P0325

In vitro Activity of Tigecycline and Comparators Against Gram-Negative Pathogens in France from Patients with Complicated Intra-Abdominal (IAI) and Skin and Soft Tissue Infections (SSTI)

D. Biedenbach[1], D. Sahm[1], M. Hackel[1], H. Leister-Tebbe[2]
[1]International Health Management Associates, Schaumburg, IL, USA
[2]Pfizer Inc., Collegeville, PA, USA

IHMA, Inc.
2122 Palmer Drive
Schaumburg, IL 60173 USA
Phone: +1.847.303.5003
Fax: +1.847.303.5601
www.ihmainc.com

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 France during the course of this surveillance study. **Methods**: Non-duplicate clinical gram-negative isolates (3,465) from multiple medical centers in France were collected during 2004-2015 from IAI and SSTI specimens. Organism identification and antibiotic susceptibility testing was performed by the local laboratories. Susceptibility testing was performed using broth microdilution according to CLSI guidelines and categorical interpretation of results was done using EUCAST breakpoints. **Results**: The table provides $MIC_{50/90}$ and (%susceptibility) data for tigecycline and comparators against key pathogens.

Organism (n)	Tigecycline	Meropenem	Pip-Tazo	Levofloxacin	Amikacin
C. freundii (95)	0.25/0.5 (100)	≤0.06/0.12 (100)	2/64 (69.5)	0.06/1 (90.5)	2/4 (98.9)
E. aerogenes (164)	0.5/2 (87.2)	≤0.06/0.25 (97.2)	8/64 (58.5)	0.06/>8 (81.1)	2/4 (96.9)
E. cloacae (608)	0.5/2 (84.4)	≤0.06/0.25 (99.4)	4/>128 (63.5)	0.06/>8 (75.5)	2/8 (96.5)
E. coli (772)	0.12/0.5 (99.6)	≤0.06/≤0.06 (100)	1/16 (88.7)	0.03/>8 (81.3)	2/4 (97.9)
K. oxytoca (246)	0.25/1 (95.5)	≤0.06/≤0.06 (99.5)	1/128 (85.0)	0.06/0.5 (93.1)	2/4 (99.2)
K. pneumoniae (395)	0.5/2 (84.8)	≤0.06/0.12 (99.2)	4/128 (77.7)	0.06/8 (78.5)	1/4 (94.9)
S. marcescens (267)	1/2 (80.2)	≤0.06/0.12 (98.7)	1/16 (87.6)	0.12/2 (87.3)	2/4 (96.2)
A. baumannii (320)	0.12/1 (NA)	0.5/16 (83.2)	4/>128 (NA)	0.12/8 (65.6)	4/32 (79.7)
P. aeruginosa (598)	8/16 (NA)	1/8 (77.8)	4/128 (75.8)	1/>8 (63.6)	4/8 (91.1)

Conclusions: Based on percent susceptibility, meropenem, amikacin, and tigecycline exhibited the most potent *in vitro* activity against *Enterobacteriaceae* from France. Tigecycline was the most active agent, based on MIC_{90}, against *A. baumannii* and activities of other agents against *P. aeruginosa* was variable. Country specific monitoring of susceptibility patterns among common gram-negative pathogens provides useful information for determining if changes in treatment strategies should be considered.

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 France during the course of this surveillance study. Comparison of susceptibility percentages among relavent antimicrobial agents are compared between two six year time periods, 2004-2009 and 2010-2015.

Materials & Methods

- Non-duplicate clinical gram-negative isolates (3,465) from multiple medical centers in France were collected during 2004-2015 from IAI and SSTI specimens and were combined for analysis purposes. 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. Susceptibility Comparison Among *E. coli* Isolates During Two Time Periods (N).

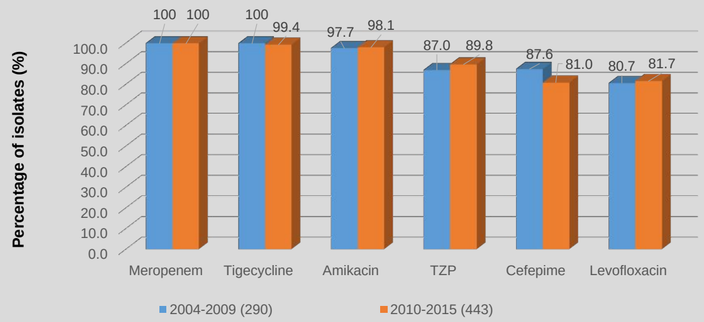

Figure 2. Susceptibility Comparison Among *Klebsiella* spp. Isolates During Two Time Periods (N).

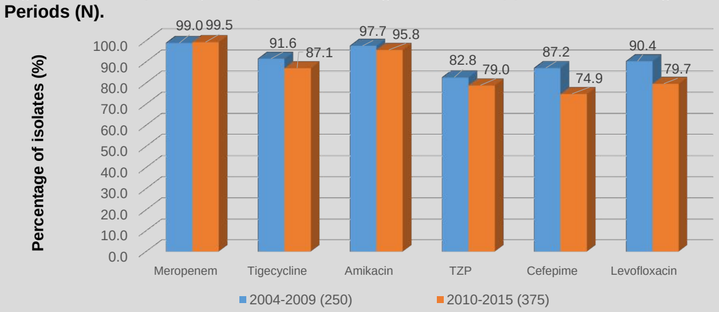

Figure 3. Susceptibility Comparison Among *Enterobacter* spp. Isolates During Two Time Periods (N).

