ABSTRACT

Background: S. aureus (SA) is a well-recognized cause of pneumonia from both the community and hospital settings. The clinical management of SA pneumonia is complicated by the invasive infection it can cause and the high prevalence of methicillin resistance (MR). Lefamulin (LEF) is the first semi-synthetic pleuromutilin antibiotic for IV and oral use in humans and it specifically inhibits bacterial protein synthesis. LEF is currently in Phase 3 trials for the treatment of community-acquired bacterial pneumonia (CABP). This study investigated the in vitro activity of LEF and comparators against SA strains collected from patients hospitalized with pneumonia in 2015.

Methods: L.173 unique SA isolates were collected from hospitalized patients with pneumonia worldwide in 28 countries (33 sites) in 2015 as part of the SENTRY surveillance program. Isolates included 401 hospital-acquired (HA) SA (259 from ICU, 152 from ventilator associated pneumonia, VAP). Susceptibility testing was conducted using the CLSI broth microdilution method and susceptibility was interpreted per CLSI 2017 B17 guidelines.

Results: LEF was the most potent compound tested, with 99.3% of all SA isolates being inhibited at a concentration of ≤0.03 mg/L (MIC50/90 values of 0.06/0.12 mg/L) and irrespective of the collection source (ICU/non-ICU). Success rates for all SA isolates were >99% for ceftaroline, vancomycin, linezolid and doxycycline. Susceptibility to azithromycin, levofloxacin and clindamycin (ICU/non-ICU, VAP/non-VAP). 31.6% of isolates (n=528; MSSA and MRSA) were resistant to clindamycin (MIC50/90 = 0.06/0.12 mg/L).

CONCLUSIONS

These data support the development of lefamulin for infections caused by S. aureus, including resistant isolates (Table 2, Figures 1 and 2). Lefamulin was the most potent compound tested with 99.3% inhibited at a lefamulin concentration of ≤0.03 mg/L (MIC50/90 values of 0.06/0.12 mg/L).

Lefamulin was the most active compound against MRSA and MSSA, including both, community-acquired and nosocomial isolates, irrespective of the resistance phenotype to other antibiotic classes including macrolides, fluoroquinolones, tetracyclines or β-lactam antibiotics.

S. aureus is largely susceptible to doxycycline (97.6%), ceftriaxone (93.3%), linezolid (99.9%) and vancomycin (100%).

Conclusion: SA is a well-recognized cause of pneumonia from both the community and hospital settings. Lefamulin is the first semi-synthetic pleuromutilin antibiotic for IV and oral use in humans and it specifically inhibits bacterial protein synthesis. LEF has the potential to play a role in the empiric treatment of CABP and is particularly useful among MRSA.

REFERENCES

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