1580. Colistin Potentiates the *In Vitro* Activity of Meropenem–Vaborbactam (M/V) Against Some, but not All KPC-producing *Klebsiella pneumoniae* (KPC-Kp)

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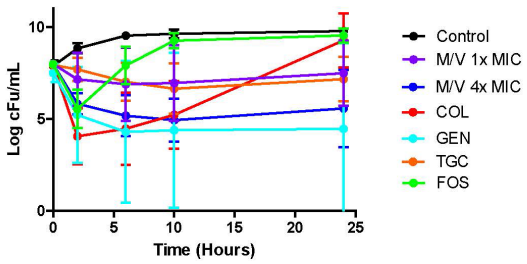
Background. M/V demonstrates potent *in vitro* activity against KPC-producing organisms. It is unclear whether the combination interacts synergistically with other active agents.

Methods. We tested isolates for responses to M/V alone (1 and 4x MIC; V fixed at 8 µg/mL), and in combination with colistin (COL; 2 µg/mL), fosfomycin (FOS; 100 µg/mL + 25 µg/mL G6P), gentamicin (GEN; 2 µg/mL), and tigecycline (TGC; 2 µg/mL) by time-kill using a starting inoculum of 1×10^8 cFu/mL. 24h was the primary endpoint.

Results. 16 KPC-Kp isolates were studied (7 KPC-2 and 9 KPC-3); all were M/V-susceptible (MIC range: 0.015 – 4 µg/mL). 44% harbored *ompK36* mutations (4 IS*5* promoter insertion, 2 134–135 DG duplication, and 1 premature stop codon). Median M/V MICs were higher against isolates with mutant *ompK36* (0.25 vs. 0.03; $P = 0.002$). Mean log-kills by M/V at 1x and 4x were -0.50 and -2.41, respectively; M/V was bactericidal (≥3-log kill) against 6% and 56%, respectively (Figure 1). Mean log-kills at 4× were greater against KPC-2 (-3.79) than KPC-3 (−1.33) isolates ($P = 0.09$), and among isolates with (−3.31) vs. without (−1.71) *ompK36* mutations ($P = 0.11$). GEN was the most active single agent (bactericidal against 56%, mean log-kill = −3.04). In combo with M/V, rates of synergy (>2-log kill in combo) with COL, FOS, GEN, and TGC were 44%, 19%, 12.5%, and 12.5%, respectively (Figure 2). Corresponding rates of bactericidal activity were 44%, 25%, 69%, and 31%, respectively. Antagonism (> 1-log kill by most active single agent) was identified for each combo against 2 isolates. Mean log-kills by M/V + GEN were greater against isolates with GEN MICs ≤1 (−7.16) vs. ≥2 (−1.66; $P = 0.001$), reflecting the activity of GEN alone. Mean log-kills by M/V + COL were greater against isolates with IS*5* insertions (-6.32) compared with wild type (−2.38) or other mutations (−1.77) in *ompK36*. Responses to M/V + FOS were not dependent upon FOS MIC, but log-kills were greater against mutant (-2.13) vs. wild-type (0.01) *ompK36* ($P = 0.03$).

Conclusion. M/V + GEN is rapidly cidal if GEN MICs are ≤1, while M/V + COL resulted in highest rates of synergy against diverse KPC-Kp. Mean log-kills were highest among isolates with IS*5* promoter insertions suggesting a potential role for COL combination therapy against KPC-Kp isolates with decreased outer membrane permeability.

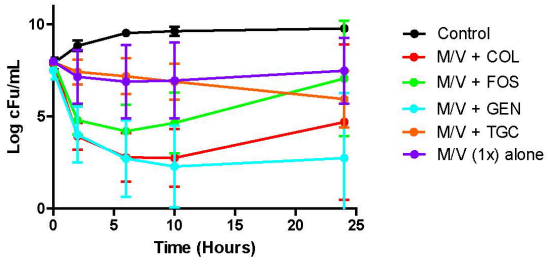
Figure 1. Mean log-kills by each agent alone against KPC-Kp (n=16)



COL = Colistin 2 µg/mL; FOS = Fosfomycin 100 µg/mL + 25 µg/mL G6P; GEN = Gentamicin 2 µg/mL; M/V = Meropenem-vaborbactam (vaborbactam fixed at 8 µg/mL); TGC = Tigecycline 2 µg/mL

Note. Error bars show the standard deviation of log-kills at each time point.

Figure 2. Mean log-kills by each M/V combination regimen against KPC-Kp (n=16)



COL = Colistin 2 µg/mL; FOS = Fosfomycin 100 µg/mL + 25 µg/mL G6P; GEN = Gentamicin 2 µg/mL; M/V = Meropenem-vaborbactam (vaborbactam fixed at 8 µg/mL); TGC = Tigecycline 2 µg/mL

Note. Error bars show the standard deviation of log-kills at each time point.

Disclosures. **All authors:** No reported disclosures.

