In Vitro Activity of RX-P873 Tested against Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter spp.

INTRODUCTION

Preclinical testing of RX-P873 demonstrated high potency and selectivity against Gram-negative and Gram-positive bacteria selected from various medical institutions located in North America and Europe. The MIC50 and MIC90 for RX-P873 against 51 strains (C. freundii) was >32 fold more active than tigecycline (MIC90, 4 µg/ml). The compound RX-P873 was shown to be very active against isolates of S. marcescens, P. aeruginosa, Acinetobacter spp., and A. baumannii. RX-P873 inhibited all isolates at ≤0.06 µg/ml with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively (Table 1). Meropenem resistance was 5.0%/4.5% by CLSI/EUCAST (2013). Meropenem MIC values were determined using Clinical and Laboratory Standards Institute (CLSI) methodology as described in CLSI document M27-A3 (2012). Quality Control (QC) strains were tested daily and QC ranges and interpretive criteria for the comparator compounds were based on CLSI (2013). The highest MIC parameters observed for all seven species/groups tested were ≤0.06 µg/ml (USA ≤0.12 µg/ml; ≥32 ≤0.06 µg/ml). RX-P873 was ≤2 µg/ml (USA ≤1 µg/ml). Gentamicin was ≤2 µg/ml (USA ≤1 µg/ml).

RESULTS

Enterobacteriaceae

The range of RX-P873 MIC values was 0.06 to 0.25 µg/ml with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively (Table 1). Only four of the 51 strains were resistant to RX-P873 with MIC values ≥2 µg/ml. Against K. pneumoniae, the range of RX-P873 MIC values was 0.12 to 2 µg/ml with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively (Table 1). Meropenem resistance was 5.0%/4.5% by CLSI/EUCAST criteria, resistance and susceptibility to RX-P873 were >32 fold more active than meropenem (MIC90 values: 0.25 and 2 µg/ml, respectively). Against E. coli, the range of RX-P873 MIC values was 0.12 to 1 µg/ml with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively. All isolates were inhibited by RX-P873 at MIC values ≤2 µg/ml (≥93% susceptible). RESISTANCE (CLSI) for other agents ranged from 0.2% for tigecycline to 46% for ciprofloxacin. For colistin, 4.1% (1 strain) of the isolates tested were not susceptible by CLSI interpretive criteria (Table 1). RX-P873 resistance against all of these strains was ≤0.06 µg/ml. A. baumannii was the only species to show resistance to ciprofloxacin, colistin, and meropenem (Table 1). RX-P873 was ≤0.06 µg/ml (USA ≤0.12 µg/ml) with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively (Table 1).

Susceptibility testing: MIC values were determined using Clinical and Laboratory Standards Institute (CLSI) broth microdilution methodology as described in CLSI document M07-A9 (2012). The compound RX-P873-P873 was highly active against P. aeruginosa, A. baumannii, K. pneumoniae, and K. oxytoca with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively. For ciprofloxacin, MIC50 and MIC90 values of 8 µg/ml were observed against E. coli (Table 2). RX-P873 inhibited all isolates at ≤0.06 µg/ml with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively (Table 2). Meropenem resistance was 5.0%/4.5% by CLSI/EUCAST (2013). Meropenem MIC values were determined using Clinical and Laboratory Standards Institute (CLSI) methodology as described in CLSI document M27-A3 (2012). Quality Control (QC) strains were tested daily and QC ranges and interpretive criteria for the comparator compounds were based on CLSI (2013). The highest MIC parameters observed for all seven species/groups tested were ≤0.06 µg/ml (USA ≤0.12 µg/ml; ≥32 ≤0.06 µg/ml). RX-P873 was ≤2 µg/ml (USA ≤1 µg/ml). Gentamicin was ≤2 µg/ml (USA ≤1 µg/ml).

REFERENCE

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Table 1. Clinical and Laboratory Standards Institute (CLSI) interpretive criteria and susceptibility testing results for RX-P873 against Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter spp. from various medical institutions located in North America and Europe.

Table 2. Activity of RX-P873 and comparator antibacterial agents when tested against 36 Enterobacteriaceae and 42 non-fermentative Gram-negative bacilli from a worldwide surveillance program.

Table 3. Activity of RX-P873 and comparator antibacterial agents tested when tested against 51 Enterobacteriaceae and 42 non-fermentative Gram-negative bacilli from a worldwide surveillance program.

Figure 1. Chemical structure of RX-P873

CONCLUSIONS

RX-P873 demonstrated high potency and selectivity against Gram-negative and non-fermentative bacilli selected from various medical institutions located in North America and Europe. The MIC90 for RX-P873 against 51 Enterobacteriaceae was ≤0.06 µg/ml. RX-P873 demonstrated high potency and selectivity against Enterobacteriaceae. RX-P873 inhibited all isolates at ≤0.06 µg/ml with MIC50 and MIC90 values of 0.25 and 0.5 µg/ml, respectively (Table 1). Meropenem resistance was 5.0%/4.5% by CLSI/EUCAST (2013). Meropenem MIC values were determined using Clinical and Laboratory Standards Institute (CLSI) methodology as described in CLSI document M27-A3 (2012). Quality Control (QC) strains were tested daily and QC ranges and interpretive criteria for the comparator compounds were based on CLSI (2013). The highest MIC parameters observed for all seven species/groups tested were ≤0.06 µg/ml (USA ≤0.12 µg/ml; ≥32 ≤0.06 µg/ml). RX-P873 was ≤2 µg/ml (USA ≤1 µg/ml). Gentamicin was ≤2 µg/ml (USA ≤1 µg/ml).

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