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Tigecycline antimicrobial activity tested against clinical bacteria from European medical centres: results from the SENTRY antimicrobial surveillance programme (2013-2015)

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Background: To evaluate the *in vitro* activity of tigecycline and comparator agents tested against bacteria causing infections in European medical centres. Tigecycline was initially approved by the European Medicines Agency in 2006 to treat adults with complicated skin and soft tissue (cSSTI) and complicated intra-abdominal infections (cIAI).

Methods: A total of 38,153 clinically significant non-duplicate bacterial isolates from multiple types of infections were collected from 53 medical centres (23 countries) across Europe from 2013 to 2015. Susceptibility testing was performed by reference broth microdilution method and results interpreted according to EUCAST breakpoint criteria. Multidrug-resistant (MDR) and extensively-drug resistant (XDR) were defined as resistant to ≥3 classes and susceptible to ≤2 classes, respectively.

Results: Isolates were mainly from SSTI (24.9%), bacteremia (23.5%) and pneumonia (21.3%). Tigecycline was highly active against gram-positive organisms with $MIC_{50/90}$ values of 0.06/0.12 mg/L for *Staphylococcus aureus* (n=6,155; 100.0% susceptible), 0.06/0.06 mg/L for enterococci (n=1,699; 99.9% susceptible) and 0.03/0.06 mg/L for beta-haemolytic streptococci (n=1,098; 100.0% susceptible). Vancomycin resistance was observed among 1.2 and 26.5% of *Enterococcus faecalis* and *E. faecium*, respectively; and the highest tigecycline MIC value among vancomycin-resistant enterococci was only 0.12 mg/L. When tested against 16,285 Enterobacteriaceae strains, tigecycline $MIC_{50/90}$ values were 0.25/1 mg/L (94.3% susceptible). No trend toward increasing tigecycline resistance (non-susceptibility) was observed for any species/group during the study period. The prevalence MDR, XDR, and carbapenem-resistant Enterobacteriaceae (CRE) were 20.3% (n=3,298), 4.3% (n=704) and 2.2% (n=359), respectively; tigecycline inhibited 85.8, 68.9 and 92.2% of these organism groups at ≤1 mg/L (EUCAST breakpoint), and 96.4, 92.5 and 99.4% at ≤2 mg/L (US-FDA breakpoint), respectively. The prevalence of *Escherichia coli* and *Klebsiella pneumoniae* with an extended-spectrum β-lactamase (ESBL) phenotype were 20.1 and 48.1%, respectively; and tigecycline was active (MIC, ≤1 mg/L) against 99.7 and 93.7% of isolates, respectively. Meropenem

and colistin were active against 71.4 and 84.4% of ESBL phenotype *K. pneumoniae* at the susceptible EUCAST breakpoint, respectively. Tigecycline was also very active against *Haemophilus influenzae* (n=1,686; $MIC_{50/90}$, 0.12/0.25 mg/L) and *Moraxella catarrhalis* (n=680; $MIC_{50/90}$, 0.03/0.06 mg/L) and demonstrated moderate activity against *Acinetobacter* spp. (n=1,316; $MIC_{50/90}$, 1/2 mg/L) and *Stenotrophomonas malthophilia* (n=469; $MIC_{50/90}$, 0.5/2 mg/L).

Conclusions: The results of this investigation showed that tigecycline generally retained potent activity against clinically important organisms isolated in European hospitals, including MDR organism subsets of gram-positive and -negative pathogens. Based on the potency and spectrum, tigecycline continues to have an important role for treating of infections caused by indicated Enterobacteriaceae organisms in Europe, including those caused by MDR isolates.