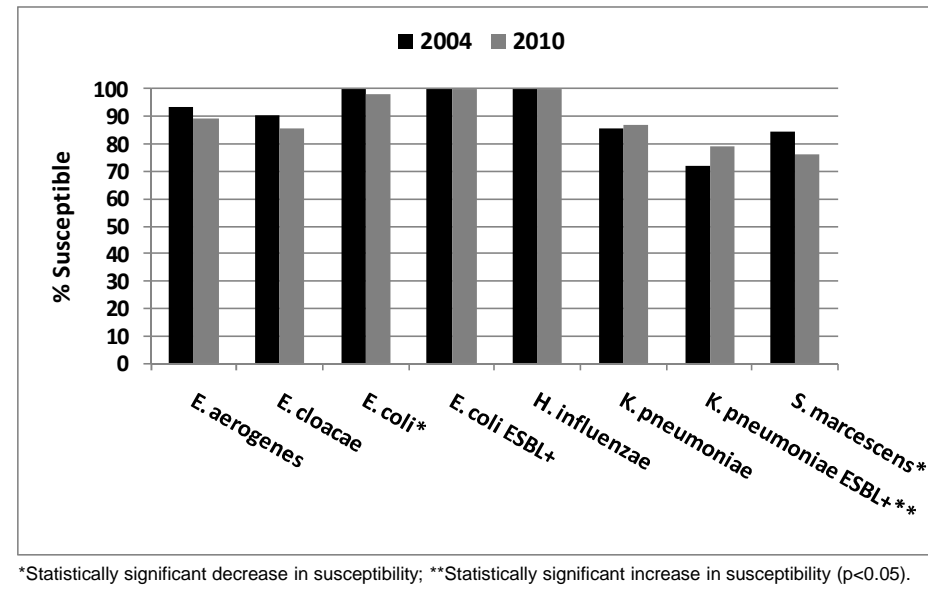


Revised Abstract

Background: The Tigecycline European Surveillance Trial (TEST) monitors the activity of tigecycline and comparators against multiple pathogens collected in Europe. Such monitoring assists in investigating resistance rates by region or by country. The current report describes trends in tigecycline susceptibility of commonly isolated gram-negative pathogens between 2004 and 2010. **Methods:** A total of 33,988 clinical isolates were collected from multiple infection sources in Europe between 2004 and 2010. Susceptibility testing was performed as per CLSI guidelines and interpreted using EUCAST clinical breakpoints. Linear trends in percent susceptible were assessed with the Cochran-Armitage test for trend. **Results:** Susceptibility to tigecycline of the 5,285 gram-negative isolates collected in 2004 and 2010 is reported below. Although % susceptible is only shown for 2004 and 2010, trends in susceptibility were assessed using all years from 2004 to 2010.



Conclusion: Susceptibility data for tigecycline show that from 2004 to 2010 susceptibility of the selected species remained largely stable. Only *E. coli* and *S. marcescens* showed statistically significant decreases in % susceptible (from 99.7 to 98.2% and 84.6 to 76.0%, respectively) over the seven-year period, while ESBL-positive *K. pneumoniae* isolates showed a slight increase in susceptibility ($p < 0.05$). While susceptibility has remained relatively stable, further susceptibility monitoring over time is warranted.

Introduction

The management of hospital-acquired bacterial infections is becoming a significant challenge for health care providers because of the increased prevalence of resistant bacteria including carbapenemase-producing *Enterobacteriaceae* and extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*. Increased morbidity and mortality, duration of hospitalization, and medical care costs are all associated with multi-drug resistant (MDR) organisms [1]. Delay of appropriate empiric antimicrobial therapy is known to increase morbidity and mortality among affected patients and inadequate therapy has been found to be associated with excess mortality and increased duration of hospitalization [2]. There is a high rate of resistance to commonly used antimicrobial agents, for example, beta-lactams (penicillins/cephalosporins), fluoroquinolones, and aminoglycosides amongst others.

Tigecycline is an antibiotic that has come into clinical use at a critical time and demonstrates *in vitro* activity against a wide range of bacteria [3,4]. The present report describes susceptibility trends of tigecycline and comparator agents against numerous gram-negative European clinical isolates collected from 2004 – 2010 as part of the Tigecycline European Surveillance Trial (TEST).

