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Abstract (oral session)

Antimicrobial activity of ceftolozane/tazobactam tested against Gram-negative bacterial isolates from hospitalised patients with pneumonia in European hospitals (2011)

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Objective: To evaluate the in vitro activity of ceftolozane/tazobactam (TOL/TAZ; formerly CXA-201) tested against Gram-negative organisms causing pneumonia in European hospitals. TOL (formerly CXA-101) is a novel oxyimino-aminothiazolyl cephalosporin with potent anti-P. aeruginosa (PSA) activity. TOL/TAZ is currently under clinical development for treatment of ventilator associated bacterial pneumonia, as well as intra-abdominal and urinary tract infections. Methods: 1124 isolates were consecutively collected in 27 hospitals from 11 countries of the European Union (EU; including Belgium, France, Germany, Greece, Ireland, Italy, Poland, Portugal, Spain, Sweden and UK) and Israel. All isolates were collected in 2011 from patients with pneumonia. Susceptibility (S) testing was performed following CLSI broth microdilution method recommendations and MIC interpretations for comparator agents were as published by EUCAST and CLSI. TOL/TAZ was tested at a fixed 4 mg/L concentrations of TAZ. Results: PSA exhibited modest S to meropenem (MER, 67.8%), cefepime (CPM, 75.8%), ceftazidime (CAZ; 70.3%), piperacillin/TAZ (P/T; 65.8%), ciprofloxacin (CIP; 63.1%) and amikacin (82.8%). TOL/TAZ was the most active beta-lactam tested against PSA and inhibited 88.1 and 85.6% of isolates at <=8 and <=4 mg/L, respectively. TOL/TAZ exhibited activity against CAZ-non-S and MER-non-S PSA isolates. All beta-lactams showed limited activity against Acinetobacter spp. TOL/TAZ was very active against E. coli, including ESBL-phenotype isolates (highest MIC, 8 mg/L). Against non-ESBL-phenotype Klebsiella spp., TOL/TAZ (MIC50/90, 0.25/0.5 mg/L) activity was similar to that of CAZ (MIC50/90, 0.12/0.5 mg/L) while ESBL-phenotype Klebsiella spp. exhibited lower S to all beta-lactams, including MER (81.6% S), as well as CIP (20.7% S) and gentamicin (57.5% S). TOL/TAZ showed greater activity than CAZ and P/T when tested against Citrobacter spp. and Enterobacter spp., and showed activity against CAZ-non-S Enterobacter spp. (Table). Conclusion: TOL/TAZ demonstrated greater in vitro activity than several currently available anti-PSA cephalosporins (CAZ and CPM) and P/T, when tested against PSA and Enterobacteriaceae isolates causing pneumonia in European hospitals (2011).

Organism (no. tested)	$MIC_{50}/MIC_{90}/\%S^a$			
	TOL/TAZ	CAZ	P/T	MER
P. aeruginosa (360)	1/>32/88.1[b]	4/>32/70.3	8/>64/65.8	1/>8/67.8
CAZ-non-S (MIC ≥16 mg/L; 107)	4/>32/60.8[b]	32/>32/0.0	>64/>64/6.5	8/>8/33.6
MER-non-S (MIC ≥4 mg/L; 116)	2/>32/68.1[b]	16/>32/38.8	64/>64/28.5	8/>8/0.0
Acinetobacter spp. (98)	16/>32/38.8[b]	>32/>32/-	>64/>64/-	>8/>8/28.5
E.coli (254)	0.25/0.5/100.0[b]	0.25/8/85.0	2/32/84.7	≤0.06/≤0.06/100.0
ESBL-phenotype (41)	0.5/2/100.0[b]	16/>32/7.3	4/>64/65.9	≤0.06/≤0.06/100.0
Klebsiella spp. (188)	0.5/>32/85.1[b]	0.5/>32/59.6	8/>64/53.7	≤0.06/0.5/91.5
ESBL-phenotype (87)	4/>32/67.8[b]	32/>32/12.6	>64/>64/9.2	≤0.06/>8/81.6
Enterobacter spp. (97)	0.25/8/92.8[b]	0.25/>32/66.0	4/64/71.1	≤0.06/≤0.06/100.0
CAZ-non-S (MIC ≥8 mg/L; 28)	4/32/75.0[b]	32/>32/0.0	64/>64/7.1	≤0.06/0.12/96.4
Serratia spp. (68)	0.5/1/100.0[b]	0.25/0.5/95.6	2/8/94.1	≤0.06/0.12/100.0
P. mirabilis (35)	0.5/1/94.3[b]	0.06/0.06/94.3	≤0.5/1/100.0	≤0.06/0.12/100.0
Citrobacter spp. (24)	0.25/4/95.8[b]	0.12/32/79.2	2/32/79.2	≤0.06/≤0.06/100.0

a. EUCAST interpretative criteria for CAZ, P/T and MER. b. % inhibited at ≤8 mg/L of TOL/TAZ.