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C a C -Ta b ba a A a R a S b E ba a a *Pseudomonas aeruginosa*, a C a S ba a -D ba a A a Ca ba - a *Acinetobacter baumannii-calcoaceticus*

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Introduction

- Cefiderocol is a siderophore-conjugated cephalosporin with broad activity against Gram-negative bacteria.
- Cefiderocol was approved by the EMA for the treatment of infections caused by Gram-negative bacteria in adult patients with limited treatment options and by the US FDA for complicated urinary tract infection, hospital-acquired bacterial pneumonia, and ventilator-associated bacterial pneumonia.
- We compared the susceptibility of cefiderocol (CFDC) and 2 Phase III combination agents, cefepime/taniborbactam (FTB) and sulbactam/durlobactam (SUD).
- FTB was tested against 101 Enterobacterales producing metallo-β-lactamases (MBLs), and 104 *Pseudomonas aeruginosa* resistant to ceftolozane-tazobactam (CT) or ceftazidime-avibactam (CZA), of which 52 produced MBLs.
- SUD was tested against 159 carbapenem-resistant *Acinetobacter baumannii-calcoaceticus* complex.

Results

- Susceptibility of 101 MBL-producing Enterobacterales to CFDC ($MIC_{50/90}$, 2/8 mg/L) was 88.1/66.3% (CLSI and FDA/EUCAST; Table 1). FTB inhibited 62.4% at ≤1 mg/L and 72.3% at ≤2 mg/L ($MIC_{50/90}$, 1/16 mg/L; Table 2, Figure 1), the EUCAST, and CLSI susceptible breakpoints for cefepime.
- Susceptibility of 104 CT or CZA-R *P. aeruginosa* to CFDC was 92.3/82.7/70.2% (CLSI/EUCAST/FDA; $MIC_{50/90}$ 0.5/4 mg/L) and FTB inhibited 51.9% at ≤8 mg/L ($MIC_{50/90}$, 8/>32 mg/L), the EUCAST susceptible-increased exposure breakpoint, and CLSI susceptible-dose dependent breakpoint for cefepime.
- CFDC showed potent activity against 52 MBL-producing *P. aeruginosa* with 94.2/92.3/80.8% susceptible (CLSI/EUCAST/FDA; $MIC_{50/90}$ 0.25/2 mg/L). FTB inhibited 63.5% at ≤8 mg/L ($MIC_{50/90}$, 8/>32 mg/L; Table 2).
- Carbapenem-resistant *A. baumannii-calcoacetius* complex susceptibility to CFDC was 96.9/95.6/90.6% (CLSI/EUCAST/FDA; $MIC_{50/90}$, 0.25/1 mg/L). SUD inhibited 95.6% at ≤4 mg/L