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Poster Session VI
MDR Gram-negatives - clinical observations

ACTIVITY OF CEFTAZIDIME-AVIBACTAM AND COMPARATORS VERSUS CHARACTERISED ESBL-POSITIVE GRAM-NEGATIVE BACTERIA ISOLATED IN THE EUROPEAN REGION: 2012 PROGRAMME

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Objectives: Avibactam is a novel non-β-lactam β-lactamase inhibitor being developed for use in combination with ceftazidime. Avibactam protects β-lactams from hydrolysis in gram-negative bacteria that produce extended-spectrum β-lactamases (ESBLs) and carbapenemases including Ambler class A and/or class C enzyme producers. In this analysis, we evaluated the activity of ceftazidime-avibactam (CAZ-AVI) and comparators against *Enterobacteriaceae* encoding ESBLs collected from European countries as part of a global surveillance study. **Methods:** Non-duplicate isolates from intra-abdominal, urinary tract, skin and soft tissue, and lower respiratory tract infections were collected from 62 European sites. Susceptibility testing was performed using CLSI broth microdilution and interpreted using EUCAST 2013 breakpoints (% susceptible at <=8 mg/L for ceftazidime-avibactam). Molecular profiling of *bla* genes was performed on *Escherichia coli*, *Klebsiella* spp., and *Proteus mirabilis* isolates with CAZ MIC of >=2 mg/L, and other *Enterobacteriaceae* spp. that were non-susceptible to any carbapenem.

% Susceptible based on EUCAST 2013

Organism (n)	AMK	FEP	CAZ	CAZ-AVI	TZP	CST	DOR	ETP	LVX	TGC
E. coli ESBL$^+$ (224)	76	7	8	100	49	100	100	99	24	97
Klebsiella spp. ESBL$^+$(254)	80	4	1	100	14	100	99	92	28	76
Proteus spp. ESBL$^+$ (25)	28	4	8	96	80	4	100	100	8	8
Other ESBL$^+$ (6)*	83	0	0	100	0	83	100	17	17	67
All *Enterobacteriaceae*										
ESBL$^+$ + AmpC (15)	40	0	0	93	27	87	100	47	20	67
ESBL$^+$ + AmpC + MBL (3)	33	0	0	0	0	100	0	0	67	67
ESBL$^+$ + KPC/OXA-48 (28)	61	0	0	96	0	93	18	7	7	79
ESBL$^+$ + MBL (1)	0	0	0	0	0	100	0	0	0	100

*Other ESBL$^+$: *Enterobacter aerogenes*, *E. cloacae*, *Serratia marcescens*; AMK-amikacin; FEP-cefepime; CAZ-ceftazidime; CAZ-AVI-ceftazidime with 4 mg/L avibactam; TZP-piperacillin-tazobactam; CST-colistin; DOR-doripenem; ETP-ertapenem; IPM-imipenem; MEM-meropenem; LVX- levofloxacin; TGC-tigecycline; MBL-metallo-b-lactamase.

Results: 889 *Enterobacteriaceae* isolates collected in European countries were molecularly characterised. *bla* genes encoding TEM, SHV, CTX-M family, VEB, GES, and OXA ESBLs were detected in 556 isolates (Austria 11/23, Belgium 20/39, Czech Republic 19/32, Denmark 3/6, France 17/41, Germany 18/37, Greece 22/61, Hungary 29/43, Italy 40/78, the Netherlands 7/17, Portugal 75/106, Romania 37/44, Russia 167/198, Spain 22/55, Sweden 8/23, Turkey 47/65, United Kingdom 14/21). Fifteen of these isolates also encoded a class C (AmpC) b-lactamase (ACC, CMY-type, DHA, ACT), 29 isolates encoded additional carbapenemases (KPC, OXA-48, VIM), and 3 isolates encoded both an ACT AmpC-family enzyme and a VIM or NDM carbapenemase. The % susceptibility of isolates that encoded only an ESBL (ESBL$^+$) was compared to that of isolates encoding an ESBL in combination with other b-lactamases.

Conclusions: CAZ-AVI displayed potent *in vitro* activity against ESBL-producing isolates (including those also encoding AmpC or non-metallo-b-lactamases), with 93-100% susceptible to this drug combination. CAZ-AVI holds great promise as an agent that could be used to treat multi-drug resistant gram-negative pathogens otherwise refractory to currently available therapy.