

Revised Abstract

Background: Tigecycline is approved for the treatment of complicated skin and skin structure infections (cSSSI) and complicated intra-abdominal infections (cIAI) and was recently approved for the treatment of community acquired pneumonia (CAP). This study describes the activity of tigecycline against *Streptococcus pneumoniae*, an important etiologic agent that was recently added by the FDA to the Tygacil® monograph for the treatment of CAP. **Methods:** 8,300 clinical isolates were collected worldwide between 2004 and 2009. MICs were determined by broth microdilution according to CLSI guidelines using identical panels and interpreted using the newly introduced breakpoints applicable to tigecycline for pneumococci. **Results:** 51% (4,235 isolates) and 29.8% (2,472 isolates) were from North America and Europe, respectively. The remaining 19.2% were from Asia, South Pacific, Middle East, Africa and Latin America. Frequency distributions of MIC data showing the activity of tigecycline and comparators against all 8,300 isolates are as follows:

MIC (mcg/ml)	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16
AmoxClav			5046	660	443	315	327	470	494	317	202	26
Azithromycin			282	1499	2131	120	19	21	65	149	161	1569
Imipenem					2624	428	320	113	5	5	3	10
Levofloxacin				88	84	322	3861	3728	159	28	12	18
Linezolid							4485	3619	196			
Tigecycline	336	2654	3295	1169	772	56	16	2				
Vancomycin					675	5415	2129	81				

Conclusions: Tigecycline exhibited good *in vitro* activity against all isolates in this study which was superior to that of the comparators. Further monitoring of susceptibility to tigecycline is warranted.

Introduction

Tigecycline is approved for the treatment of complicated skin and skin structure infections (cSSSI) and complicated intra-abdominal infections (cIAI) and was recently approved for the treatment of community acquired pneumonia (CAP). Infections due to *S. pneumoniae* continue to evolve worldwide and are a major cause of morbidity and mortality. Resistance in *S. pneumoniae* not only to penicillin but also to cephalosporins, macrolides, trimethoprim/ sulfamethoxazole, fluoroquinolones and tetracycline is well documented. 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 against *S. pneumoniae*, an important etiologic agent that was recently added by the FDA to the Tygacil® monograph for the treatment of CAP [2].

Materials & Methods

- Clinical isolates were collected and tested between January 2004 and March 2009 from a cumulative total of 1,258 investigative sites in 52 countries. Isolates were identified to the species level and tested 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. All sites identified each study isolate utilizing local laboratory criteria.
- Minimum inhibitory concentrations (MICs) were determined using plates manufactured by Trek in line with Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method [3]. Breakpoints were used as defined the CLSI [4] or by the FDA for tigecycline.

References

- Mandell, L.A., et al., *Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults*. CID, 2007. 44: p. S27-72
- Tygacil Product Monograph 2009. http://www.accessdata.fda.gov/drugsatfda_docs/lab/2009/021821s013s017s018lbl.pdf
- Clinical Laboratory Standards Institute, *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Seventh Edition*, in Document M7-A7. 2007: Clinical Laboratory Standards Institute (CLSI), 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
- Clinical Laboratory Standards Institute, *Performance Standards for Antimicrobial Susceptibility Testing*, in Document M100-S19. 2009: Clinical Laboratory Standards Institute (CLSI), 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.

Acknowledgements

This study was sponsored by a grant from Wyeth Pharmaceuticals. We gratefully acknowledge the contributions of all investigators, laboratory personnel and members of the T.E.S.T. program group.

