EV0508

In vitro Activity of Tigecycline and Comparators against Cephalosporin-Resistant Isolates of *Escherichia coli* and *Klebsiella pneumoniae* from Europe: TEST 2014-2016

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Revised Abstract

Background: Test monitors the *in vitro* activity of the glycylcycline tigecycline and comparator antimicrobial agents against clinical isolates collected in Europe from a variety of infectious processes. This study reports the *in vitro* activity of tigecycline against *K. pneumoniae* and *E.coli* including cephalosporin resistant isolates.
Methods: Non-duplicate clinical isolates were collected from defined infection sites from 21 European countries. Isolates were identified to the species level at each site. Susceptibility testing was performed by CLSI broth micro-dilution by the local laboratory using supplied panels and interpreted using EUCAST breakpoints. Confirmation of extended-spectrum-β-lactamase (ESBL) activity was performed at a central laboratory.
Results: 10332 isolates of *E. coli* and *K. pneumoniae* were collected from sites in Europe. ESBL rates were 29.9% and 18.9% for *K. pneumoniae* and *E. coli* respectively. Cephalosporin resistance (resistant to all cephems) rates were 35.5% and 16.5% for *K. pneumoniae* and *E. coli* respectively. Susceptibility of All, cephalosporin resistant and ESBL producers are shown in the following table.

Drug	Organism (n) %Susc. All/%S Cephalosporin-R			
	K. pneumoniae (4401/1562)	*K. Pneumoniae* ESBL(1315/1200)	*E. coli* (5931/980)	*E. coli* ESBL (1122/867)
TGC	84/75.3	75.7/75.1	99.4/98.8	99.2/99.1
AMK	91.7/79.1	91.7/91.5	98/92.7	93.9/93.3
FEP	60.5/0	3.2/0	77.8/0	7.8/0
CRO	59.8/0	1.4/0	77/0	1/0
LVX	64.5/21.4	27.5/24.8	63.7/14.2	17.9/14.9
MEM	89.7/71.4	87.7/86.6	99.7/98.7	99.6/99.4
TZP	71.1/38	49.1/46.6	89.5/74.6	79.9/77.4

AMK=Amikacin, FEP=Cefepime, CRO=Ceftriaxone, LVX=Levofloxacin, MEM=Meropenem, TZP=Piperacillin-Tazobactam, TGC=Tigecycline

Conclusions: Tigecycline had good *in vitro* activity against both *K. pneumoniae* and *E. coli* including ESBL producers or cephalosporin resistant with amikacin more active against *K. pneumoniae* ESBL producers. Overall activity of tigecycline was comparable to amikacin and meropenem against most isolates.

Introduction

The Tigecycline European Surveillance Trial (TEST) program is now in its 14th year of monitoring the activity of tigecycline and comparator antimicrobials against clinically significant pathogens collected in European countries from multiple infection sources. TEST continues to monitor the increasing prevalence of ESBLs in *Enterobacteriaceae* and the susceptibility of these isolates to first line antibiotics used to treat infections caused by these pathogens. This report focuses on the evaluation of *E. coli* and *K. pneumoniae*, including ESBL-producing isolates from Europe during 2014-2016 surveillance.

Materials & Methods

ESBL producing and cephalosporin resistant *E. coli* and *K. pneumoniae* were analyzed from a collection of *Enterobacteriaceae* from 817 cumulative sites in 21 European countries (Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Spain, Sweden, Switzerland and the United Kingdom) during 2014-2016. MIC values were determined by broth microdilution and interpreted using current CLSI/FDA (tigecycline) and EUCAST guidelines. Cephalosporin resistance was determined by ceftriaxone and cefepime susceptibility.

- All isolates were derived from multiple infection sources including blood, respiratory, urine, skin and skin structure. Only one isolate per patient was accepted into the study.
- Organism collection, transport, confirmation of organism identification, susceptibility testing, and development and management of a centralized database were coordinated by International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method using MicroScan (Beckman Coulter, West Sacramento, CA). All antimicrobials were supplied by the panel manufacturers.
- MIC interpretive criteria followed published EUCAST guidelines [2].
- Quality controls (QC) were performed on each day of testing using appropriate ATCC control strains, following CLSI and manufacturer guidelines. Results were included in the analysis only when corresponding QC results were within the acceptable ranges [3].

