Comparative in vitro activity of Temocillin, Meropenem, Ceftazidime, and Piperacillin/Tazobactam against panel strains and clinical isolates of *Burkholderia cepacia* complex from 9 different genomovars

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Background - B. cepacia infections treatment

- Treatment of B. cepacia infections is hampered by their intrinsic resistance to many antimicrobial agents such as:
  - aminoglycosides
  - polymyxins
  - anti-pseudomonal penicillins

- Conventional therapy include combination of drugs active in vitro against the isolate with (when possible) different mechanisms of action

Döring & Hoiby, *JCF* 2004; UK CF TRUST Antibiotic group, 2002
**Background - Temocillin**

- 6-α-methoxy-ticarcillin
- spectrum directed only on gram negative bacteria without non-fermenters (*Pseudomonas aeruginosa, Acinetobacter* spp.)
- active against all β-lactamases including ESBL and AmpC producers
- **Main Indications**:
  - urinary tract infections
  - gram negative nosocomial infections
- **Adverse Effects**: hypersensitivity to penicillins
- Recognized Orphan Drug for the treatment of *B. cepacia* infection by the EMEA and the FDA
Aim of the study

- Although temocillin has already been used in a pilot clinical studies (Taylor, JAC 1992) with success for the treatment of Bcc infections in CF patients, only a few in vitro susceptibility data are available

- Our aim was, therefore, to determine the MICs of β-lactams used in CF patients
  - meropenem
  - ceftazidime
  - piperacillin/tazobactam
  - temocillin

towards a well characterized panel of laboratory strains and clinical isolates of B. cepacia complex
Method and Strains

- MICs were determined using the CLSI broth microdilution technique including *E. coli* ATCC 25923 and *P. aeruginosa* ATCC 27853 as quality control strains.

- CLSI breakpoint for GNB non-Pseudomonas were applied for MER, CTZ, and PTZ; and that of Fuchs et al. (EJCM 1985) for temocillin for categorization.

- 100 strains from 9 different species of Bcc were used with repartition between panel strains and clinical isolates:
  - 35 *B. multivorans*
  - 30 *B. cenocepacia*
  - 5 *B. cepacia, ambifria, pyrrocinia, vietnamensis, dolosa, stabilis, anthinia*
Results – MIC distributions

**MEROPENEM**

**CEFTAZIDIME**

**PIPERACILLIN/TAZOBACTAM**

**TEMOCILLIN**
Results – Global Susceptibility

% of susceptible strains

MER | CTZ | PTZ | TMO
## Results

### Comparison between species

<table>
<thead>
<tr>
<th>% of susceptible strains</th>
<th>B. multivorans (n = 35)</th>
<th>B. cenosepacia (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MER</td>
<td>46</td>
<td>60</td>
</tr>
<tr>
<td>CTZ</td>
<td>77</td>
<td>43</td>
</tr>
<tr>
<td>PTZ</td>
<td>51</td>
<td>30</td>
</tr>
<tr>
<td>TMO</td>
<td>68</td>
<td>77</td>
</tr>
</tbody>
</table>
### Results – Particular Strains

<table>
<thead>
<tr>
<th>Strains</th>
<th>nbr of strains</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>resistant to all antibiotics</td>
<td>13</td>
<td><em>B. multivorans</em> (6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>B. cenocepacia</em> (7)</td>
</tr>
<tr>
<td>susceptible only to</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMO</td>
<td>7</td>
<td><em>B. cepacia</em> (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>B. cenocepacia</em> (5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>B. dolosa</em> (1)</td>
</tr>
<tr>
<td>CTZ</td>
<td>3</td>
<td><em>B. multivorans</em></td>
</tr>
<tr>
<td>MER</td>
<td>1</td>
<td><em>B. vietnamensis</em></td>
</tr>
<tr>
<td>PTZ</td>
<td>1</td>
<td><em>B. multivorans</em></td>
</tr>
</tbody>
</table>
Results

Comparison: Panel Strains vs. Clinical Isolates

Panel strains (n = 45) Clinical isolates (n = 55)

CTZ

PTZ
Results

Comparison: Panel Strains vs. Clinical Isolates

Panel strains (n = 45)
Clinical isolates (n = 55)

Panel strains:
- MER
- MIC (µg/ml)
- % of strains

Clinical isolates:
- TMO
- MIC (µg/ml)
- % of strains
Conclusions - Perspectives

- Temocillin was the most active β-lactam tested against these strains of *B. cepacia*.
- There might be a slightly different susceptibility pattern between *B. multivorans* and *B. cenocepacia* (especially for ceftazidime).
- There was no significant differences between panel strains and clinical isolates.

These results combined with those of the pilot study suggest a potential advantage of temocillin in *B. cepacia* infected CF patients.