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In-Vitro Activity of Cefiderocol Against Multidrug Resistant Strains of *P. aeruginosa* DTR, *A. baumannii complex* DTR, *A. xylosoxidans* MDR, *S. maltophilia* MDR & *B. cepacia* complex, by Iron-Depleted Broth Microdilution.

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Background

The emergence of multidrug-resistant (MDR) & difficult-to-treat (DTR) non-fermenter (NF) organisms pose a critical challenge for antimicrobial therapy, threatening the efficacy of existing antimicrobial and contributing to an increasing worldwide mortality rate. MDR NFs are among the most challenging organisms isolated in the clinical laboratory. Cefiderocol (CFD), a novel siderophore cephalosporin, offers an interesting approach by exploiting the bacteria's iron-acquisition system and its intrinsic stability against multiple classes of β-lactamases. In this descriptive abstract, we present the in-vitro activity of cefiderocol against multiple strains of NF organisms.

P. aeruginosa DTR	*A. baumannii* cpx DTR	*A. xylosoxidans* MDR	*S. maltophilia* MDR
Intermediate or resistant to all tested antimicrobials: • Piperacillin/tazobactam • Ceftazidime • Cefepime • Aztreonam • Meropenem • Imipenem • Ciprofloxacin • Levofloxacin	Intermediate or resistant to the following antimicrobials: • Ampicillin/sulbactam AND • Meropenem AND • One (1) more active antimicrobial	Intermediate or resistant to at least 1 agent in 3 active classes: • Anti-Pseudomonal penicillin • Cephalosporins • Carbapenems • Fluroquinolones • Tetracyclines • TMP/SXT	Intermediate or resistant to: • TMP/SXT

Difficult-To-Treat & Multi-Drug Resistant definition by organism

Cefiderocol siderophore molecule

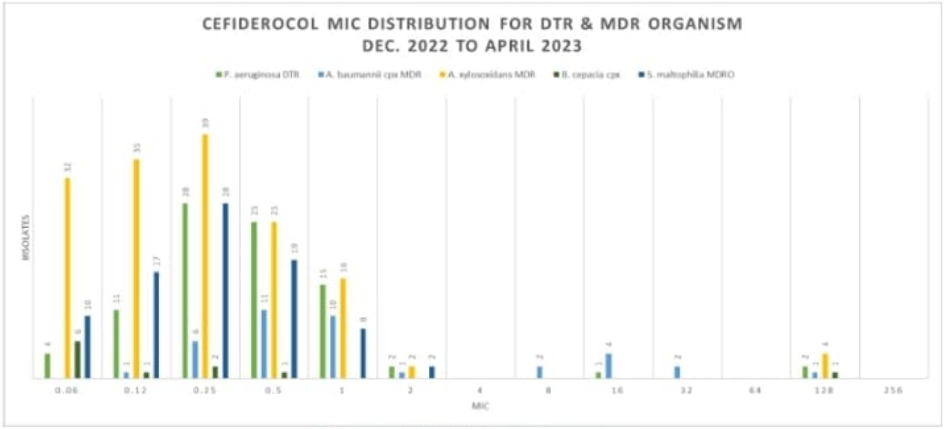
FDA-cleared Liofilchem Cefiderocol ComASP®

Methods

MIC values by iron-depleted broth microdilution (Liofilchem ComASP®) were collected and distributed by organism from December 2022 up to April 2023 at AdventHealth Orlando Microbiology Department. *P. aeruginosa* DTR (n=88), *A. baumannii* cpx DTR (n=38), *A. xylosoxidans* MDR (n=153), *S. maltophilia* MDR (n=84) & *B. cepacia* cpx (n=11). *P. aeruginosa* DTR is defined as an isolate intermediate (I) or resistant (R) to all tested antimicrobials except aminoglycosides. *A. baumannii* DTR as an isolate I or R to ampicillin/sulbactam and meropenem and one more active agent. *A. xylosoxidans* MDR as an isolate I or R to one agent in at least three active antimicrobial classes & *S. maltophilia* MDR as an isolate I or R to trimethoprim/sulfamethoxazole.

Results

The average, mode, median and range MIC (µg/mL) were calculated for each organism. *P. aeruginosa* DTR: 3.55, 0.25, 0.5, 0.06-128; *A. baumannii* DTR: 7.66, 0.5, 0.5, 0.12-128; *A. xylosoxidans* MDR: 3.66, 0.25, 0.25, 0.06-128; *S. maltophilia* MDR 0.37, 0.25, 0.25, 0.06-2; *B. cepacia* cpx: 11.77, 0.06, 0.06, 0.06-128. Using the *P. aeruginosa* susceptible CLSI BP (< =4 µg/mL) as a reference for *P. aeruginosa* DTR, *A. xylosoxidans* MDR & *B. cepacia* cpx, 96.6%, 97.39% & 90.9% respectively have an MIC value in the susceptible BP. 76.3% of *A. baumannii* DTR have an MIC < =4 µg/mL (susceptible BP) and 97.6% of *S. maltophilia* MDR have a susceptible CLSI BP < =1 µg/mL.



Cefiderocol MIC Distribution by organism

	Average MIC (µg/mL)	Mode MIC (µg/mL)	Median MIC (µg/mL)	Range MIC (µg/mL)
P. aeruginosa DTR (n=88)	3.55	0.25	0.5	0.06 - 128
A. baumannii cpx DTR (n=38)	7.66	0.5	0.5	0.12 – 128
A. xylosoxidans MDR (n=153)	3.66	0.25	0.25	0.06 - 125
S. maltophilia MDR (n=84)	0.37	0.25	0.25	0.06 – 2
B. cepacia cpx (n=11)	11.77	0.06	0.06	0.06 – 128

Cefiderocol MIC central tendency by organism

Conclusion

Although clinical outcome data is needed, cefiderocol demonstrated significant potency against the most resistant non-fermenters strains and may represent a significant therapeutic option for difficult to treat isolates.

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