

Antimicrobial Susceptibility Profiles of Bacterial Isolates from Intra-Abdominal and Skin and Skin Structure Infections in Eastern and Western Europe

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Revised Abstract

Objectives: The Tigecycline European Surveillance Trial (TEST) monitors the *in vitro* activity of tigecycline and other antimicrobials against clinically-relevant pathogens collected globally. This study reports on the activity of tigecycline and comparators against IAI and SSTI isolates collected in Eastern and Western European (EU) countries. **Methods:** Non-duplicate clinical *E. coli* and *Klebsiella* spp. isolates from IAI (2915) and *S. aureus* and β -hemolytic streptococci from SSTI (9365) were collected from medical centers in Eastern (13 countries) and Western (16 countries) EU during 2004-2015. Organism identification and antibiotic susceptibility testing was performed by the local laboratories. Susceptibility (S) testing was performed using broth microdilution according to CLSI guidelines; and categorical interpretation of results was done using EUCAST breakpoints. **Results:** The table provides MIC₅₀ and (% S) data for tigecycline and comparators against key pathogens by the two EU regions.

Organism (n)	MIC ₅₀ (%S) Eastern/Western EU					
	TGC	MEM	TZP	LXV	AMK	
<i>E. coli</i> (252/1842)	0.5(98.8/0.5)(99.3)	0.12(99.1/100.0)(99.5)	32(83.7/116)(88.4)	>8(71.8/)>8(73.7)	8(92.9/8)(97.2)	
<i>K. pneumoniae</i> (130/925)	2(97.7/2)(95.2)	1(99.7/2)(99.3)	>128(54.6/)>128(71.6)	>8(68.6/)>8(76.7)	16(87.7/16)(88.7)	
SSTI						
MSSA (859/4774)	0.25(100/0.25)(100)	0.5(92.9/0.5)(96.0)	0.5(96.0/0.5)(91.6)	1(100/1)(100)		
MRSA (351/1929)	0.25(100/0.25)(100)	8(75.5/0.5)(90.3)	32(21.4/32)(19.4)	1(100/1)(100)		
β -strep (226/1678)	0.12(100/0.06)(100)	>8(13.7/)>8(34.3)	1(97.3/1)(95.8)	0.5(100/0.5)(100)		

*TGC (tigecycline), MEM (meropenem), TZP (piperacillin-tazobactam), LXV (levofloxacin), AMK (amikacin), MIN (minocycline), VAN (vancomycin)
 **Drugs with >90% S are shaded in darker grey

Conclusions: Regardless of European region TGC exhibited potent *in vitro* activity against both the gram-negative and gram-positive species evaluated. However, given the ability of many of these species to develop antimicrobial resistance, ongoing monitoring of activity on a regional basis is warranted.

Introduction

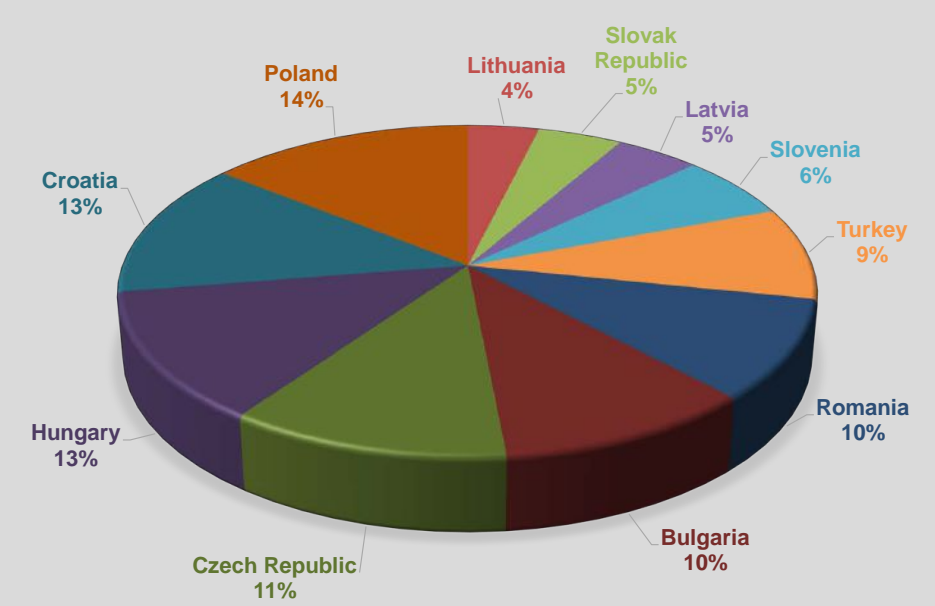
The Tigecycline European Surveillance Trial (TEST) monitors the *in vitro* activity of tigecycline and other antimicrobials against clinically-relevant pathogens collected globally. This study reports on the activity of tigecycline and comparators against IAI and SSTI isolates collected in Eastern and Western European (EU) countries.

