

Activity of Cefiderocol and Comparators Against US Enterobacterales, including Carbapenem-Resistant Isolates, from the SENTRY Antimicrobial Surveillance Program (2020-2021)

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Objective

Cefiderocol is a siderophore-conjugated cephalosporin with broad activity against Gram-negative bacteria, including carbapenem-resistant isolates.

Cefiderocol was approved by the FDA for treatment of complicated urinary tract infection, hospital-acquired bacterial pneumonia, and ventilator-associated bacterial pneumonia.

The objective in this study was the analysis of the susceptibility of cefiderocol and comparators against US Enterobacterales, including carbapenem-resistant (CRE) isolates, collected in 2020-2021.

Methods

- A total of 7,774 Enterobacterales isolates were consecutively collected from 32 US hospitals during 2020-2021.
- Isolates from all infection types were included in this analysis.
- Susceptibility testing was performed using the CLSI broth microdilution method. Cefiderocol was tested in iron-depleted cation-adjusted Mueller-Hinton broth. CLSI/FDA and EUCAST (2022) breakpoints were applied. CRE were identified as having an MIC ≥ 4 mg/L to meropenem and/or imipenem (CLSI).
- Other agents tested included the beta-lactam/beta-lactamase inhibitor (BL/BLI) combinations ceftazidime-avibactam, imipenem-relebactam, and meropenem-vaborbactam.



Results

Table 1. Susceptibilities of US Enterobacterales and Resistant Subgroups

Antimicrobial agent	mg/L		CLSI/FDA ^a	EUCAST ^a
	MIC ₅₀	MIC ₉₀	%S	%S
All (n=7,774)				
Cefiderocol	0.06	0.5	99.9	99.2
Meropenem	0.03	0.06	99.0	99.3
Meropenem-vaborbactam	0.03	0.06	99.8	99.9
Imipenem-relebactam	0.12	0.5	94.8 ^b	99.1
Ceftazidime-avibactam	0.12	0.25	99.9	99.9
CRE^c (n=68)				
Cefiderocol	0.5	4	98.5	83.8
Meropenem	16	>32	1.5	14.7
Meropenem-vaborbactam	0.12	>8	79.4	85.3
Imipenem-relebactam	0.12	8	77.9 ^b	80.9
Ceftazidime-avibactam	1	8	91.2	91.2
Meropenem-vaborbactam MIC >8 mg/L (n=10)				
Cefiderocol	2	N/A	100.0	80.0
Meropenem	32	N/A	0.0	0.0
Meropenem-vaborbactam	>8	N/A	0.0	0.0
Imipenem-relebactam	8	N/A	0.0 ^b	0.0
Ceftazidime-avibactam	2	N/A	60.0	60.0

Antimicrobial agent	mg/L		CLSI/FDA ^a	EUCAST ^a
	MIC ₅₀	MIC ₉₀	%S	%S
Imipenem-relebactam MIC >2 mg/L (n=72)				
Cefiderocol	0.015	2	100.0	95.8
Meropenem	0.12	32	81.9	81.9
Meropenem-vaborbactam	0.12	>8	83.3	86.1
Imipenem-relebactam	4	>8	0.0 ^b	0.0
Ceftazidime-avibactam	0.06	2	91.7	91.7
Ceftazidime-avibactam MIC >8 mg/L (n=8)				
Cefiderocol	2	N/A	87.5	50.0
Meropenem	8	N/A	25.0	25.0
Meropenem-vaborbactam	8	N/A	25.0	50.0
Imipenem-relebactam	4	N/A	25.0 ^b	50.0
Ceftazidime-avibactam	>32	N/A	0.0	0.0

^a Criteria as published by CLSI/FDA, and EUCAST (2022).

^b All Enterobacterales species were included in the analysis, but CLSI excludes *Morganella*, *Proteus*, and *Providencia* species while EUCAST excludes *Morganellaceae*.