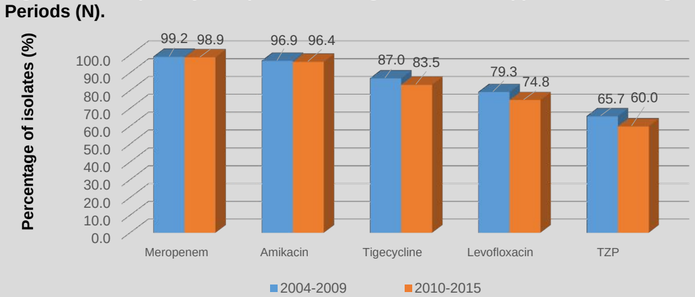

Figure 4. Susceptibility Comparison Among *S. marcescens* Isolates During Two Time Periods (N).

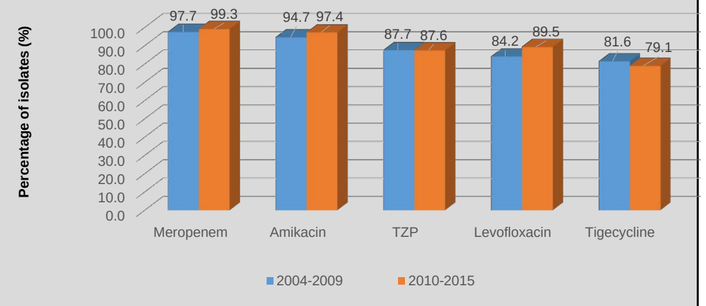

Figure 5. Susceptibility Comparison Among *P. aeruginosa* Isolates During Two Time Periods (N).

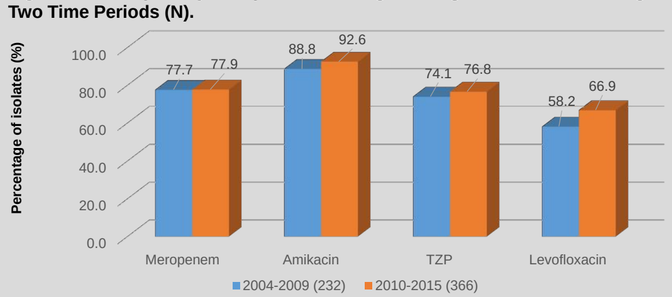

Table 1. Susceptibility Comparison Among 320 *A. baumannii* Isolates From France.

Drug	% Susceptible	% Intermediate	% Resistant	MIC_{50}	MIC_{90}
Amikacin	79.7	5.0	15.3	4	32
Levofloxacin	65.6	3.8	30.6	0.12	8
Meropenem	83.2	5.6	11.2	0.5	16
Tigecycline	na[a]	na	na	0.12	1

a. na= no breakpoints for Tigecycline and A. baumannii have been recommended by EUCAST.

Results Summary

- Based on percent susceptibility, meropenem, amikacin, and tigecycline exhibited the most potent *in vitro* activity against *Enterobacteriaceae* from France (Abstract Table).
- Susceptibility variations in France among the antimicrobials tested were minor among *E. coli* (Figure 1) and *S. marcescens* (Figure 4) during the two time periods that were compared. A decline in susceptibility was observed for nearly all agents tested among *Klebsiella* spp. (Figure 2) and *Enterobacter* spp. (Figure 3).
- Antimicrobial activities of the tested agents against *P. aeruginosa* varied (Figure 5). Tigecycline was the most active agent, based on an MIC_{90} of 1 mg/L, against *A. baumannii* (abstract table).

Conclusions

- Currently, fewer therapeutic options are now available for treating infections caused by *Enterobacteriaceae* in France.
- Tigecycline, though not approved for the treatment of *A. baumannii* infections, was the most active agent, based on MIC_{90} values observed for this species against the drugs tested in this study.
- Country specific monitoring of susceptibility patterns among common gram-negative pathogens provides useful information for determining if changes in treatment strategies should be considered.

References and Acknowledgments:

1. Tygacil®, 2014. Tigecycline FDA prescribing information. Pfizer, Inc., Collegeville, PA.
2. 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.
3. The European Committee on Antimicrobial Susceptibility Testing – EUCAST Clinical Breakpoints 2015; http://www.eucast.org/clinical_breakpoints/
4. Clinical and Laboratory Standards Institute. 2016. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Sixth Informational Supplement. CLSI Document M100S. Wayne, PA.

We gratefully acknowledge the contributions of the investigators, laboratory personnel, and all members of the Tigecycline European and Surveillance Trial group. This study was sponsored by Pfizer Inc. IHMA is a clinical research organization that has been contracted by Pfizer Inc, to manage the TEST program.