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Paper Poster Session VI

New data on new cephalosporin/beta-lactamase inhibitor combinations

In vitro activity of ceftazidime-avibactam and other agents against *Pseudomonas aeruginosa* isolated in selected countries of the European union in 2013

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Background: *P. aeruginosa* (PA) is the cause of serious healthcare associated infections and exhibits resistance to a number of different antimicrobials used to treat these infections, including resistance to currently available β-lactams. Ceftazidime-avibactam (CAZ-AVI) is a combination of ceftazidime (CAZ) with the non-β-lactam β-lactamase-inhibitor avibactam (AVI) that is under clinical development as a potential therapeutic option for the treatment of infections caused by PA. To evaluate this potential, CAZ-AVI susceptibility data generated through the INFORM Surveillance initiative were analyzed, and compared to other agents according to various PA resistance phenotypes among European Union isolates.

Methods: 891 PA isolates were collected from 66 sites in 17 countries. Isolates were collected and tested centrally at IHMA, Inc. according to CLSI guidelines for broth microdilution testing. Susceptibility (S) categories used were based on EUCAST breakpoints. No breakpoints have been defined for CAZ-AVI and a reference value of MIC ≤8 mg/L was used for comparative purposes. Multidrug resistance (MDR) was defined as resistance to three or more antimicrobial classes.

Results: The table below shows the *in vitro* activities based on MIC_{90}/%S of CAZ-AVI and comparators against PA according to various resistant phenotypes.

PA (n)	CAZ-AVI	CAZ	CEP	TZP	MEM	COL	
All (891)		8/93.5	32/78.8	16/82.7	128/71.9	>8/74.1	0.5/100
CAZ-NS (189)		32/69.3	128/0.0	>16/29.6	>128/6.9	>8/33.9	0.5/100
CAZ-NS/MBL- (163)		32/79.8	128/0.0	>16/33.7	>128/7.4	>8/39.3	0.5/100
MEM-NS (231)		32/77.5	128/45.9	>16/49.4	>128/32.0	>8/0.0	0.5/100
MEM-NS/MBL- (205)		16/86.8	64/51.7	>16/55.1	>128/35.6	>8/0.0	0.5/100
MDR (217)		32/73.3	128/24.4	>16/31.3	>128/4.6	>8/27.2	0.5/100
MBL+ (26)		>128/3.9	128/0.0	>16/3.9	>128/3.9	>8/0.0	0.5/100

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; CAZ-NS, CAZ non-susceptible; CEP, cefepime; MEM, meropenem; MEM-NS, meropenem non-susceptible; TZP, piperacillin-tazobactam; COL, colistin; MDR, multi-drug resistant; MBL+, molecularly positive for a metallo-β-lactamase.

Conclusions:

Regardless of the resistant phenotype analyzed COL and CAZ-AVI were the most active agents against PA from the European Union countries sampled. In the presence of AVI the CAZ $MIC_{90's}$ decreased 4 to 8 fold (except among the MBL-producing population). These findings demonstrate the extent to which beta-lactam resistance exists among PA and indicates that CAZ-AVI may have a role as a therapeutic option against this important species.