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ePoster Viewing
New and old beta-lactamase inhibitors

IN VITRO ACTIVITY OF CEFTAZIDIME-AVIBACTAM AND COMPARATORS AGAINST GRAM-NEGATIVE PATHOGENS IN EUROPE - THE INTERNATIONAL NETWORK FOR OPTIMAL RESISTANCE MONITORING (INFORM) 2012

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Objectives: Avibactam is a novel investigational non-β-lactam β-lactamase inhibitor that is being developed for use in combination with ceftazidime. Avibactam does not have any clinically meaningful intrinsic antibacterial activity of its own, but inhibits extended-spectrum β-lactamases (ESBLs), class C β-lactamases, serine carbapenemases including Ambler class A and class C, and some class D enzymes. The ASPIRE study began monitoring the activity of ceftazidime-avibactam and comparators in 2012. This report describes their activity against Gram-negative pathogens collected in Europe.

Methods: 5,169 clinically relevant Gram-negative pathogens from multiple sources were collected from 62 medical centres in 17 European countries. MICs were performed by CLSI broth microdilution and interpreted using EUCAST 2013 guidelines.

Results: The *in vitro* activity of ceftazidime-avibactam and a selection of six of the comparators is presented in the following table for all *Enterobacteriaceae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* from 15 EARS-Net countries representing the European Union (EU), Russia, and Turkey:

	MIC_{90} (% Susceptible) [a]						
EU, Russia, Turkey	AMK	CAZ	CAZ-AVI[b]	DOR	LVX	MEM	TZP
Enterobacteriaceae (4,146)	8 (93.3%)	64 (76.4%)	0.5 (99.4)	0.25 (97.6%)	>4 (76.9%)	0.12 (97.8%)	128 (77%)
ESBL-producers (575) [c]	32 (74.4%)	>128 (5.2%)	1 (99.1%)	0.5 (93.6%)	>4 (27%)	0.25 (93.7%)	>128 (30.6%)
H. influenzae (60)	--	0.12 (na)	<=0.03 (na)	1 (98.3%)	0.015 (100%)	0.25 (100%)	0.12 (na)
A. baumannii (256)	>32 (31.6%)	>128 (na)	128 (na)	>4 (19.9%)	>4 (18.4%)	>8 (25%)	>128 (na)
P. aeruginosa (707)	16 (88.5%)	32 (84.4%)	8 (98%)	>4 (71.2%)	>4 (66.3%)	>8 (77.7%)	128 (78.9%)
EU only							
Enterobacteriaceae (3,557)	8 (95.5)	64 (80.4%)	0.5 (99.4%)	0.25 (97.8%)	>4 (79.84%)	0.12 (98.0%)	128 (79.7%)
ESBL-producers (374) [b]	16 (80.0%)	>128 (6.2%)	1 (98.7%)	0.5 (91.2%)	>4 (28.07%)	1 (91.2%)	>128 (30.8%)
H. influenzae (56)	--	0.12 (na)	0.06 (na)	1 (100%)	0.015 (100%)	0.25 (100%)	0.12 (na)
A. baumannii (182)	>32 (37.4%)	>128 (na)	128 (na)	>4 (25.3%)	>4 (23.1%)	>8 (29.7%)	>128 (na)
P. aeruginosa (611)	8 (90.2%)	32 (85.2%)	8 (97.7%)	>4 (73.0%)	>4 (68.4%)	8 (78.9%)	128 (79.7%)

AMK, amikacin; **CAZ**, ceftazidime; **CAZ-AVI**, ceftazidime-avibactam; **DOR**, doripenem; **LVX**, levofloxacin; **MEM**, meropenem; **TZP**, piperacillin-tazobactam.

[a] EUCAST breakpoints; na= not available (no breakpoint defined); -- not tested.

[b]CAZ-AVI %S reported as % isolates with MIC ≤8mg/L.

[c] Confirmed phenotypic ESBLs from *E. coli*, *K. pneumoniae*, *K. oxytoca*, and *P. mirabilis.*

Conclusions: Ceftazidime-avibactam activity against *P. aeruginosa* was similar to that of amikacin and meropenem . Avibactam restored the *in vitro* activity of ceftazidime, lowering the MIC_{90} values at least

128-fold against *Enterobacteriaceae* (including ESBL phenotypes), 4-fold against *P. aeruginosa*, and 2- to 4-fold against *H. influenzae*. All tested antimicrobics were ineffective against *A. baumannii*.