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P1147 *In vitro* activities of ceftazidime-avibactam and comparator agents against *Pseudomonas aeruginosa* from Europe stratified by region, ATLAS Global Surveillance Program 2017

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Background: Increasing resistance in Gram-negative pathogens, including *Pseudomonas aeruginosa* (*Paer*), has been reported in Europe and elsewhere, seriously limiting treatment options. The non-β-lactam, β-lactamase inhibitor, avibactam (AVI) can inhibit Class A, C, and some Class D β-lactamases. This study examined the *in vitro* activity of ceftazidime-avibactam (CAZ-AVI) and comparators against *Paer* collected in Europe during 2017 with isolates stratified into two regions, North/Western and Central/Eastern Europe.

Materials/methods: 2097 non-duplicate *Paer* isolates were collected from 64 sites in 16 countries in Europe as part of the ATLAS surveillance study in 2017. Susceptibility testing was by broth microdilution according to the ISO standard method and interpreted using EUCAST 2018 breakpoints. CAZ was tested with a fixed concentration of 4 mg/L avibactam. Meropenem MIC values >1 mg/L triggered β-lactamase gene screening by PCR and sequencing.

Results: CAZ-AVI demonstrated potent *in vitro* activity against the collection of 1424 *Paer* isolates from North/Western Europe (MIC_{90}, 8 mg/L, 95.9% susceptible), but was less effective against the collection (n=673) from Central/Eastern Europe (MIC_{90}, 32 mg/L, 85.0% susceptible). However, when metallo-β-lactamase (MBL)-positive isolates were removed from this latter set, the activity of CAZ-AVI increased appreciably (MIC_{90}, 8 mg/L, 96.4% susceptible). The *in vitro* activity of CAZ-AVI was the highest among all comparators for both regions, and against all phenotypes.

Region/Phenotype (n)	Drug[a]									
	CAZ-AVI		CAZ		MEM		TZP		LVX	
	% S	MIC_{90} (mg/L)	% S	MIC_{90} (mg/L)	% S	MIC_{90} (mg/L)	% S	MIC_{90} (mg/L)	% S	MIC_{90} (mg/L)
North/Western Europe[b]										
All (1424)	95.9	8	80.2	32	79.6	> 8	78.0	128	67.7	> 8
MBL[c]-negative (1407)	97.0	4	81.2	32	80.5	8	79.0	128	68.5	> 8
MEM-NS[d] (291)	82.8	32	42.6	128	0.0	> 8	35.7	> 128	24.4	> 8
Central/Eastern Europe[e]										
All (673)	85.0	32	69.1	64	61.5	> 8	67.6	> 128	55.9	> 8
MBL-negative (588)	96.4	8	78.9	32	70.4	> 8	76.4	128	63.8	> 8
MEM-NS (259)	62.9	64	38.6	128	0.0	> 8	38.6	> 128	23.9	> 8

[a]CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; TZP, piperacillin-tazobactam; LVX, levofloxacin; S = susceptible
[b]Includes Sweden, Denmark, Netherlands, United Kingdom, Belgium, France, Germany, Spain, Portugal and Italy.
[c]MBL = metallo-β-lactamase.
[d]NS = non-susceptible.
[e]Includes Poland, Czech Republic, Hungary, Greece, Romania and Russia.

Conclusions: The *in vitro* activity of CAZ-AVI against the *Paer* isolates collected in North/Western Europe was higher than that against isolates from Central/Eastern Europe. This appeared to be caused by an increased

prevalence of MBL-carrying isolates from Central/Eastern Europe, as the difference between the two regions was negligible when only MBL-negative isolates were considered (97.0% susceptible for North/western vs. 96.4% susceptible for Central/Eastern Europe). More isolates were susceptible to CAZ-AVI than to any comparator, suggesting that it is a viable treatment option, especially for infections due to non-MBL harboring isolates.