Materials & Methods

- Non-duplicate clinical isolates of *E. coli*, *Klebsiella* spp., *S. aureus*, and β -hemolytic streptococci were collected during 2004-2015 in Eastern and Western European countries from IAI and SSTI. Organism identification and antibiotic susceptibility testing was performed by the local laboratories.
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method using MicroScan (Siemens Medical Solutions Diagnostics, West Sacramento, CA) or TREK (TREK Diagnostic Systems, Cleveland, OH) panels. MIC interpretive criteria followed published EUCAST guidelines.
- Quality control isolates (QC) were tested on each day 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.

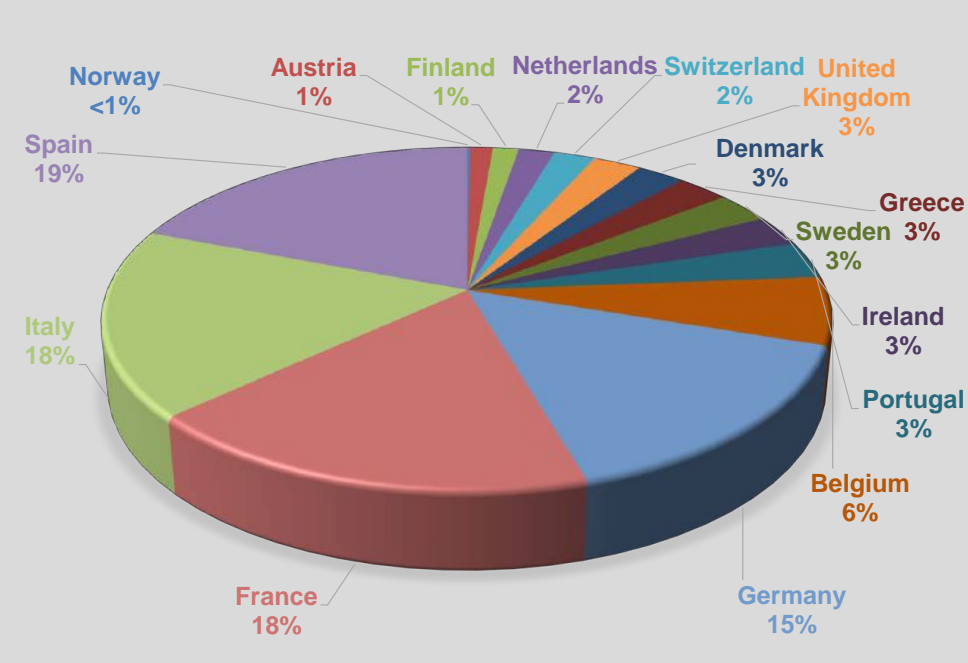
Results

Figure 1. Eastern European Country Distribution and Contribution to the TEST Program 2004-2015.*



*Reflects the percentage of isolates from each country

Figure 2. Western European Country Distribution and Contribution to the TEST Program 2004-2015.*



*Reflects the percentage of isolates from each country

Table 1. Susceptibility and MIC Values Observed Among *E. coli* and *Klebsiella* spp. Collected from Patients with IAI in Eastern European Countries.

