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Revised Abstract

Background: Tigecycline is FDA approved for the treatment of complicated skin and skin structure infections (cSSSI), complicated intra-abdominal infections (cIAI) and community acquired pneumonia (CAP). In this study we evaluated the activity of tigecycline against recent South Africa isolates from multiple body sites. Methods: MICs were determined for 2,377 isolates from 21 clinical sites during 2004 – 2009 using supplied broth microdilution panels and interpreted according to FDA / CLSI guidelines. **Results:** Isolates were from body fluids (527), blood (239), urinary tract (360), catheters/instruments (108), skin and soft tissues (436), respiratory (569) and other (138). Of the 2,377 isolates, 1029, 442, 298, 193 and 157 were *Enterobacteriaceae*, gram-negative non-*Enterobacteriaceae*, *Staphylococcus* spp., *Enterococcus* spp. and *Streptococcus pneumoniae*, respectively. For organism groups with available breakpoints, tigecycline exhibited percent susceptibilities of 96.8% against *Enterobacteriaceae*, 100% against *enterococci*, *staphylococci* and 92.9% against *S. pneumoniae*. **Conclusions:** Tigecycline exhibited promising activity against the majority of the 2,377 South African isolates that were derived from multiple body sites. Greater than 92.9% of gram-positive isolates and 96.8% of *Enterobacteriaceae* were susceptible to tigecycline.

Materials & Methods

- Clinical isolates were collected and tested between January 2004 and March 2009 from a cumulative total of 21 investigative sites in South Africa. Isolates were identified to the species level and tested at each site by the 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 site criteria.
- Organism collection, transport, confirmation of organism identification, and development and management of a centralized database, were coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- Minimum inhibitory concentrations (MICs) were determined using Trek plates in line with the CLSI recommended broth microdilution testing method [1]. Breakpoints were used as defined the Clinical and Laboratory Standards Institute or by the FDA for tigecycline [2].
- Quality controls (QC) were performed by each testing site on each day of testing using the corresponding ATCC control strains: *E. coli* ATCC 25922; *E. coli* ATCC 35218; *S. aureus* ATCC 29213; *Pseudomonas aeruginosa* ATCC 27853; *Enterococcus faecalis* ATCC 29212 and *S. pneumoniae* ATCC 49619. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI (2009) guidelines [2].

References

- [1] 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.*
- [2] 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

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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).

The purpose of this study was to investigate the *in vitro* activity of tigecycline and comparators against a wide variety of clinical isolates derived from multiple body sites in South Africa during 2004-2009. This study was part of the global Tigecycline Evaluation Surveillance Trial (T.E.S.T.).

Results

Figure 1. Distribution of organisms from multiple body sites.

