In Vitro Evaluation of Rib-X Novel Compounds’ Potency against Selected Isolates of Pseudomonas aeruginosa

Seth T. Housman, PharmD, MPA; Christina Sutherland, MT; David P. Nicolau, PharmD, FCCP, FIDSA 1 2 3

1 Center for Ant-Infective Research and Development, Hartford, Connecticut. 2 Department of Medicine, Division of Infectious Diseases Hartford Hospital, Hartford, Connecticut, USA

Poster FL-1849
51st ICAAC
Chicago, IL, USA
September 17-20, 2011

Abstract

Background
Pseudomonas aeruginosa (PA) is a frequently identified organism in the nosocomial setting. The emergence of PA in intensive care units is a significant threat to patient health because of its high resistance to clinically available antimicrobials. In vitro research has shown that Rib-X Pharmaceuticals is investigating a novel class of PA susceptible antimicrobials (PASS).

Aim
To evaluate the potency of six novel compounds, RX-P763, RX-P766, RX-P770, RX-P792, RX-P793 and RX-P808 against selected populations of resistant PA. The purpose of this study is to evaluate the efficacy of six novel compounds, RX-P763, RX-P766, RX-P770, RX-P792, RX-P793 and RX-P808 against a group of highly resistant clinical isolates.

Methods
Non-duplicate, non-urine, PSA isolates collected from 41 US hospitals over the period of October 17-20, 2011 was used in this study. Resistance was determined using the Clinical and Laboratory Standards Institute (CLSI). Triplicate MICs were done (triplicate if results were discrepant) for all agents tested. Table 3 shows the MIC distribution of Rib-X novel compounds against 200 P. aeruginosa isolates. Results

Table 1 - MDC profile of Rib-X novel compounds and comparator agents against P. aeruginosa isolates

<table>
<thead>
<tr>
<th>Agent</th>
<th>Modal MIC (µg/mL)</th>
<th>Number of isolates (%)</th>
<th>Cumulative % Inhibited at MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>0.125</td>
<td>32</td>
<td>256</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>4</td>
<td>12</td>
<td>96</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>8</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Imipenem</td>
<td>0.25</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>8</td>
<td>3</td>
<td>32</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>0.125</td>
<td>4</td>
<td>32</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>16</td>
<td>2</td>
<td>32</td>
</tr>
</tbody>
</table>

Results

• RX-P763 showed the best overall MIC performance against all resistant phenotypes compared with the comparator agents, especially against the most resistant phenotypes (R-TOB). Although RX-P763 did not show complete activity against R-TOB, it significantly reduced the MICs oftx resistant strains across the phenotypic profiles studied.

• RX-P766 was the next most effective compound against R-TOB isolates, followed by RX-P792 and RX-P770. RX-P766 and RX-P792 showed good activity against the R-IMI isolates, with RX-P766 showing the best overall MIC distribution.

• All novel compounds were found to be active against the R-TAZ isolates, with RX-P766 showing the best overall MIC distribution.

• The MIC distribution for all agents tested is summarized in Table 3.

Conclusions

• Agents with highly resistant collection of PA in vivo, the novel compounds had a narrow MIC distribution with MIC and MIC50 in the range of 0.125 µg/mL.

• MICs for the novel compounds were unchanged against different resistant phenotypes when compared with the whole collection of 200 isolates.

References

1. Seth T. Housman, PharmD, MPA; Christina Sutherland, MT; David P. Nicolau, PharmD, FCCP, FIDSA 1 2 3

2. Center for Ant-Infective Research and Development, Hartford, Connecticut. 2 Department of Medicine, Division of Infectious Diseases Hartford Hospital, Hartford, Connecticut, USA

2. Seth T. Housman, PharmD, MPA; Christina Sutherland, MT; David P. Nicolau, PharmD, FCCP, FIDSA 1 2 3

1 Center for Ant-Infective Research and Development, Hartford, Connecticut. 2 Department of Medicine, Division of Infectious Diseases Hartford Hospital, Hartford, Connecticut, USA

Acknowledgements: We would like to thank Jared Hulse for his assistance with the in vitro experimentation.