^c CRE: carbapenem-resistant Enterobacterales with meropenem and/or imipenem MIC values ≥4 mg/L. Organisms include: *Citrobacter freundii* complex (4), *Enterobacter cloacae* complex (9), *Escherichia coli* (3), *Hafnia alvei* (1), *Klebsiella aerogenes* (5), *K. oxytoca* (4), *K. pneumonia* (37), *Serratia marcescens* (3), and unspiciated *Raoultella* (2).



Results

Figure 1. MIC Distributions of CRE Isolates

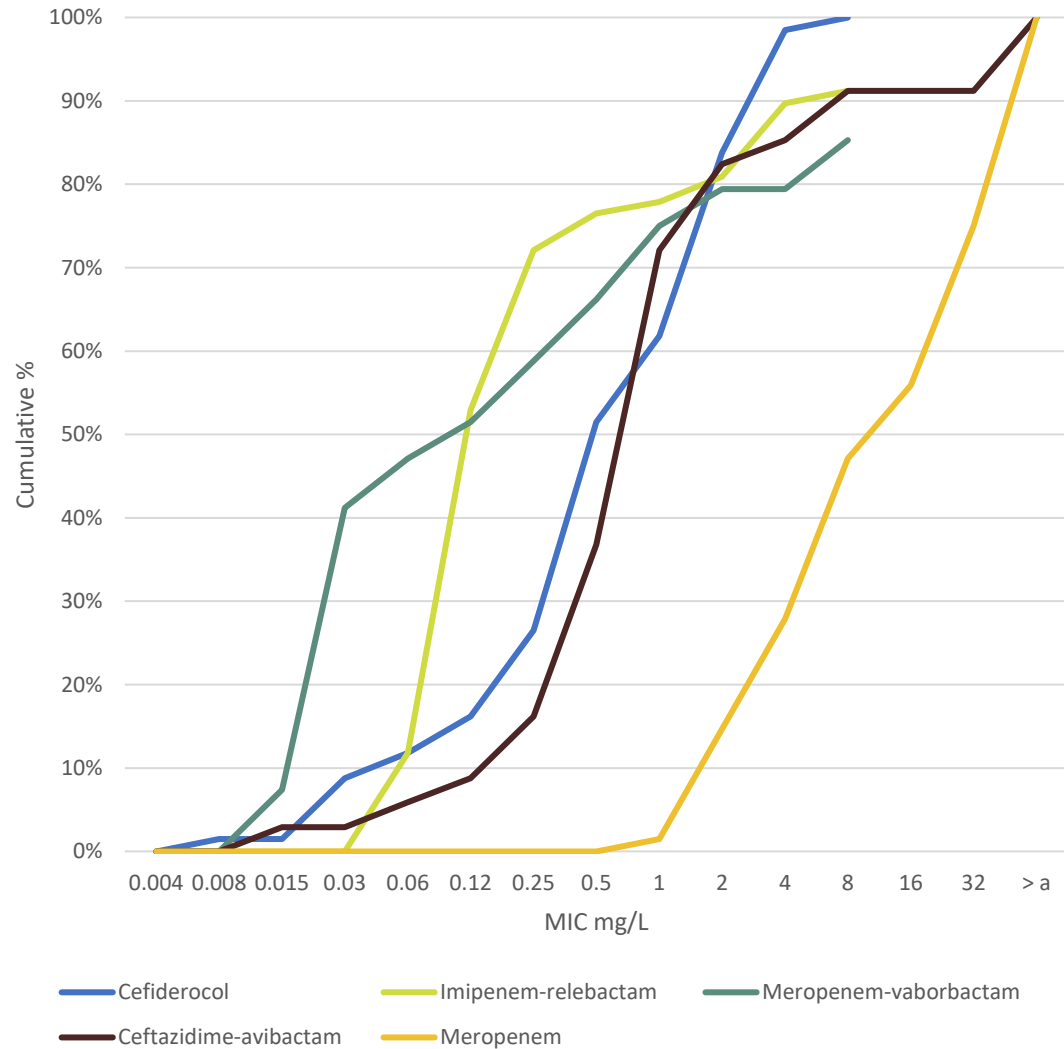
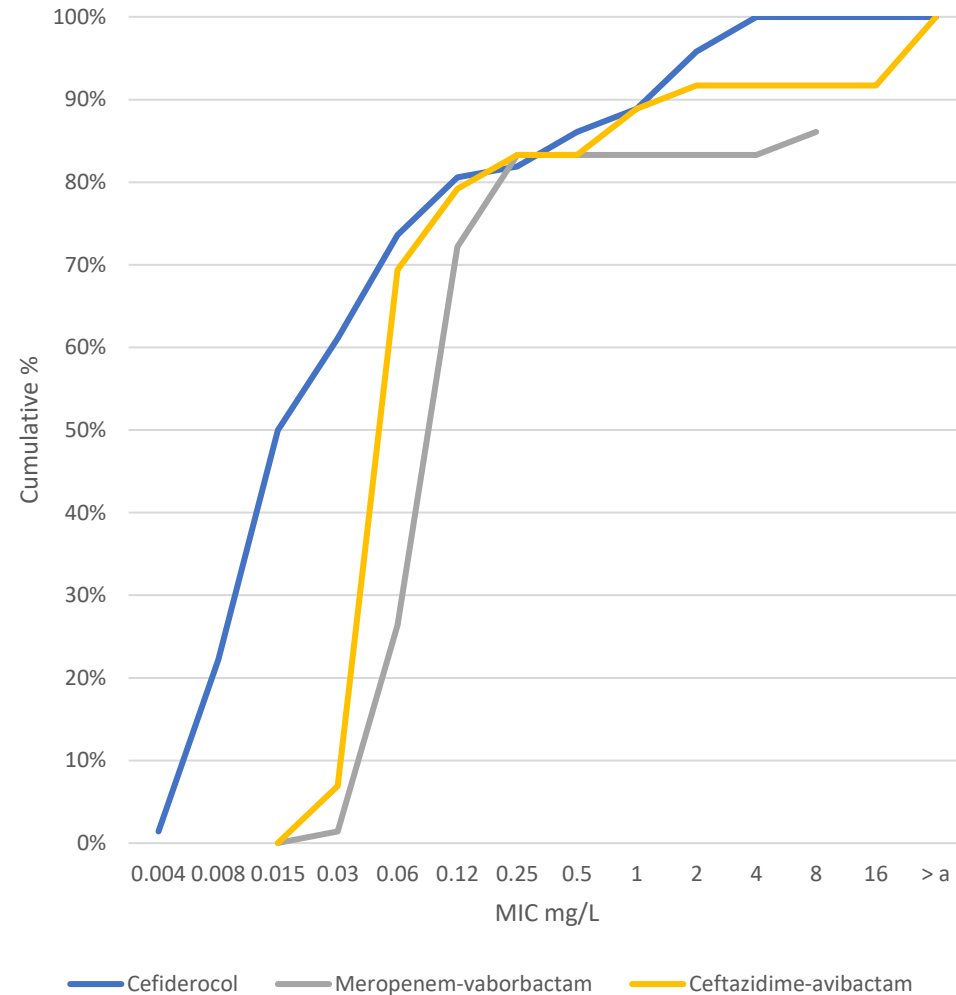


Figure 2. MIC Distributions of Imipenem-Relebactam-Resistant Isolates



^a >, MIC greater than highest concentration tested.



Results

- Most isolates were from urinary tract infections ($n=2,796$), followed by bloodstream ($n=2,047$) infections.
- The most common species was *Escherichia coli* ($n=3,285$) followed by *Klebsiella pneumoniae* (KPN, $n=1,382$).
- The susceptibilities of all tested agents were >94% against all isolates.
- CRE susceptibility to cefiderocol was 98.5/83.8% (CLSI/EUCAST).
- Cefiderocol was active against BL/BLI-resistant isolates.

Conclusions

- Cefiderocol had broad activity against US Enterobacterales isolates, including those resistant to approved BL/BLI combinations.
- These *in vitro* results suggest that cefiderocol is an important option for the treatment of infections caused by CRE and BL/BLI-resistant pathogens that have limited treatment options.

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