Materials & Methods

- A total of 33,988 isolates were collected during 2004 – 2010 in Europe and identified to the species level and MICs determined at each participating laboratory using sponsor supplied broth microdilution panels. Only one isolate per patient was accepted into the study.
- 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 by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method using MicroScan (Siemens Medical Solutions Diagnostics, West Sacramento, CA) or Sensititre (TREK Diagnostic Systems, Cleveland, OH) panels [5]. All antimicrobials were supplied by the panel manufacturers. Meropenem was fully integrated into the TEST program from 2007 for which data shown correspond to the period 2007 – 2010.
- MIC interpretive criteria followed published guidelines of the EUCAST and the most recent United States Food and Drug Administration package insert for tigecycline where applicable [6,7].
- The Cochran-Armitage test was used to assess linear trends in percent susceptible over time. A two-tailed p -value < 0.05 was considered statistically significant.

References

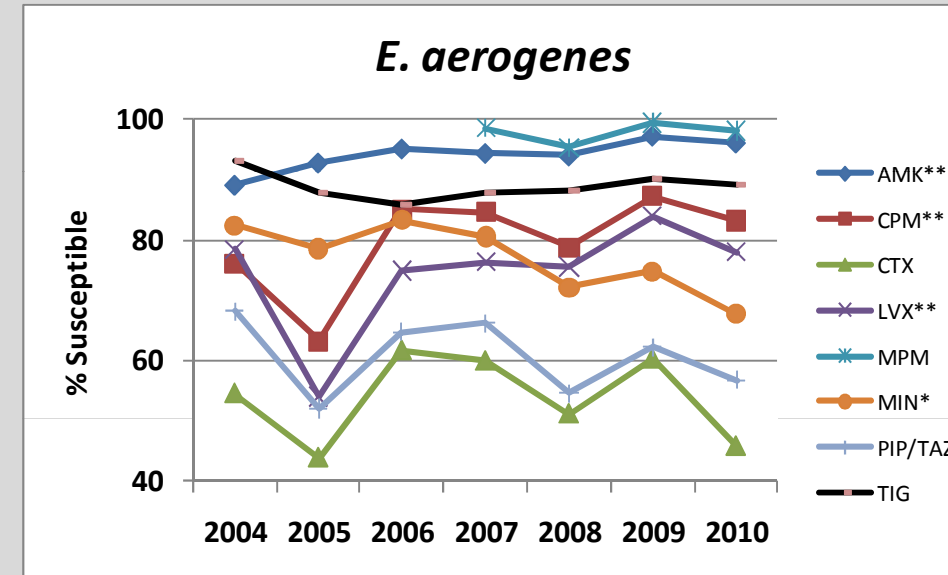
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- The European Committee on Antimicrobial Susceptibility Testing – EUCAST (www.eucast.org).

Acknowledgements

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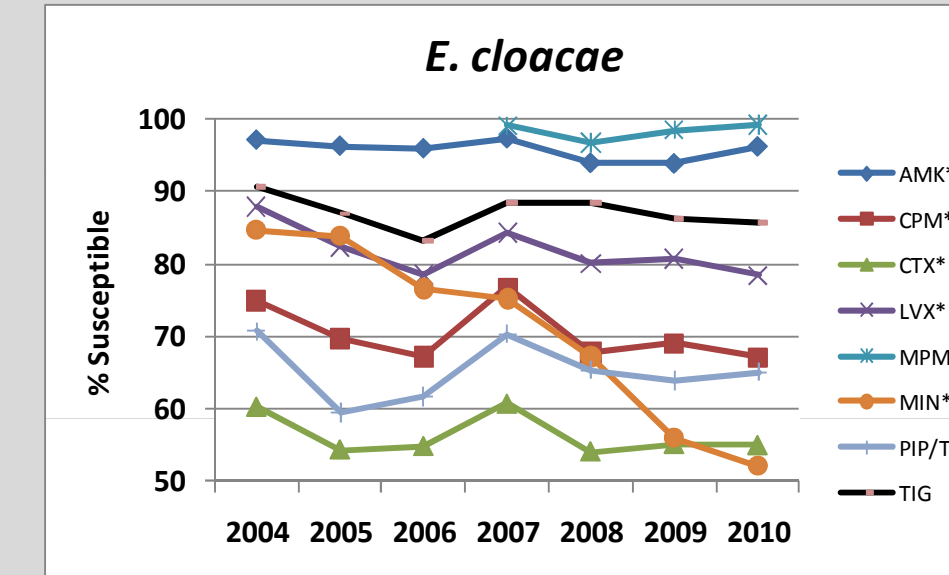
Results

Figure 1. Percent susceptibility of *E. aerogenes* (n = 1,921) from 2004 – 2010 to antimicrobial agents.



