- Aztreonam-Avibactam showed excellent *in vitro* activity against MBL-producing *Enterobacterales* isolates.
- This drug combination holds great promise as a potential treatment alternative for infections caused by these multidrug-resistant pathogens.

In vitro activity of Aztreonam-Avibactam against MBL-producing *Enterobacterales* isolates across Germany

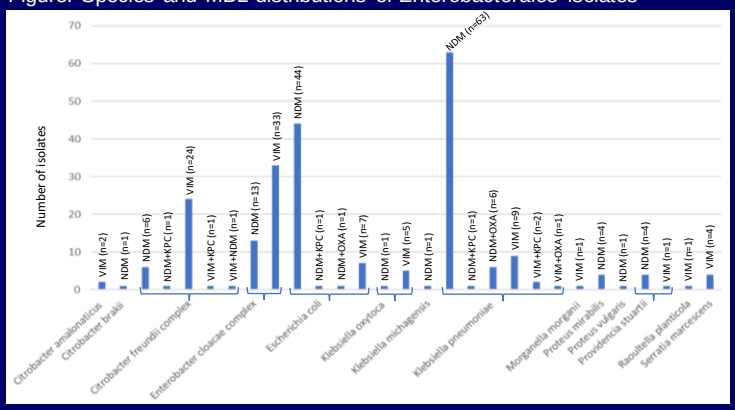
Background

Carbapenem-resistance in *Enterobacterales* due to the production of metallo-β-lactamases (MBL) is an increasing threat in healthcare facilities.[1] Although Aztreonam inhibits MBL activity, it remains ineffective in the presence of ESBL and AmpC β-lactamases, which catalyse the cleavage of aztreonam. Combination with the β-lactamase-inhibitor Avibactam can restore the activity of Aztreonam.[2,3] The aim of this study was to investigate the effect of Aztreonam-Avibactam against a collection of MBL-producing *Enterobacterales* isolates.

Results

- The main species included *Klebsiella* spp. (n=89), *Enterobacter cloacae* complex (n=46) and *Escherichia coli* (n=53). All isolates carried NDM- or VIM-like MBLs (Figure). Fifteen isolates carried additional carbapenemases (KPC- or OXA-48-like).
- Cefiderocol ≤2 mg/L was able to inhibit 55.0% (132/240) of all isolates, but 59.8% (52/87) of VIM-producing isolates and 53.6% (74/138) of NDM-producing isolates.

Figure: Species and MBL distributions of *Enterobacterales* isolates



- Aztreonam-Avibactam inhibited the majority of isolates at an Aztreonam concentration of ≤1 mg/L (91.7%, n=221) (Table). Single isolates displayed higher MIC values against the Aztreonam-Avibactam combination, including NDM-producing *E. coli* (n=15) and *K. pneumoniae* (n=1), as well as NDM- or VIM-producing *E. cloacae* complex (n=2) and *C. freundii* complex (n=2).

Table: MIC distributions and MIC_{50}-/MIC_{90}-values

Substance		MIC (mg/L)												MIC_{50} (mg/L)	MIC_{90} (mg/L)	%S	%I	%R
		≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	≥64					
Aztreonam (in-house BMD)	n	**0**	8	27	15	10	5	8	5	8	9	29	*116*	32	≥64	65	13	162
	cum-%	**0.0**	3.3	14.5	20.8	25.0	27.1	30.4	32.5	35.8	39.6	51.7	*100.0*			27.1	5.4	67.5
Meropenem (in-house BMD)	n	**0**	0	0	0	0	1	3	14	22	28	50	*122*	≥64	≥64	4	36	200
	cum-%	**0.0**	0.0	0.0	0.0	0.0	0.4	1.7	7.5	16.7	28.3	49.2	*100.0*			1.7	15.0	83.3
Cefiderocol (UMIC test kit)	n	**0**	1	7	12	16	49	47	36	30	16	12	*14*	2	32	132	-	108
	cum-%	**0.0**	0.4	3.3	8.3	14.9	35.4	55.0	70.0	82.5	89.2	94.2	*100.0*			55.0	-	45.0
Aztreonam-Avibactam (Gradient test)	n	**40**	39	61	44	18	18	8	3	6	3	0	*0*	0.12	1	No EUCAST breakpoints		
	cum-%	**16.7**	32.9	58.3	76.7	84.2	91.7	95.0	96.3	98.8	100.0	100.0	*100.0*					

Numbers in bold include isolates with MIC < value shown; numbers in italic include isolates with MIC > the highest concentration tested.
Abbreviation: BMD, broth microdilution

Methods

240 isolates were collected from 16 laboratories throughout Germany. Species identification was performed by MALDI-ToF mass spectrometry (Vitek-MS, BioMérieux, Germany). MBL-groups were identified by the study sites using PCR, sequencing or lateral flow assays. MBL-production was confirmed at the reference centre by the Rapidec® Carba NP kit (BioMérieux). Antimicrobial susceptibility testing was investigated by broth microdilution (in-house plates for Aztreonam and Meropenem, as well as UMIC® Cefiderocol test kits (Bruker-Merlin, Germany)) and by agar diffusion (Aztreonam-Avibactam gradient strips; Liofilchem, Italy).

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