Burkholderia pseudomallei

Calibration of zone diameter breakpoints to MIC values

Version 1.0
February 2020
Burkholderia pseudomallei
MIC and zone diameter correlates

- The following histograms present inhibition zone diameter distributions from EUCAST antimicrobial susceptibility testing. In most, the different colours of the bars indicate different MIC values. In some, the colours of the bars indicate a resistance gene or a resistance mechanism.

- The distributions include data for wild-type isolates and for isolates with acquired resistance mechanisms. A large number of isolates with MIC values close to the edge of the wild-type distribution and/or close to EUCAST clinical breakpoints were intentionally included. These distributions can not be used to infer resistance rates or the performance of the tests with routine isolates.

- For some agents, isolates were tested on more than one occasion, including parallel tests with disks and media from several manufacturers. When this is the case, data are presented as both the “number of isolates tested” and the “total number of MIC-zone diameter correlates”, including replicate tests and parallel tests with disks and media from different sources.
Antimicrobial susceptibility testing was performed on clinical isolates of *Burkholderia pseudomallei*. Disk diffusion was performed according to EUCAST methodology for non-fastidious microorganisms and MIC determination was performed with broth microdilution.

The distributions of MIC vs. zone diameter in this presentation are the result of a collaboration between EUCAST and several other laboratories: Cambodia Oxford Medical Research Unit, Siem Reap, Cambodia; Mahidol-Oxford Tropical Medicine Research Unit, Bangkok, Thailand; Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit, Vientiane, Laos; Royal Darwin Hospital, Darwin, Australia; Townsville Hospital, Townsville, Australia; Bundeswehr Institute of Microbiology, Munich, Germany; Robert Koch Institute, Berlin, Germany and Public Health Agency of Sweden, Stockholm, Sweden.

This presentation is based on EUCAST Clinical Breakpoint Tables v. 10.0.
Explanation of graphs:

- These graphs show zone diameter distributions with MIC values or resistance mechanisms as coloured bars. Colours are related to current EUCAST MIC breakpoints.

**Agent X**

- MIC (mg/L)
  - ≥8: Red
  - 4: Purple
  - 2: Green
  - 1: Yellow
  - 0.5: Dark blue
  - ≤0.25: Light blue

- No of observations vs. Inhibition zone diameter (mm)
- Zone diameter breakpoint
- Resistant
- Susceptible, increased exposure
- Susceptible, standard dosing regimen

**Agent Y**

- MIC (mg/L)
  - ≥64: Red
  - 32: Purple
  - 16: Green
  - 8: Yellow
  - 4: Dark blue
  - 2: Light blue
  - 1: Yellow
  - 0.5: Dark blue
  - ≤0.25: Light blue

- No of observations vs. Inhibition zone diameter (mm)

- Resistant
- Susceptible, increased exposure
Amoxicillin-clavulanic acid 20-10 µg vs. MIC
*B. pseudomallei*, 361 isolates

(8 data sources)

**Breakpoints**

| MIC (mg/L) | Breakpoint
|------------|-------------
| ≥128       | S≤0.001, R>8 mg/L
| 64         | Zone diameter S≥50, R<22 mm
| 32         | 16          | 12          | 10          | 8           | 4           | 2           | 1           | 0.5         | 0           |
|            | 6           | 8           | 10          | 12          | 14          | 16          | 18          | 20          | 22          | 24          | 26          | 28          | 30          | 32          | 34          | 36          | 38          | 40          |

**No of observations**

MIC with fixed concentration of clavulanic acid at 2 mg/L.
Ceftazidime 10 µg vs. MIC
*B. pseudomallei*, 361 isolates

(8 data sources)

No of observations

Inhibition zone diameter (mm)

Breakpoints
- MIC: $S \leq 0.001$, $R > 8$ mg/L
- Zone diameter: $S \geq 50$, $R < 18$ mm
Imipenem 10 µg vs. MIC
*B. pseudomallei*, 361 isolates

Breakpoints
- **MIC**
  - S ≤ 2, R > 2 mg/L
- **Zone diameter**
  - S ≥ 29, R < 29 mm

(8 data sources)
Meropenem 10 µg vs. MIC
*B. pseudomallei*, 361 isolates

(8 data sources)

**Breakpoints**

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>S≤2, R&gt;2 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone diameter</td>
<td>S≥24, R&lt;24 mm</td>
</tr>
</tbody>
</table>
Tetracycline 30 µg vs. Doxycycline MIC
*B. pseudomallei*, 361 isolates

(8 data sources)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Breakpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥16</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
<tr>
<td>8</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
<tr>
<td>4</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
<tr>
<td>2</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
<tr>
<td>1</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
<tr>
<td>0.5</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
<tr>
<td>0.25</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
<tr>
<td>0.125</td>
<td>S≥50, R&lt;23 mm</td>
</tr>
</tbody>
</table>

Inhibition zone diameter (mm)

Breakpoints
- Doxycycline MIC: S≤0.001, R>2 mg/L
- Tetracycline zone diameter (screen): S≥50, R<23 mm
Chloramphenicol 30 µg vs. MIC
*B. pseudomallei*, 361 isolates

(8 data sources)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥64</td>
</tr>
<tr>
<td>32</td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

Breakpoints
- **MIC**: S≤0.001, R>8 mg/L
- **Zone diameter**: S≥50, R<22 mm
Trimethoprim-sulfamethoxazole 1.25-23.75 µg vs. MIC
*B. pseudomallei*, 361 isolates

(8 data sources)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>0.5</td>
<td>10</td>
</tr>
<tr>
<td>0.25</td>
<td>5</td>
</tr>
<tr>
<td>0.125</td>
<td>5</td>
</tr>
<tr>
<td>0.06</td>
<td>5</td>
</tr>
</tbody>
</table>

**Breakpoints**
- **MIC**
  - S≤0.001, R>4 mg/L
- **Zone diameter**
  - S≥50, R<17 mm