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Activity of cefiderocol against *Stenotrophomonas maltophilia* clinical isolates collected in multi-national antimicrobial surveillance studies SIDERO-WT (2014–2019) and SENTRY (2020–2024)

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INTRODUCTION

- *Stenotrophomonas maltophilia* is an opportunistic life-threatening pathogen with high intrinsic resistance to a variety of antimicrobials, thereby limiting treatment options.
- Cefiderocol is a siderophore cephalosporin with activity against a variety of Gram-negative bacteria, including *S. maltophilia*. It was approved for clinical use in the United States (US) in 2019 and in Europe in 2020.
- This study assessed the *in vitro* activity of cefiderocol against *S. maltophilia* isolates that were collected between 2014 and 2024 in Europe and the USA, including the pre-marketing surveillance SIDERO-WT and the post-marketing surveillance SENTRY studies. Trends in cefiderocol susceptibility over time were analyzed.

MATERIALS AND METHODS

Bacterial strains

- A total of 4,202 non-duplicate clinical isolates of *S. maltophilia* were collected in the US and Europe from the SIDERO-WT surveillance study (788 isolates from the US and 1,068 isolates from Europe during 2014–2019) and the SENTRY surveillance study (1,291 isolates from the US and 1,055 isolates from Europe during 2020–2024) (**Table 1**).

Table 1. Number of isolates in SIDERO-WT and SENTRY studies

	SIDERO-WT (2014–2019)	SENTRY (2020–2024)
USA (2,079)	**788**	**1,291**
Europe (2,123)	**1,068**	**1,055**
Overall (4,202)	1,856	2,346

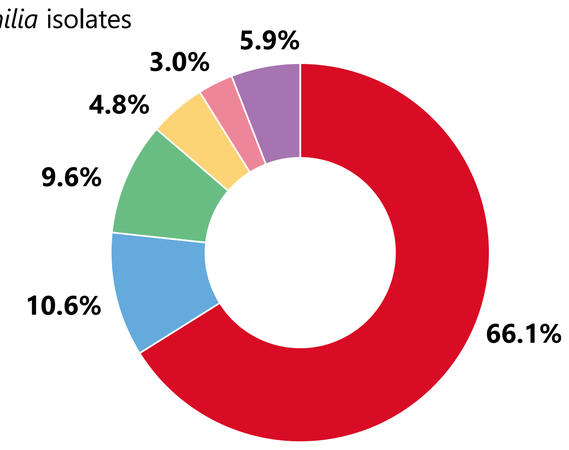
Minimum inhibitory concentration (MIC) determination

- MICs for cefiderocol and comparators were determined according to Clinical and Laboratory Standards Institute (CLSI) guidelines using broth microdilution with iron-depleted cation-adjusted Mueller-Hinton broth (ID-CAMHB) and CAMHB, respectively.
- Susceptibility to cefiderocol and comparators was determined using CLSI 2025 breakpoints.
- The MIC_{50}, MIC_{90}, and susceptibility percentages (%S) of cefiderocol across 10 years were assessed for each region (Europe and the USA).

RESULTS

- Isolates collected in this study were mainly from respiratory infections (66.1%), followed by bloodstream infections (10.6%), skin and soft tissue infections (9.6%), urinary tract infections (4.8%), and intra-abdominal infections (3.0%) (**Figure 1**).

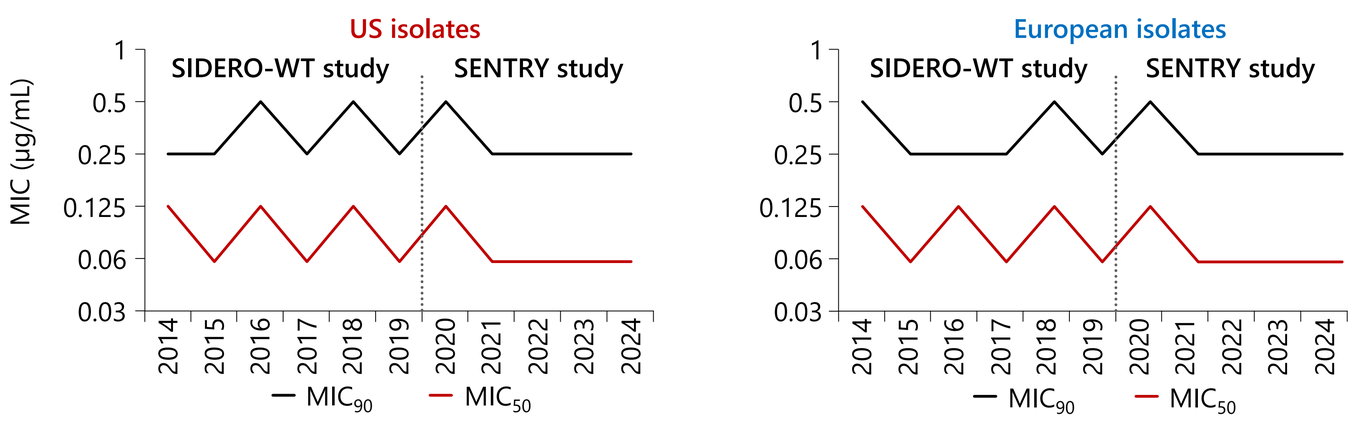
Figure 1. Prevalence of infection sources[a] of the *S. maltophilia* isolates (N=4,202) from the SIDERO-WT and SENTRY studies