Results

Table 1. In vitro susceptibility of all *E. coli* and *K. pneumoniae* collected from Europe (TEST surveillance 2014-2016)

Organism (n)	Drug	% S	% I	% R	MIC_{50}	MIC_{90}	MIC range
E. coli (5,931)	Tigecycline	99.4	0.5	0.1	0.12	0.25	≤0.008 - >8
	Amikacin	98.0	1.4	0.6	2	4	≤ 0.5 - >64
	Cefepime	77.8	5.3	16.9	≤0.5	32	≤0.5 - >32
	Ceftriaxone	77.0	0.6	22.5	≤0.06	>32	≤0.06 - >32
	Levofloxacin	63.7	1.3	35.1	0.06	>8	≤0.008 - >8
	Meropenem	99.7	0.2	0.1	≤0.06	≤0.06	≤0.06 - >16
	Pip-Tazo	89.5	2.7	7.9	1	16	≤0.06 - >128
K. pneumoniae (4,401)	Tigecycline	84.0	9.6	6.4	0.5	2	0.03 - >8
	Amikacin	91.7	5.5	2.8	2	8	≤0.5 - >64
	Cefepime	60.5	3.8	35.7	≤0.5	>32	≤0.5 - >32
	Ceftriaxone	59.8	0.7	39.5	0.12	>32	≤0.06 - >32
	Levofloxacin	64.5	3.4	32.1	0.12	>8	≤0.008 - >8
	Meropenem	89.7	1.4	8.9	≤0.06	4	≤0.06 - >16
	Pip-Tazo	71.1	4.5	24.5	4	>128	≤0.06 - >128

Table 2. In vitro susceptibility of ESBL *E. coli* and *K. pneumoniae* collected from Europe (TEST surveillance 2014-2016)

Organism (n)	Drug	% S	% I	% R	MIC_{50}	MIC_{90}	MIC range
E. coli ESBL (1,122)	Tigecycline	99.2	0.8	0	0.12	0.5	0.015 - 2
	Amikacin	93.9	3.9	2.1	4	8	≤0.5 - >64
	Cefepime	7.8	15.0	77.3	16	>32	≤0.5 - >32
	Ceftriaxone	1.0	1.2	97.9	>32	>32	≤0.06 - >32
	Levofloxacin	17.9	1.0	81.1	8	>8	≤0.008 - >8
	Meropenem	99.6	0.5	0	≤0.06	0.12	≤0.06 - 8
	Pip-Tazo	79.9	8.6	11.6	2	32	0.12 - >128
K. pneumoniae ESBL (1,315)	Tigecycline	75.7	13.9	10.3	0.5	4	0.06 - >8
	Amikacin	91.7	4.5	3.8	4	8	≤0.5 - >64
	Cefepime	3.2	5.6	91.3	>32	>32	≤0.5 - >32
	Ceftriaxone	1.4	0.4	98.2	>32	>32	≤0.06 - >32
	Levofloxacin	27.5	6.4	66.1	4	>8	0.03 - >8
	Meropenem	87.7	3.4	9.0	≤0.06	8	≤0.06 - >16
	Pip-Tazo	49.1	11.0	39.9	16	>128	0.25 - >128

Table 3. In vitro susceptibility of all Cephalosporin-R *E. coli* and *K. pneumoniae* collected from Europe (TEST surveillance 2014-2016)

