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Activity of Cefiderocol Against Non-Fermenting Gram-Negative Isolates Collected from Intensive Care Unit Patients in US and European Medical Centers as Part of the SENTRY Antimicrobial Surveillance Program (2020–2024)

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INTRODUCTION

- Intensive care units (ICUs) are a source of highly resistant Gram-negative bacteria, which may have reduced antimicrobial *in vitro* susceptibilities compared with other areas of the hospital [1].
- Cefiderocol is a siderophore-conjugated cephalosporin, which utilizes the iron-uptake systems of bacteria to facilitate cell entry, with excellent *in vitro* activity against non-fermenting Gram-negative bacteria (NFGNB) including organisms resistant to carbapenems and novel β-lactam/β-lactamase inhibitors (BL–BLIs).
- The objective of this study was to compare the *in vitro* activity of cefiderocol and comparators against NFGNB collected in ICUs and non-ICU settings.

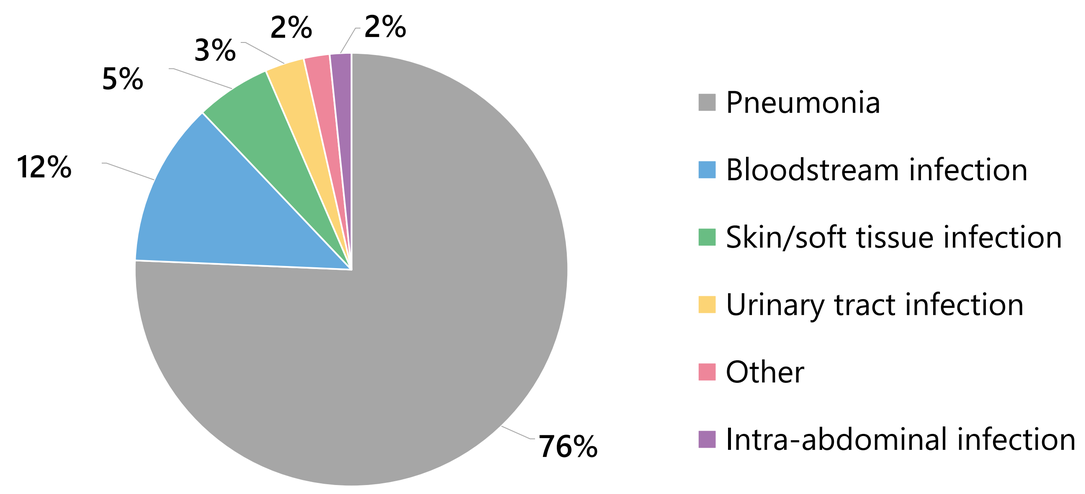
METHODS

- Isolates were collected during 2020–2024 from European and US hospitals participating in the SENTRY Antimicrobial Surveillance Program.
- Minimum inhibitory concentrations (MICs) were determined according to Clinical and Laboratory Standards Institute (CLSI) methods, using broth microdilution with cation-adjusted Mueller–Hinton broth (CAMHB) for comparator agents and iron-depleted CAMHB for cefiderocol.
- Susceptibility was determined according to 2025 CLSI, US Food and Drug Administration (FDA) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.
- Carbapenem resistance was defined as non-susceptibility to meropenem and/or imipenem by CLSI breakpoints (2025).
- Difficult-to-treat resistance was defined as non-susceptibility to piperacillin-tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem, ciprofloxacin, and levofloxacin by CLSI breakpoints (2025).

RESULTS

- Among 17,630 NFGNB isolates collected, 6,759 originated from ICU settings and were predominately from patients with pneumonia and bloodstream infections (**Figure 1**).
- *Pseudomonas aeruginosa* (54.6%) was the most common organism followed by *Acinetobacter baumannii-calcoaceticus* complex (25.4%) and *Stenotrophomonas maltophilia* (14.7%).
- Cefiderocol retained similar activity against NFGNB collected in ICUs vs. non-ICUs and was the most active agent *in vitro* against highly resistant subsets of ICU isolates, including *P. aeruginosa* resistant to novel BL–BLIs (**Tables 1–3**).
- Cefiderocol $MIC_{50/90}$ values were low for *Achromobacter* spp. (0.03/0.25 µg/mL) and *Burkholderia cepacia* species complex (0.06/0.5 µg/mL) collected from the ICU (**Table 1**).

