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Activity of Cefiderocol Against a Multinational Collection of Gram-negative Isolates Collected from Cystic Fibrosis Patients During 2020–2022

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BACKGROUND

- Cefiderocol is a siderophore-conjugated cephalosporin with activity against a broad range of Gram-negative pathogens.
- Cefiderocol is approved in the United States (US) for the treatment of patients with complicated urinary tract infections and hospital-acquired/ventilator-associated bacterial pneumonia caused by susceptible Gram-negative pathogens. Cefiderocol is approved in Europe for the treatment of infections caused by susceptible Gram-negative bacteria with limited treatment options.
- Patients with cystic fibrosis (CF) are often colonized with multidrug-resistant Gram-negative bacteria, such as *Pseudomonas aeruginosa*, which may cause pulmonary infections.
- In this study, the *in vitro* activity of cefiderocol was evaluated against Gram-negative isolates collected from patients with CF.

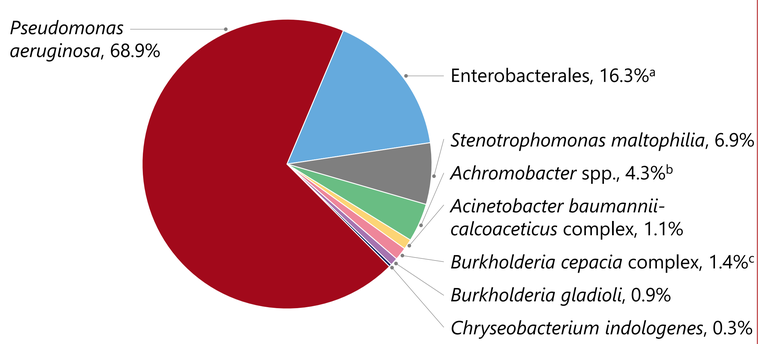
METHODS

- 350 Gram-negative bacterial isolates were collected during 2020–2022 from hospitalized patients with CF from US and European hospitals as part of the SENTRY Antimicrobial Surveillance Program.
- Minimum inhibitory concentrations (MICs) were determined according to Clinical and Laboratory Standards Institute (CLSI) guidelines using broth microdilution with cation-adjusted Mueller–Hinton broth (CAMHB) for comparator agents and iron-depleted CAMHB for cefiderocol.
- Susceptibility was assessed according to 2024 CLSI, US Food and Drug Administration (FDA), and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.
- Carbapenem-non-susceptible subsets were defined as non-susceptible to meropenem and imipenem using CLSI breakpoints.

RESULTS

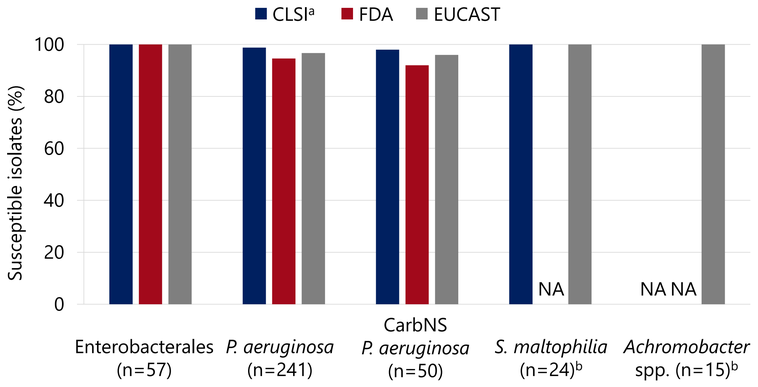
- The majority of Gram-negative isolates collected from patients with CF were *P. aeruginosa* (**Figure 1**).
- Cefiderocol showed good *in vitro* activity against most Gram-negative isolates, including carbapenem-non-susceptible isolates. Activity against *Burkholderia* species varied, with MIC values ranging from ≤0.004 to >64 mg/L (**Figure 2** and **Table 1**).
- Compared with other agents, the highest susceptibility rate was observed with cefiderocol, particularly against carbapenem-non-susceptible isolates (**Table 2**).

