F-1512

ABSTRACT

Background: F-1512 is a new glycopeptide antimicrobial agent. In this study, time-kill and post-antibiotic effect (PAE) experiments were performed to evaluate its in vitro activity of SP2078 tested against MRSA and VISA strains.

Methods: One strain each of vancomycin-susceptible S. aureus (VSSA; ATCC 29213), vancomycin-intermediate S. aureus (VISA, NRS 17), and vancomycin-resistant (VanA) S. aureus (Vancomycin-resistant, VanA) (ATCC 51559) were selected for testing. Inocula were prepared aerobically and each strain was exposed to 2, 4, 8, and 16 µg/mL of F-1512 for 24 h. To determine the bactericidal or bacteriostatic activity, colony counts were performed at T0, T2, T4, T8 and T24. A killing effect was obtained for F-1512 at 8 and 16 µg/mL against a VISA strain within 24h, while static results were observed within 24h against a VISA. F-1512 concentrations tested inhibited the bacterial growth (3-5 log10). When tested at 2 and 4 µg/mL, F-1512 showed bacteriostatic activity against a VISA strain (≥4 log10). Vancomycin showed static activity when tested against the VISA strain (≥4 log10), while bactericidal activity was observed at 16 µg/mL.

RESULTS

Bacterial isolates. One strain each of vancomycin-susceptible S. aureus (VSSA; ATCC 29213), vancomycin-intermediate S. aureus (VISA, NRS 17) and vancomycin-resistant (VanA) S. aureus (ATCC 51559) were selected for this study. Inocula were prepared aerobically for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; Approved Standard: Ninth edition (M07-A9, 2012) and CLSI guidelines. F-1512 was utilized as an investigational compound followed the CLSI recommendations for vancomycin resistant (Table 1). Inocula were prepared with 10^8-10^9 CFU/mL for the time-kill experiments. To determine the bactericidal or bacteriostatic activity, colony counts were performed at T0, T2, T4, T8 and T24.

Bacterial susceptibility testing (Table 1). Inoculates were tested for susceptibility by broth microdilution methods following the Clinical and Laboratory Standards Institute (CLSI) guidelines. F-1512 concentration (µg/mL) was determined by the agar dilution method (M07-A9, 2012). The Clinical and Laboratory Standards Institute (M07-A9, 2012) provides the concentration-activity values of 0.5 µg/mL to ≥4 µg/mL for determining bactericidal activity of antimicrobial agents; Approved Standard: Ninth edition (M07-A9, 2012). Susceptibility testing was performed in cation-supplemented Mueller-Hinton broth (CAM-HNB) using standardized microtiter plate forms. F-1512 was supplemented with the surfactant polysorbate-80 (0.002%). MIC results were expressed as the minimal concentration that prevented visible bacterial growth for 24 h (Table 2). Vancomycin MIC values were provided by the Clinical and Laboratory Standards Institute (M07-A9, 2012).

Potency and PAE. F-1512 is a novel glycopeptide agent (SP2078; see poster ICAAC 2012) in preclinical development for the treatment of severe clinical conditions of patients infected by these pathogens and severe clinical conditions of patients infected by these pathogens. In this study, time-kill and post-antibiotic effect (PAE) experiments were performed to evaluate the F-1512 in vitro activity against selected strains.

Vancomycin has long been the gold standard agent for the empirical management of serious gram-positive infections, including those caused by MRSA and VISA. Despite this, vancomycin resistance continues to rise, recognized limitations, including low cidal activity, tolerance, and high resistance rates. New glycopeptide agents are being developed to treat infections caused by these pathogens and severe clinical conditions of patients infected by these pathogens. 

F-1512 demonstrated the effectiveness of the antibiotic activity against various strains. Therefore, the antibiotic activity of F-1512 is in preclinical development for the treatment of serious clinical conditions of patients infected by these pathogens. In this study, time-kill and post-antibiotic effect (PAE) experiments were performed to evaluate the F-1512 in vitro activity against selected strains.

REFERENCES

1. Clinical and Laboratory Standards Institute (CLSI) guidelines. F-1512 is a novel glycopeptide agent (SP2078; see poster ICAAC 2012) in preclinical development for the treatment of severe clinical conditions of patients infected by these pathogens and severe clinical conditions of patients infected by these pathogens. In this study, time-kill and post-antibiotic effect (PAE) experiments were performed to evaluate the F-1512 in vitro activity against selected strains.

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