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

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Introduction

- Cefiderocol is a novel siderophore-conjugated cephalosporin with broad activity against Gram-negative bacteria, including carbapenem-resistant isolates.
- Cefiderocol was recently approved by the EMA for the treatment of infections caused by Gram-negative bacteria in adult patients with limited treatment options and the FDA for complicated urinary tract infection (UTI), hospital-acquired bacterial pneumonia, and ventilator-associated bacterial pneumonia.
- 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 *Enterobacterales* isolates, including CRE, collected in 2020 as a part of the SENTRY Antimicrobial Surveillance Program.

Materials and Methods

- A total of 3,844 *Enterobacterales* 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 iron-depleted Mueller-Hinton broth.
- CLSI/FDA and EUCAST (2021) breakpoints were used.
  - Cefiderocol breakpoints for CLSI and FDA are ≤4/8/≥16 mg/L.
  - Cefiderocol breakpoints for EUCAST are ≤2/-/>2 mg/L.
- CRE were identified as having an MIC >2 mg/L to meropenem and/or imipenem.
- Multi-drug 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 ceftazidime-avibactam, imipenem-relebactam, and meropenem-vaborbactam as well as meropenem and imipenem.

Results

- The most common *Enterobacterales* isolate was *Escherichia coli* (n=1,619) then *Klebsiella pneumoniae* (n=757; 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 *Enterobacterales* 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 ceftazidime-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 ceftazidime-avibactam resistant.
- 7.6% of the isolates were MDR and 0.7% were XDR (Table 1).
  - The cumulative % MIC distributions of MDR and XDR isolates are shown for cefiderocol and the 3 BL/BLI comparators in Figures 3 and 4.
- Cefiderocol was very active against both MDR (98.0/92.5% susceptible, CLSI/EUCAST) and XDR (96.4/92.5%; Table 1 and Figures 3 and 4).
  - The 3 comparators had susceptibililities >93% for MDR and >89% for XDR isolates. Imipenem-relebactam was the least active BL/BLI tested.

Figure 1. Species prevalence of *Enterobacterales* isolated from all infection types in US patients (2020)

