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Activity of cefiderocol against clinical isolates of *Stenotrophomonas maltophilia* collected from five European countries as part of the SENTRY antimicrobial surveillance programme 2020–2023

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BACKGROUND

Stenotrophomonas maltophilia is an important healthcare-associated pathogen that is intrinsically resistant to many β-lactam antibiotics, including carbapenems, due to the presence of the chromosomal L1 metallo-β-lactamase. Cefiderocol is a siderophore-conjugated cephalosporin approved by European Medicines Agency for treatment of aerobic Gram-negative bacterial infections with limited treatment options and one of the few agents with activity against isolates carrying metallo-β-lactamases.

OBJECTIVE

The objective of this study was to elucidate the *in vitro* activity of cefiderocol against contemporary isolates of *S. maltophilia* collected from European patients.

METHODS

- Isolates were collected between 2020–2023 as part of the SENTRY surveillance programme[1].
- Minimum inhibitory concentrations (MICs) were determined according to Clinical and Laboratory Standards Institute guidelines using broth microdilution with iron-depleted cation-adjusted Mueller-Hinton broth for cefiderocol and cation-adjusted Mueller–Hinton broth for comparator agents.
- Comparator agents included trimethoprim-sulfamethoxazole, minocycline and levofloxacin as well as the β-lactam/β-lactamase inhibitor combination aztreonam-avibactam.
- Susceptibility was interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidance v14. Aztreonam-avibactam has no EUCAST breakpoints for pathogens other than Enterobacterales, so only $MIC_{50/90}$ and MIC ranges are reported.

RESULTS

- Of 1,781 *S. maltophilia* isolates collected between 2020–2023, 612 originated from Europe and 68% (n=418) were from France, Germany, Italy, Spain and the UK.
- All isolates were susceptible to cefiderocol (MIC ≤2 mg/L) and a comparison between countries showed similar MIC distributions with a combined modal MIC of 0.06 mg/L (Figure 1).
- Isolates from all five countries showed high susceptibility to comparators except levofloxacin, for which only 17–35% isolates were susceptible (Table 1).
- $MIC_{50/90}$ values for aztreonam-avibactam were 4/4 mg/L for isolates from all five countries except Italy, which showed a higher MIC_{90} value of 8 mg/L.

Figure 1: Cefiderocol MIC distributions for 418 *S. maltophilia* isolates from 5 European countries: SENTRY 2020–2023

