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

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BACKGROUND

Acinetobacter baumannii complex is an important pathogen that is highly resistant to many first-line antibiotics and associated with high mortality. Cefiderocol is a siderophore-conjugated cephalosporin approved by the European Medicines Agency for treatment of aerobic Gram-negative bacterial infections with limited treatment options.

OBJECTIVE

The objective of this study was to elucidate the *in vitro* activity of cefiderocol against contemporary isolates of *A. baumannii* complex 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 (CLSI) 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 meropenem and colistin as well as the β-lactam/β-lactamase inhibitor combinations ampicillin-sulbactam and sulbactam-durlobactam.
- Susceptibility was interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) v14 breakpoints where available. Sulbactam-durlobactam was interpreted according to US Food and Drug Administration (FDA) breakpoint of ≤4 mg/L. Carbapenem resistance (CR) was defined according to EUCAST breakpoints as MIC >8 mg/L to meropenem or >4 mg/L imipenem.

RESULTS

- A total of 1,289 *A. baumannii* isolates were collected from European hospitals with 49% (n=630) originated from France, Germany, Italy, Spain and UK.
- Susceptibility to carbapenems differed greatly between countries (Figure 1) with the highest rates in Italy (77% resistant) and Spain (42% resistant), while no carbapenem resistance was detected in the 31 isolates collected from the UK.
- Overall, 97% of isolates had MICs to cefiderocol that were ≤2 mg/L. This was similar for carbapenem-resistant isolates (96%).
- MIC distributions for CRAB were similar between countries with a modal MIC of 0.12–0.25 mg/L (Figure 2).
- Isolates from all countries showed high susceptibility to comparators, except ampicillin-sulbactam which lost activity against CR strains (Table 1).
- Sulbactam-durlobactam is not approved in Europe, but applying the FDA breakpoint, it showed similar activity to cefiderocol for most CR isolates, including those from Italy (89% vs 93% respectively).
- Cefiderocol retained activity against 4 isolates resistant to sulbactam-durlobactam (all from Italy).

Figure 1: Distribution of CR *A. baumannii* complex isolates across 5 European countries: SENTRY 2020–2023

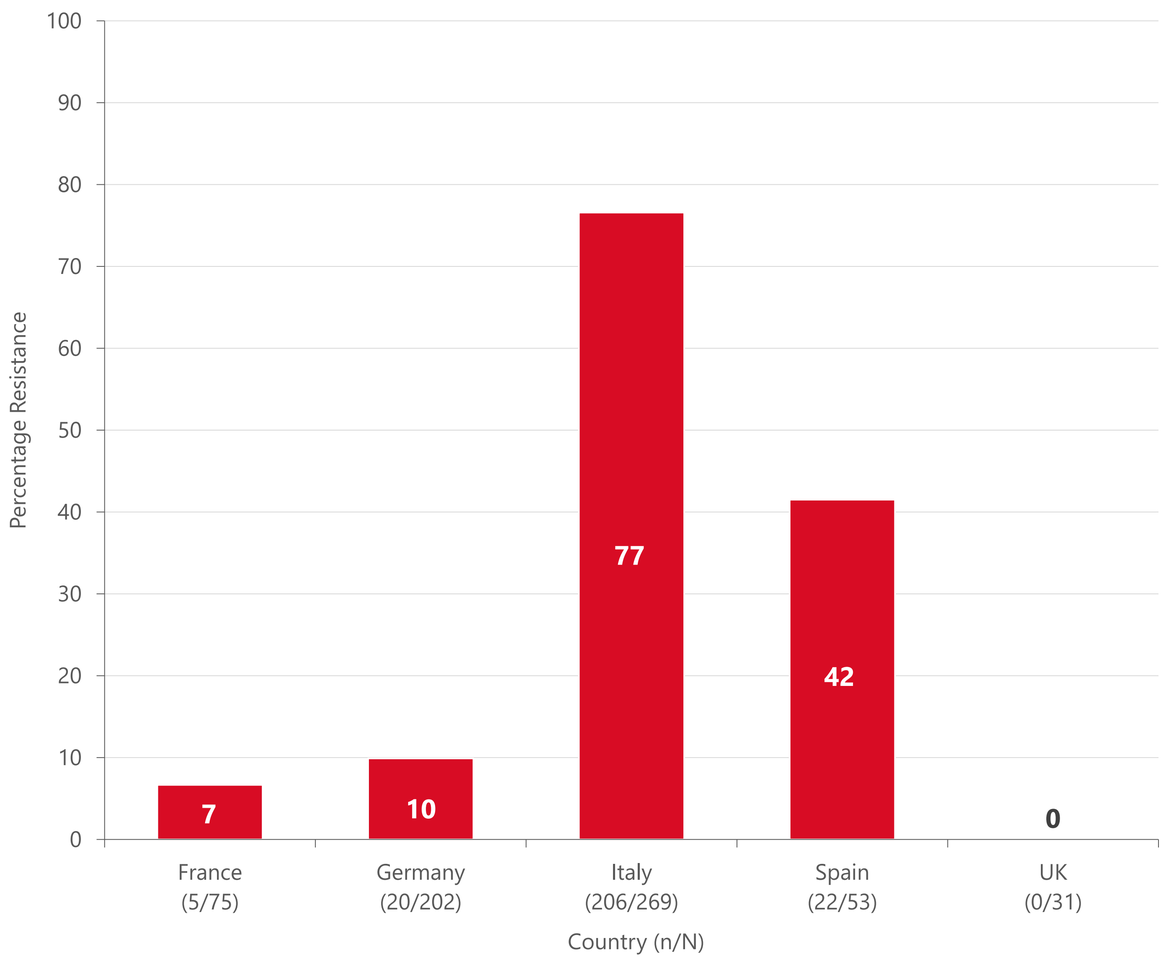

Figure 2: Cefiderocol MIC distributions for 253 CR *A. baumannii* complex isolates from 4 European countries: SENTRY 2020–2023

