In vitro activity of cefiderocol against Gram-negative pathogens circulating in Germany

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Background: Cefiderocol, an investigational catechol-substituted siderophore cephalosporin, possesses potent activity against multidrug resistant aerobic Gram-negative pathogens, including carbapenemase-producing strains. The purpose of the present study was twofold, to provide data on the in vitro activity of cefiderocol against i) a representative collection of Gram-negative pathogens obtained from patients with nosocomial infections in intensive care units (collection I), as well as ii) a collection of Gram-negative strains producing various types of carbapenemases (collection II).

Materials/methods: Collection I comprised 213 first isolates from patients collected during a multicentre surveillance study conducted by the Paul-Ehrlich-Society in 2013, namely 146 Enterobacterales (including 17 ESBL-producing strains), 13 Acinetobacter baumannii group isolates, and 54 Pseudomonas aeruginosa. Collection II included 59 CPE-producing strains from our stock collection. Minimum inhibitory concentrations (MICs) of cefiderocol and comparative antibacterial agents were determined using the microdilution method according to the standard ISO 20776-1. The provisional CLSI breakpoint of cefiderocol for susceptibility is ≤4 mg/L.

Results: Cefiderocol inhibited 99% of the collection I at ≤4 mg/L (Table). MIC50/90 values of cefiderocol for Enterobacterales isolates were 0.12/1 mg/L. However, cefiderocol was more active against ESBL-negative isolates than against ESBL-producing Enterobacterales (isolates with MIC >1 mg/L: 4/129 [3.1%] ESBL-negative isolates vs 7/17 [41%] ESBL-producing isolates). In contrast, cefiderocol inhibited all Acinetobacter isolates at 0.12 mg/L and all P. aeruginosa isolates at 1 mg/L (Table). The highest cefiderocol MICs observed for collection II strains were 16 mg/L. Cefiderocol inhibited all seven carbapenemase-producing A. baumannii at 0.25 mg/L. MIC50/90 values for Enterobacterales (n=30) and P. aeruginosa (n=22) were 1/4 mg/L and 0.5/2 mg/L, respectively.

Conclusions: Cefiderocol showed excellent activity against A. baumannii (including carbapenemase-producing strains). Cefiderocol showed also good activity against carbapenemase-producing Enterobacterales and P. aeruginosa, though about one third of strains required concentrations of >1 mg/L for inhibition. Also, about 40% of the ESBL-producing Enterobacterales isolates required inhibitory concentrations of >1 mg cefiderocol per L. Overall, cefiderocol inhibited 202/208 (97%) Gram-negative strains at ≤4 mg/L.
### Table: In vitro activity of cefiderocol against Gram-negative pathogens

<table>
<thead>
<tr>
<th>Species / Bacterial group</th>
<th>n</th>
<th>MIC (mg/L)</th>
<th>≤0.03</th>
<th>0.06</th>
<th>0.12</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>16</th>
<th>32</th>
<th>64</th>
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<tr>
<td>Entero-bacteriales</td>
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<td>22</td>
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