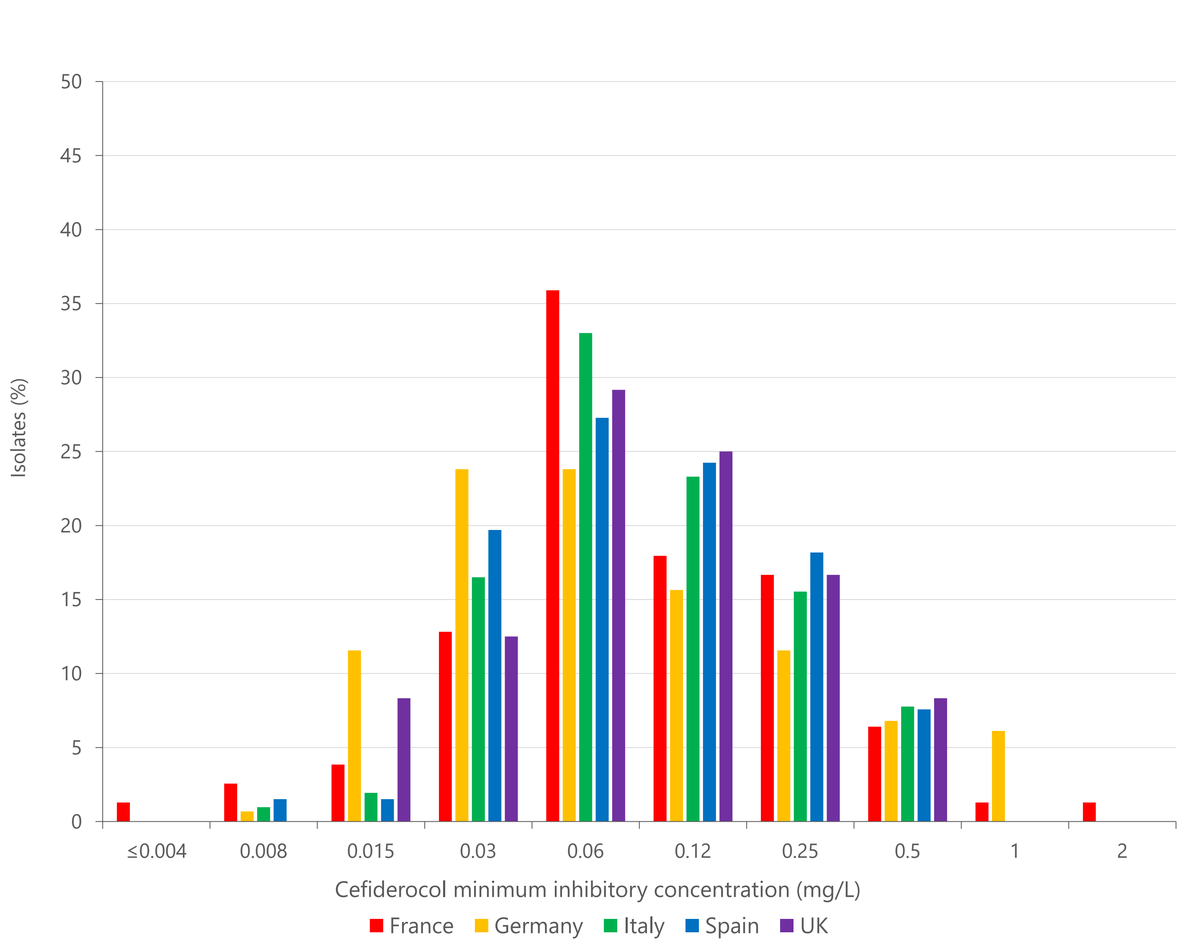

Table 1: Activity of cefiderocol and comparator antibiotics against clinical isolates of *Stenotrophomonas maltophilia* from 5 European countries (2020–2023)

Country (n) Agent	MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC range (mg/L)	EUCAST (%S)[a]
All (418)				
Cefiderocol	0.06	0.25	≤0.004–2	100
Aztreonam-avibactam	4	4	0.25–>16	-
Trimethoprim-sulfamethoxazole	<0.12	0.5	≤0.12–>4	98
Minocycline	0.5	1	<0.06–8	99
Levofloxacin	1	4	0.12–16	27
France (78)				
Cefiderocol	0.06	0.25	≤0.004–2	100
Aztreonam-avibactam	2	4	1–16	-
Trimethoprim-sulfamethoxazole	<0.12	0.5	≤0.12–>4	98
Minocycline	0.5	1	≤0.6–4	99
Levofloxacin	1	4	0.12–16	26
Germany (147)				
Cefiderocol	0.06	0.5	0.008–1	100
Aztreonam-avibactam	2	4	1–16	-
Trimethoprim-sulfamethoxazole	<0.12	0.5	≤0.12–>4	98
Minocycline	0.5	1	0.12–8	99
Levofloxacin	1	2	0.25–8	35
Italy (103)				
Cefiderocol	0.06	0.25	0.008–2	100
Aztreonam-avibactam	4	8	0.25–>16	-
Trimethoprim-sulfamethoxazole	<0.12	0.5	≤0.12–>4	97
Minocycline	0.5	1	0.12–4	99
Levofloxacin	1	4	0.25–16	17
Spain (66)				
Cefiderocol	0.06	0.25	0.008–0.5	100
Aztreonam-avibactam	2	4	2–>16	-
Trimethoprim-sulfamethoxazole	<0.12	0.5	≤0.12–>4	99
Minocycline	0.5	1	≤0.06–4	97
Levofloxacin	1	8	0.25–16	24
UK (24)				
Cefiderocol	0.06	0.25	0.015–0.5	100
Aztreonam-avibactam	2	4	1–8	-
Trimethoprim-sulfamethoxazole	<0.12	0.5	≤0.12–2	100
Minocycline	0.5	1	0.12–1	100
Levofloxacin	1	4	0.25–4	25

S, susceptible or susceptible with increased exposure; n, number of isolates.
a. Interpretations according to EUCAST breakpoint table v14 and Guidance on what to do when no breakpoints. Cefiderocol, breakpoint of <4 mg/L for *Pseudomonas* and other non-fermenters; Aztreonam-avibactam, no breakpoints or guidance have been established for *S. maltophilia*; Trimethoprim-sulfamethoxazole, breakpoint of <8 mg/L; Minocycline R breakpoint of <4 mg/L; Levofloxacin breakpoint of <1 mg/L. **Key:** Green, >90%; Amber, 50-90%; Red <50% susceptible.

CONCLUSIONS

Isolates of *S. maltophilia* from 5 European countries remained largely susceptible to standard-of-care antibiotics except for levofloxacin, which had poor levels of susceptibility in all countries.

Cefiderocol showed higher potency than aztreonam-avibactam and remained active against 100% of isolates tested, including those resistant to standard-of-care antibiotics. Cefiderocol should be considered as a treatment option for patients with limited treatment options.

References

1. Shortridge D, et al. Microbiol Spectr. 2022;10(2):e0271221.

Acknowledgments

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