[a]Infection site was unknown for one isolate.

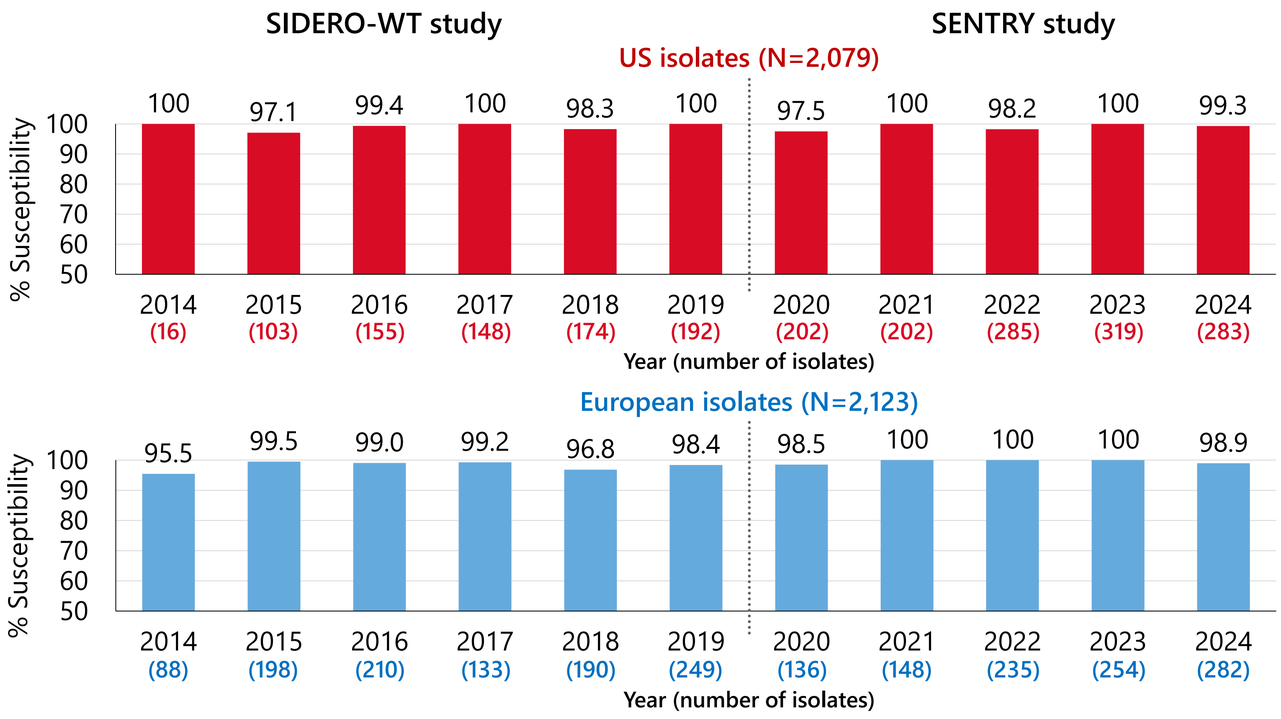
- Overall, a consistent high activity (MIC_{50}, MIC_{90}, and %S) of cefiderocol against *S. maltophilia* was observed over time, with MIC_{50} values ranging from 0.06 to 0.12 µg/mL, MIC_{90} values ranging from 0.25 to 0.5 µg/mL, and %S ranging from 95.5% to 100%, irrespective of region (**Figures 2 and 3**).

Figure 2. Susceptibility (MIC_{50}, MIC_{90}) trend of cefiderocol by year against *S. maltophilia* isolates collected from the US and European hospitals in the SIDERO-WT (2014–2019) and SENTRY studies (2020–2024)



MIC, minimum inhibitory concentration.

