P1783
Poster Session VI
MDR Gram-negatives - clinical observations

ACTIVITY OF CEFTAZIDIME-AVIBACTAM AND COMPARATORS VERSUS CHARACTERISED CLASS-C ?-LACTAMASE POSITIVE GRAM-NEGATIVE PATHOGENS ISOLATED GLOBALLY IN THE 2012 INTERNATIONAL NETWORK FOR OPTIMAL RESISTANCE MONITORING (INFORM) PROGRAMME

K. Kazmierczak[1], S. Hickman[1], M. Hackel[1], R. Badal[1], D. Biedenbach[1], I. Morrissey[2], S. Bouchillon[1], W. Nichols[3]

Objectives: Avibactam is a novel non-β-lactam β-lactamase inhibitor that protects against hydrolysis of β-lactams in Gram-negative bacteria that produce Ambler class A (extended-spectrum b-lactamases [ESBLs], serine carbapenemases), class C (AmpC) and some class D enzymes. We evaluated the activity of avibactam (AVI) in combination with ceftazidime (CAZ) against *Enterobacteriaceae* encoding AmpC b-lactamases collected as part of the INFORM global surveillance study.

Methods: Non-duplicate isolates from intra-abdominal, urinary tract, skin and soft tissue, and lower respiratory tract infections were collected from 132 global sites. Susceptibility testing was performed using CLSI broth microdilution and interpreted using EUCAST 2013 breakpoints; as no formal interpretative criteria have yet been defined, % of isolates with a CAZ-AVI MIC of <= 8 mg/L was used as a tentative breakpoint based on PK/PD data. Detection and sequencing of *bla* genes was performed on *Escherichia coli*, *Klebsiella* spp., and *Proteus mirabilis* isolates with CAZ MIC of >= 2 mg/L, and other *Enterobacteriaceae* that were non-susceptible to any carbapenem.

Results: 2,274 *Enterobacteriaceae* isolates were molecularly characterised. *bla* genes encoding ACC, ACT, CMY-type, DHA, FOX, MIR, and MOX enzymes were detected in 290 isolates from seven regions (Africa 7/70, Asia 93/484, Europe 86/889, Latin America 35/417, Middle East 10/101, North America 24/173, South Pacific 35/140). Isolates in which genes for both AmpC and ESBL enzymes were detected were seen in all regions, with proportionately more collected from Asia (41/484) and the South Pacific (7/140). Isolates encoding both AmpC enzymes and carbapenemases were only detected in Asia (8/484), Europe (8/889), North America (2/173), and the South Pacific (1/140). Notably, ten of these isolates encoded a metallo-b-lactamase (China 3, Greece 3, Romania 2, Thailand 1, Austria 1). The % susceptibility of isolates that encoded an AmpC enzyme was compared to that of isolates that encoded multiple b-lactamases.

	% Susceptible based on EUCAST 2013									
Enterobacteriaceae (n)	AMK	FEP	CAZ	CAZ-AVI	TZP	CST	DOR	MEM	LVX	TGC
AmpC only (198)	92	72	17	99	48	88	98	99	53	80
AmpC + ESBL (73)	66	5	0	99	27	99	100	99	22	79
AmpC + ESBL* + KPC (2)	50	50	0	100	0	100	0	50	50	50
AmpC + ESBL* + MBL (4)	50	0	0	0	0	100	0	25	50	75
AmpC + KPC (7)	29	14	14	100	14	71	14	14	29	86
AmpC + MBL (5)	80	20	0	20	20	80	0	0	40	60
AmpC + KPC + MBL (1)	0	0	0	0	0	100	0	0	0	100

AMK-amikacin; FEP-cefepime; CAZ-ceftazidime; CAZ-AVI-ceftazidime with 4 mg/L avibactam; TZP-piperacillin-tazobactam; CST-colistin; DOR-doripenem; MEM-meropenem; LVX- levofloxacin; TGC-tigecycline; MBL-metallo-b-lactamase.

Conclusions: Genes encoding AmpC b-lactamases were detected in approximately 13% of the characterized *Enterobacteriaceae* and were more prevalent in isolates from Asia (19% of collected) and South Pacific (25% of collected). Isolates encoding both AmpC enzymes and carbapenemases were rare. b-lactamase inhibitors such as tazobactam tend to be less effective against AmpC enzymes, and only 41% of isolates encoding AmpC enzymes were susceptible to TZP in this study. In contrast, 99-100% of isolates encoding AmpC enzymes alone or in combination with ESBLs or serine carbapenemases were presumptively susceptible to CAZ-AVI, suggesting that this drug combination

may hold considerable therapeutic promise.