**ABSTRACT**

**Background:** WCK 4282 (cefepime-tazobactam) is currently under clinical development at 5mg/L as a 90 min infusion. In this investigation, we evaluated the in vitro potency and the spectrum of activity against cefepime-resistant Enterobacteriaceae.

**Materials and Methods:** A total of 40 unique patient isolates collected as part of a global clinical trial were tested in a MIC assay against cefepime alone or combined with tazobactam at 5mg/L and 10mg/L using CLSI broth microdilution. The MIC endpoints were calculated by CLSI strain disk results (MIC ≤8 μg/mL for Cefepime, 1 mg/L for Tazobactam) and CLSI breakpoints (≤4 mg/L for 1g q 8 hours or 2g q12 hours dosages and ≤8 mg/L for 2g q8 hours dosages). CLSI strain disk results (≤2 mg/L for 1g q 8 hours dosages), ≤4 mg/L for 1g q 8 hours or 2g q12 hours dosages and ≤8 mg/L for 2g q8 hours dosages.

**Results:** Cefepime-resistant Enterobacteriaceae showed a broad spectrum of activity against Enterobacteriaceae spp. (96.2/95.5% from USA/Latin America inhibited at 0.06/0.5 μg/mL). Isolates were divided into two groups: non-ESBL negative Enterobacteriaceae (46.7%) and ESBL producers (53.3%), respectively. Cefepime and tazobactam showed a synergistic effect against 100% of isolates. Cefepime resistance was not associated with tazobactam resistance. Cefepime-resistant Enterobacteriaceae were susceptible to CefTaz4 (98.2%), CefTaz8 (89.9%) and Cefepime (95.6%).

**Conclusions:** Cefepime resistance was not associated with tazobactam resistance. Cefepime-resistant Enterobacteriaceae were susceptible to CefTaz4 (98.2%), CefTaz8 (89.9%) and Cefepime (95.6%).

**Materials and Methods**

<table>
<thead>
<tr>
<th>Table 1. Summary of cefepime-tazobactam (basoactam at fixed 8 mg/L) activity stratified by geographic region.</th>
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<tbody>
<tr>
<td><strong>Geographic Region</strong></td>
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<tr>
<td>USA</td>
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<tr>
<td>Latin America</td>
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**Table 2. Activity of cefepime-tazobactam (WCK 4282) combinations (basoactam at fixed 4 and 8 mg/L) and comparator agents tested against bacterial isolates from USA and Latin America.**

**Table 3. Cumulative frequency distributions of cefepime and WCK 4282 (CefTaz8; cefepime + basoactam at fixed concentrations of 8 mg/L) MIC results when tested against 3,008 bacterial isolates (USA).**

**Acknowledgements**

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**References**

1. Borges E, Melton JL, Clear SK (2015). Evaluating outcomes of Enterobacteriaceae treatment using CLSI broth microdilution, CLSI strain disk results (MIC ≤8 μg/mL for Cefepime, 1 mg/L for Tazobactam) and CLSI breakpoints (≤4 mg/L for 1g q 8 hours or 2g q12 hours dosages and ≤8 mg/L for 2g q8 hours dosages). CLSI strain disk results (≤2 mg/L for 1g q 8 hours dosages), ≤4 mg/L for 1g q 8 hours or 2g q12 hours dosages and ≤8 mg/L for 2g q8 hours dosages.


