In Vitro Bactericidal Activity of KPI-10, a Next-Generation Fluoroquinolone (FQ), Against FQ-Susceptible (FQ-S) and FQ-Resistant (FQ-R) Gram-Negative and Gram-Positive Isolates

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Abstract

Background: KPI-10 demonstrates potent broad-spectrum activity against key nosocomial pathogens, including FQ-R isolates. The aim of the study was to assess the in vitro activity of KPI-10 against selected FQ-S and FQ-R strains.

Methods: The MIC was measured using CLSI methods. Time-kill curves were performed at 0.125× to 16× MIC against a panel of key pathogens, including FQ-S and FQ-R strains. A flask of inoculated cation-adjusted MH broth with no antibiotic served as the negative control. Post-antibiotic effect (PAE) was determined by exposure to a drug concentration equivalent to 4× the MIC for 30 min. The MICs were determined in cation-supplemented MH broth by the CLSI microdilution method.

Results: Bactericidal activity (≥3 log10 CFU/mL) was achieved for KPI-10 against all FQ-S isolates, except for a FQ-R A. baumannii strain exhibiting a decrease of 2.53 log10 CFU/mL. KPI-10 exhibited bactericidal activity against all FQ-S isolates, including FQ-R strains. The MICs of KPI-10 and comparators (ciprofloxacin (CIP) and levofloxacin (LVX)) are summarized in Table 1 and Table 2 for Gram-positive and Gram-negative isolates, respectively. Time-kill curves are shown for Gram-positive and Gram-negative isolates in Figure 1 and Figure 2, respectively. FIC index results are summarized in Table 3 and Table 4. PAE data are shown in Table 5.

Discussion / Conclusion

- KPI-10 showed broad-spectrum activity and lower MICs than comparators against almost all Gram-positive and Gram-negative bacteria.
- KPI-10 demonstrated excellent bactericidal activity against all pathogen tested, including fluoroquinolone-resistant gram-negative pathogens.
- Additivity was the main interaction observed between KPI-10 and each partner drug against all the strains tested in the present study. No antagonism was detected with KPI-10 against Gram-negative bacteria, including in combination with amikacin, tigecycline, cefazidime, telithromycin, and meropenem. A positive synergistic interaction (FIC index of ≤0.5) was observed between KPI-10 and other drugs with:
  - Tigecycline against FQ-S and FQ-R strains.
  - Meropenem against FQ-R and FQ-R strains.
  - As previously demonstrated with other fluoroquinolones, antagonism was observed between KPI-10 and other drugs with:
    - Amikacin against both FQ-S and FQ-R strains.

- On the basis of these findings, further studies of KPI-10 are warranted to explore the in vivo activity of this new fluoroquinolone against both Gram-positive and Gram-negative pathogens in various animal experimental models.