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P1807 Do we have any clue of what we are doing to optimise empiric therapy? The *Pseudomonas aeruginosa* example

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Background: Inappropriate empiric therapy is a modifiable risk factor for mortality. Antimicrobial stewardship programs utilize combination antibiograms to optimize empiric therapy. Correct interpretation of combination antibiograms requires assessment of appropriate breakpoints and dose optimized regimens, neither of which is routinely considered. The purpose of this analysis was to demonstrate how these impact optimal empiric therapy selection using *P. aeruginosa* as an example.

Materials/methods: Unique *P. aeruginosa* isolated in 2017 at Michigan Medicine were included. The optimal empiric regimen was assessed by constructing a combination antibiogram to evaluate cross resistance between beta-lactams and combination agents using various breakpoints. Old (≤1 mg/L) and new (≤0.5 mg/L) CLSI breakpoints for ciprofloxacin and current CLSI (tobramycin ≤4 mg/L and amikacin ≤16 mg/L) and proposed USCAST (tobramycin ≤1 mg/L and amikacin ≤2 mg/L) breakpoints for aminoglycosides were compared. Additionally, dose optimized beta-lactam breakpoints, determined using published PK/PD data for achieving a probability of target attainment of ~90% for the 1-2 log kill targets, were assessed as monotherapy.

Results: 3836 unique *P. aeruginosa* isolates were analyzed (table). Using current breakpoints, beta-lactam + amikacin combinations appeared optimal. However, when proposed USCAST breakpoints were applied, amikacin added minimal additional coverage to beta-lactam monotherapy, and tobramycin combinations provided "optimal coverage." While dose optimization of cephalosporins and piperacillin/tazobactam did not substantially improve activity, use of extended/continuous infusion meropenem or high-dose ceftolozane/tazobactam monotherapy provided superior activity compared to all combination regimens.

Conclusions: Use of simplistic combination antibiograms alone and failure to evaluate dose optimization strategies can lead to selection of suboptimal empiric regimens.

	Mono therap y	**Tobr amycin**	**Amik acin**	**Cipr ofloxa cin**			
		Curr ent	**Prop osed**	**Curr ent**	**Prop osed**	**Old	**New
Cefe pime	82%	94%	91%	96%	85%	87%	86%
Ceft azidim e	85%	95%	94%	97%	89%	90%	89%
**Mero penem	80%	94%	90%	96%	84%	85%	83%
**Pipe racill							

racill in/taz obacta m	77%	94%	90%	96%	83%	85%	83%
	Mono therap y	**Tobr amycin**	**Amik acin**	**Cipr ofloxa cin**			
Ceft olozan e/tazo bactam **3 g q8h**	97%						
Pipe racill in/taz obacta m **4.5 g q6h (EI: 4h)** **18 g (CI)**	82%						
Mero penem **2 g q8h (EI: 3h)**	90%						
Mero penem **3 g (CI)**	90-94%						
Mero penem **6 g (CI)**	97%						
Cefe pime **2 g q8h (EI: 3-4h)	67-91%						
Cefe pime **6 g (CI)**	82-91%						
Ceft azidim e **2 g q8h** **(EI: 2h)**	85-89%						
Ceft azidim e	89%						

6 g (CI)	89% Mono therap y	Tobr amycin	Amik acin	Cipr ofloxa			