

P1782

Poster Session VI

MDR Gram-negatives - clinical observations

ACTIVITY OF CEFTAZIDIME-AVIBACTAM VERSUS PSEUDOMONAS AERUGINOSA, INCLUDING MULTIPLE-DRUG RESISTANT ISOLATES IN EUROPE --THE 2012 INFORM PROGRAMME

S. Bouchillon<sup>1</sup>, D. Hoban<sup>1</sup>, M. Hackel<sup>1</sup>, R. Badal<sup>1</sup>, I. Morrissey<sup>2</sup>, D. Biedenbach<sup>1</sup>, W. Nichols<sup>3</sup>

**Objectives:** Avibactam is a novel investigational non-β-lactam β-lactamase inhibitor that is being developed for use in combination with ceftazidime (CAZ). Avibactam does not have any clinically meaningful intrinsic antibacterial activity, but inhibits Ambler class A β-lactamases including extended-spectrum enzymes (ESBLs) and KPCs, class C β-lactamases, and some class D enzymes. It thus restores the activity of CAZ against difficult to treat Gram-negative pathogens such as *Pseudomonas aeruginosa* (PA) including multiple-drug resistant (MDR) isolates.

**Methods:** 707 clinically relevant PA from multiple sources were collected in 2012 at 62 centres in 17 European countries as part of the International Network for Optimal Resistance Monitoring (INFORM) programme. MICs were measured as specified by CLSI broth microdilution and interpreted following EUCAST 2013 guidelines; for ceftazidime-avibactam, a presumptive susceptible interpretive criterion of ≤8 mg/L was used based on PK/PD data.

**Results:** The *in vitro* activity of ceftazidime-avibactam and 9 comparators are presented in the following table for all PA, meropenem-non-susceptible (MEM-NS), ceftazidime-non-susceptible (CAZ-NS), and MDR PA isolates:

Drug	All <i>P. aeruginosa</i> (n=707)		MEM-NS PA (n=158)		CAZ-NS PA (n=110)		MDR PA (n=152)	
	MIC <sub>90</sub>	%Sus	MIC <sub>90</sub>	%Sus	MIC <sub>90</sub>	%Sus	MIC <sub>90</sub>	%Sus
Ceftazidime-Avibactam	8	98.0 <sup>a</sup>	8	91.8 <sup>a</sup>	16	87.3 <sup>a</sup>	8	90.8 <sup>a</sup>
Ceftazidime	32	84.4	64	54.4	64	0.0	64	36.8
Amikacin	16	88.5	>32	64.6	>32	60.9	>32	57.9
Aztreonam	32	3.5	64	0.0	128	0.0	64	0.1
Cefepime	16	84	>16	52.5	>16	32.7	>16	32.2
Doripenem	>4	71.2	>4	1.3	>4	20.9	>4	14.5
Imipenem	>8	76.8	>8	10.8	>8	41.8	>8	32.2
Levofloxacin	>4	66.3	>4	25.3	>4	28.2	>4	14.5
Meropenem	>8	77.7	>8	0.0	>8	34.6	>8	25.7
Piperacillin-Tazobactam	128	78.9	>128	37.3	>128	10.0	>128	15.1

<sup>a</sup>Ceftazidime-avibactam: a presumptive susceptible interpretive criterion of ≤8 mg/L was used.

**Conclusions:** Ceftazidime-avibactam was the most active *in vitro* antimicrobial agent against the combined *P. aeruginosa* collected in Europe, including non-susceptible phenotypes. Avibactam restored the *in vitro* activity of ceftazidime, lowering the MIC<sub>90</sub> values 2- to 8-fold against *P. aeruginosa*, including meropenem- and ceftazidime-non-susceptible, and multidrug-resistant isolates.