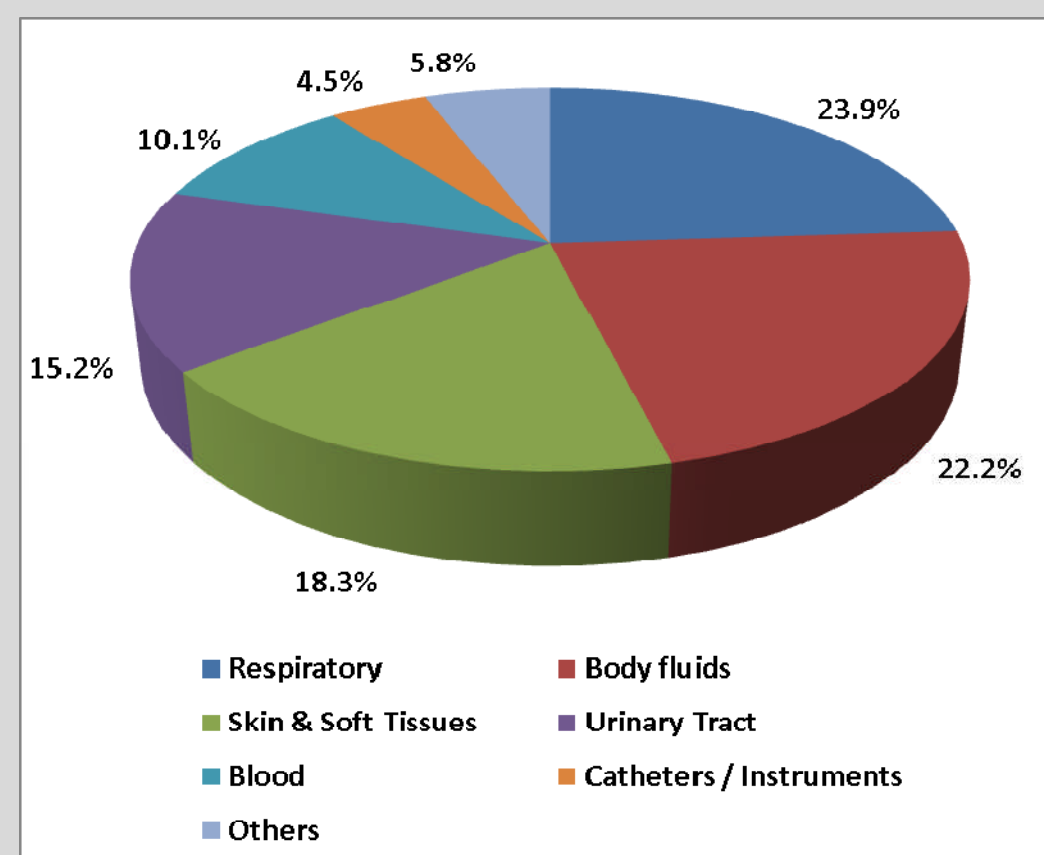
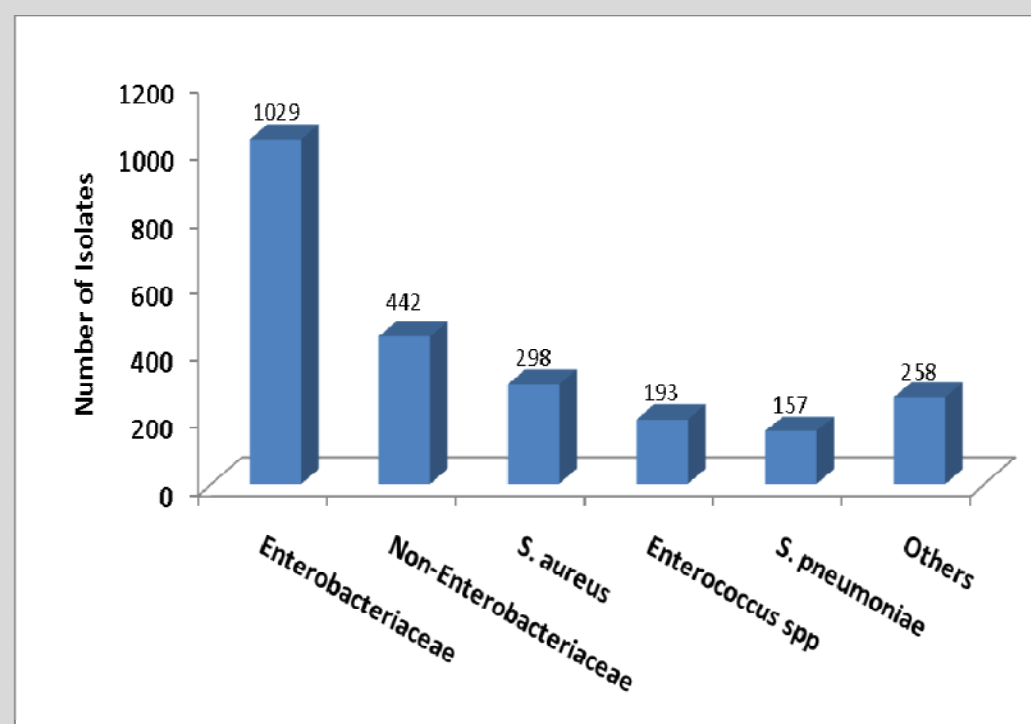


Figure 2. Distribution of organisms by organism group.



