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Abstract (poster session)

Activity of ceftaroline/avibactam tested against multidrug-resistant Enterobacteriaceae and methicillin-resistant Staphylococcus aureus collected from USA hospitals in 2011

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Objective: To evaluate the activity of ceftaroline (CPT) combined with avibactam (formerly NXL-104) tested against resistant subsets of Enterobacteriaceae (ENT) and MRSA strains. CPT is a broad-spectrum cephalosporin with activity against Gram-negative and -positive (including MRSA and multidrug-resistant [R] S. pneumoniae) organisms. Avibactam is a novel non-beta lactam beta-lactamase (BL) inhibitor that inhibits Ambler class A, C, and D enzymes (eg, ESBL, KPC, and AmpC). Methods: CPT/avibactam (CPA; avibactam at fixed 4 mg/L) and various comparators were tested for susceptibility (S) by CLSI broth microdilution methods against 1502 ENT, including ESBL-phenotype E. coli (43) and Klebsiella spp. (KSP; 67), AmpC derepressed Enterobacter spp. (ESP; 60), carbapenem (CB)-non-S (most were KPC-producing) KSP (13) and ESP (2), ciprofloxacin-R ENT (224) and gentamicin-R ENT (120), among other R phenotypes. 1496 S. aureus, including 738 MRSA strains were also tested. The strains were consecutively collected in 2011 from 52 medical centres located in the 9 USA Census Regions. Results: 99.6% of ENT and 99.1% of MRSA strains were inhibited at CPA MIC of <=1 mg/L (see Table). Highest CPA MIC was only 4 mg/L (1 S. marcescens strain; 0.06% of ENT). The most active compounds tested against the ESBL-phenotype and CB-non-S KSP were CPA (95.5% and 76.9% inhibited at <=0.5 mg/L [USA-FDA S breakpoint for CPT], respectively), tigecycline (95.5/85.1% and 100.0/92.3% S by CLSI/EUCAST criteria, respectively) and gentamicin (65.7/61.2% and 69.2/69.2% S by CLSI/EUCAST criteria, respectively). All MRSA strains were inhibited at <=2 mg/L of CPA, and CPT MIC results were not affected by the addition of avibactam. Against methicillin-S S. aureus, CPA inhibited all at MIC <=0.5 mg/L and was 16-fold more active than ceftriaxone. Conclusions: Avibactam can effectively lower CPT MIC values for ENT strains producing the most clinically significant BLs found in USA hospitals. CPA was highly active against ENT-producing KPC, various ESBL types, and AmpC (chromosomally derepressed or plasmid mediated), and MRSA. CPA represents a promising therapeutic option for treatment of infections caused by multidrug-R ENT and MRSA.

	No. of isolates (cumulative %) inhibited at ceftaroline/avibactam MIC (mg/L) of:							
Organism (no. tested)	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**
Citrobacter spp. (100)	29 (29.0)	46 (75.0)	20 (95.0)	3 (98.0)	1 (99.0)	1 (100.0)	-	-
Ceftazidime-R (11)	0 (0.0)	3 (27.3)	7 (90.9)	1 (100.0)	-	-	-	-
Enterobacter spp. (337)	56 (16.6)	117 (51.3)	91 (78.3)	49 (92.9)	15 (97.3)	6 (99.1)	3 (100.0)	-
Ceftazidime-R (60)	1 (1.7)	11 (20.0)	8 (33.3)	21 (68.3)	10 (85.0)	6 (95.0)	3 (100.0)	-
Meropenem-non-S (2)			1 (50.0)	0 (50.0)	0 (50.0)	0 (50.0)	1 (100.0)	-
E. coli (435)	356 (81.8)	65 (96.8)	11 (99.3)	3 (100.0)	-	-	-	-
ESBL-phenotype (43)	25 (58.1)	8 (76.7)	7 (96.0)	3 (100.0)	-	-	-	-
Klebsiella spp. (539)	218 (40.5)	209 (79.2)	72 (92.6)	29 (98.0)	8 (99.4)	2 (99.8)	1 (100.0)	-
ESBL-phenotype (67)	12 (17.9)	15 (40.3)	19 (68.7)	13 (88.1)	5 (95.5)	2 (98.5)	1 (100.0)	-
Meropenem-non-S (13)	0 (0.0)	1 (7.7)	2 (23.1)	6 (69.2)	1 (76.9)	2 (92.3)	1 (100.0)	-
Indole-positive *Proteae* (91)	58 (63.7)	24 (90.1)	8 (98.9)	1 (100.0)	-	-	-	-
S. marcescens (148)	0 (0.0)	1 (0.7)	14 (10.1)	57 (48.7)	60 (89.2)	13 (98.0)	1 (98.7)	1 (100.0)
S. aureus (1496)	1 (0.1)	6 (0.5)	182 (12.6)	601 (52.8)	551 (89.6)	148 (99.5)	7 (100.0)	-
MRSA (738)	1 (0.1)	0 (0.1)	2 (0.4)	40 (5.4)	543 (79.0)	148 (99.1)	7 (100.0)	-