P1446

Abstract (poster session)

Activity of the novel antimicrobial ceftolozane/tazobactam (CXA-201) tested against contemporary clinical strains from European hospitals

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Objective: To evaluate the in vitro activity of ceftolozane/tazobactam (CXA-201) against Gram-negative organisms isolated from patients in European (EU) hospitals in 2011. CXA-201 is a combination of the novel oxyimino-aminothiazolyl cephalosporin ceftolozane and tazobactam (TAZ), and is currently under clinical development for treatment of complicated intraabominal (cIAI) and urinary tract infections (cUTI). Methods: CXA-201 and comparators were susceptibility (S) tested by CLSI broth microdilution methods against 3210 clinical strains, which included 519 P. aeruginosa (PSA; 25.8% ceftazidime [CAZ]-non-S and 28.5% meropenem [MER]-non-S), 1174 E. coli (17.2% ESBL-phenotype), 485 Klebsiella spp. (33.4% ESBL-phenotype and 3.3% MER-non-S), and 239 Enterobacter spp. (26.8% ceftriaxone-non-S), among others. Results: When tested against PSA, CXA-201 was at least 4-fold more active than CAZ or cefepime and inhibited 76.4% of MER-non-S strains at MIC of <=4 mg/L. CXA-201 exhibited activity against PSA CAZ-non-S (MIC50/90, 4/>32 mg/L), MER-non-S (MIC50/90, 2/>32 mg/L) and both CAZ and MER-non-S strains (MIC50/90, 4/>32 mg/L). Piperacillin/TAZ (P/T; MIC50/90, 8/>64 mg/L) was active against 68.4% of PSA at S breakpoint of <=16 mg/L. CXA-201 activity against ESBL-negative E. coli and Klebsiella spp. was similar to that of CAZ, in contrast, CXA-201 was 16- to 32-fold more active than CAZ when tested against ESBL producers. Against Enterobacter spp. and Citrobacter spp., CXA-201 was slightly more active than CAZ (Table). Conclusions: CXA-201 demonstrated higher activity than currently available anti-PSA cephalosporins (CAZ and CPM) and P/T when tested against PSA and Enterobacteriaceae strains from EU hospitals and may represent a valuable treatment option for Gram-negative infections, including those caused by resistant organisms causing cIAI, cUTI and HABP.

Table. Activity of ceftolozane/tazobactam tested against Gram-negative organisms from European hospitals

	no. of isolates (cumulative %) inhibited at ceftolozane/tazobactam MIC (mg/L) of:								
Organism (no. tested)	≤0.12	0.25	0.5	1	2	4	8	16	32
P. aeruginosa (519)	0(0.0)	10(1.9)	201(40.7)	191(77.5)	36(84.4)	41(92.3)	10(94.2)	1(94.4)	4(95.2)
Ceftazidime-S (385)	0(0.0)	10(2.6)	200(54.5)	165(97.4)	10(100.0)	-	-	-	-
CAZ-non-S (134)	0(0.0)	0(0.0)	1(0.7)	26(20.1)	26(39.6)	41(70.1)	10(77.6)	1(78.4)	4(81.3)
MER-S (371)	0(0.0)	10(2.7)	181(51.5)	143(90.0)	19(95.2)	13(98.7)	5(100.0)	-	-
MER-non-S (148)	0(0.0)	0(0.0)	20(13.5)	48(46.0)	17(57.4)	28(76.4)	5(79.7)	1(80.4)	4(83.1)
CAZ & MER-non-S (80)	0(0.0)	0(0.0)	0(0.0)	7(8.8)	10(21.3)	28(56.3)	5(62.5)	1(63.8)	4(68.8)
E. coli (1174)	493(42.0)	469(81.9)	125(92.6)	48(96.7)	16(98.0)	11(99.0)	4(99.3)	2(99.5)	3(99.7)
ESBL phenotype (202)	9(4.5)	43(25.7)	68(59.4)	44(81.2)	15(88.6)	11(94.1)	4(96.0)	2(97.0)	3(98.5)
ESBL negative (972)	484(49.8)	426(93.6)	57(99.5)	4(99.9)	1(100.0)	-	-	-	-
Klebsiella spp. (485)	104(21.4)	159(54.2)	77(70.1)	53(81.0)	22(85.6)	21(89.9)	10(92.0)	6(93.2)	9(95.1)
ESBL phenotype (162)	5(3.1)	6(6.8)	24(21.6)	36(43.8)	21(56.8)	21(69.8)	10(75.9)	6(79.6)	9(85.2)
ESBL negative (323)	99(30.7)	153(78.0)	53(94.4)	17(99.7)	1(100.0)	-	-	-	-
Enterobacter spp. (239)	26(10.9)	100(52.7)	48(72.8)	14(78.7)	16(85.4)	12(90.4)	9(94.1)	4(95.8)	4(97.5)
Citrobacter spp. (101)	18(17.8)	49(66.3)	9(75.2)	9(84.2)	1(85.1)	3(88.1)	3(91.1)	7(98.0)	1(99.0)
Indole-pos. Proteae (109)	19(17.4)	43(56.9)	37(90.8)	8(98.2)	2(100.0)	-	-	-	-
P. mirabilis (142)	3(2.1)	40(30.3)	79(85.9)	10(93.0)	4(95.8)	2(97.2)	2(98.6)	2(100.0)	-