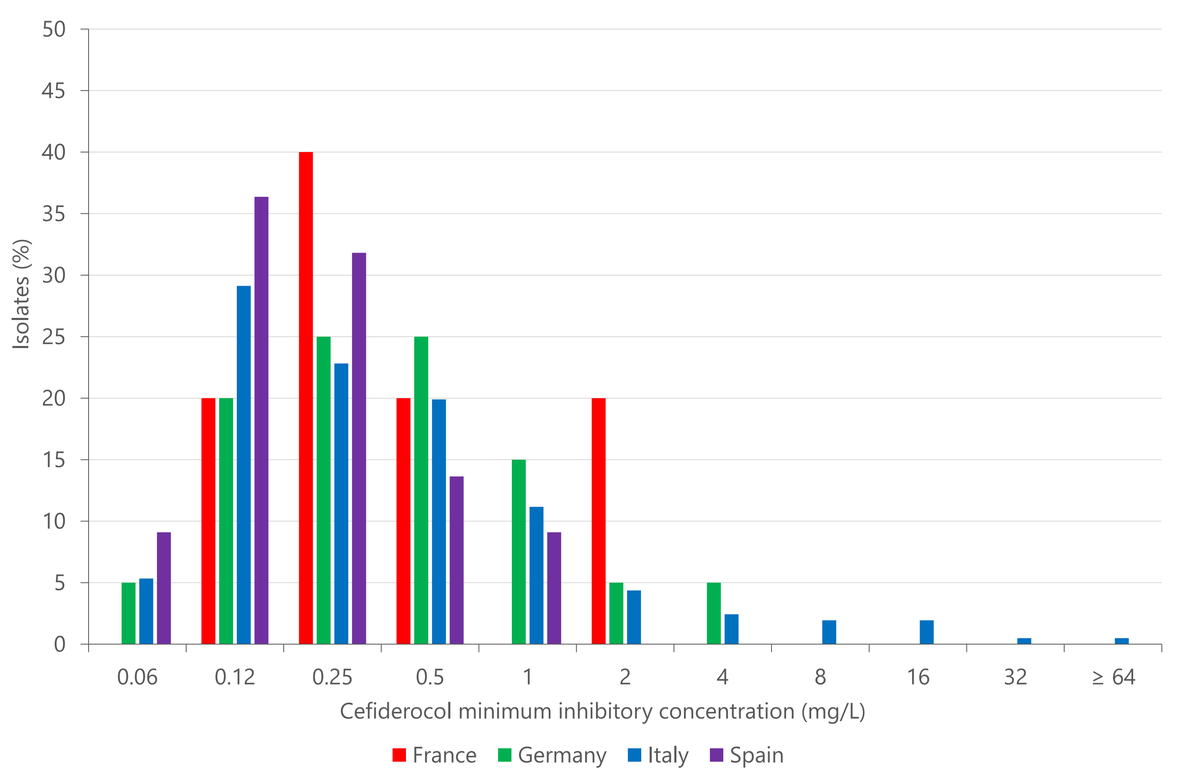

Table 1: Susceptibility of cefiderocol and comparator antibiotics against 630 carbapenem-susceptible and 253 carbapenem-resistant isolates of *A. baumannii* complex from 5 European countries: SENTRY 2020–2023

Country (n) Agent	France	Germany	Italy	Spain	UK
All *A. baumannii* complex (n=630)	**75**	**202**	**269**	**53**	**31**
Cefiderocol	99%	99%	94%	100%	100%
Meropenem	93%	90%	23%	58%	100%
Ampicillin-sulbactam	85%	89%	23%	57%	87%
Sulbactam-durlobactam	100%	100%	93%	100%	100%
Colistin	97%	96%	94%	98%	100%
Carbapenem-resistant *A. baumannii* (n=253)	**5**	**20**	**206**	**22**	**0**
Cefiderocol	100%	95%	93%	100%	-
Meropenem	0%	0%	0%	0%	-
Ampicillin-sulbactam	20%	14%	0%	0%	-
Sulbactam-durlobactam	100%	100%	89%	100%	-
Colistin	100%	55%	93%	100%	-
Sulbactam-durlobactam resistant (n=4)	**0**	**0**	**4**	**0**	**0**
Cefiderocol	-	-	100%	-	-
Meropenem	-	-	0%	-	-
Ampicillin-sulbactam	-	-	0%	-	-
Sulbactam-durlobactam	-	-	0%	-	-
Colistin	-	-	100%	-	-

Interpretations according to EUCAST breakpoint table v14 and Guidance on what to do when no breakpoints. Carbapenem resistant, EUCAST breakpoint of >8 mg/L to meropenem or >4 mg/L imipenem; Cefiderocol, breakpoint of ≤2 mg/L for *Pseudomonas* and other non-fermenters; Ampicillin-sulbactam, breakpoint of ≤8 mg/L; Sulbactam-durlobactam (only 168/630 tested), FDA breakpoint of ≤4 mg/L; Colistin, bracketed breakpoint of ≤2 mg/L: **Key**: >90% green, 50-90% Amber, <50% red.

CONCLUSIONS

A difference in susceptibility to carbapenems was observed between *A. baumannii* from five European countries with Italy and Spain having highest rates of resistance. Cefiderocol showed high susceptibility against isolates resistant to carbapenems or sulbactam-durlobactam and should be considered as a treatment for patients with limited treatment options.

References

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

Acknowledgments

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