1581. Comparative *In Vitro* Activity of Ceftolozane/tazobactam and Comparator Agents Against *Enterobacteriaceae* and *Pseudomonas Aeruginosa* Clinical Isolates in Colombia

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Background. Multidrug-resistant Enterobacteriaceae (Ent) and Pseudomonas aeruginosa (Pae) are involved in a considerable number of healthcare-associated infections, thus representing a therapeutic challenge. Ceftolozane–tazobactam (C/T) is a combination of a novel cephalosporin with a known β-lactamase inhibitor. Ceftolozane has high affinity for penicillin-binding proteins, improved outer membrane permeability, increased stability against efflux and enhanced stability against chromosomal AmpC β-lactamases compared with other β-lactam antibiotics. This agent is not active against carbapenemases. We evaluated the in vitro activity of C/T against clinical isolates of Ent and Pae collected from 2016- 2017 and compared it to the activity of broad-spectrum antimicrobial agents.

Methods. 1.644 Ent and Pae non-duplicate clinical isolates were collected in 13 medical centers located in 12 Colombian cities. Minimum inhibitory concentrations (MIC) were performed by broth microdilution and interpreted according to current CLSI guidelines. Isolates tested included 813 *Escherichia coli* (Eco), 441 *Klebsiella pneumoniae* (Kpn), 82 *Enterobacter* spp., (Enb); 60 *Serratia marcescens* (Sma) and 248 Pae. Comparator agents were ceftriaxone (CRO), cefotaxime (CTX), ceftazidime (CAZ), cefepime (FEP), piperacillin/tazobactam (TZP), ertapenem (ETP), imipenem (IMI), meropenem (MEM).

Results. Susceptibilities to C/T and comparators of 4 Ent species and Pae are shown in Table 1. Compared with other β-lactams such as CRO, CAZ, TZP, and FEP, C/T had considerably higher susceptibility rates against ESBL, non-carbapenem-resistant (CR) Eco and Kpn isolates. C/T MIC50/90 were: Eco (≤1/≤1); Kpn (≤1/128); Enb (≤1/64); Sma (≤1/≥256); Pae (≤1/≥256). In the case of P.aeruginosa despite the high resistance rates observed in the study, C/T had the best susceptibility, even higher than the carbapenems.

Conclusion. Overall, C/T demonstrated higher in vitro activity than currently available cephalosporins and TZP when tested against Ent and Pae. C/T provides an important treatment option against infections caused by non-carbapenemase producing Gram-negative pathogens. Further studies are warranted to identify an emerging mechanism of resistance in Colombia.

Table 1. Susceptibility rates of C/T and comparators agents against 1644 *Enterobacteriacea* and *P. aeruginosa* clinical isolates from Colombia [a]

Organisms	C/T%S	CRO%S	CTX%S	CAZ%S	TZP%S	FEP%S	ETP%S	IMI%S	MEM%S
Eco (813)	94	72	72	79	84	82	91	95	95
Eco ESBL-non-CR (156)	97	0	2	33	42	92	100	100	100
Kpn (441)	70	50	51	52	62	57	69	74	76
Kpn ESBL-non-CR (83)	82	0	6	20	25	54	100	98	100
Sma (60)	68	-	-	62	63	63	70	67	73
Sma ETP *susceptible* (39)	92	-	-	92	95	87	100	92	100
Ent (82)	60	-	-	48	48	57	59	70	74
Ent ETP-*susceptible* (48)	88	-	-	73	73	83	100	100	100
Pae (248)	66	-	-	55	59	57	-	30	47
Pae MEM-*susceptible* (117)	97	-	-	86	88	91	-	63	100
Pae MEM-*non-susceptible* (131)	39	-	-	27	29	30	-	1	0

[a] ESBL phenotype defined as a MIC at ≥ 2 mg/L for ceftriaxone

Disclosures. **All authors:** No reported disclosures.

1582. Delafloxacin Activity Against Drug-Resistant *Streptococcus pneumoniae*, *Haemophilus influenzae*, Haemophilus parainfluenzae, and *Moraxella catarrhalis* from US Medical Centers (2014–2018)

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Background. Delafloxacin (DLX) is an anionic fluoroquinolone (FQ) antimicrobial that was approved in 2017 by the United States (US) Food and Drug Administration for the treatment of acute bacterial skin and skin structure infections. DLX recently successfully completed a clinical trial for the treatment of community-acquired bacterial pneumonia (CABP). In the present study, *in vitro* susceptibility (S) results for DLX and comparator agents were determined for CABP pathogens including *Streptococcus pneumoniae* (SPN), *Haemophilus influenzae* (HI), *H. parainfluenzae* (HP) and *Moraxella catarrhalis (*MC) clinical isolates from US hospitals participating in the SENTRY Program during 2014–2018.

Methods. A total of 1,975 SPN, 1,128 HI, 684 MC, and 43 HP isolates were collected from community-acquired respiratory tract infections (CARTI) during 2014–2018 from US hospitals. Sites included only 1 isolate/patient/infection episode. Isolate