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

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ABSTRACT

Background: RX-P873 (RX) is a novel antibiotic which is the lead compound in a series that targets a biologically-conserved region in the bacterial ribosome. RX-P873 is from the pyrrolocytosine series, one of three de novo-designed molecular scaffolds with high tiding activity and potential that have been rationally developed to target multidrug-resistant (MDR) Gram-negative and Gram-positive bacilli. This antibiotic has shown in vitro activity and preclinical efficacy against multidrug resistant (MDR) Gram-negative and Gram-positive bacilli selected from various medical institutions located in North America and Europe to represent the contemporary distribution of antibiotic resistance. RX-P873 also demonstrated susceptibility profiles within each organism species or group as follows: Enterobacteriaceae (202 strains), Klebsiella pneumoniae (200 strains); E. coli (11 strains), Proteus mirabilis (two strains); Klebsiella oxytoca (two strains); Enterobacter aerogenes (51 strains); Acinetobacter spp. (50 strains); Pseudomonas aeruginosa (200 strains); P. stuartii (20 strains); and non-fermentative Gram-negative bacilli (two strains).

OBJECTIVE: To determine the in vitro activity of RX-P873 against a contemporary, broad-spectrum panel of Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter spp. from various medical institutions located in North America and Europe.

MATERIALS AND METHODS

Enterobacteriaceae (A. baumannii, P. aeruginosa, and Acinetobacter spp.) isolates were collected as part of a worldwide surveillance program were selected from various medical institutions located in North America and Europe to represent the contemporary distribution of antibiotic resistance. RX-P873 was tested against these isolates using dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved by Clinical Laboratory Standards Institute (CLSI) document M07-A9 (2012). Quality Control (QC) strains were tested as published in CLSI M100-S24 (2014); tested QC ranges and interpretive criteria were selected. Isolates from various medical institutions located in North America and Europe to represent the contemporary distribution of antibiotic resistance.

RESULTS: The range of RX-P873 MIC values was 0.06 to 2 µg/ml with MIC90 values of 0.5 and 2 µg/ml respectively (Table 1). Against E. coli, resistance to all other comparator agents (except tigecycline) was >24.0% for meropenem. For non-fermentative Gram-negative bacilli (two strains), RX-P873 was ≤0.12 µg/ml, with MIC90 values of 0.06 and 0.5 µg/ml, respectively (Table 2).

CONCLUSIONS: RX-P873 demonstrated high and consistent potency against MDR Enterobacteriaceae and non-fermentative bacilli selected from various medical institutions located in North America and Europe, providing a broad-spectrum, potent and highly active agent against this contemporary set of Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter spp. RX-P873 was shown to be very active against Enterobacteriaceae strains due to its ability to provide susceptible and resistant resistance to pipeline/bactericidal, ceftriaxone, ceftazidime, colistin, gentamicin, meropenem and tigecycline.

REFERENCE


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Introduction

Pharmacology

Clinical

Biologic Data

Toxicity

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