Results

Figure 1. Cumulative total of investigator sites

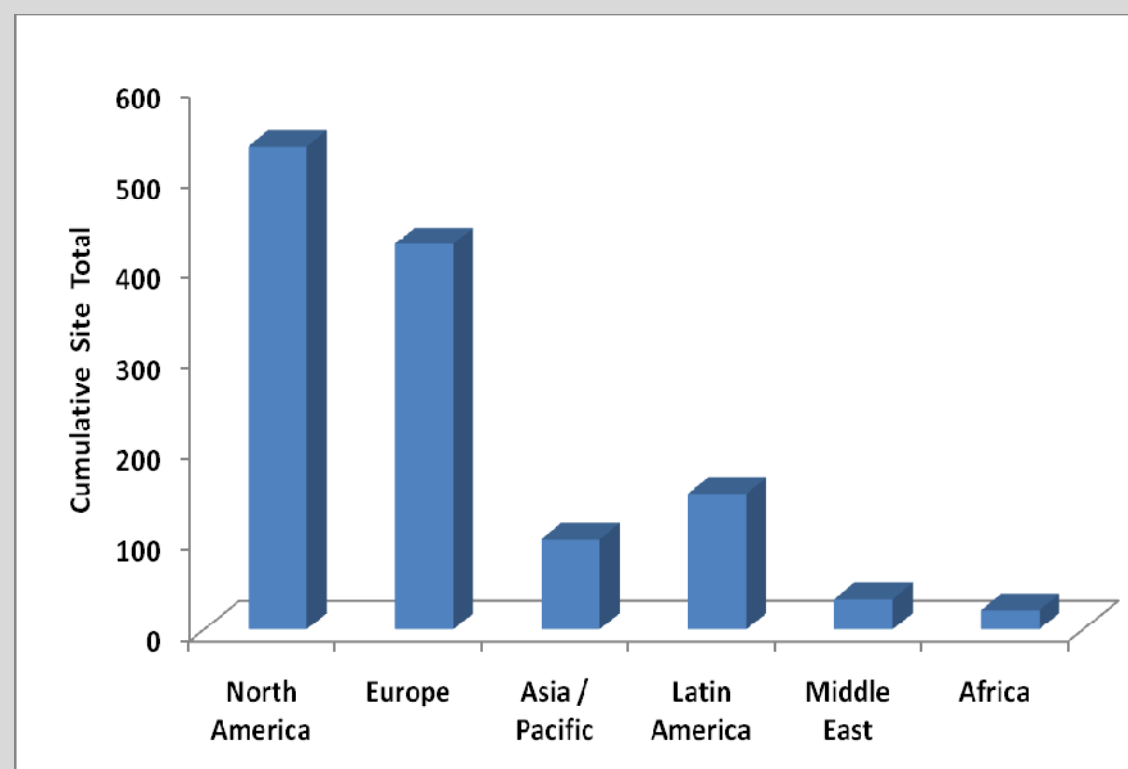


Figure 2. Percent cumulative total of investigator sites

