P0322

In vitro Activity of Tigecycline and Comparator Agents Against *Enterobacteriaceae* from Intra-Abdominal Infection (IAI) Isolates Collected in Italy

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Revised Abstract

Background: *Enterobacteriaceae* cause serious intra-abdominal infections (IAIs) among hospitalized patients. Tigecycline European Surveillance Trial (TEST) program data were used to evaluate the *in vitro* activity of several key drugs against enteric pathogens causing IAI among patients from Italy. **Material/methods:** A total of 489 *Enterobacteriaceae* isolates were collected from IAI sources in Italy during 2010-2015. Isolates were identified to the species level and MICs determined at each participating laboratory using supplied broth microdilution panels and following EUCAST guidelines. Only one isolate per patient was accepted into the study. All data were collected centrally at IHMA for analysis using EUCAST breakpoint criteria. **Results:** The activities of drugs against all isolates and MDR (multidrug-resistant; resistant to drugs representing ≥3 drug classes) and for CRE (carbapenem-resistant *Enterobacteriaceae*) are provided in the table below.

	Enterobacteriaceae (489)			MDR (239)			CRE (59)		
Drug	**%S**	**MIC_{50}**	**MIC_{90}**	**%S**	**MIC_{50}**	**MIC_{90}**	**%S**	**MIC_{50}**	**MIC_{90}**
Tigecycline	87.9	0.5	2	79.1	0.5	2	52.5	1	4
Pip-Tazo	54.0	8	> 128	14.6	128	> 128	0	> 128	> 128
Meropenem	85.1	≤0.06	> 16	69.5	0.12	> 16	0	> 16	> 16
Levofloxacin	54.4	0.5	> 8	17.2	> 8	> 8	1.7	> 8	> 8
Cefepime	54.6	1	> 32	15.1	32	> 32	0	> 32	> 32
Amikacin	82.4	2	16	66.1	4	32	8.5	16	64

Overall the MDR rates and CRE rates in Italy among IAI *Enterobacteriaceae* isolates were 48.9% and 12.1%, respectively.

Conclusions: Based on percent susceptibility tigecycline was the most active agent against all IAI isolates, and against the MDR and CRE subpopulations. These variations in antimicrobial susceptibilities and the increase in the antimicrobial resistance among *Enterobacteriaceae* emphasize the need for continued monitoring of antimicrobial activities among *Enterobacteriaceae* from IAIs in Italy.

Introduction

Enterobacteriaceae cause serious infections among hospitalized patients, including intra-abdominal infections (IAI). Tigecycline European Surveillance Trial (TEST) program data were used to evaluate the *in vitro* activity of several key drugs against pathogens causing IAI among patients from Italy. The species included in this study were from the following groups: *Enterobacter* spp., (five species), *Klebsiella* spp., (two species), *Citrobacter spp*., (two species), *Serratia* spp., (two species) and *E. coli*.

Materials & Methods

- Between 2010 and 2015 a total of 30 sites from Italy participated in the TEST program. A total of 489 *Enterobacteriaceae* isolates were identified to the species level and MICs determined at each participating laboratory using supplied broth microdilution panels. All isolates were derived from intraabdominal infections (IAI) from hospitalized patients. 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) or TREK (Thermo Fisher Scientific, Oakwood, OH) panels [1]. All antimicrobics were supplied by the panel manufacturers.
- MIC interpretive criteria followed EUCAST guidelines [2].
- Quality control (QC) was 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 [2].

Results

Figure 1. MIC Distributions of Tigecycline and Comparators Against 489 *Enterobacteriaceae* Isolates

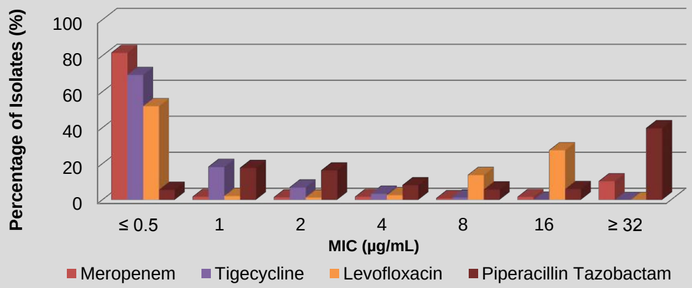


Figure 2. MIC Distributions of Tigecycline and Comparators Against 134 *E. coli* Isolates

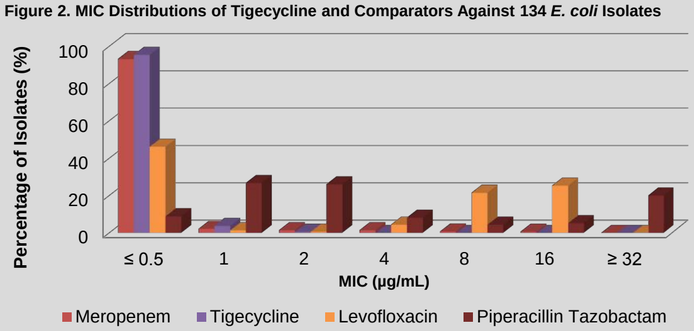
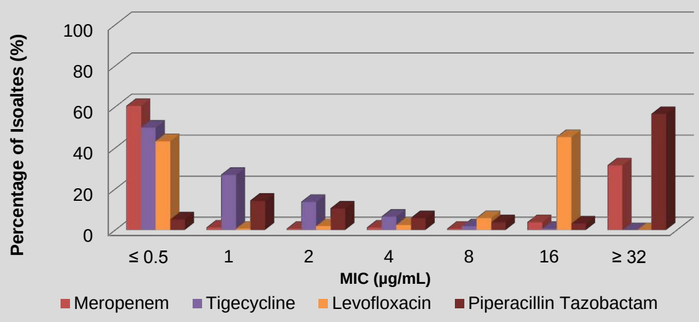


