P0331
Paper Poster Session
Susceptibility trends for old and new antibiotics

In vitro activity of aztreonam-avibactam (ATM-AVI) against Gram-negative pathogens from Europe collected in 2014

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Background: Avibactam (AVI) is a non-β-lactam β-lactamase inhibitor with activity against class A, class B, and some class D β-lactamases, including extended-spectrum β-lactamases (ESBLs) and KPCs. Aztreonam (ATM) is stable to hydrolysis by metallo-β-lactamases (MBL). ATM-AVI is being developed for use against carbapenem-resistant *Enterobacteriaceae*, especially those producing MBLs that often co-carry serine β-lactamases. This study evaluated the *in vitro* activity of ATM-AVI and comparators against *Enterobacteriaceae* and *P. aeruginosa* collected in 2014 in Europe.

Material/methods: Non-duplicate clinical isolates were collected from 78 centers in 18 European countries. Susceptibility testing was performed using CLSI broth microdilution and interpreted using EUCAST 2015 breakpoints. Aztreonam-avibactam was tested at a fixed concentration of 4 mg/L avibactam. PCR and sequencing were used to determine the β-lactamase genes present in isolates that were non-susceptible to carbapenems (meropenem, imipenem, doripenem), phenotypically positive for ESBL, and those with ceftazidime MICs ≥ 16 mg/L.

Results: The MIC data for *Enterobacteriaceae* and *P. aeruginosa* are provided in the table. ATM-AVI demonstrated good activity against *Enterobacteriaceae*, with MIC_{90} values of 0.12-1 mg/L for all groups. 99.9% of the isolates, including those that produced MBLs, were inhibited by ≤ 8 mg/L of ATM-AVI. VIM- and NDM-type MBLs were found in 17 *K. pneumoniae*, 7 *E. cloacae*, 3 *C. freundii*, 3 *S. marcescens*, 2 *P. mirabilis*, and 1 *P. stuartii* collected in Greece, Romania, Hungary, Russia, Italy, Turkey, Germany and the United Kingdom. No IMP-type MBLs were found in isolates from Europe. All MBL-producing *Enterobacteriaceae* isolates co-carried one or more plasmid- or chromosomally-mediated serine β-lactamases, including CTX-M-15 and OXA-48. ATM-AVI showed only modest activity against *P. aeruginosa*.

Species/ phenotype[a] (n)	Drug (MIC_{90} [mg/L], % Susceptible)									
	ATM-AVI		ATM		MEM		COL		TGC	
Enterobacteriaceae All (7453)	0.12	NA	64	74.1%	0.12	97.3%	>4	82.7%	2	84.6%
ESBL-positive (1367)	0.25	NA	>128	1.4%	2	91.1%	2	91.7%	2	83.6%
Meropenem-S (7250)	0.12	NA	64	76.1%	0.12	100%	>4	83.0%	2	84.9%
Meropenem-NS (203)	0.5	NA	>128	4.4%	>8	0	>4	72.4%	2	70.9%
MBL-negative (7420)	0.12	NA	64	74.4%	0.12	97.6%	>4	82.7%	2	84.6%
MBL-positive (33)	1	NA	>128	21.2%	>8	21.2%	>4	78.8%	2	72.7%
P. aeruginosa All (2091)	32	NA	32	4.4%	>8	72.5%	2	99.6%	>8	NA

ATM-AVI, aztreonam-avibactam; ATM, aztreonam; MEM, meropenem; COL, colistin; TGC, tigecycline; NA, no breakpoints available; NS, non-susceptible.
[a]ESBL, extended-spectrum β-lactamase; MBL, metallo-β-lactamase.

Conclusions: ATM-AVI had good activity against *Enterobacteriaceae* isolated in Europe, including those that produced ESBLs and MBLs. ATM-AVI was highly active against all MBL-containing *Enterobacteriaceae*, regardless of species or country of isolation. The promising *in vitro* activity of ATM-AVI against carbapenem-resistant *Enterobacteriaceae*, especially those producing MBLs that are disseminating around the globe, warrants further development of this combination for future use against these pathogens.