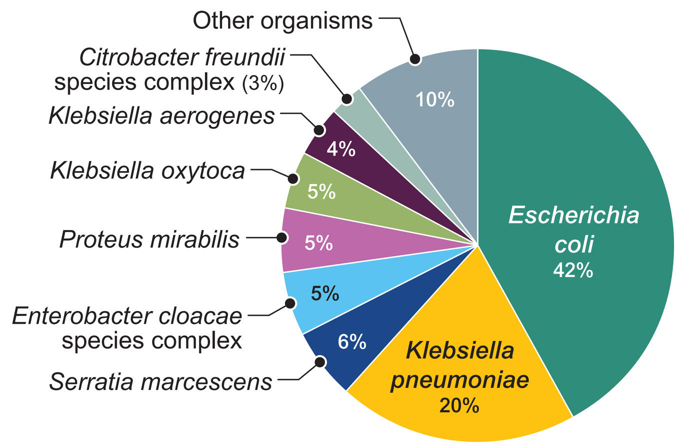
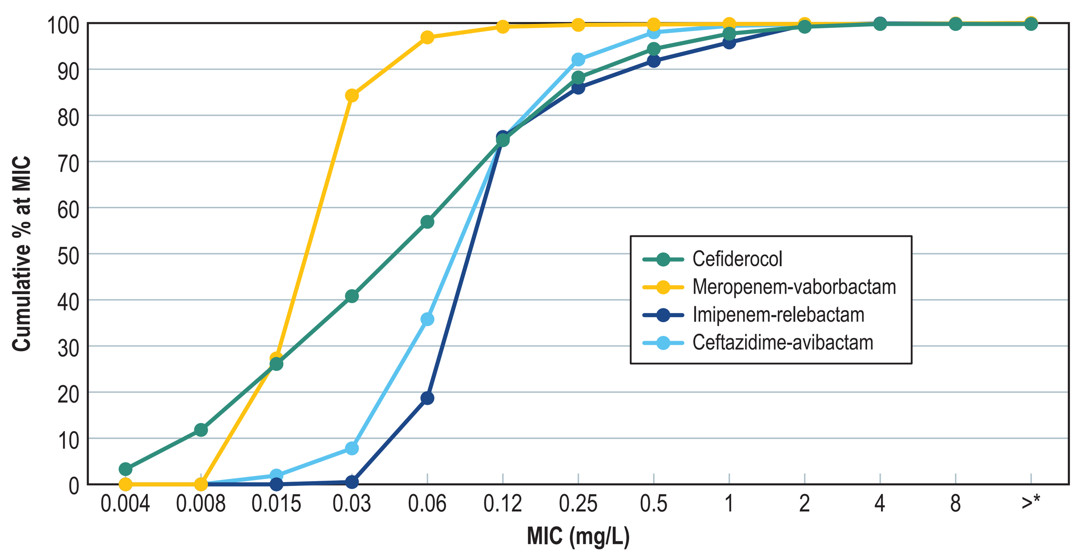
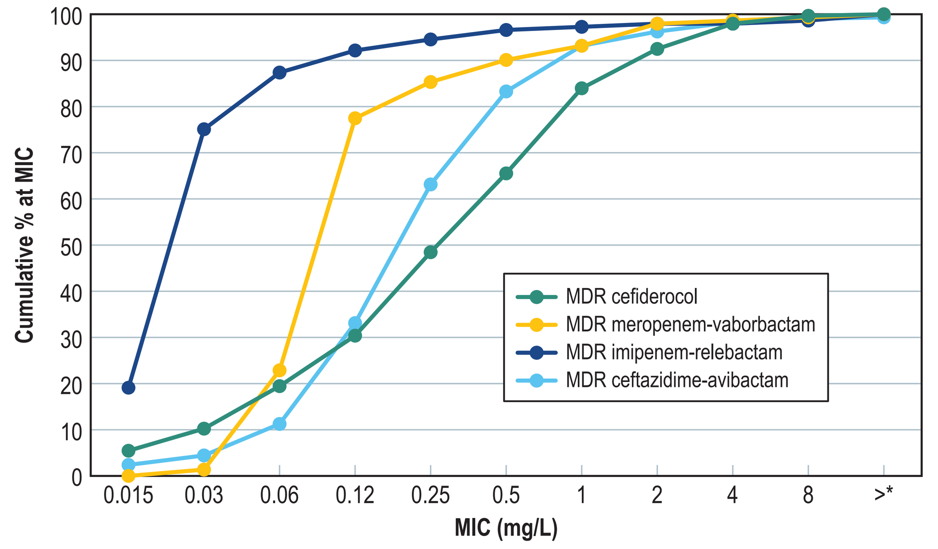


Figure 2. Cumulative % MIC distributions of *Enterobacterales* (n=3,844) for cefiderocol and comparators



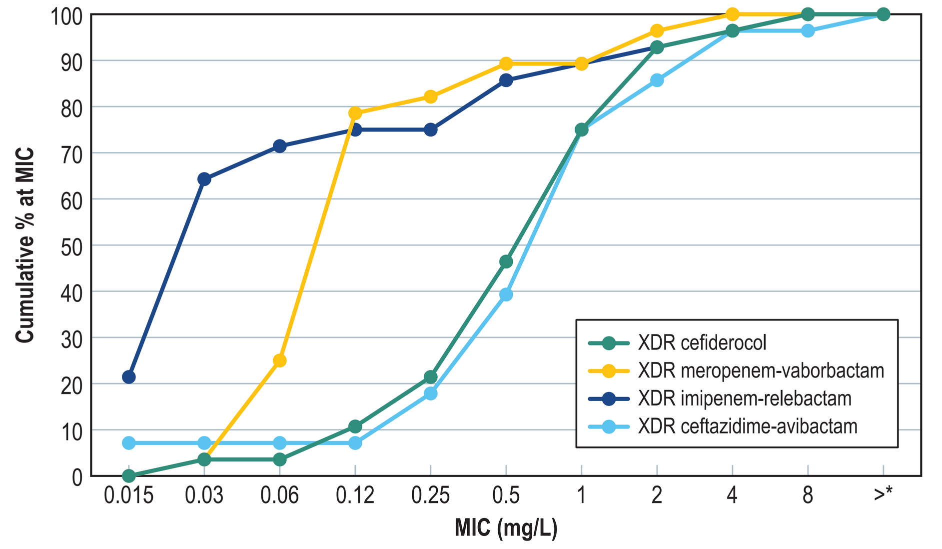
* MIC value greater than the highest dilution tested