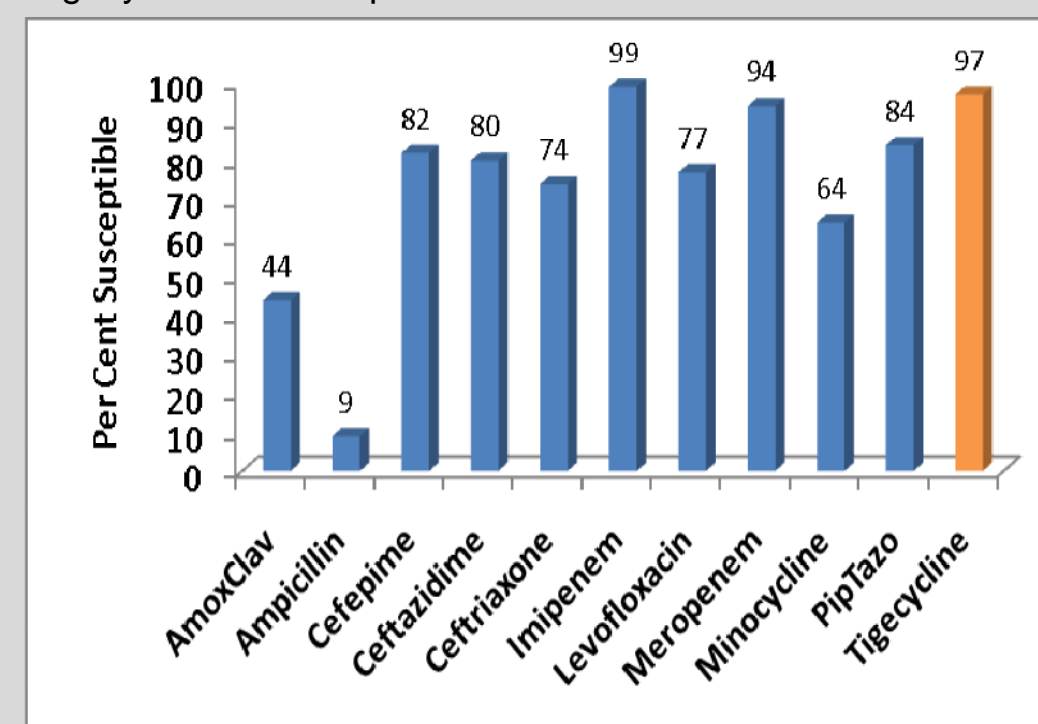
* Selected organisms according to study protocol.

Table 1. MIC₉₀ and percent susceptibility of major organism groups to tigecycline

| Organism Group (n) | MIC ₉₀ (mcg/ml) | Percent susceptible* |
|----------------------------------|----------------------------|----------------------|
| <i>Enterobacteriaceae</i> (1029) | 1 | 96.8 |
| Non-enterobacteriaceae (442) | >16 | NB** |
| <i>S. aureus</i> (298) | 0.25 | 100 |
| <i>Enterococcus</i> spp. (193) | 0.12 | 100 |
| <i>S. pneumoniae</i> (157) | 0.06 | 92.9 |

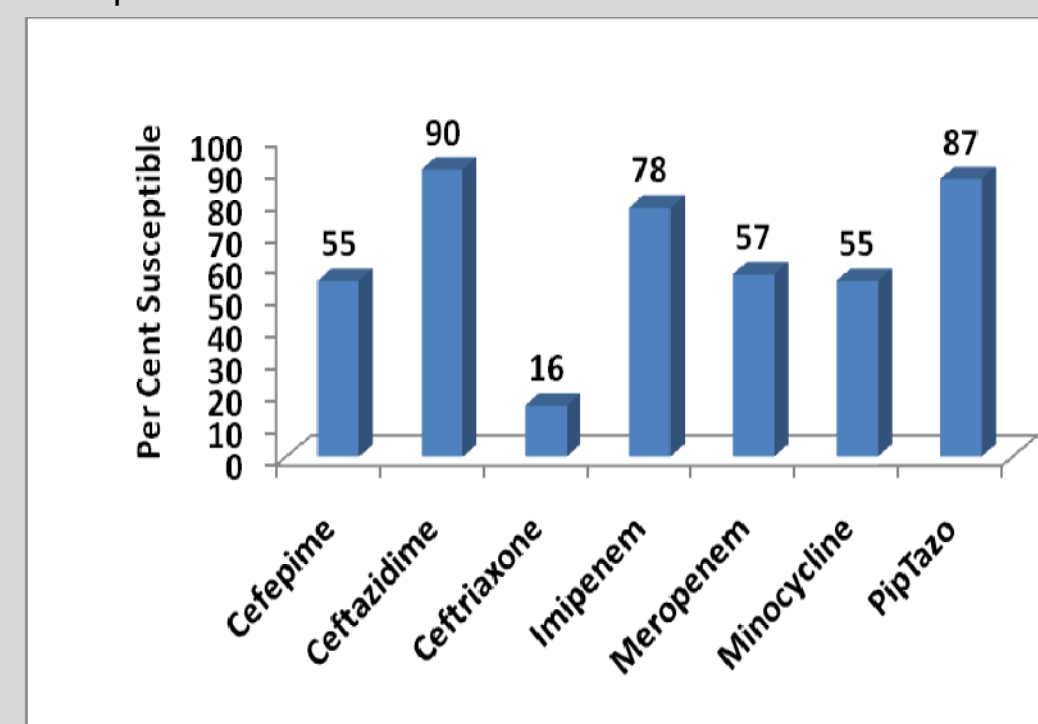
*Tigecycline breakpoints defined by FDA (Tygacil®, 2009); ** No clinical breakpoint for this organism group.