Figure 3. MIC Distributions of Tigecycline and Comparators Against 152 *Klebsiella spp.*[a] Isolates



[a] *K. pneumoniae* (124 isolates), and *K. oxytoca* (28 isolates)

Table 1. Activity of Tigecycline and Comparators Against All and MDR *Enterobacteriaceae*[a]

	All	(N=489)	All MDR (N=239)		MDR=3 (N=94)		MDR=4 (N=76)		MDR>=5 (N=69)	
Drug	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**
Tigecycline	87.9	2	79.1	2	95.7	1	84.2	2	50.7	4
Pip-Tazo	54.0	> 128	14.6	> 128	37.2	> 128	0	> 128	0	> 128
Meropenem	85.1	> 16	69.5	> 16	96.8	0.5	85.5	4	14.5	> 16
Levofloxacin	54.4	> 8	17.2	> 8	41.5	> 8	1.3	> 8	1.5	> 8
Cefepime	54.6	> 32	15.1	> 32	28.7	> 32	11.8	> 32	0	> 32
Amikacin	82.4	16	66.1	32	92.6	8	81.6	16	13.0	64

[a]MDR: Multi-Drug Resistant: MDR=3, resistant to three drugs; MDR=4, resistant to four drugs; MDR>= 5, resistant to five or more drugs.

Table 2. Activity of Tigecycline and Comparators Against All and MDR *E. coli*[a]

	All	(N=134)	All MDR (N=57)		MDR=3 (N=38)		MDR>=4 (N=19)	
Drug	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**
Tigecycline	99.3	0.5	98.3	0.5	100	0.5	73.7	16
Pip-Tazo	74.6	128	43.9	> 128	65.8	128	5.3	> 32
Meropenem	97.0	0.25	93.0	2	100	0.12	0	> 8
Levofloxacin	47.8	> 8	3.5	> 8	5.3	> 8	79.0	8
Cefepime	59.7	> 32	12.3	> 32	15.8	> 32	0	> 128
Amikacin	91.8	8	84.2	16	89.5	16	94.7	1

[a]MDR: Multi-Drug Resistant: MDR=3, resistant to three drugs; MDR>=4, resistant to four or more drugs.

Table 3. Activity of Tigecycline and Comparators Against All and MDR *Klebsiella spp.*[a]

	All	(N=152)	All MDR (N=92)		MDR=3 (N=21)		MDR=4 (N=12)		MDR>=5 (N=59)	
Drug	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**	**%S**	**MIC_{90}**
Tigecycline	77.0	2	63.0	4	90.5	1	72.7	4	52.5	4
Pip-Tazo	40.1	> 128	8.7	> 128	38.1	> 128	0	> 128	0	> 128
Meropenem	62.5	> 16	38.0	> 16	95.2	0.25	63.6	16	11.9	> 16
Levofloxacin	44.1	> 8	10.9	> 8	47.6	> 8	18.2	> 8	0	> 8
Cefepime	37.5	> 32	5.4	> 32	28.6	> 32	0	> 32	0	> 32
Amikacin	62.5	32	38.0	32	90.5	8	90.9	8	10.2	64

[a]MDR: Multi-Drug Resistant: MDR=3, resistant to three drugs; MDR=4, resistant to four drugs; MDR>= 5, resistant to five or more drugs.

Table 4. Activity of Tigecycline and Comparators Against CRE Isolates[a]

Drug	**%S**	**%I**	**%R**	**MIC_{50}**	**MIC_{90}**	**Range**
Tigecycline	52.5	28.8	18.6	1	4	0.25 - >8
Pip-Tazo	0	0	100	> 128	> 128	128 - >128
Meropenem	0	0	100	> 16	> 16	16 - >16
Levofloxacin	1.7	1.7	96.6	> 8	> 8	0.25 - >8
Cefepime	0	0	100	> 32	> 32	32 - >32
Amikacin	8.5	47.5	44.1	16	64	1 - >64

[a]CRE: 54 *K. pneumoniae*, 2 *Citrobacter spp.*, 2 *E. cloacae*, 1 *E. coli*

Conclusions

- Based on susceptibility percentages, tigecycline, meropenem, and amikacin were the most active drugs against all *Enterobacteriaceae* isolated from intra-abdominal infections in Italy (Table 1).
- Tigecycline was the most active agent against MDR *Enterobacteriaceae,* including those resistant to five or more drugs (Tables 1-3).
- Monitoring variation in antimicrobial susceptibilities among clinically significant *Enterobacteriaceae* from IAIs in Italy helps to establish antibiotic treatment guidelines in this country. Antimicrobial surveillance should be continued on an ongoing basis.

References and Acknowledgments:

1. Clinical Laboratory Standards Institute. 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards -- Tenth Edition. CLSI document M07-A10 Wayne, PA.
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