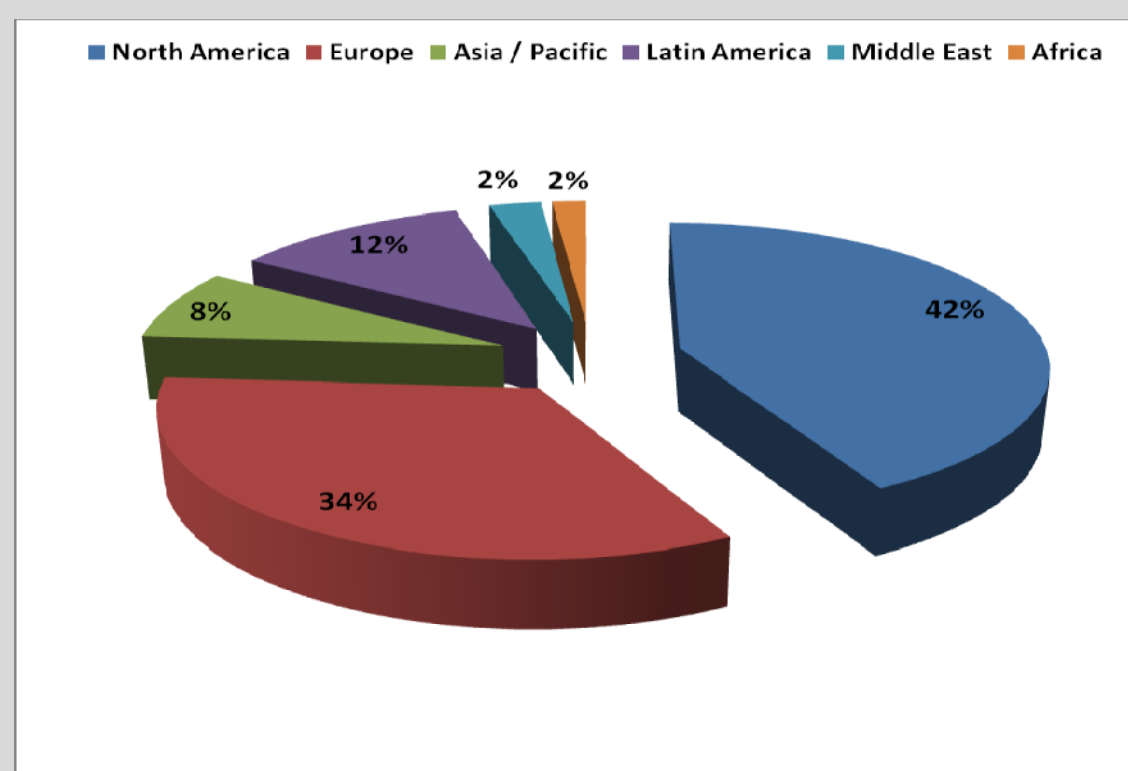


Figure 3. Number of organisms by region

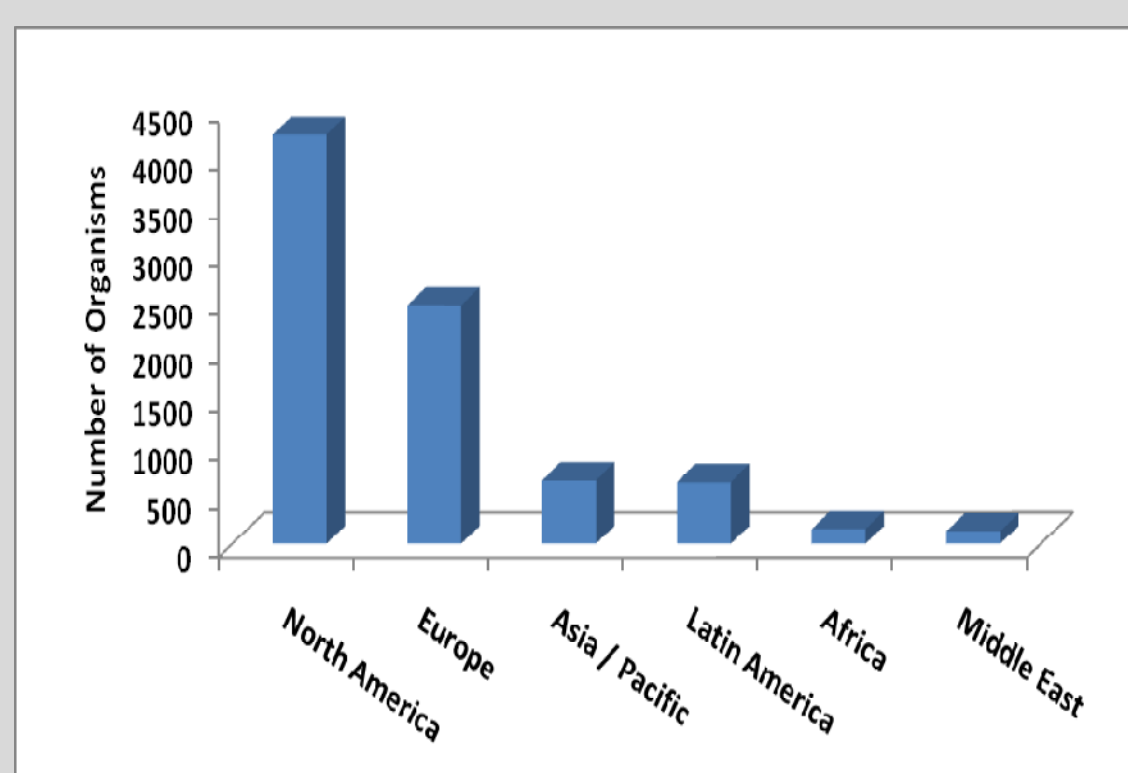


Figure 4. Percent number of organisms by region

