Potent activity of BAY 73-7388, a novel aminomethylcycline, against susceptible and resistant Gram-positive and Gram-negative organisms

Boston, USA

Objectives: BAY 73-7388 is the first of a new class of antibiotics, the aminomethylcyclines, which evolved from the tetracycline (TET) family. BAY 73-7388 has potent activity against antibiotic susceptible and resistant Gram-positive and Gram-negative pathogens. The present study compared the activity in vitro of BAY 73-7388 and 10 other agents including vancomycin (VAN), linezolid (LIN), levofloxacin (LVX) and TET against recent clinical isolates including MRSA, VAN-resistant Enterococcus faecium (Efa VRE), Enterococcus faecalis (Ef), penicillin-resistant Streptococcus pneumoniae (Spn PENR), Groups A and B beta-haemolytic streptococci (BHS), Escherichia coli (Ec), and other pathogens. Potential microbiological interactions between BAY 73-7388 and other antibiotics were also assessed.

Methods: Microdilution MIC tests were performed according to NCCLS guidelines. The activity of BAY 73-7388 in the presence of other antibacterial agents was assessed using standard chequerboard MIC methods. TET-resistance determinants were identified using multiplex PCR.

Results: Susceptibility in vitro (MIC90 mg/L) for selected agents is shown in the table below.

<table>
<thead>
<tr>
<th>Strains</th>
<th>BAY 73-7388</th>
<th>VAN</th>
<th>LIN</th>
<th>LVX</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA (n = 39)</td>
<td>0.5</td>
<td>1.0</td>
<td>2.0</td>
<td>32.0</td>
</tr>
<tr>
<td>Efa VRE (n = 19)</td>
<td>0.5</td>
<td>&gt;64.0</td>
<td>2.0</td>
<td>&gt;64.0</td>
</tr>
<tr>
<td>Ef (n = 31)</td>
<td>0.5</td>
<td>2.0</td>
<td>2.0</td>
<td>32.0</td>
</tr>
<tr>
<td>Spn PENR (n = 23)</td>
<td>0.06</td>
<td>0.25</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>BHS (n = 48)</td>
<td>0.25</td>
<td>0.5</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Ec (n = 23)</td>
<td>2.0</td>
<td>NA</td>
<td>NA</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Conclusions: BAY 73-7388 has potent activity in vitro against a range of common pathogens, including those resistant to currently available antibiotics: most notably MRSA, VRE and penicillin-resistant S. pneumoniae. Chequerboard studies in vitro demonstrate BAY 73-7388 does not affect, and is not affected by, the activity of other antibiotics.

(BAY 73-7388 was discovered by Paratek Pharmaceuticals Inc., Boston, MA, and designated PTK 0796.)
**POTENT ACTIVITY OF BAY 73-7388, A NOVEL AMINOMETHYLCCYCLINE, AGAINST SUSCEPTIBLE AND RESISTANT GRAM-POSITIVE AND GRAM-NEGATIVE ORGANISMS**

**Abstract**

**Objectives:**

- To determine the activity of BAY 73-7388 alone and in combination with other antibiotics against isolates of Gram-positive and Gram-negative bacteria.

**Methods:**

- Microbiological MIC tests were performed according to NCCLS guidelines.
- Growth of target organisms was achieved using cation-adjusted Mueller Hinton broth and standard broth microdilution methods.

**Results:**

- BAY 73-7388 inhibited all strains of Staphylococcus aureus, Enterococcus faecalis, and Enterococcus faecium.
- The combination of BAY 73-7388 with other antibiotics showed synergistic effects.

**Conclusions:**

- BAY 73-7388 is a potent new antimicrobial agent with broad-spectrum activity against both Gram-positive and Gram-negative bacteria.

---

**References**