Figure 3. Percent susceptibility of *Enterobacteriaceae* to tigecycline and comparators.



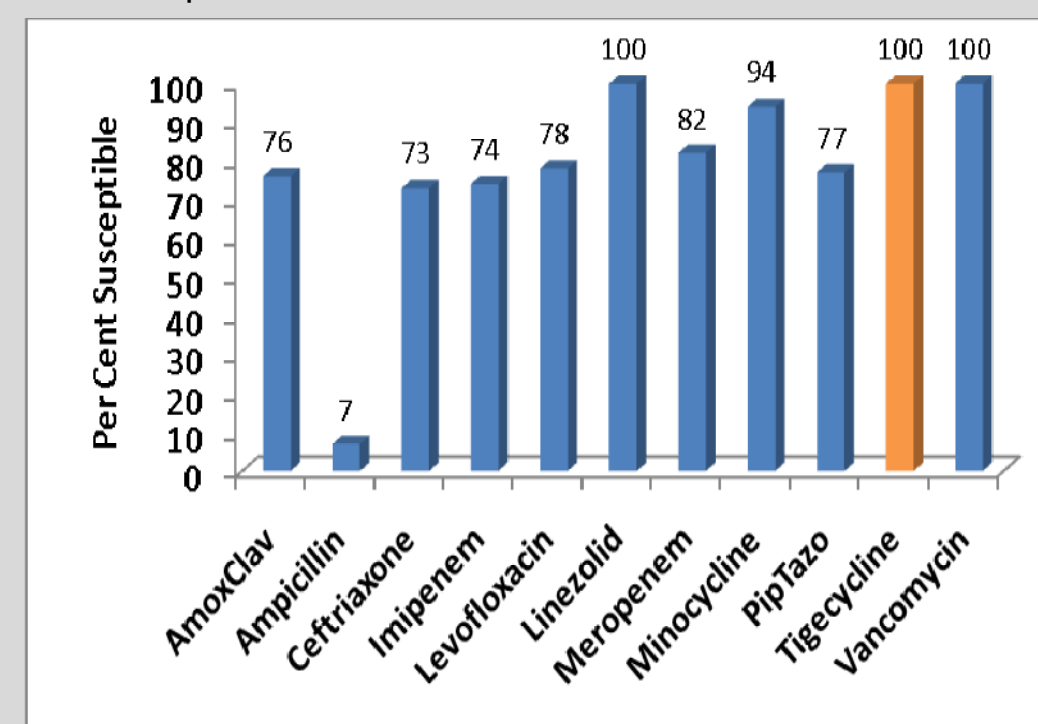
* Susceptibility breakpoints defined by CLSI document M100-S19 (2009), where available. Tigecycline breakpoints defined by FDA (Tygacil®, 2009).

Figure 4. Percent susceptibility of non-enterobacteriaceae to comparators.



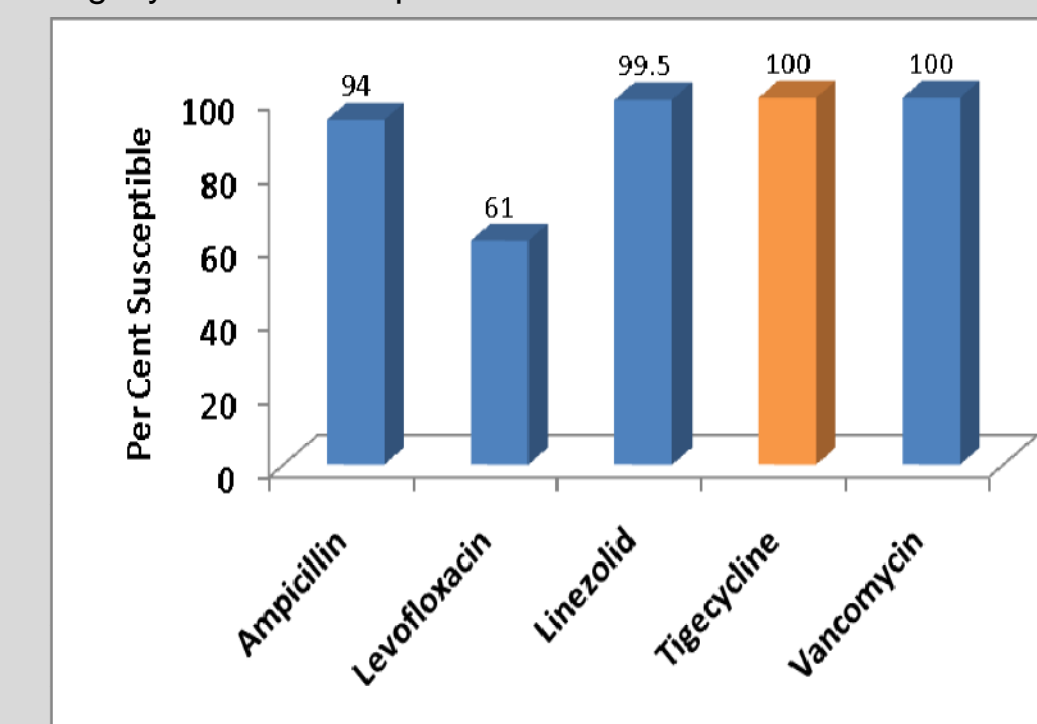
* Susceptibility breakpoints defined by CLSI document M100-S19 (2009), where available. No breakpoints exist for tigecycline for non-enterobacteriaceae.