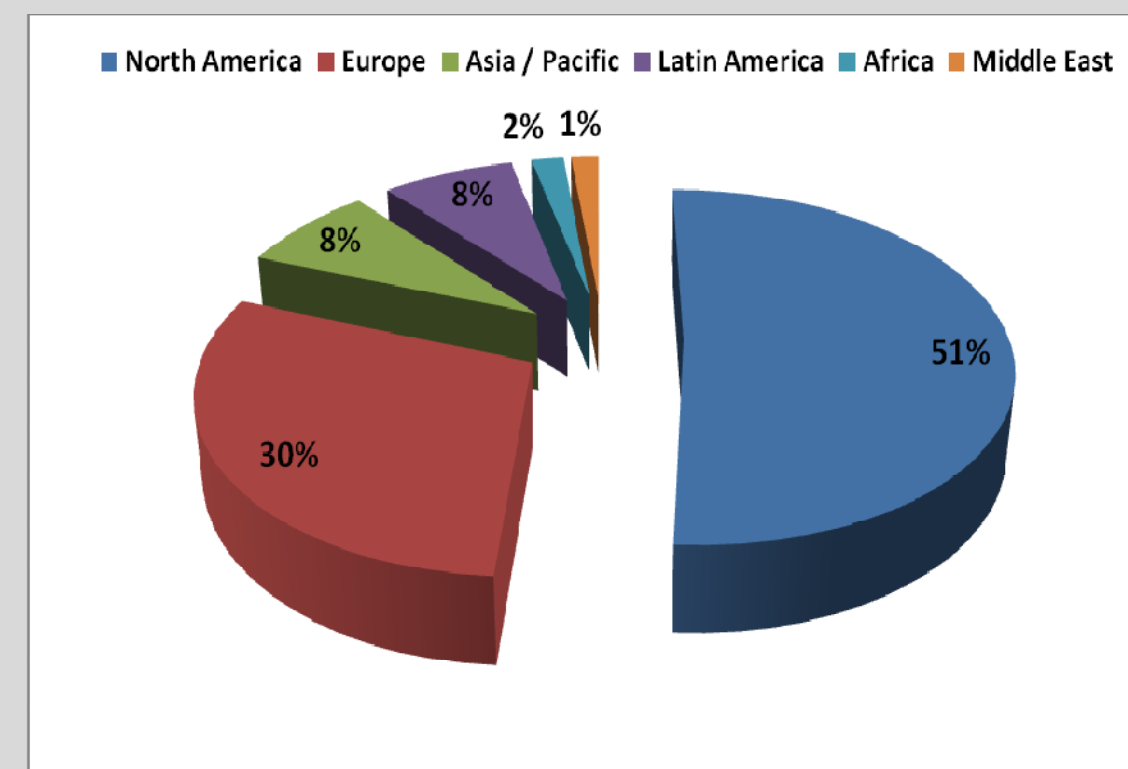


Figure 5. Modal MIC of tigecycline and comparators

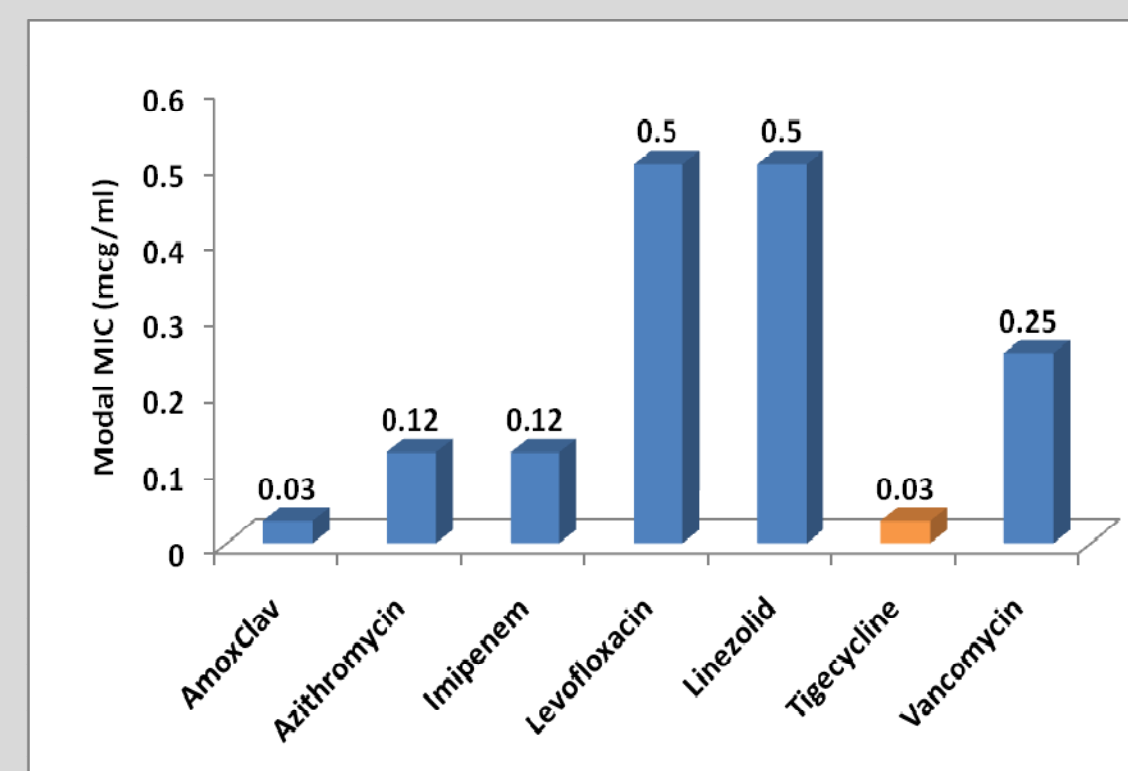


Figure 6. MIC90 of tigecycline and comparators.

