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Activity of Cefiderocol and Comparator Agents against European Isolates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii-calcoaceticus* species complex, and *Stenotrophomonas maltophilia* from the SENTRY Antimicrobial Surveillance Program (2020–2022)

Dee Shortridge, Rodrigo Mendes, Mariana Castanheira
JMI Laboratories, North Liberty, Iowa, USA

Introduction

- Cefiderocol is a siderophore-conjugated cephalosporin with broad activity against Gram-negative bacteria, including multidrug-resistant organisms.
- 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.
- Non–glucose-fermenting (NGF) species are often extensively drug resistant (XDR), presenting serious treatment challenges.
- The activity of cefiderocol and comparator agents was investigated against European NGF isolates collected in 2020–2022 as part of the SENTRY Antimicrobial Surveillance Program.

Materials and Methods

- A total of 3,063 *Pseudomonas aeruginosa*, 1,010 *Acinetobacter baumannii-calcoaceticus* species complex, and 352 *Stenotrophomonas maltophilia* isolates were consecutively collected from 40 hospitals in 18 European countries, Turkey, and Israel.
- Susceptibility testing was performed using broth microdilution with cation-adjusted Mueller-Hinton broth (CAMHB) for comparators and iron-depleted CAMHB for cefiderocol.
- CLSI and EUCAST breakpoints were applied.
  - EUCAST cefiderocol PK/PD breakpoints were used for *A. baumannii-calcoaceticus* complex and *S. maltophilia.*
  - CLSI criteria defined XDR as non-susceptible to at least 1 agent in all but 2 or fewer drug classes.
- Other agents tested included the newer β-lactam/β-lactamase inhibitor (BL/BLI) combinations ceftazidime-avibactam, ceftolozane-tazobactam, imipenem-relebactam, and meropenem-vaborbactam as well as meropenem.

Results

- The most common infection that isolates were collected from was pneumonia (*n*=2,151), followed by skin/skin structure infection (*n*=800), bloodstream infection (*n*=755), urinary tract infection (*n*=372), intrabdominal infection (*n*=168), and other sites (*n*=179).
- For all *P. aeruginosa* isolates, cefiderocol and BL/BLI susceptibilities were >95%, except meropenem-vaborbactam, which was 90.9% (EUCAST; Table 1).
- Cefiderocol was the most active agent against XDR *P. aeruginosa* and *P. aeruginosa* isolates resistant to the newer BL/BLI combinations, with >90% being susceptible to cefiderocol (Table 1, Figure 1).
- Cefiderocol had potent activity ($MIC_{50/90}$ 0.25/1 mg/L; 98.4/96.8% susceptibility, CLSI/EUCAST) against *A. baumannii-calcoaceticus* complex, and susceptibility percentages of >96% against XDR, meropenem-, and imipenem-relebactam–resistant *A. baumannii-calcoaceticus* complex isolates (Table 2; Figure 1).
- Cefiderocol was very active against *S. maltophilia*, with 99.4/100.0% susceptibility (CLSI/EUCAST; $MIC_{50/90}$ 0.06/0.5 mg/L; Table 2; Figure 1).

Conclusions

- Cefiderocol was the most active β-lactam against contemporary European isolates of *P. aeruginosa*, *A. baumannii-calcoaceticus* complex, and *S. maltophilia*, including resistant subsets for which treatment options are limited.
- These *in vitro* data suggest that cefiderocol is an important option for the treatment of infections caused by *P. aeruginosa*, *A. baumannii-calcoaceticus* complex, and *S. maltophilia*, including meropenem-resistant, BL/BLI-resistant and XDR isolates.

