Introduction

• Key strategies are required to successfully treat multidrug-resistant gram-negative pathogens.

The antitubercular TpHx vaccine strategy: selecting strains with unique transport mechanisms.

The resulting siderophore-Fe complexes are then taken up by bacterial cells to provide iron for iron-siderophore synthesis.

This process allows efficient delivery of antimicrobials into cells of gram-negative species that possess iron permeable outer membranes.

GT-1 (previously LB-1010) is a new siderophore cephalosporin (Figure 1) with broad-spectrum activity against gram-negative bacteria.

This study reports on the in vitro antimicrobial activity of GT-1 against sets of Pseudomonas aeruginosa and Acinetobacter spp. clinical isolates with specific resistance phenotypes or genotypes.

Materials and Methods

Organism group/organism

• Pseudomonas aeruginosa and Acinetobacter spp. isolates were collected from 110 medical centers in 34 countries.

• P. aeruginosa (18 isolates)

• Acinetobacter spp. (99 isolates)

• Wild-type susceptible (susceptible to colistin and meropenem; 18 isolates)

• Colistin-resistant (95 isolates)

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• Where indicated, the presence of specific β-lactamase genes was confirmed by PCR analysis or whole-genome sequencing.

Siderophores

• Siderophore cephalosporin GT-1

• GT-1 (ID-CAMHB)

• Meropenem-resistant (51 isolates)

• Ceftazidime-resistant and meropenem-susceptible (9 isolates)

• Wild-type (22)

• VIM-1 (1), and unspeciated (51)

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Susceptibility testing

• Unless otherwise indicated, susceptibility testing followed current CLSI guidelines and interpretive criteria, when applicable.

• Bacterial inoculum densities were monitored by colony counts.

• MIC values were validated by concurrently tested CLSI-recommended quality control strains (Escherichia coli ATCC 25922 and P. aeruginosa ATCC 27853).

• Isolates were tested against GT-1 using a broth microdilution method (Table 1).

• Previous investigations evaluating the susceptibility of multidrug-resistant P. aeruginosa and Acinetobacter spp. isolates of different geographic locations showed that bacteriicidal activity was achieved at or near the MIC.

• Because some isolates (particularly Acinetobacter spp.) exhibit a "yielding inhibition of growth" phenomenon in the presence of GT-1 (a known property of siderophore cephalosporins), GT-1 MIC values were read as the lowest concentration of compound that exhibited a significant reduction in growth relative to the growth control.

• The criterion was based on the alternative MAC methodology described by Shangri & Co. in their analysis of the CLSI Methods Development and Standardization Working Group concerning their siderophore cephalosporin GT-1.

Results

Table 1. Activity of GT-1 and comparator agents against phenotypically and genotypically characterized Pseudomonas aeruginosa clinical isolates

<table>
<thead>
<tr>
<th>Organism Group/Isolate</th>
<th>GT-1 (MIC; µg/mL)</th>
<th>Comparator Agents (MIC; µg/mL)</th>
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<tbody>
<tr>
<td>Wild-type (18)</td>
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<tr>
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Table 2. Activity of GT-1 and comparator agents against phenotypically and genotypically characterized Acinetobacter clinical isolates

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Conclusions

GT-1 exhibited potent in vitro activity against a diverse global collection of multidrug-resistant P. aeruginosa and Acinetobacter spp. isolates.

As shown in Table 1, GT-1 maintained good activity against GT-1-exposed isolates that were carbapenem-resistant due to the expression of class A β-lactamases, class B enzymes, and/or the presence of metallo-β-lactamase (Table 2).

Where indicated, the presence of specific β-lactamase genes was confirmed by PCR analysis or whole-genome sequencing.

Table 3. Activity of GT-1 and comparator agents against phenotypically and genotypically characterized Enterobacteriaceae clinical isolates

<table>
<thead>
<tr>
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References


Visit https://www.jmilabs.com/data/posters/ASM2018 for additional data.