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Objective
POL7001 represents a member of a novel class of outer membrane protein targeting antibiotics. Like murepavadin POL7001 is a pathogen-specific antibiotic with a very potent and selective antibacterial activity1. POL7001 specifically interacts with LpD and inhibits LPS transport2. The MIC of POL7001 towards the infecting organisms covered a range from 0.063 mg/L to 0.25 mg/L which covers the MIC range of POL7001 against this organism (0.125 mg/L).

In these studies the efficacy of POL7001 was assessed in neutropenic murine models of pneumonia due to UDR and Pseudomonas aeruginosa clinical isolates.

Methods
- All isolates were tested by the CLSI broth microdilution method (M07-A82, 2009) in cation-adjusted Mueller-Hinton broth.
- CD-1 mice were inoculated intranasally with a pipette with 0.05 mL of bacteria suspension containing approximately 108 CFU.
- The mice were treated subcutaneously in the neck region with a single dose at 2 hour post infection or with b.i.d dosing at 2 and 14 hours post infection.
- The total daily dose ranged from 1.88 mg/kg given as a single dose to 60 mg/kg given b.i.d. Comparator antibiotics were used.
- The mice were then euthanized; the lungs were collected for determining the CFU counts.
- The lung bacterial burden was determined at 2 and 26 hrs post inoculation.

References
3 CLSI. M07-A8. Clinical Laboratory Standards Institute, 2009. Wayne PA

Results

Table 1: MICs of the strains evaluated in vivo

<table>
<thead>
<tr>
<th>Strain</th>
<th>ATCC 27853</th>
<th>ATCC BAA 2113</th>
<th>ATCC 15697</th>
<th>X11045</th>
<th>X11046</th>
</tr>
</thead>
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<tr>
<td>MIC (mg/L)</td>
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Figure 1: A diagram of the procedures followed

- Treatment of infected mice with POL7001.
- Time course of infection.
- Homogenization of lung tissue to count CFU.

- From the 9 isolates tested 5 are considered MDR.
- The MICs of the isolates ranged from 0.063 to 0.25 mg/L of which 6 were equal to the MIC90.
- POL7001 displays a potent in vitro activity towards these isolates.
- The models displayed a robust infection with generally a 3-log growth from start of treatment.
- Comparator antibiotics often showed little effect in this model.

Figure 2: Effect of POL7001 in the murine neutropenic lung infection model

- Clinical Isolate 12
- NCTC 13437
- A. baumannii
- ATCC BAA2113
- Loss of respiratory function

Table 2: Efficacy of POL7001 against isolates in the murine neutropenic lung infection model

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Conclusion
- POL7001 is highly efficacious in the neutropenic murine pneumonia model against both non-MDR and MDR P. aeruginosa.