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Activity of Cefiderocol Against Resistant Isolates Collected From Bloodstream Infections During 2020 to 2024 as Part of the SENTRY Antimicrobial Surveillance Program

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INTRODUCTION

- Bloodstream infections (BSIs) caused by Gram-negative bacteria can become life threatening for patients, and many of these pathogens are becoming increasingly resistant to antimicrobials.
- The main objective of this surveillance study was to evaluate the *in vitro* activity of cefiderocol against contemporary Gram-negative bloodstream infection isolates, collected as part the SENTRY Surveillance Program, particularly those with limited treatment options due to high levels of resistance.

METHODS

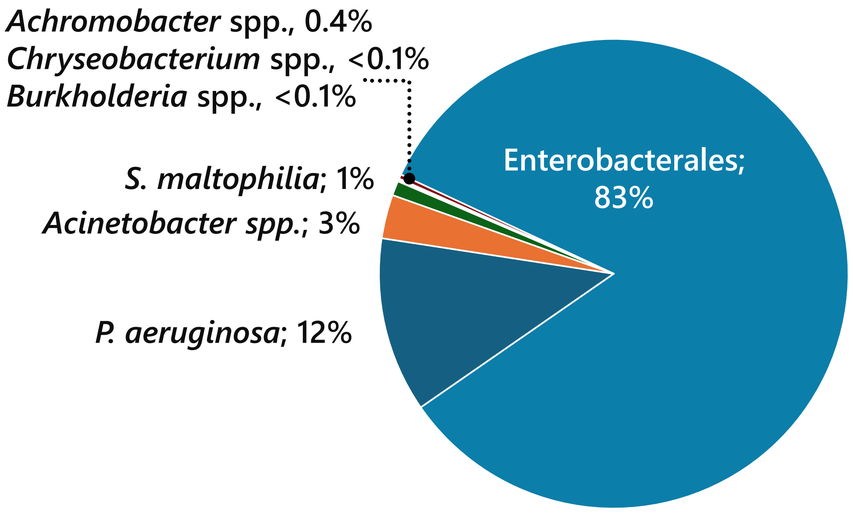
- Isolates from patients with BSIs caused by Gram-negative pathogens were consecutively collected in US (*n*=62 sites), European (*n*=37), Israeli (*n*=2) and Turkish (*n*=2) hospitals during 2020–2024 as part of the SENTRY Antimicrobial Surveillance Program.
- Minimum inhibitory concentrations (MICs) 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.
- Non-susceptibility for comparator agents was based on CLSI breakpoints and susceptibility for cefiderocol was assessed according to CLSI, US Food and Drug Administration, and European Committee on Antimicrobial Susceptibility Testing breakpoints. Resistance phenotypes are defined in **Table 1.**

RESULTS

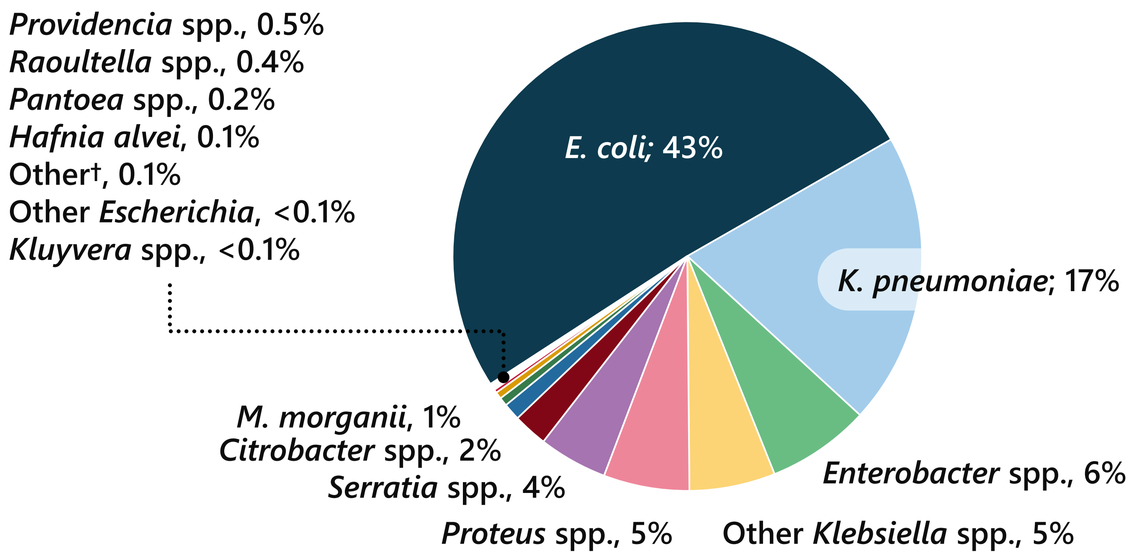
- A total of 14,916 Gram-negative bacterial isolates were collected. The majority of isolates were Enterobacterales, with *Escherichia coli* being the most prevalent species (**Figure 1**).
- Susceptibility to cefiderocol remained high for multidrug-resistant, carbapenem-resistant (CR), and extensively drug-resistant Enterobacterales and *Pseudomonas aeruginosa*, as well as for difficult-to-treat resistant *P. aeruginosa*, CR *Acinetobacter baumannii-calcoaceticus* species complex, and *Stenotrophomonas maltophilia* (**Table 1**).
- Cefiderocol showed low MIC values (MIC ranges 0.008–1 µg/mL) against *Burkholderia cepacia* species complex, *Achromobacter* spp., and *Chryseobacterium* spp. isolates (**Table 2**).