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Table 1. Susceptibilities of *P. aeruginosa* isolates and resistant subgroups tested against cefiderocol and comparator agents

Organism/organism group Antimicrobial agent	MIC_{50} (mg/L)	MIC_{90} (mg/L)	%S CLSI[a]	%S EUCAST[a]
All isolates (*n*=3,063)				
Cefiderocol	0.12	0.25	99.8	99.5
Meropenem	0.5	8	79.3	79.3
Meropenem-vaborbactam	0.5	8		90.9
Imipenem-relebactam	0.25	1	95.3	95.3
Ceftolozane-tazobactam	0.5	2	95.1	95.1
Ceftazidime-avibactam	2	4	96.2	96.2
XDR[b] (*n*=290)				
Cefiderocol	0.12	1	98.6	97.2
Meropenem	16	>32	6.2	6.2
Meropenem-vaborbactam	>8	>8		37.6
Imipenem-relebactam	2	>8	57.9	57.9
Ceftolozane-tazobactam	4	>16	56.6	56.6
Ceftazidime-avibactam	8	>32	65.9	65.9
Meropenem MIC >8 mg/L (*n*=275)				
Cefiderocol	0.12	1	98.5	97.1
Meropenem	16	>32	0.0	0.0
Meropenem-vaborbactam	>8	>8		4.4
Imipenem-relebactam	2	>8	53.5	53.5
Ceftolozane-tazobactam	4	>16	58.8	58.8
Ceftazidime-avibactam	8	>32	58.8	58.8
Meropenem-vaborbactam MIC >8 mg/L (*n*=278)				
Cefiderocol	0.12	0.5	98.9	97.5
Meropenem	16	>32	0.0	0.0
Meropenem-vaborbactam	>8	>8		0.0
Imipenem-relebactam	2	>8	54.3	54.3
Ceftolozane-tazobactam	4	>16	58.8	58.8
Ceftazidime-avibactam	8	>32	58.8	58.8
Ceftolozane-tazobactam MIC >4 mg/L (*n*=149)				
Cefiderocol	0.25	2	96.6	93.3
Meropenem	32	>32	9.4	9.4
Meropenem-vaborbactam	>8	>8		23.5
Imipenem-relebactam	8	>8	32.9	32.9
Ceftolozane-tazobactam	>16	>16	0.0	0.0
Ceftazidime-avibactam	16	>32	38.3	38.3
Ceftazidime-avibactam MIC >8 mg/L (*n*=115)				
Cefiderocol	0.25	2	96.5	92.2
Meropenem	32	>32	6.1	6.1
Meropenem-vaborbactam	>8	>8		18.3
Imipenem-relebactam	8	>8	29.6	29.6
Ceftolozane-tazobactam	>16	>16	20.0	20.0
Ceftazidime-avibactam	32	>32	0.0	0.0

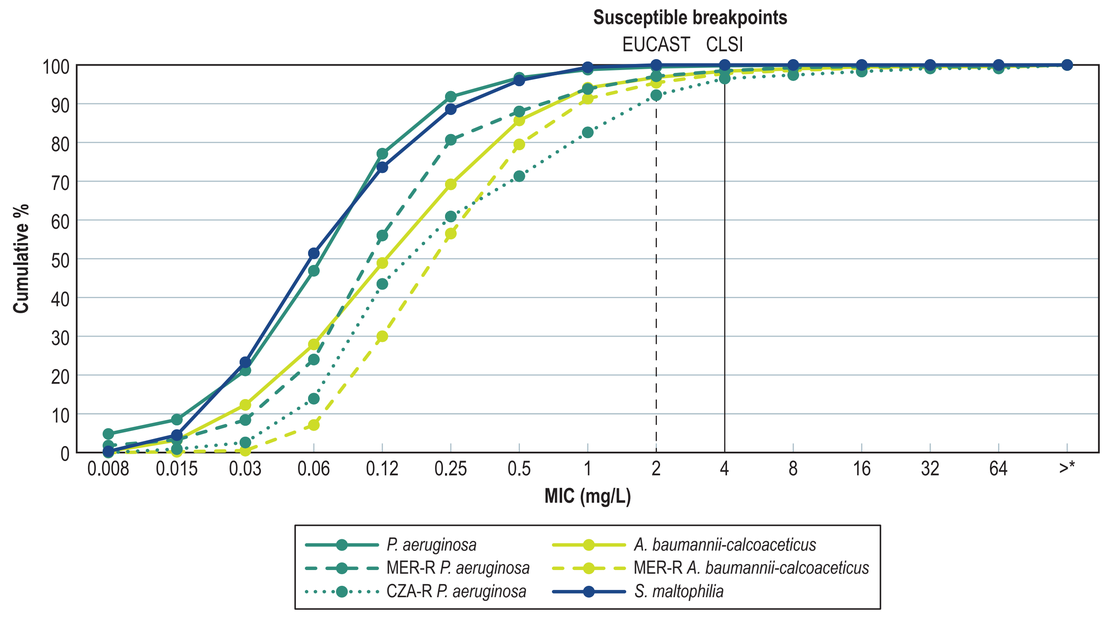
Abbreviations: XDR, extensively drug resistant.
[a] Breakpoints as published by CLSI or EUCAST (2022).
[b] XDR, defined as resistant to all but 2 or fewer drug classes using CLSI breakpoints (2022).

