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P1859 *In vitro* activity of cefiderocol against Gram-negative pathogens circulating in Germany

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Background: Cefiderocol, an investigational catechol-substituted siderophore cephalosporin, possesses potent activity against multidrug resistant aerobic Gram-negative pathogens, including carbapenemase-producing strains. The purpose of the present study was twofold, to provide data on the *in vitro* activity of cefiderocol against i) a representative collection of Gram-negative pathogens obtained from patients with nosocomial infections in intensive care units (collection I), as well as ii) a collection of Gram-negative strains producing various types of carbapenemases (collection II).

Materials/methods: Collection I comprised 213 first isolates from patients collected during a multicentre surveillance study conducted by the Paul-Ehrlich-Society in 2013, namely 146 Enterobacterales (including 17 ESBL-producing strains), 13 *Acinetobacter baumannii* group isolates, and 54 *Pseudomonas aeruginosa*. Collection II included 59 CPE-producing strains from our stock collection. Minimum inhibitory concentrations (MICs) of cefiderocol and comparative antibacterial agents were determined using the microdilution method according to the standard ISO 20776-1. The provisional CLSI breakpoint of cefiderocol for susceptibility is ≤4 mg/L.

Results: Cefiderocol inhibited 99% of the collection I at ≤4 mg/L (Table). MIC50/90 values of cefiderocol for Enterobacterales isolates were 0.12/1 mg/L. However, cefiderocol was more active against ESBL-negative isolates than against ESBL-producing Enterobacterales (isolates with MIC >1 mg/L: 4/129 [3.1%] ESBL-negative isolates vs 7/17 [41%] ESBL-producing isolates). In contrast, cefiderocol inhibited all *Acinetobacter* isolates at 0.12 mg/L and all *P. aeruginosa* isolates at 1 mg/L (Table). The highest cefiderocol MICs observed for collection II strains were 16 mg/L. Cefiderocol inhibited all seven carbapenemase-producing *A. baumannii* at 0.25 mg/L. MIC50/90 values for Enterobacterales (n=30) and *P. aeruginosa* (n=22) were 1/4 mg/L and 0.5/2 mg/L, respectively.

Conclusions: Cefiderocol showed excellent activity against *A. baumannii* (including carbapenemase-producing strains). Cefiderocol showed also good activity against carbapenemase-producing Enterobacterales and *P. aeruginosa*, though about one third of strains required concentrations of >1 mg/L for inhibition. Also, about 40% of the ESBL-producing Enterobacterales isolates required inhibitory concentrations of >1 mg cefiderocol per L. Overall, cefiderocol inhibited 202/208 (97%) Gram-negative strains at ≤4 mg/L.

Table: *In vitro* activity of cefiderocol against Gram-negative pathogens

Species / Bacterial group	n	MIC (mg/L)												
		≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Collection I, representative clinical isolates (n=213)														
Entero-bacterales	146	42	14	22	31	14	12	5	4	2				
ESBL-producing Entero-bacterales	17	1	1	1	2	2	3	2	4	1				
A. baumannii group	13		8	5										
P. aeruginosa	54	8	9	13	15	6	3							
Total	213	50	31	40	46	20	15	5	4	2				
Collection II, carbapenemase-producing strains (n=59)														
Entero-bacterales	30	1	5		1	7	5	6	3	1	1			
A. baumannii	7		1	3	3									
P. aeruginosa	22			1	3	8	3	5		2				
Total	59	1	6	4	7	15	8	11	3	3	1			