

P1615

Abstract (poster session)

**Activity of aztreonam combined with the beta-lactamase inhibitor avibactam tested against metallo beta-lactamase-producing organisms**

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**Objective:** To evaluate the in vitro activity of aztreonam (ATM) alone, ATM combined with avibactam (AVI) and comparator antimicrobial agents tested against a collection of metallo-beta-lactamase (MBL)-producing multidrug-resistant Gram-negative strains. The emergence of NDM-producing isolates has renewed discussions about the threat and limitations to therapeutic options for infections caused by MBL-producing organisms.

**Methods:** 133 MBL-producers (68 Enterobacteriaceae [ENT; 10 species], 47 Pseudomonas spp. [PSP] and 18 Acinetobacter spp. [ASP]) were susceptibility tested against ATM with and without AVI and comparator agents using reference broth microdilution method according to CLSI documents. Isolates produced 23 different MBL-types, including 13 IMP-variants, 9 VIM-types and NDM-1. **Results:** ATM-AVI (MIC<sub>50/90</sub>, 0.25/1 mg/L) was very active against MBL-producing ENT; inhibiting 67 of 68 (98.5%) at ≤2 mg/L (Table). Among different species, ATM-AVI MIC<sub>50</sub> values were 1, 0.25, 0.12 and 0.06 mg/L for E. coli (6 strains), K. pneumoniae (24 strains), E. cloacae (25 strains) and other ENT, respectively. One NDM-1-producing E. coli had an ATM-AVI MIC of 8 mg/L. ATM-AVI (MIC<sub>50/90</sub>, 0.25/1 mg/L) was the most active compound tested against ENT strains. Against PSP producing MBLs, the activity of ATM alone (MIC<sub>50</sub>, 16/>64 mg/L) was similar to that of the ATM-AVI combination. All other compounds exhibited very limited activity against these organisms, with the exception of colistin (MIC<sub>50/90</sub>, 1/2 mg/L; 100.0% susceptible by CLSI and EUCAST criteria). ATM-AVI (MIC<sub>50/90</sub>, 32/64 mg/L), ATM alone (MIC<sub>50/90</sub>, 32/>64 mg/L) and other beta-lactam agents tested exhibited limited activity against ASP. MIC values of ≥ two-doubling dilutions for ATM-AVI (>64 mg/L) compared to ATM alone (32 mg/L) were observed for three IMP-1-producing ASP. **Conclusions:** ATM-AVI was generally active against a large collection of MBL-producing ENT strains, regardless of bacterial species or type of MBL produced. ATM-AVI inhibited 94.1% of the MBL-producing ENT compared to 27.9% for ATM alone. ATM-AVI activity against MBL-producing PSP and ASP was similar to that of ATM alone. MBL-producing strains represent a challenge to antimicrobial therapy and the combination ATM-AVI might be an option for the treatment of infections caused by these pathogens.

Antimicrobial Agent Organism (no. tested)	no. of organisms (cumulative %) inhibited at MIC (mg/L) of:							
	≤0.5	1	2	4	8	16	32	≥64
<i>Enterobacteriaceae</i> (68)								
Aztreonam-avibactam	56(82.3)	8(94.1)	3(98.5)	0(98.5)	1(100.0)	-	-	-
Aztreonam	17(25.0)	2(27.9)	0(27.9)	1(29.4)	0(29.4)	5(36.8)	3(41.2)	40(100.0)
<i>Pseudomonas</i> spp. (47)								
Aztreonam-avibactam	-	-	3(6.4)	7(21.3)	6(34.0)	15(66.0)	8(83.0)	8(100.0)
Aztreonam	-	-	1(2.1)	5(12.8)	4(21.3)	15(53.2)	7(68.1)	15(100.0)
<i>Acinetobacter</i> spp. (18)								
Aztreonam-avibactam	-	-	2(11.1)	1(16.7)	0(16.7)	4(38.9)	3(55.6)	8(100.0)
Aztreonam	-	-	1(5.6)	0(5.6)	3(22.2)	2(33.3)	9(83.3)	3(100.0)