Figure 5. Percent susceptibility of *S. aureus* to tigecycline and comparators.



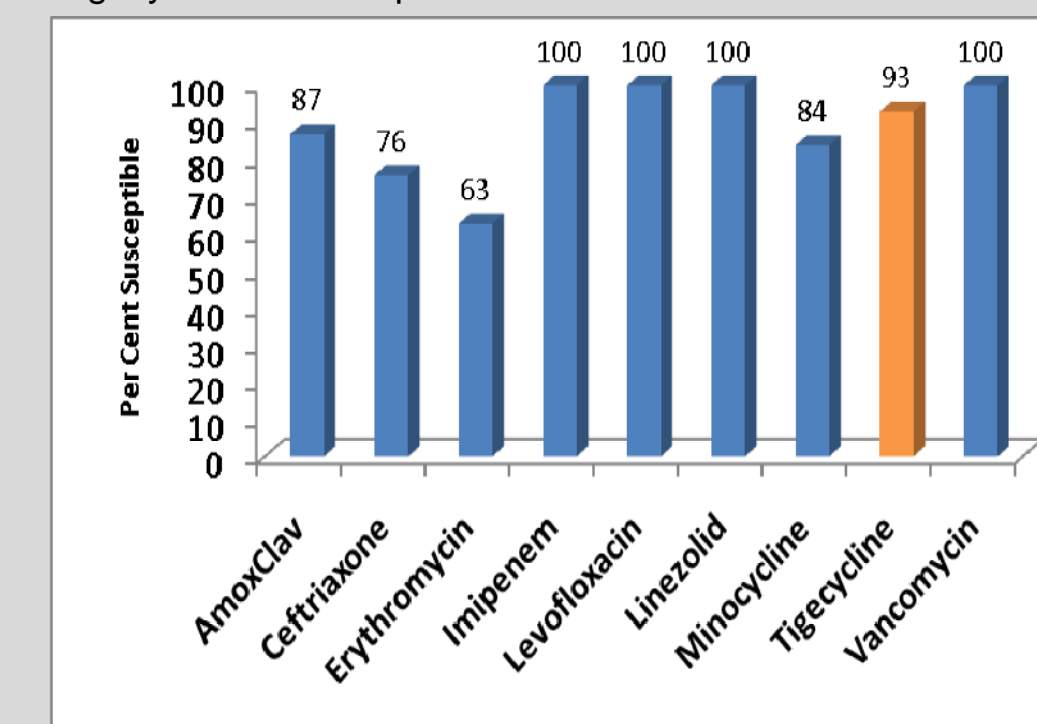
* Susceptibility breakpoints defined by CLSI document M100-S19 (2009), where available. Tigecycline breakpoints defined by FDA (Tygacil®, 2009).

Figure 6. Percent susceptibility of *Enterococcus* spp. to tigecycline and comparators.



* Susceptibility breakpoints defined by CLSI document M100-S19 (2009), where available. Tigecycline breakpoints defined by FDA (Tygacil®, 2009).

Figure 7. Percent susceptibility of *S. pneumoniae* to tigecycline and comparators.



* Susceptibility breakpoints defined by CLSI document M100-S19 (2009), where available. Tigecycline breakpoints defined by FDA (Tygacil®, 2009).

Conclusions

- Tigecycline exhibited promising activity against the majority of South African isolates derived from multiple body sites.
- 100% of *S. aureus*, including MRSA, and 96.8% of *Enterobacteriaceae*, including ESBL producers, were susceptible to tigecycline in this *in vitro* study.