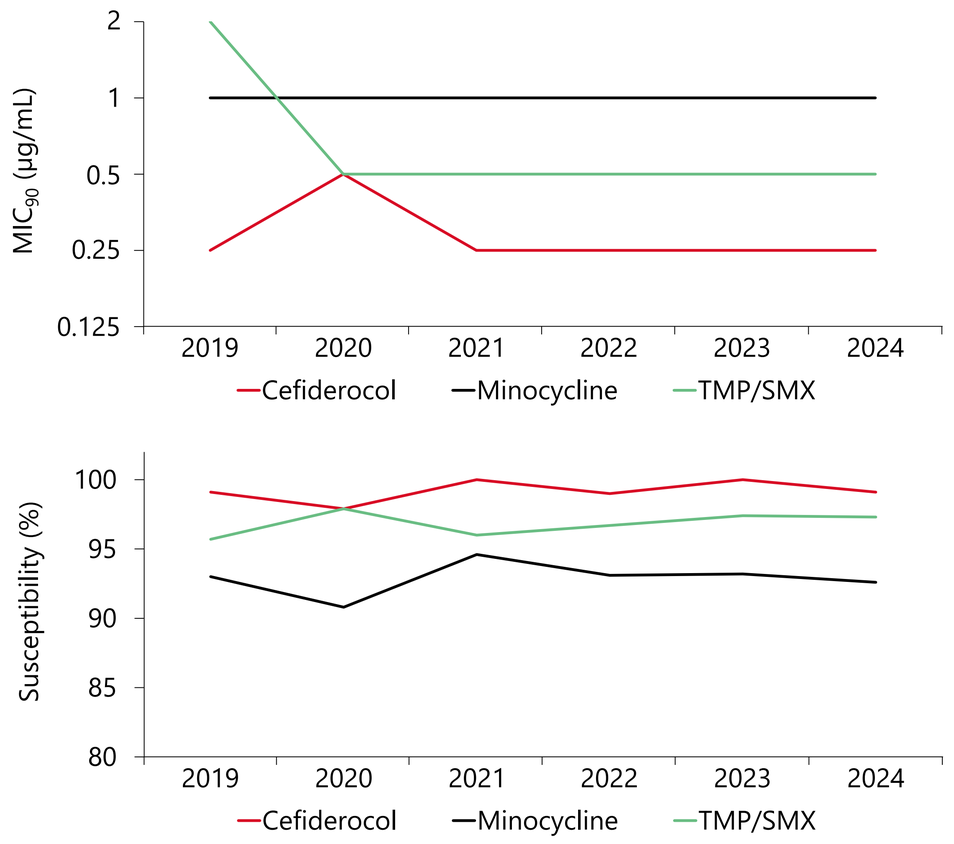
Figure 3. Susceptibility percentages (%S) of cefiderocol by year against *S. maltophilia* isolates collected from the US and European hospitals in the SIDERO-WT (2014–2019) and SENTRY studies (2020–2024)



The susceptibility percentage by year was determined based on the CLSI breakpoints. CLSI, Clinical and Laboratory Standards Institute.

- In comparison to comparator agents (trimethoprim/sulfamethoxazole, levofloxacin, and minocycline), cefiderocol showed the highest %S (97.9–100%) and lowest MIC_{90} (0.25–0.5 µg/mL) from year 6 in the SIDERO-WT study (2019) and across 5 years from the SENTRY study (2020–2024) (**Figure 4** and **Table 2**).

Figure 4. Susceptibility (MIC_{90}, %S) trend of cefiderocol and comparators by year against *S. maltophilia* isolates collected from the US and European hospitals in the SIDERO-WT (2019) and SENTRY studies (2020–2024)



MIC, minimum inhibitory concentration; %S, susceptibility percentage; TMP/SMX, trimethoprim/sulfamethoxazole.

Table 2. Susceptibility of cefiderocol and comparators against *S. maltophilia* isolates collected from the US and European hospitals in the SIDERO-WT (2019) and SENTRY studies (2020–2024)

Antimicrobials	N	Range (mg/L)	MIC_{50} (mg/L)	MIC_{90} (mg/L)	%S[a]	%I	%R
Cefiderocol	2787	≤0.03 to >64	0.06	0.25	99.2	-[b]	-[b]
Trimethoprim/ sulfamethoxazole	2786	≤0.25 to >4	≤0.25	1	96.9	-[b]	3.1
Minocycline	2786	≤0.06 to 16	0.5	1	92.9	5.2	1.9

[a]%S, %I, and %R were determined based on CLSI 2025 breakpoints. [b]No breakpoints defined.
CLSI, Clinical and Laboratory Standards Institute; I, intermediate; R, resistant; S, susceptible.

CONCLUSIONS

- Cefiderocol consistently demonstrated high activity against *S. maltophilia* over a 10-year period, with no significant change in susceptibility before or after its market introduction.
- Continued monitoring of cefiderocol susceptibility is warranted to assure its activity is maintained over time.

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