Activity of Cefiderocol and Comparators against US Enterobacteriales, including Carbapenem-Resistant Isolates

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Carbapenem-resistant Enterobacterales (CRE) isolates have disseminated worldwide, presenting a treatment challenge. In this study, we have analyzed the susceptibility of cefiderocol and comparators tested against US Enterobacteriales isolates, including CRE, collected in 2020 as a part of the SENTRY Antimicrobial Surveillance Program.

Materials and Methods

A total of 3,844 Enterobacteriales isolates were consecutively collected from 30 US hospitals during 2020. Only 1 isolate per patient per infection episode were submitted.

Susceptibility testing was performed using the CLSI broth microdilution method.
- Cefiderocol was tested in 96-deep well Mueller-Hinton broth.
- CLSI/FDA and EUCAST (2021) breakpoints were used.
- Cefiderocol breakpoints for CLSI and FDA are ≤2/≤8/16 mg/L.
- Cefiderocol breakpoints for EUCAST are ≤2/–/2 mg/L.
- CRE were identified as having an MIC >2 mg/L for meropenem and/or imipenem.
- Multidrug-resistant isolates (MDR) were defined as having resistance to at least 1 drug in ≥3 drug classes.
- Extensively-drug resistant (XDR) isolates were defined as susceptible to ≤2 drug classes.
- Other agents tested included β-lactam/β-lactamase inhibitor (BL/BLI) combinations cefazidime-avibactam, imipenem-relebactam, and meropenem-vaborbactam as well as meropenem and imipenem.

Results

The most common Enterobacteriales isolate was Escherichia coli (n=3,615) then Klebsiella pneumoniae (n=751; Figure 1).
- Most isolates were from UTI (n=1,378), bloodstream infection (n=1,034), and pneumonia (n=925).
- The susceptibilities of cefiderocol and comparators for all isolates and isolate groups are shown in Table 1. The MIC distributions of Enterobacteriales for cefiderocol and the 3 BL/BLI combinations are shown in Figure 2.
- The susceptibilities of all tested agents were ≥95% against all isolates.
- The CRE rate was 0.9% (33/3,844), of which 51.5% were K. pneumoniae.
- Against CRE, cefiderocol had a susceptibility of 97.0/87.9% (CLSI/EUCAST). The BL/BLI combinations had susceptibilities to CRE ranging from 81.8/87.9% for imipenem-relebactam and meropenem-vaborbactam to 90.9/90.9% for cefazidime-avibactam.
- A small number of isolates were resistant to the BL/BLI inhibitors: 16 isolates were imipenem-relebactam resistant, 4 were meropenem-vaborbactam resistant, and 3 were cefazidime-avibactam resistant.
- 7.6% of the isolates were MDR and 0.7% were XDR (Table 1).

Discussion

- Cefiderocol was very active against MDR and XDR isolates.

Conclusions

- Cefiderocol had potent activity against US Enterobacteriales isolates, including those resistant to carbapenems.
- Cefiderocol was very active against MDR and XDR isolates.
- These in vitro results suggest that cefiderocol is an important option for the treatment of infections caused by CRE and other drug-resistant Enterobacteriales.

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References


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