Antimicrobial Activity of Meropenem-WCK 4243 (WCK 5999) against Clinical Isolates of Acinetobacter spp. Collected Worldwide and Stratified by Infection Type

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Introduction

Background: WCK 5999 consists of WCK 4234 (WCK), a novel carbapenemase inhibitor with enhanced activity against class D carbapenemases, which was evaluated against a global collection of clinical isolates of Acinetobacter spp. collected during 2013 (China) and 2015 (worldwide) and stratified by infection type. Methods: A total of 639 isolates were from the United States (172), Europe (521) Acinetobacter spp. (567, and Latin America (38); MIC values for MEM-WCK and comparators were determined by reference broth microdilution methodology. Isolates were stratified by infection type and breakpoint interpretative criteria for comparators followed CLSI guidelines. Results: MEM-WCK was very active against ASP isolates (MIC< 2/8 µg/mL; 65.6% and 83.6% inhibited at 2/4µg/mL, respectively). The addition of WCK to MEM significantly increased the percentage of ASP isolates with MIC values ≤4 µg/mL (based on meropenem dose of 2g TID) from 39.5% (MEM-WCK) and meropenem when tested against clinical isolates of Acinetobacter spp., followed by amikacin (MIC≤32/32 µg/mL; 31.8% susceptible), and ceftazidime (MIC≤8/8 µg/mL; 39.7% susceptible), meropenem (MIC≤2/2 µg/mL; 32.0% susceptible), meropenem (MIC≤32/32 µg/mL; 32.8/32.6% susceptible), aztreonam (MIC≤0.5/1 µg/mL; 32.0% susceptible), imipenem (MIC≤4/4 µg/mL; 33.0% susceptible), and chloramphenicol (MIC<8/8 µg/mL; 32.6% susceptible). Table 1 susceptibility rates were very high for all comparators, except COL. These data support the continued development of meropenem-WCK 4243 (WCK 5999) to treat Acinetobacter spp. infections.

Materials and Methods

Susceptibility testing

Minimal inhibitory concentration (MIC) values were determined for the meropenem-WCK 4243 combination (WCK 4243 at fixed concentration of 8 µg/mL) and comparator agents using the Clinical and Laboratory Standards Institute (CLSI) reference broth microdilution method (M100-S27). Quality control (QC) reference strains were tested daily and the inoculum density monitored by colony counts. QC ranges and interpretive criteria for comparator compounds were published in CLSI M100-S27 and EUCAST v7.0 (2011) documents. The tested QC reference strains included Escherichia coli ATCC 25922, Klebsiella pneumoniae ATCC 7048, Enterobacter aerogenes ATCC 27775, and Pseudomonas aeruginosa ATCC 27863.

Organism collection

Acinetobacter spp. (639) isolates were selected for testing from the 2015 SENTRY worldwide surveillance program. These isolates were collected during 2015 (except for China, which were collected in 2013) from 103 medical institutions worldwide, including Europe (EU; 31 medical centers), United States (US; 44, Latin America (LA; 8), the Asia-Pacific (APAC) region (excluding China, 10), and China (10)). All isolates were obtained from documented infections and only 1 isolate per patient-infection episode was included in the surveillance collection. Species identifications were confirmed by matrix-assisted laser desorption-time of flight mass spectrometry (MALDI-TOF MS), using the Bruker Daltronics MALDI Biotyper (Billericia, MA, USA).

Results

• Meropenem-WCK 4234 was very active against Acinetobacter spp. isolates with MIC≤4/4 µg/mL and 61.0% inhibited at 2/4 µg/mL, respectively (Table 1 and Figure 2).

Conclusions

• Meropenem-WCK 4234 (WCK 5999) was very active against Acinetobacter spp. isolates and demonstrated enhanced activity over meropenem alone.

• Resistance rates were very high for all comparators, except colistin.

• These data support the continued development of meropenem-WCK 4243 (WCK 5999) to treat Acinetobacter spp. infections.

Acknowledgements

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References


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Table 1 Activity of meropenem-WCK 4243 fixed at 633 isolates of Acinetobacter spp. and comparator antimicrobial agents when tested against 633 isolates of Acinetobacter spp. stratified by type of infection

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>MIC (µg/mL)</th>
</tr>
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<tbody>
<tr>
<td>MEM-WCK</td>
<td>2/8</td>
</tr>
<tr>
<td>MEM</td>
<td>2/8</td>
</tr>
<tr>
<td>WCK</td>
<td>≤2/8</td>
</tr>
<tr>
<td>CAZ</td>
<td>50/90</td>
</tr>
<tr>
<td>AMP</td>
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<tr>
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<td>≥32/32</td>
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<td>≥32/32</td>
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<tr>
<td>LEV</td>
<td>≥32/32</td>
</tr>
<tr>
<td>COL</td>
<td>≥32/32</td>
</tr>
</tbody>
</table>

Figure 1 Compound structure of WCK 4243

Figure 2. MIC distributions for WCK 5999 (meropenem-WCK 4234; MEM-WCK) and meropenem when tested against Acinetobacter spp. isolates and demonstrated enhanced activity over meropenem alone.

Figure 3. Antimicrobial activity of WCK 5999 (meropenem-WCK 4243; MEM-WCK) and comparator agents tested against clinical isolates of Acinetobacter spp., stratified by type of infection.

Figure 1 Compound structure of WCK 4243

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Figure 3. Antimicrobial activity of WCK 5999 (meropenem-WCK 4243; MEM-WCK) and comparator agents tested against clinical isolates of Acinetobacter spp., stratified by type of infection.