

**P1823 In vitro activity of lefamulin against contemporary *Staphylococcus aureus* isolates from patients in Europe (SENTRY 2016)**

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**Background:** Lefamulin is the first semi-synthetic pleuromutilin antibiotic for IV and oral treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI). Lefamulin specifically inhibits bacterial protein translation by binding to the peptidyl transferase center (“induced fit”). Lefamulin is highly active in the lung *in vivo* and has recently completed a Phase 3 clinical trial for the treatment of CABP in adults showing non-inferiority to moxifloxacin (+/-linezolid). *Staphylococcus aureus* is a well-recognized cause of pneumonia, ABSSSI, and bloodstream infections (BSI), and management can be challenging due to high antibacterial resistance rates. This study investigated the activity of lefamulin and comparators against contemporary *S. aureus* isolates.

**Materials/methods:** 550 unique *S. aureus* isolates were collected from hospitalised patients with BSI (50.0%), ABSSSI (30.0%), and pneumonia (20.0%) in 19 European countries (37 sites) during 2016 as part of the SENTRY Surveillance Program. Susceptibility testing was conducted using the CLSI broth microdilution method and susceptibility was interpreted per EUCAST 2017 breakpoint criteria.

**Results:** Lefamulin was one of the most potent compounds tested, with 99.6% of all isolates inhibited at a concentration of  $\leq 0.25$  mg/L (MIC<sub>50/90</sub> values of 0.06/0.12 mg/L). Susceptibility rates were >90% for clindamycin (MIC<sub>50/90</sub>,  $\leq 0.25$  mg/L/ $\leq 0.25$  mg/L), doxycycline (MIC<sub>50/90</sub>,  $\leq 0.06/0.25$  mg/L), tigecycline (MIC<sub>50/90</sub>,  $\leq 0.06/0.12$  mg/L), vancomycin (MIC<sub>50/90</sub>, 0.5/1 mg/L), linezolid (MIC<sub>50/90</sub>, 1/1 mg/L) and ceftaroline (MIC<sub>50/90</sub>, 0.25/1 mg/L). Oxacillin-resistant isolates (MRSA) totaled 28.2% and were inhibited by lefamulin (MIC<sub>99</sub>, 0.25 mg/L), tigecycline (MIC<sub>99</sub>, 0.25 mg/L), vancomycin (MIC<sub>99</sub>, 1 mg/L) and linezolid (MIC<sub>99</sub>, 2 mg/L), while demonstrating high resistance rates to azithromycin (55.5%), levofloxacin (71.0%) and clindamycin (21.3%).

**Conclusions:** *S. aureus* strains collected from patients with BSI, ABSSSI, and pneumonia were highly susceptible to lefamulin regardless of resistance phenotype to the other antibiotics tested. Due to its potent activity against the most prevalent typical and atypical respiratory pathogens, including MRSA and the availability of IV and oral formulations, lefamulin has the potential to play a role in the empiric treatment of CABP and ABSSSI.