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P2415 Activity of the novel extended-spectrum beta-lactamase inhibitor AAI101 in combination with cefepime against Enterobacteriaceae collected from US and European hospitals during 2014/2015

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Background: AAI101 is a novel extended-spectrum β-lactamase inhibitor (BLI), active against ESBLs and a broad array of other β-lactamases. AAI101 combined with cefepime (FEP) is in Ph 2 development. Emergence of new extended-spectrum β-lactamases (ESBLs) amongst *Enterobacteriaceae* has compromised the clinical efficacy of β-lactam/β-lactamase inhibitor combinations such as piperacillin-tazobactam (PIP/TAZ). This study assessed the *in vitro* activity of FEP/AAI101 against *Enterobacteriaceae* isolated from patients in the USA and Europe during 2014/2015.

Materials/methods: *E. coli*, *K. pneumoniae*, and *Enterobacter* isolates (n = 1,696) were collected during 2014/2015 from the USA (50%) and France, Germany, Italy, Spain and the UK (10% each). ESBLs were identified by genotyping. MICs were determined by broth microdilution following CLSI methodology.

Results: MIC_{90} data for FEP/AAI101 and β-lactam comparators are shown in the Table. Against *K. pneumoniae* FEP/AAI101 activity was far superior to ceftolozane-tazobactam (TOL/TAZ) or PIP/TAZ, and similar to ceftazidime-avibactam (CAZ/AVI). Against *E. coli* FEP/AAI101 activity was superior to PIP/TAZ, particularly ESBL-producing isolates, and similar to CAZ/AVI or TOL/TAZ. FEP/AAI101 activity *vs. Enterobacter* isolates was much greater than that of PIP/TAZ or TOL/TAZ, and was similar to CAZ/AVI.

Pathogen (n)	MIC_{90} (mg/L)					
	FEP	FEP/AAI 101[4*]	FEP/AAI 101[8*]	CAZ/AVI [4*]	TOL/TAZ [4*]	PIP/TAZ [4*]
K. pneumoniae (799)	>64	0.5	0.5	0.5	8	>128
- ESBL *K. pneumoniae* (87)	>64	0.5	0.5	0.5	16	>128
E. coli (697)	16	0.12	0.12	0.25	0.5	8
- ESBL *E. coli* (103)	>64	0.25	0.12	0.25	1	64
E. aerogenes (100)	0.5	0.25	0.25	0.5	4	64
E. cloacae (100)	16	2	1	0.5	16	128

*fixed BLI concentration (mg/L)

Conclusions: Addition of AAI101, a potent β-lactamase inhibitor, to cefepime renders this cephalosporin active against ESBL-producing *K. pneumoniae* and *E. coli*, and other *Enterobacteriaceae.* Improved susceptibility of ESBL-producing *Enterobacteriaceae* to cefepime-AAI101 compared to PIP/TAZ suggests that cefepime-AAI101 may be useful in hospitals where resistance to PIP/TAZ is significant. Cefepime-AAI101 warrants further clinical investigation as a treatment for infections caused by ESBL-producing *Enterobacteriaceae*.