Table 2. Susceptibilities of *Acinetobacter baumannii-calcoaceticus* species isolates and resistant subgroups, and *Stenotrophomonas maltophilia* tested against cefiderocol and comparator agents

Organism/organism group Antimicrobial agent	MIC_{50} (mg/L)	MIC_{90} (mg/L)	%S CLSI[a]	%S EUCAST[a]
All *A. baumannii-calcoaceticus* (*n*=1,010)				
Cefiderocol	0.25	1	98.4	96.8
Meropenem	>32	>32	37.0	37.0
Imipenem-relebactam	>8	>8		37.0
Ampicillin-sulbactam	32	>64	36.0	
Colistin	0.5	>8		84.9
XDR[b] (*n*=618)				
Cefiderocol	0.25	1	98.1	95.6
Meropenem	>32	>32	0.3	0.3
Imipenem-relebactam	>8	>8		0.3
Ampicillin-sulbactam	64	>64	0.6	
Colistin	0.5	>8		76.1
Meropenem MIC >8 mg/L (*n*=634)				
Cefiderocol	0.25	1	97.8	95.4
Meropenem	>32	>32	0.0	0.0
Imipenem-relebactam	>8	>8		0.0
Ampicillin-sulbactam	64	>64	1.7	
Colistin	0.5	>8		76.7
Imipenem-relebactam MIC >2 mg/L (*n*=636)				
Cefiderocol	0.25	1	97.8	95.4
Meropenem	>32	>32	0.0	0.0
Imipenem-relebactam	>8	>8		0.0
Ampicillin-sulbactam	64	>64	1.7	
Colistin	0.5	>8		76.7
S. maltophilia (*n*=352)				
Cefiderocol	0.06	0.5	99.4	100.0
Levofloxacin	1	4	85.5	
Trimethoprim-sulfamethoxazole	≤0.12	0.5	96.0	96.9

Abbreviations: XDR, extensively drug resistant.
[a] Breakpoints as published by CLSI or EUCAST; PK/PD breakpoints shown for cefiderocol (2022).
[b] XDR, resistant to all but 2 or fewer drug classes using CLSI breakpoints (2022).

Figure 1. Cefiderocol MIC distributions of *P. aeruginosa* isolates, all isolates and isolates resistant to meropenem or ceftazidime-avibactam; *A. baumannii-calcoaceticus* complex, all isolates and isolates resistant to meropenem; all *S. maltophilia*



*Greater than the highest concentration tested.
Abbreviations: MER-R, meropenem resistant; CZA-R, ceftazidime-avibactam resistant.

References

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Contact

Dee Shortridge
JMI Laboratories
345 Beaver Kreek Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Fax: (319) 665-3371
Email: dee-shortridge@jmilabs.com

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