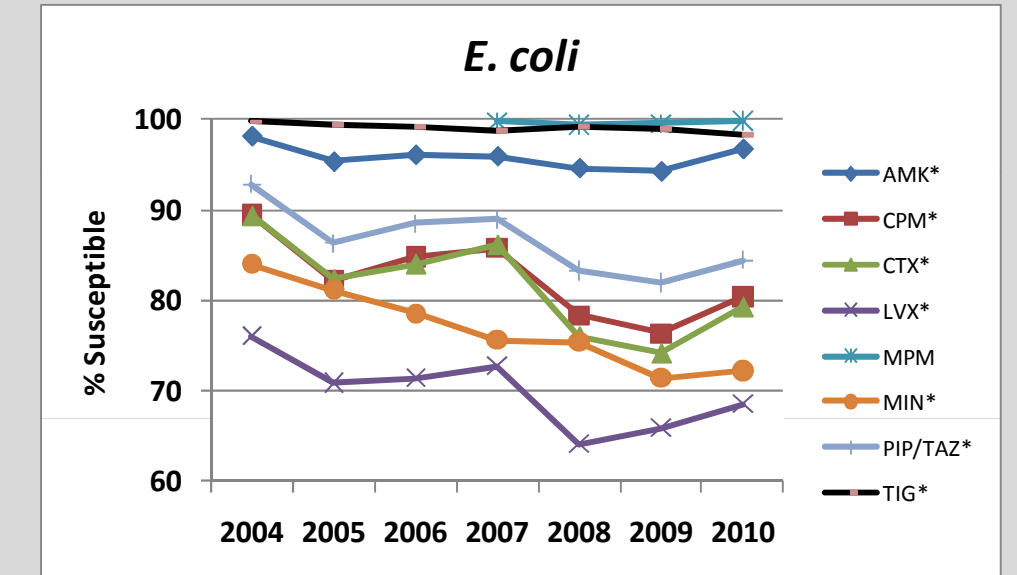
AMK, amikacin; CPM, cefepime; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).
** Statistically significant increasing trend in %S ($p < 0.05$).

Figure 2. Percent susceptibility of *E. cloacae* (n = 6,989) from 2004 – 2010 to antimicrobial agents.



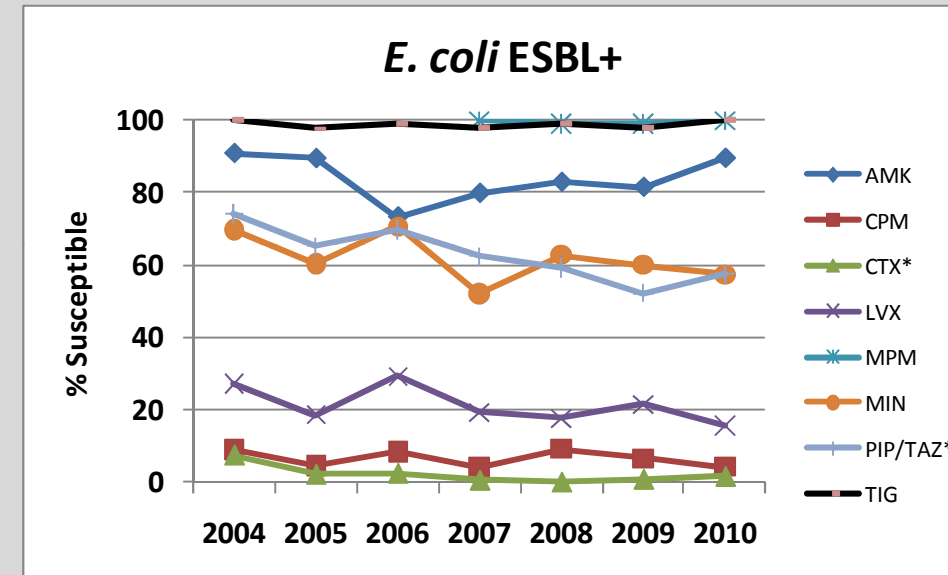
AMK, amikacin; CPM, cefepime; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).

Figure 3. Percent susceptibility of *E. coli* (n = 10,038) from 2004 – 2010 to antimicrobial agents.



