Antimicrobial Activity and Spectrum of compounds from the RX-04 class of Novel Protein Synthesis Inhibitors

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Abstract

The RX-04 class of protein synthesis inhibitors demonstrates broad antimicrobial activity against contemporary Gram-negative bacilli. In addition, the RX-04 compounds are efficacious in mouse models of infection. To more fully characterize the antibacterial spectrum of the RX-04 compounds, current studies describe activity against MDR strain sets from different locations.

Methods

A total of 100 non-duplicate clinical isolates were collected from medical centers located across the United States during 2009 (30) and 2010 (70). All isolates were collected over a 2 year period and were confirmed MDR by CLSI MDR interpretive criteria. The RX-04 compounds were selected for their broad spectrum of activity against contemporary Gram-negative pathogens.

Results

Table 1. Activity profile of RX-04 compounds against Gram-negative organisms.

Table 2. Activity profile of RX-04 compounds against C. freundii and S. marcescens.

Table 3. Activity profile of RX-04 compounds against A. baumannii and P. aeruginosa.

Table 4a. Activity profile of RX-04 compounds against Gram-negative organisms by phenotype.

Table 4b. Activity profile of RX-04 compounds against Gram-negative organisms by phenotype.

Table 5. MIC distributions of RX-04 compounds against Gram-negative organisms.

Table 6a. Activity profile of RX-04 compounds against Gram-negative organisms by phenotype.

Table 6b. Activity profile of RX-04 compounds against Gram-negative organisms by phenotype.

Table 7. MIC distributions of RX-04 compounds against MDR organisms.

Conclusions

Similar to the data shown for the more commonly isolated Gram-negative pathogens, organisms such as A. baumannii and P. aeruginosa also demonstrate reduced susceptibility to many currently marketed drugs. RX-P770 is one of the best performing agents against these organisms with the most potent compounds having MIC50/90s no greater than 1-2 µg/mL. In addition, the RX-P770 MIC distribution against both A. baumannii and P. aeruginosa is notably more uniform against these MDR strain sets.

References