Figure 1. BSI isolates collected as part of the SENTRY program (2020–2024). A. Prevalence of Gram-negative isolates (*n*=14,916), B. Enterobacterales isolates (n=12,435)*.

A.



B.



BSI, bloodstream infection.
* Percentages shown as percentage of total number of isolates. † Includes Gram-negative rods in the family of *Enterobacteriaceae* (*n*=1), *Leclercia adecarboxylata* (*n*=3), *Lelliottia amnigena* (*n*=2), *Phytobacter diazotrophicus* (*n*=2), *Pluralibacter gergoviae* (*n*=5), *Rahnella aquatilis* (*n*=2), unspeciated *Erwinia* (n=1), and *Yersinia enterocolitica* (*n*=2).

Table 2. MIC distribution (number and cumulative percentage of isolates) of cefiderocol against rare Gram-negative BSI isolates collected as part of the SENTRY program (2020–2024). MIC_{50} and MIC_{90} (for n≥10) values are shaded light and dark grey, respectively.

Species (*n*)	Number and cumulative percentage of isolates inhibited at cefiderocol MIC (µg/mL) of:							
	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1
***B. cepacia* species complex (*n*=13)**	1 (7.7%)	2 (23.1%)	2 (38.5%)	4 (69.2%)	2 (84.6%)	2 (100%)		
***Achromobacter* spp. (*n*=57)[a]**	3 (5.3%)	29 (56.1%)	9 (71.9%)	6 (82.5%)	5 (91.2%)	3 (96.5%)	1 (98.2%)	1 (100%)
***Chryseobacterium* spp. (*n*=7)[b]**			1 (14.3%)	0 (14.3%)	4 (71.4%)	1 (85.7%)	1 (100%)	

BSI, bloodstream infection; MIC, minimum inhibitory concentration; $MIC_{50/90}$, MIC required to inhibit growth of ≥50%/90% of isolates.
[a]Organisms included: *Achromobacter insolitus* (*n*=1), *A. xylosoxidans* (*n*=11), unspeciated *Achromobacter spp.* (*n*=45) [b]Organisms included: *Chryseobacterium arthrosphaerae* (*n*=2), *C. hominis* (*n*=1), *C. indologenes* (*n*=4).

Table 1. Activity of cefiderocol against BSI isolates collected as part of the SENTRY program (2020–2024).

Isolate set	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC range (µg/mL)	CLSI[a] %S	FDA[a] %S	EUCAST[a] %S
Enterobacterales (*n*=12,435)	0.06	0.5	≤0.004–>64	99.7	99.7	99.0
Multidrug-resistant (*n*=3,508)[b]	0.25	2	≤0.004–>64	99.0	99.0	96.6
Carbapenem-resistant (*n*=309)[c]	1	4	0.015–>64	92.9	92.9	82.8
Extensively drug-resistant (*n*=114)[d]	2	8	0.015–32	84.2	84.2	71.9
P. aeruginosa (*n*=1,723)	0.12	0.5	≤0.004–32	99.8	98.8	99.5
Multidrug-resistant (*n*=211)[b]	0.25	1	≤0.004–32	98.1	93.4	95.7
Carbapenem-resistant (*n*=253)[c]	0.12	0.5	≤0.004–32	98.4	94.5	96.4
Extensively drug-resistant (*n*=62)[d]	0.25	2	0.008–32	95.2	88.7	91.9
Difficult-to-treat resistant (*n*=43)[e]	0.25	1	0.008–32	97.9	93.0	95.3
A. baumannii-calcoaceticus species complex (*n*=356)	0.25	2	0.008–>64	95.8	88.8	–
Carbapenem-resistant (*n*=240)[c]	0.25	2	0.03–>64	94.6	85.0	–
S. maltophilia (*n*=219)	0.06	0.25	0.008–16	99.5	99.5	–

BSI, bloodstream infection; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; I, intermediate; MIC, minimum inhibitory concentration; $MIC_{50/90}$, MIC required to inhibit growth of ≥50%/90% of isolates; R, resistant; S, susceptible.
[a]Criteria as published by CLSI (2025), US FDA (2025), and EUCAST (2025). [b]Non-susceptible to ≥1 agent in three or more antimicrobial categories by CLSI breakpoints; [c]Resistant to meropenem and/or imipenem by CLSI breakpoints; [d]Non-susceptible to ≥1 agent in all but two or fewer antimicrobial categories by CLSI breakpoints; [e]Non-susceptible to β-lactams and fluoroquinolones by CLSI breakpoints.

CONCLUSION

Highly resistant Gram-negative isolates collected from BSIs, for which treatment options are limited, remained susceptible to cefiderocol.

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Conflict of interest: 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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