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Surveillance of cefiderocol in-vitro activity against Gram-negative clinical isolates collected in Europe: SIDERO-WT-2014

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Background: The emergence and dissemination of potent resistance mechanisms among gram-negative species underscores the need for the development of new and effective therapeutic choices to treat the infections caused by these challenging organisms. Cefiderocol (formerly S-649266) is a novel parenteral siderophore cephalosporin with potent activity against a wide variety of gram-negative pathogens including carbapenem-resistant strains. This study evaluated the *in vitro* activity of cefiderocol and comparator agents against resistant clinical isolates collected in 2014-2015 from Europe.

Material/methods: A total of 3015 Enterobacteriaceae, 823 *Acinetobacter baumannii*, 751 *Pseudomonas aeruginosa*, 271 *Stenotrophomonas maltophilia*, and five *Burkholderia cepacia* collected from 11 European countries in 2014 - 2015 were tested. MICs were determined for cefiderocol, cefepime (FEP), ceftazidime-avibactam (CZA), ceftolozane-tazobactam (C/T), ciprofloxacin (CIP), colistin (CST), and meropenem (MEM) by broth microdilution and interpreted according to CLSI 2016 guidelines, with the exception that cefiderocol was tested in iron-depleted cation-adjusted Mueller Hinton broth. Carbapenem-resistant (CR) isolates were defined using

EUCAST breakpoints of MEM (resistant, >8 µg/mL). EUCAST MIC breakpoints for CZA (resistant, >8 µg/mL) and C/T (resistant, >1 µg/mL) were used. For colistin, EUCAST MIC breakpoints for Enterobacteriaceae were applied (resistant, >2 µg/mL). Quality control testing was performed on each day of testing.

Results: As shown in the following table, cefiderocol exhibited potent *in vitro* activity against 4865 strains of gram-negative bacteria with MIC90 of 1 mg/L. MIC90 of cefiderocol against *P. aeruginosa*, *A. baumannii*, *S. maltophilia* and Enterobacteriaceae including the subset of CR or CZA resistant isolates were 4 mg/L or less. Cefiderocol also inhibited the growth of 98.0% of the isolates at 4 mg/L although 14.8%, 29.3% and 15.0% showed resistance to CZA, C/T and CST.

Conclusions: The potent *in vitro* activity that cefiderocol demonstrated against CR *A. baumannii*, CR *P. aeruginosa*, and CR Enterobacteriaceae isolates collected from Europe, with greater than 99% of isolates having MIC values ≤4 mg/L, indicates this agent has high potential for treating infections caused by these problematic organisms.

Organisms		MIC90 (**mg/L**)						
	N	Cefiderocol	FEP	CZA	C/T	CIP	CST	MEM
E. coli	774	0.5	64	0.25	0.5	8	1	0.06
K. pneumoniae	745	2	64	1	64	>8	1	8
CZA-resistant *K. pneumoniae*	22	8	64	64	64	>8	>8	64
CR *K. pneumoniae*	74	4	64	64	64	>8	1	32
P. aeruginosa	751	0.5	32	8	4	8	2	16
C/T resistant *P. aeruginosa*	127	1	64	64	64	>8	8	64
CR *P. aeruginosa*	83	2	64	64	64	8	1	64
A. baumannii	823	1	64	64	64	>8	8	64
CR *A. baumannii*	590	1	64	64	64	8	8	64
S. malthophilia	271	0.25	64	32	64	8	8	64