Activity of linezolid when tested against contemporary European bacterial clinical isolates (2015)

Robert Flamm*1, Rodrigo E. Mendes1, Jennifer M. Streit1, Helio Sader1, Patricia A. Hogan2, Ronald N. Jones3

1Jmi Laboratories, North Liberty, United States
2Pfizer Inc., New York, United States
3Jmi Laboratories, North Liberty, Ia, United States

Background: International bacterial surveillance has shown that although very uncommon, linezolid resistance has been observed among coagulase-negative staphylococci (CoNS) in more frequency than enterococci. Resistance remains even lower among Staphylococcus aureus and streptococci. In this study, an interim evaluation of in vitro activity of linezolid and comparators against isolates from the European and Israeli component of the 2015 Zyvox® Annual Appraisal of Potency and Spectrum (ZAAPS) surveillance program are presented.

Methods: More than 4,000 isolates were collected from over 30 sites in Europe and Israel in 2015. Isolates were received from the following organism groups: S. aureus, CoNS, Enterococcus spp., Streptococcus pneumoniae, viridans group streptococci, and β-haemolytic streptococci. Isolates from each country were sent to a central monitoring laboratory for confirmatory identification and CLSI broth microdilution susceptibility testing. Susceptibility interpretations followed EUCAST breakpoint tables (Version 5.0, 2015). Isolates displaying elevated linezolid MIC results (≥4 mg/L) were retested using frozen broth microdilution, Etest and disk diffusion methods. PCR and sequencing were performed to detect mutations in 23S rRNA, L3, L4, and L22 genes, and acquired determinants (cfr, optrA).

Results: All S. aureus were susceptible to linezolid (MIC50/90, 1/1 mg/L), daptomycin, tigecycline, and vancomycin. MRSA represented 20.8% of S. aureus. Enterococci (MIC50/90, 1/2 mg/L), β-haemolytic streptococci (MIC50/90, 1/1 mg/L), viridans group streptococci (MIC50/90, 1/1 mg/L) and S. pneumoniae (MIC50/90, 1/1 mg/L) were all susceptible to linezolid. S. pneumoniae had overall penicillin and erythromycin resistant rates of 31.8% (MIC, ≥2mg/L) and 26.6%, respectively. Linezolid susceptibility for CoNS (64.7% methicillin-resistant CoNS) was 99.4%. Three linezolid-resistant CoNS were found. These were hospital-acquired isolates recovered from blood (two) and wound (one) specimens. These isolates originated from two sites in Italy and had linezolid MIC values of 16, 32 and 64 mg/L. Alterations in the 23S rRNA were observed in all three CoNS, but one isolate also carried cfr (linezolid MIC, 64 mg/L).

Conclusions: In this interim view of the 2015 European component of ZAAPS, linezolid-resistance remains uncommon (<1%). A linezolid resistance phenotype was only observed among CoNS, which were hospital-acquired isolates exhibiting a common linezolid resistance mechanism (target site alteration in 23S rRNA). Additionally, one isolate also had a plasmid-mediated resistance (cfr), emphasizing the importance of ongoing surveillance and molecular characterization of resistant isolates.