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Activity of Cefiderocol and Comparator Agents Against Global Isolates of *Stenotrophomonas maltophilia* from the SENTRY Antimicrobial Surveillance Program (2020–2023)

Motoyasu Onishi[1], Hidenori Yamashiro[1], Joshua M. Maher[2], Hank Kimbrough[2], Rodrigo Mendes[2], Boudewijn L.M. DeJonge[3], Sean Nguyen[3], Christopher Longshaw[4], Miki Takemura[1], and Yoshinori Yamano[1]

[1]Shionogi & Co., Ltd., Osaka, Japan, [2]Element Materials Technology, North Liberty, IA, USA, [3]Shionogi Inc., NJ, USA, [4]Shionogi B.V. London, UK

Contact information:
Motoyasu Onishi
3-1-1, Futaba-cho, Toyonaka,
Osaka 561-0825, Japan
Phone: +81-80-8537-0702
Email: motoyasu.oonishi@shionogi.co.jp

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BACKGROUND

- *Stenotrophomonas maltophilia* is a ubiquitous multidrug-resistant opportunistic pathogen, for which limited treatment options are available.
- Infections caused by *S. maltophilia* have limited β-lactam treatment options due to the intrinsic resistant mechanisms such as the production of chromosomal L1 metallo-type carbapenemase and L2 extended-spectrum type β-lactamase.
- Cefiderocol (FDC) is a siderophore-conjugated cephalosporin with broad activity against Gram-negative bacteria, including *S. maltophilia*.

OBJECTIVE

- Determine susceptibility of FDC and comparator agents against *S maltophilia* clinical isolates, collected from the US and Europe in 2020-2023 as part of the SENTRY Antimicrobial Surveillance Program.

MATERIALS AND METHODS

- A total of 1,781 *S. maltophilia* isolates were consecutively collected from the US and Europe from 2020-2023. Minimum inhibitory concentrations (MICs) were determined according to Clinical and Laboratory Standards Institute (CLSI) broth microdilution methodology using cation-adjusted Mueller–Hinton broth (CAMHB) for comparator antimicrobial agents and iron-depleted CAMHB for FDC.
- Susceptibility was assessed according to CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) pharmacokinetic (PK)-pharmacodynamic (PD) breakpoints.

RESULTS

- The most common infection type from which isolates were collected was pneumonia (n=1,192), followed by bloodstream (n=208), skin and skin structure (n=166), urinary tract (n=56), and intra-abdominal infections (n=38) (Figure 1).
- Cumulative MIC distributions showed FDC was the most active agent against *S. maltophilia* with $MIC_{50/90}$ of 0.06/0.25 µg/mL (Figure 2, Table 1).
- MIC_{90} values of levofloxacin (LVX), trimethoprim-sulfamethoxazole (SXT), and minocycline (MIN) were 4, 0.5, and 1 µg/mL, respectively, and the MIC_{90} values of remaining comparator agents were >8 µg/mL (Figure 2, Table 1).
- 99.3, 83.1, 97.0, and 93.0% of the isolates were susceptible to FDC, LVX, SXT, and MIN respectively, according to CLSI breakpoints (Table 1).
- Against LVX-, SXT- or MIN-non-susceptible isolates, FDC retained activity (>98% susceptibility) according to both CLSI and EUCAST breakpoints, whereas the comparator agents were much less active (<90% susceptibility) (Table1).

Figure 1: Prevalence and infection type of *S. maltophilia* isolates collected from medical centers in the US and Europe

