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ePoster Viewing
New and old beta-lactamase inhibitors

ACTIVITY OF CEFTAZIDIME-AVIBACTAM AND COMPARATORS AGAINST COLISTIN NON-SUSCEPTIBLE ENTEROBACTERIACEAE AND PSEUDOMONAS AERUGINOSA ISOLATED IN 2012: THE INTERNATIONAL NETWORK FOR OPTIMAL RESISTANCE MONITORING (INFORM) STUDY

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Objectives: Due to the increase in multidrug resistance (MDR) in Gram-negative (GN) organisms, colistin is increasingly being used to treat serious GN infections. While resistance to polymyxins is low, trends towards increasing resistance are being reported. Avibactam (AVI) is a novel β-lactamase inhibitor being developed for combination with beta-lactams, including ceftazidime (CAZ). AVI protects β-lactams from hydrolysis in GN bacteria that produce Ambler class A β-lactamases including extended-spectrum enzymes (ESBLs) and *K. pneumoniae* carbapenemases (KPCs), class C β-lactamases, and some class D enzymes. We evaluated the activity of CAZ-AVI and comparators against colistin non-susceptible isolates from the 2012 INFORM global surveillance study. **Methods:** 9,278 *Enterobacteriaceae* (8,046 from species without intrinsic resistance to colistin, 1,232 from species with intrinsic colistin resistance including *Proteus* spp., *Providencia* spp., *M. morganii* and *S. marcescens*) and 1,558 *P. aeruginosa* 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. AVI was tested at a fixed 4 mg/L concentration. Colistin was supplemented with 0.002% polysorbate-80. MICs were interpreted using EUCAST 2013 breakpoints. No breakpoints are available for CAZ-AVI and a MIC of <=8 mg/L was used based on the 2g q8h dose of CAZ infused over 2h. **Results**: 70 *Enterobacteriaceae* without intrinsic colistin resistance (0.9%) and 16 *P. aeruginosa* (1.0%) were colistin non-susceptible. Regional percentage rates were (*Enterobacteriaceae*/*P. aeruginosa*, respectively): Asia 0.7/0, Europe 1.0/1.1, Latin America 0.8/2.9, Middle East 0.4/0, and North America 0.9/0.8. Susceptibilities are summarized below; values >=90% are shaded.

	% Susceptible									
Organism (N)	AMK	CAZ	CAZ-AVI**	CPE	COL	DOR	ERT	IPM	MER	TIG
All EBAC (8046)	94	71	99	76	99	98	96	97	98	90
COL NS EBAC (70)	91	69	99	77	0	90*	90*	89*	90*	76*
INTR COL NS (1232)	94	93	100	90	0	98	99	79	100	21
All PA (1558)	89	82	97	83	99	70	na	74	75	na
COL NS PA (16)	75	75	94	94	0	56	na	56	63	na

EBAC- *Enterobacteriacae*; INTR COL NS- intrinsically colistin resistant; PA- *Pseudomonas aeruginosa*; NS- non-susceptible; AMK-amikacin; CAZ-ceftazidime; CAZ-AVI-ceftazidime with 4 mg/mL avibactam; CPE-cefepime; COL-colistin; DOR-doripenem; ERT-ertapenem; IPM-imipenem; MER-meropenem; TIG-tigecycline

*Statistically significant decrease in susceptibility for colistin non-susceptible isolates (Fisher's exact test, P<0.05).

**% CAZ-AVI MIC of <=8 mg/L.

Conclusions: CAZ-AVI demonstrated potent activity against colistin non-susceptible isolates of *Enterobacteriaceae* and *P. aeruginosa* from a global population, with an MIC of <=8 mg/L in >99% and 94%, respectively. There was no significant difference in CAZ-AVI susceptibility between colistin-susceptible and -non-susceptible isolates. The carbapenems and tigecycline were significantly less active against the colistin non-susceptible isolates. These results may reflect selective pressure as colistin is increasingly used empirically to treat KPC and metallo-β-lactamase producing isolates. These *in vitro* results suggest that CAZ-AVI may be a valuable option for the treatment of increasingly difficult to treat serine beta-lactamase- producing pathogens.