Figure 3. Cumulative MIC distribution of MDR (n=293) isolate subset for cefiderocol and comparators



* MIC value greater than the highest dilution tested
MDR, multi-drug resistant

Figure 4. Cumulative MIC distribution of XDR (n=28) isolate subset for cefiderocol and comparators



* MIC value greater than the highest dilution tested
XDR, extensively drug resistant

Table 1. Susceptibilities of cefiderocol and comparators tested against US *Enterobacterales* isolates and resistant groups

Antimicrobial agent	No. of isolates	mg/L		CLSI/FDA[a]	EUCAST[a]
		MIC_{50}	MIC_{90}	%S	%S
All					
Cefiderocol[b]	3,844	0.06	0.5	99.8	99.2
Meropenem-vaborbactam	3,839	0.03	0.06	99.8	99.9
Imipenem-relebactam	3,844	0.12	0.5	95.8[c]	99.6
Ceftazidime-avibactam	3,842	0.12	0.25	99.9	99.9
CRE[d]					
Cefiderocol	33	0.5	4	97.0	87.9
Meropenem-vaborbactam	33	0.03	>8	81.8	87.9
Imipenem-relebactam	33	0.12	4	81.8[c]	87.9
Ceftazidime-avibactam	33	1	8	90.9	90.9
MDR					
Cefiderocol	293	0.5	2	98.0	92.5
Meropenem-vaborbactam	293	0.03	0.12	98.0	98.6
Imipenem-relebactam	293	0.12	0.5	93.2	98.0
Ceftazidime-avibactam	293	0.25	1	99.0	99.0
XDR					
Cefiderocol	28	1	2	96.4	92.9
Meropenem-vaborbactam	28	0.03	2	92.9	96.4
Imipenem-relebactam	28	0.12	2	89.3	96.4
Ceftazidime-avibactam	28	1	4	96.4	96.4
Imipenem-relebactam R					
Cefiderocol	16	0.03	2	100.0	93.8
Meropenem-vaborbactam	16	0.25	>8	75.0	75.0
Imipenem-relebactam	16	4	>8	0.0[c]	0.0
Ceftazidime-avibactam	16	0.06	>32	87.5	87.5

[a] Criteria as published by CLSI, FDA, and EUCAST (2021).
[b] Cefiderocol breakpoints for CLSI and FDA are ≤4/8/≥16 mg/L and EUCAST breakpoints are ≤/-/>2 mg/L. FDA breakpoints were published on 2020SEP25.
[c] FDA breakpoints were published on 2020JUN04 and have been applied to all *Enterobacterales* other than *Morganella*, *Proteus*, and *Providencia*
[d] CRE, carbapenem-resistant *Enterobacterales*. Organisms include: *Citrobacter freundii* species complex (3), *Enterobacter cloacae* species complex (4), *Escherichia coli* (1), *Klebsiella aerogenes* (2), *K. oxytoca* (4), *K. pneumoniae* (17), and unspeciated *Raoultella* (2).

Conclusions

- Cefiderocol had potent activity against US *Enterobacterales* 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 *Enterobacterales*.

Acknowledgements

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References

CLSI. *M07 Eleventh edition. Methods for Dilution Antimicrobial Susceptibility Testing for Bacteria That Grow Aerobically.* Clinical and Laboratory Standards Institute, Wayne, PA, 2018.

CLSI. *M100 31st edition. Performance Standards for Antimicrobial Susceptibility Testing.* Clinical and Laboratory Standards Institute, Wayne, PA, 2021.

EUCAST. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, v 11.0, January 1, 2021. http://www.eucast.org (Access Date Jan 31, 2021).

FDA Susceptibility Test Interpretive Criteria: https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria. Accessed May, 2021.

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