Figure 1. ICU source of infection (N=6759).



ICU, intensive care unit.

Table 1. Activity of cefiderocol against NFGNB isolated from ICU and non-ICU settings as part of the SENTRY program (2020–2024)

Isolate set	n	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC range (µg/mL)	CLSI[a] %S	FDA[a] %S	EUCAST[a] %S
P. aeruginosa							
ICU	3695	0.12	0.5	≤0.004–>64	99.5	98.2	99.1
Non-ICU	6652	0.12	0.5	≤0.004–64	99.7	98.6	99.4
CRPA[b]							
ICU	885	0.12	0.5	≤0.004–>64	98.4	95.0	97.5
Non-ICU	939	0.12	0.5	≤0.004–64	98.7	94.7	97.2
DTR PA[c]							
ICU	159	0.25	2	≤0.004–>64	97.5	88.1	96.2
Non-ICU	232	0.12	2	≤0.004–64	97.0	87.9	95.3
ABC complex							
ICU	1714	0.25	1	0.008–>64	95.9	90.7	93.8
Non-ICU	2197	0.25	1	≤0.004–>64	97.5	93.7	96.2
CRAB[b]							
ICU	957	0.25	2	0.008–>64	93.8	85.9	90.3
Non-ICU	837	0.25	2	0.015–>64	94.1	85.5	90.9
S. maltophilia							
ICU	991	0.06	0.25	≤0.004–4	99.3	99.3	99.8
Non-ICU	1037	0.06	0.25	≤0.004–>64	99.2	99.2	99.6
***Achromobacter* spp.**							
ICU	83	0.03	0.25	≤0.004–8	–	–	–
Non-ICU	173	0.03	0.25	≤0.004–2	–	–	–
***B. cepacia* species complex**							
ICU	103	0.06	0.5	≤0.004–64	–	–	–
Non-ICU	134	0.06	4	≤0.004–>64	–	–	–

ABC complex, *Acinetobacter baumannii-calcoaceticus* complex; CLSI, Clinical and Laboratory Standards Institute; CRAB, carbapenem-resistant *A. baumannii-calcoaceticus* complex; CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; DTR PA, difficult-to-treat resistant *P. aeruginosa*; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; ICU, intensive care unit; MIC, minimum inhibitory concentration; $MIC_{50/90}$, MIC required to inhibit growth of ≥50%/90% of isolates; NFGNB, non-fermenting Gram-negative bacteria; S, susceptible. [a]Criteria as published by CLSI (2025), US FDA (2025), and EUCAST (2025). [b]Resistant to meropenem and/or imipenem by CLSI breakpoints. [c]Non-susceptible to piperacillin-tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem, ciprofloxacin, and levofloxacin by CLSI breakpoints (2025).

Table 2. Activity of cefiderocol and comparators against highly resistant NFGNB ICU isolates collected as part of the SENTRY program (2020-2024)