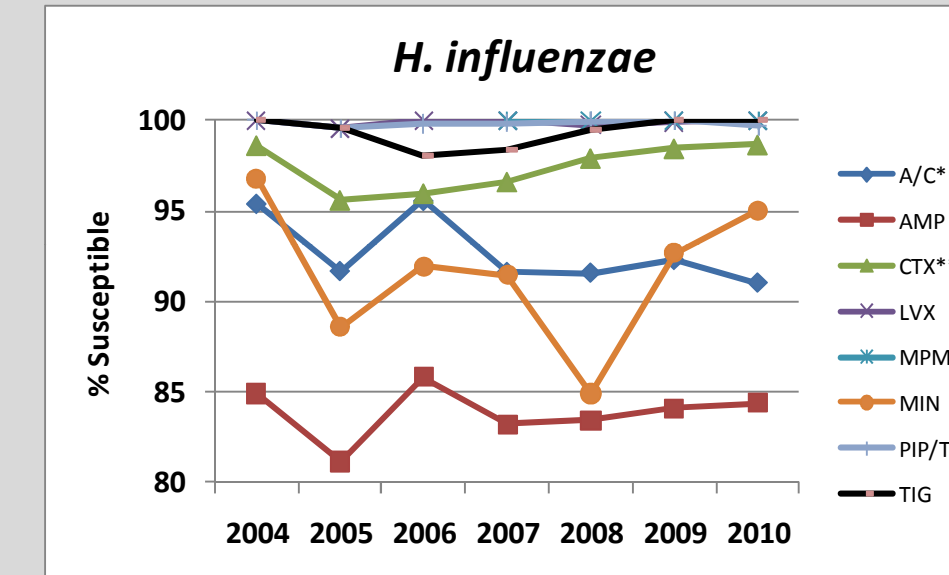
AMK, amikacin; CPM, cefepime; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).

Figure 4. Percent susceptibility of *E. coli* ESBL+ (n = 1,481) from 2004 – 2010 to antimicrobial agents.



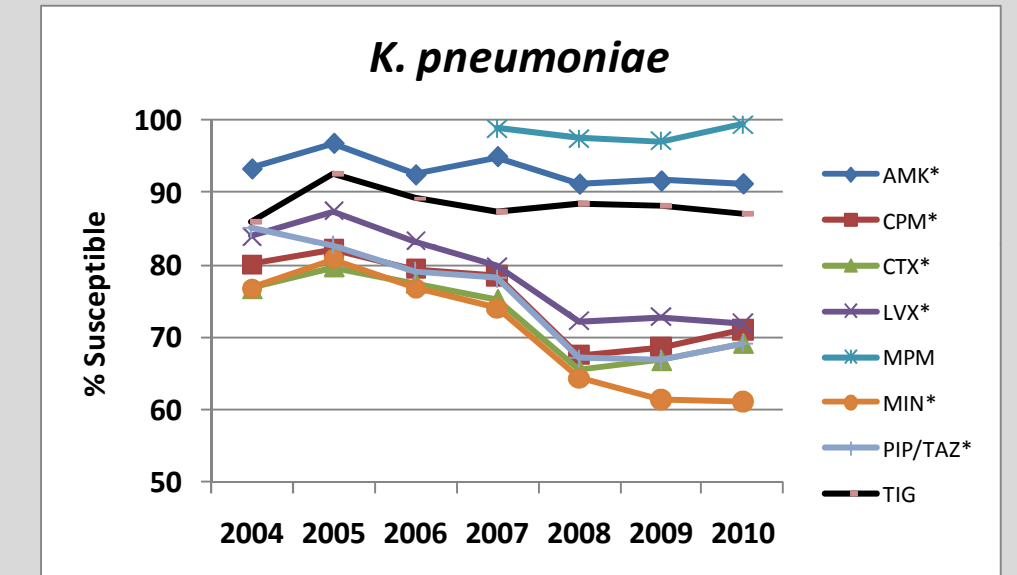
AMK, amikacin; CPM, cefepime; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).

Figure 5. Percent susceptibility of *H. influenzae* (n = 4,370) from 2004 – 2010 to antimicrobial agents.