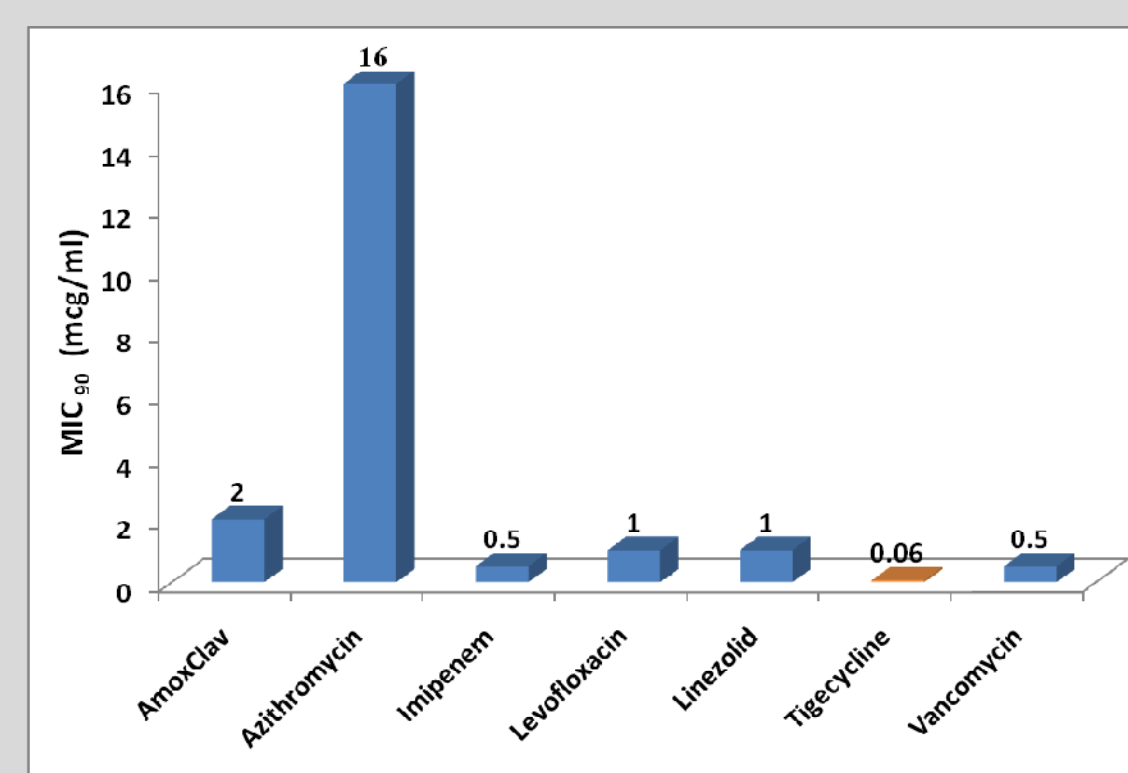


Table 1. MIC frequency distributions for tigecycline and comparators.

MIC (mcg/ml)	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16
AmoxClav			5046	660	443	315	327	470	494	317	202	26
Azithromycin			282	1499	2131	120	19	21	65	149	161	1569
Imipenem					2624	428	320	113	5	5	3	10
Levofloxacin				88	84	322	3861	3728	159	28	12	18
Linezolid							4485	3619	196			
Tigecycline	336	2654	3295	1169	772	56	16	2				
Vancomycin					675	5415	2129	81				

Table 2. Percent susceptibility of pneumococci to tigecycline and comparators

Antibiotic	Percent Susceptible
Amox-Clav	93.4
Azithromycin	67.4
Imipenem	99.6
Levofloxacin	99.3
Linezolid	100
Tigecycline	87
Vancomycin	100

Conclusions

- Tigecycline exhibited good *in vitro* activity against all isolates in this study which was comparable to that of the comparators.
- Further monitoring of susceptibility to tigecycline is warranted.