Isolate set, N	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC range (µg/mL)	CLSI[a] %S	FDA[a] %S	EUCAST[a] %S
CR *P. aeruginosa* (N=885)[b]						
Cefiderocol	0.12	0.5	≤0.004–>64	98.4	95.0	97.5
Imipenem-relebactam	1	8	0.25–>8	81.4	81.4	81.4
Ceftazidime-avibactam	4	32	0.5–>32	82.0	82.0	82.0
Ceftolozane-tazobactam	1	>16	0.25–>16	81.9	81.9	81.9
Cefepime	8	>32	1–>32	54.4	54.4	54.4
Piperacillin-tazobactam	32	>128	4–>128	42.3	42.3	42.3
Ciprofloxacin	0.5	>4	0.03–>4	60.3	60.3	–
Amikacin	4	32	≤0.25–>32	87.3[c]	87.3	87.3
Colistin	0.5	1	0.12–8	0	99.8	–
DTR *P. aeruginosa* (N=159)[d]						
Cefiderocol	0.25	2	≤0.004–>64	97.5	88.1	96.2
Imipenem-relebactam	4	>8	0.25–>8	45.9	45.9	45.9
Ceftazidime-avibactam	16	>32	1–>32	44.7	44.7	44.7
Ceftolozane-tazobactam	8	>16	1–>16	48.4	48.4	48.4
Amikacin	16	>32	≤0.25–>32	64.8[c]	64.8	64.8
Colistin	1	1	0.12–2	0	100	–
CR *A. baumannii-calcoaceticus* complex (N=957)[b]						
Cefiderocol	0.25	2	0.008–>64	93.8	85.9	90.3
Ampicillin-sulbactam	64	>64	4–>64	1.9	1.9	–
Minocycline	8	16	0.12–>32	17.0	17.0	–
Sulbactam-durlobactam (n=335)	2	4	≤0.25–>32	93.4	93.4	–
Colistin	0.5	>8	0.12–>8	0	–	82.8
***S. maltophilia* (N=991)**						
Cefiderocol	0.06	0.25	≤0.004–4	99.3	99.3	99.8
Aztreonam-avibactam	4	4	0.12–>16	–	–	–
Levofloxacin	1	4	≤0.015–>32	84.7	–	–
Minocycline	0.5	1	≤0.06–8	92.9	–	–
SMX/TMP	≤0.12	0.5	≤0.12–>4	97.2	–	97.2

CLSI, Clinical and Laboratory Standards Institute; CR, carbapenem-resistant; DTR, difficult-to-treat resistant; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; ICU, intensive care unit; MIC, minimum inhibitory concentration; $MIC_{50/90}$, MIC required to inhibit growth of ≥50%/90% of isolates; NFGNB, non-fermenting Gram-negative bacteria; S, susceptible; SMX/TMP, sulfamethoxazole/trimethoprim. [a]Criteria as published by CLSI (2025), US FDA (2025), and EUCAST (2025). [b]Resistant to meropenem and/or imipenem by CLSI breakpoints. [c]Using urinary tract infection breakpoints only. [d]Non-susceptible to piperacillin-tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem, ciprofloxacin, and levofloxacin by CLSI breakpoints (2025).

Table 3. Activity of cefiderocol and comparators against ICU isolates of *Pseudomonas aeruginosa* resistant to BL–BLIs.

Resistance phenotype (*resistant to*)	n	%Susceptible per CLSI/FDA/EUCAST[a]						
		Cefiderocol			CAZ-AVI	C-T	IMI-REL	MEM-VAB
		CLSI	FDA	EUCAST				
CAZ-AVI	195	91.3	79.5	87.7	0	27.2	44.1	0/0/21.0
C-T	200	91.5	79.0	88.0	29.0	0	41.0	0/0/30.5
IMI-REL	168	94.0	85.0	91.1	34.7	29.8	0	0/0/6.5
MEM-VAB	442	96.6	91.6	95.2	65.1	68.6	64.5	0

BL–BLI, β-lactam–β-lactamase inhibitor; CAZ-AVI, ceftazidime-avibactam; CLSI, Clinical and Laboratory Standards Institute C-T, ceftolozane/tazobactam; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; ICU, intensive care unit; IMI-REL, imipenem-relebactam; MEM-VAB, meropenem-vaborbactam. [a]If only one value is shown, the CLSI, FDA, and EUCAST breakpoints are equivalent.

CONCLUSIONS

- Cefiderocol demonstrated excellent *in vitro* activity against NFGNB collected in ICUs, with no meaningful differences compared with isolates from non-ICU settings.
- These data suggest that cefiderocol is an important treatment option for patients with infections due to a broad range of suspected or confirmed NFGNB in the ICU, including those with resistance to carbapenems and novel BL–BLIs.

References: 1. Sader HS, et al. Diagn Microbiol Infect Dis. 2022 Jan;102(1):115557.

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Conflict of interest: SS, STN, BLMD, CL, HY, YY are employees of the SHIONOGI Group. JMM and REM are employees of Element, which received funding for this study.

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