Organism (n)	Drug	% Susceptible	% Resistant	MIC ₅₀	MIC ₉₀	MIC range
<i>E. coli</i> (252)	Ceftriaxone	77.4	21.4	≤ 0.06	> 32	≤ 0.06 - > 32
	Cefepime	78.2	15.9	≤ 0.5	16	≤ 0.5 - > 32
	Meropenem	99.1	0.0	≤ 0.06	0.12	≤ 0.06 - 8
	TZP ^a	83.7	11.5	2	32	≤ 0.06 - > 128
	Levofloxacin	71.8	27.4	0.06	> 8	≤ 0.008 - > 8
	Amikacin	92.9	3.6	2	8	≤ 0.5 - > 64
Tigecycline	98.8	0.0	0.25	0.5	≤ 0.008 - 2	
<i>K. pneumoniae</i> (130)	Ceftriaxone	43.9	54.6	32	> 32	≤ 0.06 - > 32
	Cefepime	43.1	50.8	8	> 32	≤ 0.5 - > 32
	Meropenem	90.7	2.5	≤ 0.06	1	≤ 0.06 - > 16
	TZP	54.6	39.2	8	> 128	0.25 - > 128
	Levofloxacin	56.9	40.8	0.5	> 8	≤ 0.008 - > 8
	Amikacin	87.7	6.9	2	16	≤ 0.5 - > 64
Tigecycline	87.7	3.9	0.5	2	0.06 - 8	
<i>K. oxytoca</i> (37)	Ceftriaxone	81.1	10.8	≤ 0.06	8	≤ 0.06 - > 32
	Cefepime	89.2	8.1	≤ 0.5	4	≤ 0.5 - > 32
	Meropenem	100.0	0.0	≤ 0.06	≤ 0.06	≤ 0.06 - 0.25
	TZP	89.2	10.8	2	32	0.12 - > 128
	Levofloxacin	91.9	8.1	0.06	1	0.03 - > 8
	Amikacin	100.0	0.0	2	4	1 - 8
Tigecycline	97.3	2.7	0.25	0.5	0.12 - 4	

^a TZP = Piperacillin-tazobactam

Table 2. Susceptibility and MIC Values Observed Among *E. coli* and *Klebsiella* spp. Collected from Patients with IAI in Western European Countries.

Organism (n)	Drug	% Susceptible	% Resistant	MIC ₅₀	MIC ₉₀	MIC range
<i>E. coli</i> (1,842)	Ceftriaxone	81.6	17.5	≤ 0.06	> 32	≤ 0.06 - > 32
	Cefepime	82.3	12.6	≤ 0.5	8	≤ 0.5 - > 32
	Meropenem	99.5	0.1	≤ 0.06	≤ 0.06	≤ 0.06 - > 16
	TZP ^a	88.4	8.6	1	16	≤ 0.06 - > 128
	Levofloxacin	73.7	24.9	0.06	> 8	≤ 0.008 - > 8
	Amikacin	97.2	0.7	2	8	≤ 0.5 - > 64
Tigecycline	99.3	0.1	0.12	0.5	≤ 0.008 - > 8	
<i>K. pneumoniae</i> (925)	Ceftriaxone	66.2	33.0	0.12	> 32	≤ 0.06 - > 32
	Cefepime	66.9	27.2	≤ 0.5	> 32	≤ 0.5 - > 32
	Meropenem	90.3	8.4	≤ 0.06	2	≤ 0.06 - > 16
	TZP	71.6	25.4	4	> 128	≤ 0.06 - > 128
	Levofloxacin	73.4	24.0	0.12	> 8	≤ 0.008 - > 8
	Amikacin	88.7	5.5	2	16	≤ 0.5 - > 64
Tigecycline	85.2	6.3	0.5	2	≤ 0.008 - > 8	
<i>K. oxytoca</i> (403)	Ceftriaxone	81.6	16.9	≤ 0.06	8	≤ 0.06 - > 64
	Cefepime	85.9	6.2	≤ 0.5	4	≤ 0.5 - > 32
	Meropenem	98.9	0.5	≤ 0.06	≤ 0.06	≤ 0.06 - 0.25
	TZP	80.2	18.4	2	32	0.12 - > 128
	Levofloxacin	91.3	6.5	0.06	1	0.03 - > 8
	Amikacin	99.3	0.0	2	4	1 - 8
Tigecycline	96.5	0.7	0.25	0.5	0.12 - 4	

^a TZP = Piperacillin-tazobactam

Figure 3. ESBL rates for *E. coli* and *Klebsiella* spp. IAI isolates collected from Eastern and Western European Countries.