Figure 1. Gram-negative pathogens collected during 2020–2022 from hospitalized patients with CF from US and European hospitals (N=350)



[a]Organisms included: *Citrobacter koseri* (n=1), *Enterobacter cloacae* (n=2), *Enterobacter cloacae* complex (n=4), *Escherichia coli* (n=13), *Klebsiella aerogenes* (n=2), *Klebsiella oxytoca* (n=5), *Klebsiella pneumoniae* (n=11), *Proteus mirabilis* (n=3), *Serratia liquefaciens* (n=4), *Serratia liquefaciens* complex (n=2), *Serratia marcescens* (n=10); [b]Organisms included: *Achromobacter xylosoxidans* (n=2), unspeciated *Achromobacter* (n=13); [c]Organisms included: *Burkholderia multivorans* (n=1), unspeciated *Burkholderia cepacia* complex (n=4).

Figure 2. Cefiderocol susceptibility of Gram-negative isolates from patients with CF



Only species with n>10 are shown.
[a]According to 2024 CLSI, FDA, EUCAST breakpoints; [b]Based on EUCAST PK-PD breakpoint (2 mg/L).
CarbNS, carbapenem-non-susceptible; NA, no breakpoint available.

Table 1. *In vitro* activity of cefiderocol against less frequent Gram-negative isolates from patients with CF

Pathogen	N	MICs (mg/L)
Acinetobacter baumannii-calcoaceticus complex	4	0.12, 0.25, 1 and 2
CarbNS *A. baumannii-calcoaceticus* complex	2	0.12 and 2
Chryseobacterium indologenes[a]	1	0.25
Achromobacter xylosoxidans[a]	1	0.5
Burkholderia cepacia complex	5	≤0.004, ≤0.004, 0.015, 2 and >64
Burkholderia gladioli	3	2, 4 and 64

Only species with n <10 are shown.
[a]Carbapenem-non-susceptible isolate.
N, number of isolates; MIC, minimum inhibitory concentration; NA, not applicable as breakpoints are not available.

Table 2. Susceptibility of cefiderocol and comparator agents against Gram-negative isolates from patients with CF

		Susceptible (%)[a]											
Pathogen	N	CFDC	MEM	MEV	CAZ	CZA	IPM	IMR	CT	LVX	AN	MI	SXT	CL[b]
Enterobacterales	57	**100**	**98.2**	**100**	82.5	**100**	**94.7**	**94.7**	**93.0**	84.2	**94.7**	89.5	73.7	66.1
Pseudomonas aeruginosa	241	**98.8**	77.2	NA	77.6	**94.6**	67.6	**92.9**	**90.0**	58.1	78.8	NA	NA	**98.3**
CarbNS *P. aeruginosa*	50	**98.0**	0	NA	34.0	81.6	0	68.0	66.0	42.0	58.0	NA	NA	**96.0**
Acinetobacter baumannii-calcoaceticus complex	4	**100**	50.0	NA	50.0	NA	50.0	NA	NA	50.0	50.0	50.0	50.0	75.0
CarbNS *A. baumannii-calcoaceticus* complex	2	**100**	0	NA	0	NA	0	NA	NA	0	0	0	0	50.0
Stenotrophomonas maltophilia	24	**100**	NA	NA	16.7	NA	NA	NA	NA	58.3	NA	**100**	**91.7**	NA
Achromobacter spp.	15	NA	86.7	NA	60.0	NA	**93.3**	NA	NA	26.7	0	**93.3**	**93.3**	NA
Burkholderia cepacia complex	5	NA	40.0	NA	60.0	NA	NA	NA	NA	0	NA	60.0	40.0	NA
Chryseobacterium indologenes	1	NA	0	NA	**100**	NA	0	NA	NA	**100**	0	**100**	**100**	NA

% susceptibility ≥90% indicated in red bold.
[a]According to 2024 CLSI breakpoints; [b]According to 2024 EUCAST breakpoints. CFDC, cefiderocol; MEM, meropenem; MEV, meropenem-vaborbactam; CAZ, ceftazidime; CZA, ceftazidime-avibactam; IPM, imipenem; IMR, imipenem-relebactam; CT, ceftolozane-tazobactam; LVX, levofloxacin; AN, amikacin; MI, minocycline; SXT, trimethoprim-sulfamethoxazole; CL, colistin; N, number of isolates; NA, no breakpoint available; CarbNS, carbapenem-non-susceptible.

CONCLUSIONS

- Cefiderocol demonstrated potent activity against a wide range of Gram-negative isolates collected from patients with CF, including carbapenem-non-susceptible isolates.
- Cefiderocol could be an important agent for patients with CF when treatment options are limited.

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