Organism (n)	Drug	% S	% I	% R	MIC_{50}	MIC_{90}	MIC range
E. coli (980)	Tigecycline	98.8	1.1	0.1	0.25	0.5	0.015 - >8
	Amikacin	92.7	4.4	3.0	8	8	≤0.5 - >64
	Cefepime	0	0	100	>32	>32	8 - >32
	Ceftriaxone	0	0	100	>32	>32	4 - >32
	Levofloxacin	14.2	0.9	84.9	>8	>8	≤0.008 - >8
	Meropenem	98.7	1.0	0.3	≤0.06	0.12	≤0.06 - >16
	Pip-Tazo	74.6	9.1	16.3	16	64	0.12 - >128
K. pneumoniae (1,562)	Tigecycline	75.3	15.1	9.6	2	2	0.06 - >8
	Amikacin	79.1	13.8	7.1	16	16	≤0.5 - >64
	Cefepime	0	0	100	>32	>32	8 - >32
	Ceftriaxone	0	0	100	>32	>32	4 - >32
	Levofloxacin	21.4	4.8	73.8	>8	>8	0.03 - >8
	Meropenem	71.4	3.7	24.9	>16	>16	≤0.06 - >16
	Pip-Tazo	38.0	9.4	52.6	>128	>128	0.25 - >128

Table 4. In vitro susceptibility of all ESBL Positive and Cephalosporin-R *E. coli* and *K. pneumoniae* collected from Europe (TEST surveillance 2014-2016)

Organism (n)	Drug	% S	% I	% R	MIC_{50}	MIC_{90}	MIC range
E. coli ESBL (867)	Tigecycline	99.1	0.9	0	0.25	0.5	0.015 - 2
	Amikacin	93.3	4.2	2.5	8	8	≤0.5 - >64
	Cefepime	0	0	100	>32	>32	8 - >32
	Ceftriaxone	0	0	100	>32	>32	8 - >32
	Levofloxacin	14.9	0.9	84.2	>8	>8	≤0.008 - >8
	Meropenem	99.4	0.6	0	≤0.06	0.12	≤0.06 - 8
	Pip-Tazo	77.4	9.2	13.4	16	32	0.12 - >128
K. pneumoniae ESBL (1,200)	Tigecycline	75.1	14.3	10.6	2	4	0.06 - >8
	Amikacin	91.5	4.5	4.0	4	8	≤0.5 - >64
	Cefepime	0	0	100	>32	>32	8 - >32
	Ceftriaxone	0	0	100	>32	>32	8 - >32
	Levofloxacin	24.8	6.1	69.2	>8	>8	0.03 - >8
	Meropenem	86.6	3.7	9.8	1	8	≤0.06 - >16
	Pip-Tazo	46.6	11.9	41.5	>128	>128	0.25 - >128

Figure 1. Susceptibility Percentages Observed Among *E. coli*, *E. coli* Cephalosporin Resistant, ESBL E. coli, and ESBL *E. coli* Cephalosporin Resistant from Europe

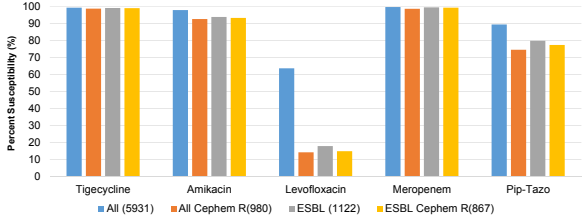
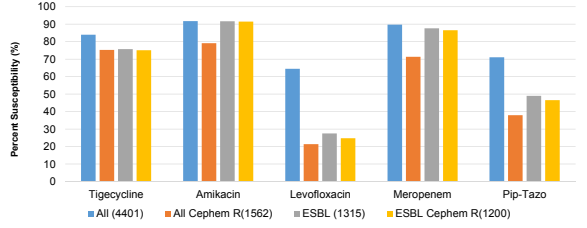


Figure 2. Susceptibility Percentages Observed Among *K. pneumoniae*, *K. pneumoniae* Cephalosporin Resistant, ESBL *K. pneumoniae*, and ESBL *K. pneumoniae* Cephalosporin Resistant from Europe



Conclusions

- Tigecycline maintained good *in vitro* activity against *E. coli* and *K. pneumoniae* including ESBL producers and cephalosporin resistant isolates.
- ESBL-positive and cephalosporin resistant *K. pneumoniae* isolates were less susceptible to most agents tested when compared to ESBL-positive or cephalosporin resistant *E. coli*.
- Continent wide and country specific monitoring is essential to follow the susceptibility patterns of ESBL and cephalosporin producing isolates of common *Enterobacteriaceae* species.

References

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