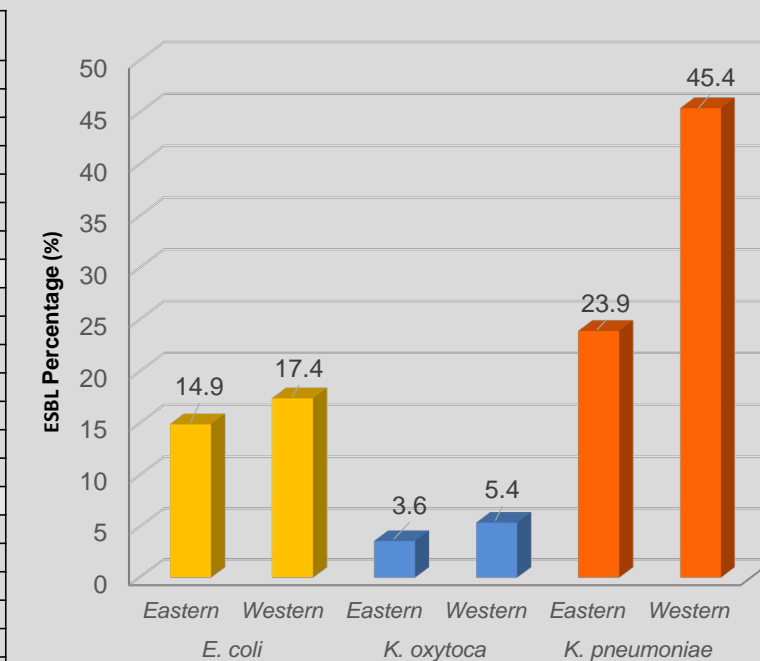


Table 3. Susceptibility and MIC Values Observed Among Gram-Positive Pathogens Collected from Patients with SSTI in Eastern and Western European Countries.

Region (n)	MIC ₉₀ (% susceptible)			
	Tigecycline	Minocycline	Levofloxacin	Vancomycin
Eastern Europe				
MSSA (859)	0.25 (100)	0.5 (92.9)	0.5 (96.0)	1 (100)
MRSA (351)	0.25 (100)	8 (75.5)	32 (21.4)	1 (100)
β -strep (226)	0.12 (100)	>8 (13.7)	1 (97.3)	0.5 (100)
Western Europe				
MSSA (4774)	0.25 (100)	0.5 (96.0)	0.5 (91.6)	1 (100)
MRSA (1929)	0.25 (100)	0.5 (90.3)	32 (19.4)	1 (100)
β -strep (1678)	0.06 (100)	>8 (34.3)	1 (95.8)	0.5 (100)

Conclusions

- ESBL rates for the three *Enterobacteriaceae* spp. were higher in Western European countries in comparison to Eastern European countries.
- Regardless of European region TGC exhibited potent *in vitro* activity against both the gram-negative and gram-positive species evaluated.
- Minimal differences among the drugs tested in both European regions was observed against the gram-positive species. Differences in susceptibility among the gram-negative pathogens were likely due to differences in ESBL rates in these two regions.
- Given the ability of many of these species to develop antimicrobial resistance, ongoing monitoring of activity on a regional basis is warranted.

References and Acknowledgments:

- Tygacil®, 2014. Tigecycline FDA prescribing information. Pfizer, Inc., Collegeville, PA.
- 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.
- The European Committee on Antimicrobial Susceptibility Testing - EUCAST Clinical Breakpoints 2015; http://www.eucast.org/clinical_breakpoints/
- Clinical and Laboratory Standards Institute. 2016. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Sixth Informational Supplement. CLSI Document M100S. Wayne, PA.

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