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P1153 *In vitro* activity of aztreonam-avibactam and comparator agents against *Enterobacteriaceae* from Europe collected during the ATLAS Global Surveillance Program 2015-2017

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Background: Avibactam (AVI) is a non-β-lactam β-lactamase inhibitor with activity against class A, class C, 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* collected in 2015-2017 in Europe.

Materials/methods: Non-duplicate clinical isolates were collected from Northern/Western Europe (Belgium, Denmark, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, United Kingdom) and Central/Eastern Europe (Austria, Czech Republic, Greece, Hungary, Poland, Romania, Russia, Turkey). Susceptibility testing was performed using CLSI broth microdilution and interpreted using EUCAST 2018 breakpoints. ATM-AVI was tested at a fixed concentration of 4 mg/L avibactam. PCR and sequencing were used to determine the β-lactamase genes present in all isolates with meropenem (MEM) MIC >1 mg/L, and *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* phenotypically positive for ESBL activity (2015) or with ATM or ceftazidime MIC >1 mg/L (2016-2017).

Results: % susceptibility for ATM and MEM varied slightly for the regions, but ATM-AVI demonstrated good activity against *Enterobacteriaceae*, with MIC_{90} values of 0.12-0.5 mg/L in both European regions for all subsets of isolates (Table). In both regions, >99.9% of isolates, including all that produced MBLs, were inhibited by ≤8 mg/L of ATM-AVI. The percentages of MEM-non-susceptible isolates in Northern/Western and Central/Eastern Europe were 2.5 and 5.6%, respectively, and the percentages of MBL-positive isolates were 0.4 and 1.9%, respectively. 109 NDM- and 104 VIM-type MBLs were found in 13 species and 15 countries. No IMP-type MBLs were found. The majority of MBL-producing *Enterobacteriaceae* isolates co-carried one or more plasmid- or chromosomally-mediated serine β-lactamases, including CTX-M-15 and OXA-48.

	Drug (MIC_{90} [mg/L, % Susceptible]											
	Northern/Western						Central/Eastern					
Species/phenotype (n per region)	ATM-AVI		ATM		MEM		ATM-AVI		ATM		MEM	
Enterobacteriaceae, All (13652/8198)	0.12	NA	32	78.5	0.12	97.5	0.12	NA	128	69.0	0.12	94.4
ESBL-positive (1731/1810)	0.25	NA	>128	1.4	2	90.1	0.25	NA	>128	0.4	>8	83.2
Meropenem-S (13316/7736)	0.12	NA	32	80.3	0.12	100	0.12	NA	64	72.6	0.12	100
Meropenem-NS (336/462)	0.5	NA	>128	3.6	>8	0.0	0.5	NA	>128	8.9	>8	0.0
MBL-negative (13595/8043)	0.12	NA	32	78.7	0.12	97.9	0.12	NA	128	70.1	0.12	96.0
MBL-positive (57/155)	0.5	NA	>128	14.0	>8	15.8	0.5	NA	>128	16.1	>8	11.6

ATM-AVI, aztreonam-avibactam; ATM, aztreonam; MEM, meropenem; NA, no breakpoints available; NS, non-susceptible; 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.