**ABSTRACT**

Background: WCK 4282 (ceftazidime-tazobactam) is currently under clinical development at ≥2g p.i. and ≥12h doses. We evaluated the spectrum of activity of WCK 4282 (ceftazidime-tazobactam) tested against contemporary Gram-negative organisms isolated as part of the SENTRY Antimicrobial Surveillance Program (AP), and against Enterobacteriaceae isolated from patients treated at 15 centers located in high-risk regions from the Asia-Pacific region (APAC) and ≥17 sites from 10 medical centers located in China. All isolates were collected in 2014, except those from China, which were collected in 2013.

Methods: A total of 4,319 unique patient isolates, including 2,852 from Europe (EU), 1,020 from North America (NA), 417 from China (CHN) and 94 from Japan (JP), were tested against WCK 4282 (ceftazidime-tazobactam) at fixed concentrations of ≤4 mg/L and ≤8 mg/L and ≤8 mg/L for 2g q8 hours (2g q8h) or ≤16 mg/L for 2g q12 hours (2g q12h) dosages and ≤8 mg/L for 2g q8h (high dose). The studies were performed in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines and were submitted to the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Minimal inhibitory concentration (MIC) results were interpreted using CLSI and EUCAST breakpoints. Percentage inhibited at 49:311 ≤4 mg/L for 1g q 8 hours or 2g q12 hours dosages and ≤8 mg/L for 2g q8 hours (high dose).

Antimicrobial susceptibility testing: MIC values for ceftazidime-tazobactam and ceftazidime alone were determined using CLSI broth microdilution methodology as described above. The minimum concentration required to inhibit ≥90% of all Enterobacteriaceae (MIC90) and ≥99% of P. aeruginosa (MIC99) was determined for each isolate. When tested against Enterobacteriaceae, ceftazidime-tazobactam activity (MIC90) of <64 mg/L for 2g q8h or ≤64 mg/L for 2g q12h, was similar to that observed for MIC90 of <32 mg/L for cefepime, ≤8 mg/L for meropenem, ≤8 mg/L for meropenem, and MIC90 of ≤4 mg/L for imipenem. When tested against P. aeruginosa, MIC90 of ≤64 mg/L for 2g q8h or ≤64 mg/L for 2g q12h was similar to that observed for MIC90 of ≤32 mg/L for cefepime, ≤8 mg/L for meropenem, ≤8 mg/L for meropenem, and MIC90 of ≤4 mg/L for imipenem.

Table 1. Summary of ceftazidime-tazobactam activity stratified by geographic region.

<table>
<thead>
<tr>
<th>Organism</th>
<th>EU (%)</th>
<th>AP (%)</th>
<th>NA (%)</th>
<th>CHN (%)</th>
<th>JP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ceftazidime</td>
<td>98.7</td>
<td>98.7</td>
<td>98.7</td>
<td>98.7</td>
<td>98.7</td>
</tr>
<tr>
<td>tazobactam</td>
<td>98.7</td>
<td>98.7</td>
<td>98.7</td>
<td>98.7</td>
<td>98.7</td>
</tr>
<tr>
<td>cefepime</td>
<td>99.5</td>
<td>99.5</td>
<td>99.5</td>
<td>99.5</td>
<td>99.5</td>
</tr>
</tbody>
</table>

Conclusion: Cefepime+tazobactam combination may represent a valuable option for the treatment of serious infections caused by Gram-negative bacteria, including multidrug-resistant isolates.

**REFERENCES**

2. Bajpai, D., Singh, A., Singh, V. - Proceedings of the Asia Pacific Society of Tropical Medicine and Parasitology (2014): Antimicrobial activity of WCK 4282 (ceftazidime-tazobactam) tested at fixed concentrations of ≤4 mg/L and ≤8 mg/L for 2g q8h dosages and ≤8 mg/L for 2g q12h (high dose). The studies were performed in accordance with the CLSI and EUCAST guidelines. Percentage inhibited at 49:311 ≤4 mg/L for 1g q 8 hours or 2g q12 hours dosages and ≤8 mg/L for 2g q8 hours (high dose).

**CONCLUSIONS**

- Cefepime+tazobactam combination demonstrated excellent activity against Enterobacteriaceae, including ESBLs, clavulanate-potentiated β-lactam-resistant Enterobacteriaceae, and P. aeruginosa. This combination may represent a valuable option for the treatment of serious infections caused by Gram-negative bacteria, including multidrug-resistant isolates.

**ACKNOWLEDGEMENTS**

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