Doripenem European Surveillance: Antimicrobial Activity Against 6,480 Contemporary Pathogens (2004)

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Doripenem (formerly S-4661), a parenteral carbapenem in late-stage clinical development, confers stability to β-lactamases and resistance to renal dehydropeptidases.

MATERIALS AND METHODS

Bacterial Strain Collection

A total of 6,480 non-duplicate clinical isolates were selected from 24 medical centers located in Europe (21 sites), Turkey (2 sites) and Israel (1 site) as part of an international surveillance program. Isolates originated from patients with confirmed bacteremia, sepsis, and skin and soft tissue, and urinary tract infections. The distribution of species and groups is shown in Table 1.

RESULTS

• Doripenem was very active against the most common species of Enterobacteriaceae (Table 2) and Staphylococcus spp. (Table 3).
• Doripenem was highly potent against oxacillin-susceptible S. aureus and oxacillin-resistant S. epidermidis.
• Doripenem displayed similar activity against Enterococcus faecalis and E. faecium.
• Doripenem exhibited enhanced potency (two-fold; MIC ≤ 0.06 mg/L) among extended-spectrum carbapenem-resistant Enterobacteriaceae tested against doripenem and was non-susceptible (MIC > 2 mg/L) to imipenem and meropenem against Enterococcus spp.

Table 2. Antimicrobial activity of doripenem and five other broad-spectrum beta-lactams tested against contemporary uropathogenic Escherichia coli strains

<table>
<thead>
<tr>
<th>Species</th>
<th>Doripenem</th>
<th>Meropenem</th>
<th>Imipenem</th>
<th>Piperacillin/Tazobactam</th>
<th>Cefepime</th>
<th>Ertapenem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli (525)</td>
<td>0.06</td>
<td>0.5</td>
<td>0.5</td>
<td>16</td>
<td>&gt;16</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Enterococcus faecalis (52)</td>
<td>0.06</td>
<td>0.03</td>
<td>0.016</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>Staphylococcus (24)</td>
<td>0.06</td>
<td>0.03</td>
<td>0.016</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Table 3. Antimicrobial activity of doripenem tested against Gram-positive organisms, compared to selected β-lactam agents.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Doripenem</th>
<th>Meropenem</th>
<th>Imipenem</th>
<th>Piperacillin/Tazobactam</th>
<th>Cefepime</th>
<th>Ertapenem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (750)</td>
<td>0.02</td>
<td>0.12</td>
<td>1</td>
<td>8</td>
<td>&gt;16</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Enterococcus faecalis (52)</td>
<td>0.06</td>
<td>0.03</td>
<td>0.016</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• Carbapenems are assuming a greater therapeutic role in many nations, as multidrug-resistant and multidrug-nonsusceptible Enterobacteriaceae and Gram-negative bacilli with various β-lactamase resistance mechanisms.
• The collection of doripenem from 24 medical centers in Europe, Turkey, and Israel represented a broad range of pathogens and antimicrobial susceptibility.
• Doripenem consistently displayed activity against staphylococci and streptococci (MIC ≤ 0.12 mg/L) and most importantly—enzymes in Ambler class B (metallo-β-lactamases) spreads.
• Resistance to extended-spectrum β-lactamase (ESBL)-producing and AmpC β-lactamase producers was also high.
• Enterococci and staphylococci were susceptible to doripenem.

SELECTED REFERENCES