COLISTIN-RESISTANT ORGANISMS

ABSTRACT

Background: CB-182,804 is a novel synthetic polymyxin B analog that inhibits bacterial growth and has shown rapid bactericidal activity against various Gram-negative bacteria, including multidrug-resistant (MDR) organisms.

Methods: A35 strains selected from various surveillance programs were assessed for susceptibility to CB-182,804 by a broth microdilution method. The activity of CB-182,804 against clinical isolates of various Gram-negative bacteria was determined to understand the potential role of CB-182,804 in the treatment of infections due to MDR bacteria.

Results: Of 35 bacterial species tested, CB-182,804 was active against all except one (P. aeruginosa). CB-182,804 was also active against 20% and 60% of Enterobacteriaceae and carbapenemase-producing P. aeruginosa, respectively. CB-182,804 was very active against Acinetobacter spp. and MDR clinical isolates.

Conclusions: CB-182,804 exhibited in vitro activity and appears similar to colistin (EC; 80), P. aeruginosa (EC; 80), Proteae (IPP; 10), and indole-positive Proteae (IPP; 10).

INTRODUCTION

The continued worldwide emergence of Gram-negative bacterial infections is leading to the development of resistance among clinical isolates. The lack of new therapeutic agents that can be used for the treatment of infections caused by these organisms is a major concern.

RESULTS

Bacterial isolates

A total of 35 Gram-negative bacterial strains were studied, and the susceptibility of these strains to CB-182,804 was determined. The results are summarized in Table 1.

Table 1: Activity of CB-182,804 and comparator agents tested against clinical isolates of Gram-negative bacilli.

| Organism            | MIC (μg/ml) | Comparator | S. marcescens | Enterobacter | Klebsiella pneumoniae | Acinetobacter | P. aeruginosa | Proteae (IPP) | Proteae (IPP) | Proteae (IPP) | E. coli (80) | CB-182,804 | Comparator |
|---------------------|-------------|-----------|---------------|--------------|-----------------------|---------------|---------------|---------------|---------------|---------------|--------------|------------|------------|-----------|
| Aeromonas spp.      | 0.5-8       | Colistin  | 94.7 / 5.3    | 75.0 / 25.0  | 67.9 / 32.1           | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 84.0 / 16.0 | 84.0 / 16.0 |
| Citrobacter spp.    | >16         | Colistin  | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0           | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0 | 100.0 / 0.0 |
| Citrobacter spp.    | >16         | CB-182,804| 87.7 / 10.0   | 75.0 / 25.0   | 87.7 / 12.3           | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 100.0 / 0.0   | 84.0 / 16.0 | 84.0 / 16.0 |

CONCLUSIONS

CB-182,804 exhibited in vitro activity and a potential clinical role similar to that of colistin, which is currently the only agent available for treatment of infections caused by MDR Gram-negative bacteria.

This study was funded by Cubist Pharmaceuticals.

References:


5. Sader HS, Ferraro MJ, Reller B, Schreckenbrger P, Swenson JM, 50th Interscience Conference on Antimicrobial Agents and Chemotherapy, September 12-16, 2009, Boston, MA, USA. This study was funded by Cubist Pharmaceuticals.