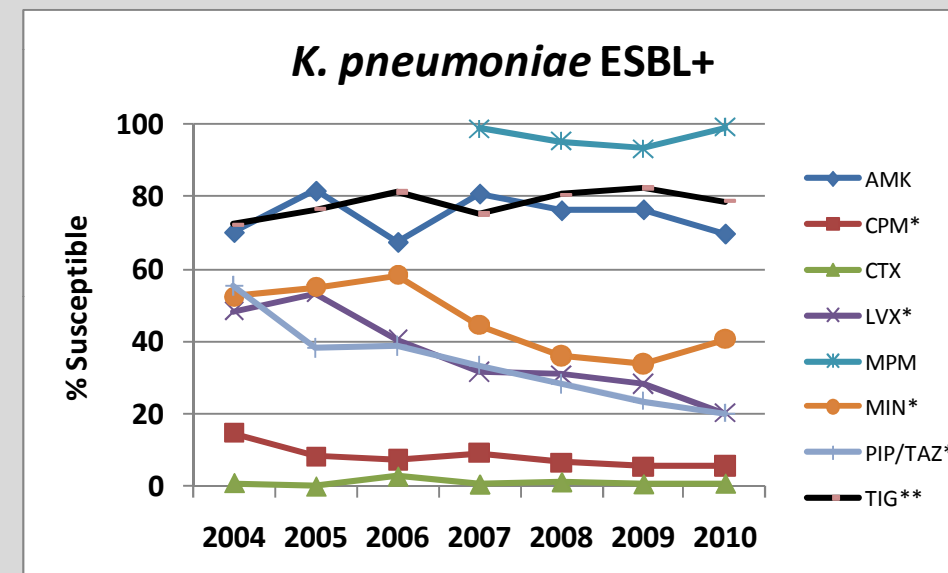
A/C, amoxicillin-clavulanic acid; AMP, ampicillin; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).
** Statistically significant increasing trend in %S ($p < 0.05$).

Figure 6. Percent susceptibility of *K. pneumoniae* (n = 7,157) from 2004 – 2010 to antimicrobial agents.



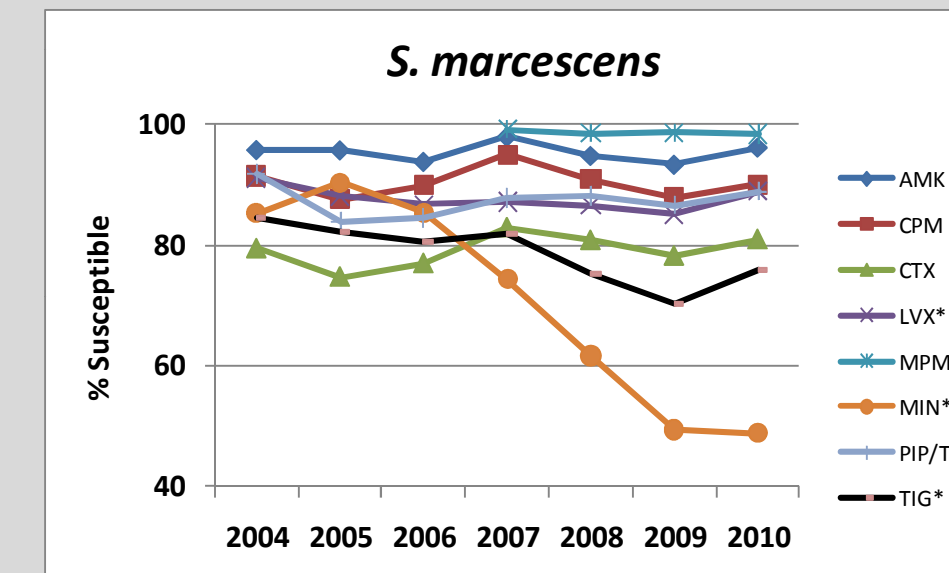
AMK, amikacin; CPM, cefepime; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).

Figure 7. Percent susceptibility of *K. pneumoniae* ESBL+ (n = 1,523) from 2004 – 2010 to antimicrobial agents.



AMK, amikacin; CPM, cefepime; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).
** Statistically significant increasing trend in %S ($p < 0.05$).

Figure 8. Percent susceptibility of *S. marcescens* (n = 3,513) from 2004 – 2010 to antimicrobial agents.



AMK, amikacin; CPM, cefepime; CTX, ceftioxone; LVX, levofloxacin; MPM, meropenem; MIN, minocycline; PIP/TAZ, piperacillin-tazobactam; TIG, tigecycline
* Statistically significant decreasing trend in %S ($p < 0.05$).

Conclusions

- Trending analyses of the six gram-negative species showed that susceptibility to tigecycline largely remained stable during 2004 – 2010.
- Statistically significant decreases in tigecycline susceptibility were observed only for *E. coli* and *S. marcescens* ($p < 0.05$) during 2004 – 2010.
- On the contrary, susceptibility of ESBL-positive *K. pneumoniae* isolates to tigecycline showed a slight but significant increase ($p < 0.05$) during 2004 – 2010.
- Susceptibility to comparator antimicrobial agents also significantly decreased ($p < 0.05$) during 2004 – 2010 though the decreases were largely drug / organism specific.
- Further trending analyses of the susceptibility of gram-negative organisms to tigecycline and comparators is ongoing.