	>16	0	1	100
MSSA	9	0.25	100	na	na	1	100	>16	22.2	na	na	4	100	4	77.8	2	100	4	100	0.5	100	>8	22.2	4	100	1	100
<i>S. pneumoniae</i>	44	0.06	100	na	na	8	77.3	8	na	na	na	2	86.4	1	97.7	2	100	1	72.7	>8	na	4	50.0	8	na	0.5	100
penicillin resistant	11	0.03	100	na	na	8	9.1	16	na	na	na	2	45.5	1	90.9	1	100	1	0	>8	na	8	0	8	na	0.5	100
penicillin intermediate	11	0.06	100	na	na	0.5	100	2	na	na	na	0.25	100</														