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Abstract (poster session)

Antimicrobial spectrum and potency of ceftaroline/avibactam when tested against bacterial isolates from complicated urinary tract infections in the United States

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Objective: To evaluate the activity of ceftaroline (CPT) combined with avibactam (CPA; avibactam at fixed 4 mg/L) against isolates from complicated urinary tract infections (cUTI) collected in USA medical centres. CPT is a broad-spectrum cephalosporin and avibactam is a novel non-beta-lactam beta-lactamase (BL) inhibitor that inhibits Ambler class A, C, and some D enzymes. Methods: CPA and comparators were tested for susceptibility (S) by CLSI broth microdilution methods against 1131 strains, including Escherichia coli (348; 8.0% ESBL-phenotype), Klebsiella spp. (326; 7.7% ESBL-phenotype and 1.5% meropenem-resistant [R]), group B streptococci (GBS; 176), Enterococcus faecalis (78), coagulase-negative staphylococci (CoNS; 77; 57.1% oxacillin-R), Proteus mirabilis (61) and Morganella morganii (34). Non-fermentative bacilli were not included. Isolates were collected in 2009-2010 from 65 medical centres located in all nine USA Census Regions. Results: Overall, 98.4% of strains were inhibited at <=2 mg/L of CPA and all 18 isolates with CPA MIC at >=4 (4-16) mg/L were E. faecalis (Table). E. coli and Klebsiella spp. were very S to CPA with MIC50/90 of <=0.03/0.06 and 0.06/0.12 mg/L, respectively. Ceftriaxone and ciprofloxacin were active against 92.0% and 73.9% of E. coli and 92.3% and 94.2% of Klebsiella spp., respectively; and 1.5% of Klebsiella spp. were R to meropenem. Among P. mirabilis and M. morganii, the highest CPA MIC values were only 0.5 and 0.25 mg/L, and R rates to ciprofloxacin were 29.5% and 35.3%, respectively. The highest CPA MIC value among Enterobacter spp. was only 0.5 mg/L (MIC50/90, 0.06/0.5 mg/L). All GBS were inhibited at CPA MIC of <=0.06 mg/L. CPA showed activity against E. faecalis (MIC50/90, 2/8 mg/L) and was very active against CoNS (MIC50/90, 0.25/0.5 mg/L; 57.1% oxacillin-R). Conclusions: CPA exhibited potent activity against a large collection of Enterobacteriaceae and Gram-positive organisms from patients with cUTI. Avibactam can effectively lower CPT MIC values for Enterobacteriaceae that produced the most clinically significant BLs occurring in USA hospitals.

Organism	No. of isolates (cumulative %) inhibited at CPA MIC (mg/L) of [a]:										
(no. tested)	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	MIC_{50}	MIC_{90}
E. coli (348)	205 (58.9)	1115 (92.0)	24 (98.9)	3 (99.7)	1 (100.0)	-	-	-	-	≤0.03	0.06
Klebsiella spp. (326)	72 (22.1)	173 (75.2)	50 (90.5)	22 (97.2)	7 (99.4)	2 (100.0)	-	-	-	0.06	0.12
P. mirabilis (61)	2 (3.3)	16 (29.5)	34 (85.3)	7 (96.7)	2 (100.0)	-	-	-	-	0.12	0.25
M. morganii (34)	12 (35.3)	15 (79.4)	5 (94.1)	2 (100.0)	-	-	-	-	-	0.06	0.12
Group B strep. (176)	174 (98.9)	2 (100.0)	-	-	-	-	-	-	-	≤0.03	≤0.03
E. faecalis (78)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)	10 (14.1)	49 (76.9)	8 (87.2)	5 (93.6)	2	8
CoNS (77)	2 (2.6)	15 (22.1)	21 (49.4)	21 (76.6)	15 (96.1)	2 (98.7)	1 (100.0)	-	-	0.25	0.5

[a] Concentrations reported in the table for ceftaroline/avibactam (CPA) refer to the concentration of ceftaroline tested with fixed 4-mg/L avibactam concentration.