eP440
ePoster Viewing
New and old beta-lactamase inhibitors

COMPARATIVE IN VITRO ACTIVITY OF CEFTAZIDIME (CAZ) AND CEFTAZIDIME-AVIBACTAM (CAZ-AVI) IN A EUROPEAN COLLECTION OF PSEUDOMONAS AERUGINOSA FROM CYSTIC FIBROSIS (CF) PATIENTS.

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Objectives: Resistance of *Pseudomonas aeruginosa* to antipseudomonal cephalosporins is causing increasing concern for CF patients, especially if they have received multiple antibiotic treatments. Carbapenems are now increasingly used in this setting, promoting the risk of selecting strains resistant to one of the last lines of therapy. In this context, avibactam (AVI), a novel, broad-spectrum beta-lactamase inhibitor, could prove of value in restoring activity of antipseudomonal cephalosporins such as CAZ against resistant Pa. Our aim was to examine the shift of MIC distribution of CAZ in a European collection of Pa isolates from CF patients when AVI is added to CAZ.

Methods: 342 Pa isolates were collected in United Kingdom (n=99), Belgium (n=91), France (n=81) and Germany (n=71) from CF patients who had received multiple antibiotic therapies. MICs were determined by microdilution in cation-adjusted Muller Hinton broth without or with AVI (4 mg/L), following CLSI recommendations and using Pa strain ATCC 27853 as quality control. MIC distributions and correlations between MICs were analysed using basic statistics and susceptibility/resistance patterns assessed using the interpretative criteria set by EUCAST (Version 3.1, 2013. http://www.eucast.org) and CLSI (Table 2B-1, M02 and M07; January 2013) for CAZ. Correlation between MICs of CAZ vs. CAZ-AVI against individual strains was examined using quantile density contour analysis (JMP 10.0.2, SAS Institute Inc., Cary, NC).

Results: The MICs (mg/L) and the percentage of susceptible and resistant Pa for CAZ and CAZ-AVI are summarized in the Table and the correlation between CAZ MICs of individual strains in the presence of AVI *vs.* values in the absence of AVI is presented in the Figure. Only 36% of isolates in this collection were susceptible to CAZ alone whereas 76 % of these isolates were in the range of susceptibility to CAZ after addition of AVI. Based on CLSI breakpoints, the presence of AVI also resulted in a smaller proportion of intermediate isolates than were observed for CAZ alone. The correlation shows that 54% of the strains categorized as resistant according to EUCAST for CAZ alone could be categorized as susceptible after addition of AVI.
Conclusions: AVI restores CAZ activity against a high proportion of CAZ-resistant Pa from CF patients. CAZ-AVI could represent a useful addition to our antimicrobial armamentarium for microbiologically-documented infections in this patient population.

Drug	MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC (mg/L) range		Susceptibility according to				
					EUCAST [a]		CLSI [a]		
			min	max	% S	%R	% S	%I	%R
CAZ	32	512	0.5	>512	36	64	36	9	55
CAZ-AVI	4	64	0.03	>512	76	24	76	5	19

[a] based on current Pa breakpoints for CAZ alone (EUCAST: S≤8, R>8; CLSI: S≤8, I=16, R≥32)

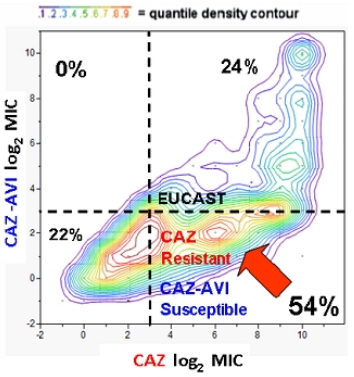

Figure: Correlation between MICs of CAZ combined with AVI (CAZ-AVI; ordinate) and MICs of ceftazidime alone (CAZ; abscissa) for all strains. The colour gives information on the proportion of strains in each zone of the diagram. The dotted lines show the S/R limits according to EUCAST interpretative criteria for CAZ, with the figures showing the % of strains categorized as CAZ-susceptible and CAZ-resistant, respectively. The lower right quadrant shows which strains categorized as CAZ-resistant were brought to a presumptively susceptible MIC level by the addition of AVI, based on the current EUCAST CAZ susceptibility breakpoint for Pa.