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Paper Poster Session
Susceptibility trends for old and new antibiotics

Activity of ceftazidime-avibactam against carbapenem-non-susceptible Enterobacteriaceae isolated from patients in Europe 2012–2014

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Background: Increasing resistance in Gram-negative pathogens, including resistance to carbapenems, has been reported worldwide, seriously limiting treatment options in some regions. Avibactam is a novel non-β-lactam β-lactamase inhibitor that restores the *in vitro* activity of ceftazidime against *Enterobacteriaceae* that produce class A (including KPC), class C, and some class D β-lactamases. In this study we evaluated the *in vitro* activity of ceftazidime-avibactam and comparator agents against a collection of carbapenem-non-susceptible *Enterobacteriaceae* isolated from European countries participating in the 2012–2014 INFORM surveillance program.

Material/methods: MICs were determined using CLSI broth microdilution guidelines. The percent susceptible was assessed using the FDA breakpoint of ≤8 mg/L for ceftazidime-avibactam and EUCAST guidelines for other comparators. Carbapenem-non-susceptible *Enterobacteriaceae* were defined as non-susceptible to meropenem using the EUCAST breakpoint of ≥4 mg/L.

Results: 448 out of 18,377 *Enterobacteriaceae* (2.4%) were meropenem-non-susceptible. The percent susceptible (%S) for ceftazidime-avibactam and comparative antimicrobial agents are shown in the table. Ceftazidime-avibactam provided activity against 99.6% of all *Enterobacteriaceae*, and against 85.5% of meropenem-non-susceptible isolates from Europe, and was the most active drug tested. Ceftazidime-avibactam showed potent activity against meropenem-non-susceptible *Klebsiella pneumoniae*, where the most common mechanism of carbapenem resistance was KPC production, but showed reduced activity against other meropenem-non-susceptible *Enterobacteriaceae*, where resistance was mainly due to the presence of metallo-β-lactamases (MBLs). Country differences were apparent, with lower activity in countries that showed higher incidence of MBLs.

***In Vitro* Activity of Ceftazidime-Avibactam and Comparators against *Enterobacteriaceae* from Europe**

	Percent Susceptible			
Organism (N)	Europe	Greece	Russia	Romania
Enterobacteriaceae	N=18,377	N=1,110	N=1,961	N=697
CAZ-AVI	99.6	96.9	99.6	98.0
CAZ	74.7	75.1	46.8	69.4
MEM	97.6	86.0	96.6	95.0
COL	82.2	76.4	84.3	80.6
TGC	81.6	79.0	80.4	81.4
Enterobacteriaceae, MEM NS	N=448	N=155	N=67	N=35
CAZ-AVI	85.5	82.6	91.0	62.9
CAZ	2.5	0.7	6.0	0.0
COL	72.4	65.2	96.4	35.3
TGC	66.3	63.9	64.2	88.6
Klebsiella pneumoniae, MEM NS	N=390	N=139	N=64	N=28
CAZ-AVI	90.8	89.2	92.2	78.6
CAZ	2.3	0.0	6.3	0.0
COL	71.3	64.1	96.3	35.7
TGC	66.9	64.8	65.6	92.9
Other *Enterobacteriaceae*, MEM NS	N=58	N=16	N=3	N=7
CAZ-AVI	50.0	25.0	66.7	0.0
CAZ	3.5	6.3	0.0	0.0
COL	81.8	80.0	100	33.3
TGC	62.1	56.3	33.3	71.4

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; COL, colistin; TGC, tigecycline; MEM-NS, meropenem non-susceptible

Conclusions: Ceftazidime-avibactam demonstrated good *in vitro* potency against meropenem-non-susceptible *Enterobacteriaceae* isolates from Europe. It was the most active agent tested, but activity was diminished by the presence of MBLs. The incidence of these amongst different countries explains the different degrees of activity observed in these countries.