ABSTRACT

Delafloxacin (DLX) is a broad-spectrum fluoroquinolone which has been approved by the FDA for the treatment of adults of EC and PA. For EC, isolates with DLX MICs ≤0.25 μg/mL comprised 97.8% for stasis at an MIC of 0.25 μg/mL, and 99.3% for 1-log10 bacterial reduction, for each organism and strain. Delafloxacin demonstrated dose-dependent killing of E. coli and P. aeruginosa both 

INTRODUCTION

Delafloxacin (DLX) is a novel fluoroquinolone currently under FDA review for the treatment of adult skin and skin structure infections. Delafloxacin is a member of the quinolone class of antibiotics and is a novel fluorinated analog of lomefloxacin. DLX has been shown to have in vitro activity against Gram-positive and Gram-negative organisms. Delafloxacin's pharmacodynamic (PD) profile is characterized by high and sustained free AUC/MIC values, which have been correlated with therapeutic success. Delafloxacin has demonstrated activity against Enterococcus faecalis, Staphylococcus aureus, and Pseudomonas aeruginosa (PA) in vitro, including isolates resistant to several fluoroquinolones.

Delafloxacin MICs

Delafloxacin was evaluated at concentrations of 0.008–320 μg/mL. The MIC distribution was determined by broth microdilution, with the breakpoints regarded as follows: susceptible (SUS), intermediate (INT), and resistant (RES). The MIC distribution of the three isolates was represented by the mean MIC, which was lower than the susceptibility breakpoint of 0.25 μg/mL.

Delafloxacin MIC Distributions and Weighted PK/PD Target Attainment

The target attainability for DLX was determined by fitting curves to the results of the mouse efficacy experiments with doses ranging from 0.5 to 320 mg/kg. The target attainment probability curves are shown overlaid on the MIC distributions in Figure 4 and Figure 5. The probability of achieving a 1-log10 bacterial reduction was high (~100%) for all DLX doses tested, indicating that DLX concentrations were adequate to treat the majority of isolates of E. coli and P. aeruginosa.

CONCLUSION

The ability of DLX to target dangerous bacterial isolates, including those with MICs ≤0.25 μg/mL, has been demonstrated in vivo. The potential of DLX to inhibit bacteria, bacterial selection, and reduction of bacterial load (MIC ≤0.25 μg/mL), indicates that DLX may be effective in treating infections caused by these organisms. Further studies are needed to evaluate the efficacy of DLX in treating infections caused by resistant isolates.