

P1620

Abstract (poster session)

**Antimicrobial activity of ceftaroline combined with avibactam tested against contemporary (2012) bacteria collected from USA patients with acute bacterial skin and skin structure infections (ABSSSI)**

H.S. Sader\*, R.K. Flamm, R.N. Jones (North Liberty, US)

**Objective:** To evaluate the activity of ceftaroline (CPT)-avibactam (AVI) tested against bacteria from ABSSSI collected in USA hospitals in 2012. CPT fosamil is a novel parenteral cephalosporin approved by the European Medicines Agency and USA Food and Drug Administration for treatment of complicated skin and soft tissue infections and ABSSSI, respectively, including those caused by MRSA. AVI is a novel non-beta-lactam beta-lactamase inhibitor of Ambler class A, C, and some D enzymes. **Methods:** 5140 isolates were consecutively collected in 2012 from 90 USA medical centres. Susceptibility (S) testing for CPT-AVI (AVI at fixed 4 mg/L), CPT alone and comparators was performed by CLSI broth microdilution methods. S interpretations were per EUCAST and CLSI breakpoints. **Results:** The most common organisms were *S. aureus* (SA; 3481; 50.5% MRSA), *E. coli* (EC; 444; 13.3% ESBL-phenotype), beta-haemolytic streptococci (BHS; 389) and *Klebsiella* spp. (KSP; 338, 13.3% ESBL-phenotype and 5.3% meropenem [MER]-non-S). All EC, including ESBL-phenotype strains, were inhibited at CPT-AVI MIC values of only  $\leq 0.5$  mg/L (EUCAST and CLSI S breakpoint for CPT), and 99.3% of EC had CPT-AVI MIC  $\leq 0.12$  mg/L. CPT-AVI was also active against KSP (MIC<sub>90</sub>, 0.25 mg/L), including ESBL-phenotype (MIC<sub>90</sub>, 0.5 mg/L) and MER-non-S strains (MIC<sub>90</sub>, 0.5 mg/L), and *Enterobacter* spp. (MIC<sub>90</sub>, 0.25 mg/L), including ceftazidime (CAZ)-resistant (R) strains (MIC<sub>90</sub>, 1 mg/L). Only 2 *Enterobacteriaceae* (0.2%) had CPT-AVI MIC at  $>1$  mg/L, one *K. pneumoniae* and one *S. marcescens*, both with CPT-AVI MIC of 4 mg/L (Table). All oxacillin-S (MSSA) and -R SA (MRSA) strains were inhibited at  $\leq 0.5$  and  $\leq 2$  mg/L of CPT-AVI respectively; and CPT MIC results were not adversely affected by the addition of AVI. CPT-AVI was 16-fold more active than ceftriaxone against MSSA. BHS, viridans group streptococci and coagulase-negative staphylococci were CPT-AVI-S with MIC<sub>90</sub> values of  $\leq 0.015$ , 0.03 and 0.5 mg/L, respectively. **Conclusions:** CPT-AVI and CPT were the most potent beta-lactam agents tested against staphylococci and streptococci collected from patients with ABSSSI in USA hospitals in 2012. MRSA was particularly S to CPT-AVI and CPT (MIC<sub>50/90</sub>, 0.5/1 mg/L). CPT-AVI was also highly active against *Enterobacteriaceae*-producing KPC serine carbapenemase, various ESBL types, and AmpC (chromosomal or plasmid-mediated) enzymes. CPT-AVI demonstrated potent in vitro efficacy against resistant pathogens associated with ABSSSI in the USA.

cumulative % inhibited at CPT-AVI MIC (mg/L) of:

Organism (no. tested)	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4
<i>E. coli</i> (444)	26.1	74.8	98.0	99.3	99.8	100.0	-	-	-
Non-ESBL (385)	28.6	79.2	99.5	100.0	-	-	-	-	-
ESBL (59)	10.2	45.8	88.1	94.9	98.3	100.0	-	-	-
<i>Klebsiella</i> spp. (338)	1.8	32.3	77.5	88.8	96.5	99.7	99.7	99.7	100.0
non-ESBL (293)	2.1	35.9	85.0	93.9	99.0	100.0	-	-	-
ESBL (45)	-	8.9	28.9	55.6	80.0	97.8	97.8	97.8	100.0
MER-non-S (18)	-	-	-	22.2	66.7	94.4	94.4	94.4	100.0
<i>Enterobacter</i> spp. (102)	3.8	10.8	36.3	75.5	90.2	98.0	100.0	-	-
Ceftazidime-S (85)	4.7	12.9	43.5	87.1	98.8	100.0	-	-	-
Ceftazidime-R (17)	-	-	-	5.9	47.1	88.2	100.0	-	-
<i>Citrobacter</i> spp. (77)	2.6	19.5	74.0	94.8	98.7	100.0	-	-	-
<i>M. morgani</i> (27)	11.1	48.2	70.4	88.9	92.6	96.3	100.0	-	-
<i>S. marcescens</i> (51)	-	-	-	7.8	19.6	70.6	98.0	98.0	100.0
<i>S. aureus</i> (3481)	-	<0.1	0.5	7.4	49.0	90.2	99.5	100.0	-
MSSA (1723)	-	<0.1	0.9	14.9	96.8	100.0	-	-	-
MRSA (1758)	-	-	-	-	2.2	80.5	98.9	100.0	-
β-haemolytic strep. (389)	96.1	99.7	100.0	-	-	-	-	-	-
CoNS (185)	1.1	8.7	31.9	42.2	89.2	100.0	-	-	-
Viridans group strep. (46)	37.0	93.5	100.0	-	-	-	-	-	-