P0297
Paper Poster Session
Bacterial strain typing

In vitro activity of ceftazidime-avibactam and comparators against Pseudomonas aeruginosa from Europe 2012–2014

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Background: Avibactam is a novel 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, but inhibits Ambler class A β-lactamases including extended-spectrum enzymes and KPCs, class C β-lactamases, and some class D enzymes. It is able to restore the activity of ceftazidime against the often resistant ESKAPE pathogen *Pseudomonas aeruginosa.* This study reports ceftazidime-avibactam susceptibility data for recent clinical isolates from Europe generated through the INFORM Surveillance initiative.

Material/methods: 3,893 clinically relevant *P. aeruginosa* isolates from multiple sources were collected between 2012 and 2014 in 19 European countries. MICs were determined as specified by CLSI broth microdilution and interpreted following FDA guidelines for ceftazidime-avibactam (≤8 µg/mL susceptible), and EUCAST 2015 guidelines for comparators.

Results: The table below shows the *in vitro* activities based on MIC_{90}/% susceptible (S) of ceftazidime-avibactam and comparators against *P. aeruginosa* according to various resistant phenotypes. Ceftazidime-avibactam exhibited potent *in vitro* antimicrobial activity against *P. aeruginosa* collected in Europe, with 92.6% of all isolates testing as susceptible. Of the meropenem-non-susceptible isolates, 74.2% were susceptible to ceftazidime-avibactam, but that increased to 86.2% in the metallo-β-lactamase (MBL)-negative subset. Country differences in *in vitro* activity were noted, with consistently high activity in countries with no MBLs (exemplified by Denmark and The Netherlands), and decreased activity in countries where MBLs are more prevalent (exemplified by Russia and Romania).

***In Vitro* Activity of Ceftazidime-Avibactam and Comparators against *P. aeruginosa* from Europe**

		MIC_{90}/%S					
Region	N	CAZ-AVI	CAZ	CEP	MEM	TZP	COL
Europe	3893	8/92.6	64/77.4	16/78.8	>8/72.9	>128/69.4	2/99.5
Europe-MEM NS	1056	32/74.2	128/41.3	>16/41.0	>8/0	>128/27.0	2/99.4
Europe, no MBL	3740	8/96.2	32/80.5	16/81.9	>8/75.8	128/72.1	2/99.5
Europe-MEM NS, no MBL	904	16/86.2	128/47.9	>16/47.6	>8/0	>128/31.1	4/99.2
Russia	376	32/75.3	64/57.5	>16/57.7	>8/52.7	>128/50.7	2/100
Russia, no MBL	309	8/90.9	64/69.3	>16/70.2	>8/64.1	>128/61.8	2/100
Romania	114	32/79.0	128/64.9	>16/61.4	>8/61.4	>128/53.5	2/100
Romania, no MBL	103	16/87.4	128/71.8	>16/68.0	>8/68.0	>128/59.2	2/100
Denmark	149	4/99.3	8/93.3	8/93.3	2/91.3	32/85.2	2/100
Denmark, no MBL	149	4/99.3	8/93.3	8/93.3	2/91.3	32/85.2	2/100
Netherlands	79	4/100	16/89.9	8/98.7	4/89.9	16/91.1	2/100
Netherlands, no MBL	79	4/100	16/89.9	8/98.7	4/89.9	16/91.1	2/100

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; CEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; COL, colistin; MEM-NS, meropenem non-susceptible; MBL, metallo-β-lactamase.

Conclusions: Ceftazidime-avibactam showed potent *in vitro* antimicrobial activity against *P. aeruginosa* collected in Europe, but activity was compromised by MBLs. The incidence of these play a role in the reduced activity of ceftazidime-avibactam in some countries.