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Poster Session IV
Resistance surveillance in Gram-negatives

ANTIBIOTIC RESISTANCE IN A COLLECTION OF PSEUDOMONAS AERUGINOSA ISOLATED FROM CYSTIC FIBROSIS PATIENTS THROUGH EUROPE (BELGIUM, FRANCE, GERMANY AND UNITED KINGDOM).

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Objectives: *Pseudomonas aeruginosa* is the predominant microorganism causing respiratory tract infections in cystic fibrosis (CF) patients older than 25 years (CF Foundation Patient Registry report 2012, Bethesda, MD). These patients therefore require repetitive and prolonged antibiotic treatments with antipseudomonal drugs. Our aim was to determine MIC distributions and resistance rates to major antipseudomonal antibiotics against strains isolated from CF patients in 4 centres through Europe.
Methods: Bacterial strains. 342 *P. aeruginosa* strains were collected in 4 Cystic Fibrosis centers from different countries (Hôpital des enfants malades Reine Fabiola/Erasme, Belgium, n = 91; Hôpital Jean Minjoz, Besançon, France, n = 81; University Hospital of Münster, Germany, n = 71; Queen's University of Belfast, UK, n = 99).
Susceptibility testing. Minimal Inhibitory Concentrations (MIC) were measured by microdilution in cation- adjusted Mueller-Hinton broth following CLSI recommendations, with ATCC 27853 used as quality control strain. Susceptibility was assessed according to EUCAST and CLSI breakpoints. **Analysis.** Cross-resistance was assessed using *quantile density contour analysis* (QDCI; 0.1 to 0.9) using JMP software v 10.0.2.
Results: Table 1 shows that, based on EUCAST interpretative criteria, more than half of the strains was resistant to amikacin, ceftazidime**,** piperacillin-tazobactam, and ciprofloxacin; 20-25 % to tobramycin and meropenem, and only 7 % to colistin. Lower resistance rates were recorded for all drugs except ceftazidime and piperacillin-tazobactam when using CLSI interpretative criteria. Table 2 shows that cross-resistance [EUCAST] was rare with colistin, 26 % among aminoglycosides, 18-62 % among beta-lactams, and 35-44 % among drugs from different classes with high resistance rates (CIP**,** TZP, CAZ, AMK).
Conclusions: Resistance and cross-resistance rates are worryingly high in this collection, most probably related to frequent antibiotic usage in this patient population, with best options remaining tobramycin, meropenem, and colistin. High concentrations (such as those obtained by inhaled formulations) may be increasingly essential, but will still need to define appropriate pharmacodynamic targets.

Table 1: MIC distributions and susceptibility breakpoints

Antibiotic	MIC distribution (mg/L)				% Resistant Strains	
	min	max	MIC_{50}	MIC_{90}	EUCAST[a]	CLSI[b]
Amikacin [AMK]	1	>512	32	128	54	39
Tobramycin [TOB]	0.064	>512	2	16	26	15
Piperacillin-tazobactam [TZP]	0.5	>512	64	512	69	50
Ceftazidime [CAZ]	0.5	>512	32	512	64	55
Meropenem [MEM]	0.016	256	2	32	18	34
Ciprofloxacin [CIP]	0.016	64	1	8	51	26
Colistin [COL]	0.125	>512	1-2	4	7	7

[a] EUCAST breakpoints : AMK R > 16; TOB R > 4; CAZ R > 8; MEM R > 8; TZP R > 16; CIP R > 1; COL R > 4.
[b] CLSI breakpoints : AMK R ≥ 64; TOB R ≥ 16; CAZ R ≥ 32; MEM R ≥ 8 ; TZP R> 64; CIP R ≥ 4; COL R ≥ 8.

Table 2: Percentage of cross resistance among tested antibiotics (using EUCAST breakpoints)

TOB	TZP	CAZ	MEM	CIP	COL	antibiotics
26	44	42	15	35	6	AMK
	23	22	8	20	4	TOB
		62	18	40	6	TZP
			18	39	6	CAZ
				16	3	MEM
					4	CIP