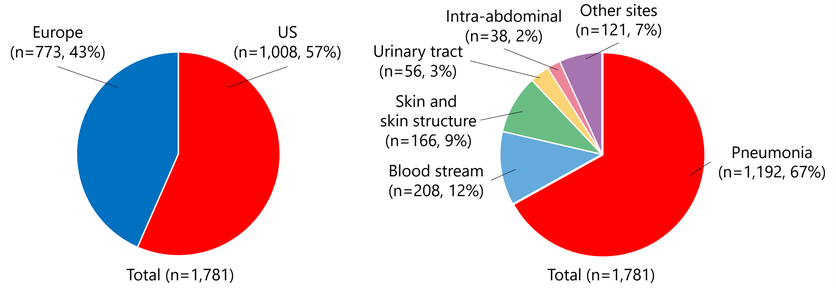
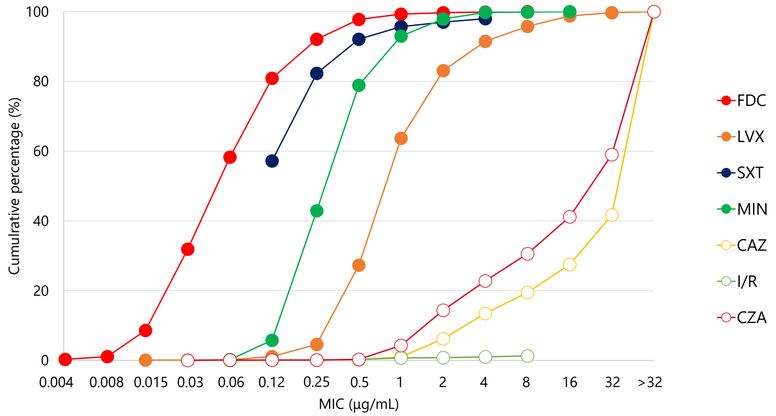


Figure 2: Cumulative percentage distributions of cefiderocol and comparators MICs against *S maltophilia* (n=1,781)



Cefiderocol (FDC), levofloxacin (LVX), trimethoprim-sulfamethoxazole (SXT), minocycline (MIN), ceftazidime (CAZ), imipenem-relebactam (I/R), ceftazidime-avibactam (CZA)

Table 1: Susceptibility of cefiderocol and comparator agents against *S. maltophilia* isolates collected from medical centers in the US and Europe during 2020-2023

Isolate set	MIC_{50}	MIC_{90}	MIC range	%Susceptibility	
Antimicrobial agents	µg/mL			CLSI[a]	EUCAST[b]
All (N=1,781)					
FDC (n=1,781)	0.06	0.25	≤0.004 - 8	99.3	99.7
LVX (n=1,779)	1	4	≤0.015 - >32	83.1	27.3
SXT (n=1,780)	≤0.125	0.5	≤0.12 - >4	97.0	N/A
MIN (n=1,780)	0.5	1	≤0.06 - 16	93.0	N/A
CAZ (n=1,779)	>32	>32	0.12 - >32	N/A	13.5
I/R (n=1,781)	>8	>8	0.12 - >8	N/A	0.8
CZA (n=1,779)	32	>32	0.06 - >32	N/A	30.6
LVX NS[a] (n=301)					
FDC (n=301)	0.06	0.25	≤0.004 - 4	99.7	99.7
SXT (n=301)	0.25	4	≤0.12 - >4	88.7	N/A
MIN (n=301)	1	4	0.12 - 16	65.6	N/A
SXT NS[a] (n=53)					
FDC (n=53)	0.125	0.5	0.008 - 2	98.1	100
LVX (n=53)	8	32	0.5 - >32	35.8	9.4
MIN (n=53)	1	4	0.12 - 16	62.3	N/A
MIN NS[a] (n=125)					
FDC (n=125)	0.06	0.25	0.008 - 1	99.7	100
LVX (n=125)	8	32	0.06 - >32	16.8	1.6
SXT (n=125)	0.5	>4	≤0.12 - >4	84.0	N/A

Non-susceptible (NS), susceptible (S), N/A (not applicable), cefiderocol (FDC), levofloxacin (LVX), trimethoprim-sulfamethoxazole (SXT), minocycline (MIN), ceftazidime (CAZ), imipenem-relebactam (I/R), ceftazidime-avibactam (CZA), [a]FDC S ≤1, LVX S ≤2, SXT S ≤2/38, MIN S ≤1, breakpoints as published by CLSI (2024), [b]FDC S ≤2, LVX S ≤0.5, CAZ S≤4, I/R S ≤2, CZA S ≤8, PK-PD breakpoints as published by EUCAST (2023)

CONCLUSIONS

- FDC showed potent *in vitro* activity against *S. maltophilia* clinical isolates collected in the US and Europe from 2020-2023, including clinical isolates non-susceptible to LVX, SXT, or MIN.
- FDC should be considered as a therapeutic option to treat infections caused by *S. maltophilia*.

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