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Paper Poster Session
Cefepime-tazobactam

WCK4282 (high-dose cefepime-tazobactam) antimicrobial activity against Gram-negative organisms from United States (USA) and Latin American medical centres (2014)

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Background: WCK4282 (cefepime-tazobactam) is currently under clinical development at 2g/2g q8 as well as q12 hours dosage. We evaluated the in vitro activity of FEP/TAZ8 against clinical bacteria.

Material/methods: 3,008 isolates from USA and 647 from 4 Latin American (LA) countries (Argentina, Brazil, Chile, Mexico) were collected in 2014 by the SENTRY Antimicrobial Surveillance Program and susceptibility tested by a reference broth microdilution method against cefepime-tazobactam (tazobactam at fixed 8 mg/L) and comparator agents.

Results: Isolates were mainly from pneumonia (26.8%), urinary tract infection (23.8%) and bacteremia (21.2%). Cefepime-tazobactam and cefepime inhibited (USA/LA) 98.3/94.4% and 94.7/72.5% of Enterobacteriaceae strains at ≤8 mg/L (high dose, CLSI; Table), and 97.6/91.4% and 92.2/64.8% at ≤2 mg/L (low dose), respectively. Cefepime-tazobactam activity against Enterobacteriaceae was comparable to that of meropenem (97.9/94.8% susceptible in USA/LA) and greater than that of piperacillin-tazobactam (92.0/82.6% susceptible [CLSI] in USA/LA). Except *Klebsiella* spp. (KSP), all Enterobacteriaceae species from USA had ≥98.9% of isolates inhibited at ≤8 mg/L of cefepime-tazobactam. Extended-spectrum β-lactamase (ESBL)-phenotype rates among *E. coli* and KSP were higher in LA (37.4 and 53.9%, respectively) compared to USA (14.4 and 15.6%, respectively). Cefepime-tazobactam inhibited 99.0-100.0% of ESBL-phenotype *E. coli* at ≤8 mg/L; and retained activity against some ESBL-phenotype KSP (72.2-73.8% inhibited at ≤8 mg/L). Meropenem (67.6-73.3% susceptible) also showed more limited activity against ESBL-phenotype KSP. Cefepime-tazobactam inhibited 99.2/98.2% of *Enterobacter* spp. from USA/LA at ≤8 mg/L; and retained activity against most ceftazidime-non-susceptible *Enterobacter* spp. (96.2/95.5% from USA/LA inhibited at ≤8 mg/L). Cefepime-tazobactam, cefepime, piperacillin-tazobactam and meropenem exhibited similar activity against *P. aeruginosa* from USA (84.4-86.2% susceptible) and LA (75.2-79.8% susceptible). *Acinetobacter* spp. exhibited low susceptibility rates for all β-lactams.

Conclusions: Resistance rates were higher among isolates from LA compared to USA. Cefepime-tazobactam was highly active against Enterobacteriaceae, including ESBL-phenotype *E. coli* and ceftazidime-non-susceptible *Enterobacter* spp. and *P. aeruginosa*. These in vitro results support the further clinical development of WCK 4282.

Organism (n)	MIC_{50}/MIC_{90} (% susceptible[a])			
	Cefepime-tazobactam	**Cefepime**	**Piperacillin-tazobactam**	**Meropenem**
Enterobacteriaceae				
USA (2,466)	≤0.03/0.25 (98.3)[b]	0.06/1 (92.2)	2/16 (92.0)	0.03/0.06 (97.9)
LA (466)	0.06/1 (94.4)[b]	0.06/64 (64.8)	4/>64 (82.6)	0.03/0.06 (94.8)
E. coli				
USA (720)	≤0.03/0.12 (99.9)[b]	0.06/2 (90.6)	2/8 (95.0)	≤0.015/0.03 (100.0)
LA (179)	0.06/0.25 (100.0)[b]	0.06/>64 (65.9)	2/16 (94.4)	≤0.015/0.03 (100.0)
Klebsiella spp.				
USA (932)	≤0.03/0.25 (95.9)[b]	≤0.03/4 (88.9)	2/32 (89.6)	0.03/0.03 (95.0)
LA (167)	0.06/64 (85.0)[b]	4/>64 (49.7)	8/>64 (64.7)	0.03/8 (85.6)
Enterobacter spp.				
USA (239)	0.06/0.5 (99.2)[b]	0.06/2 (94.6)	2/64 (82.8)	0.03/0.06 (98.7)
LA (56)	0.06/1 (98.2)[b]	0.06/16 (78.6)	4/64 (78.6)	0.03/0.06 (100.0)
P. aeruginosa				
USA (390)	2/16 (85.9)[b]	2/16 (84.4)	4/32 (86.2)	0.5/4 (85.6)
LA (109)	4/32 (79.8)[b]	4/32 (77.1)	4/>64 (76.1)	0.5/16 (75.2)

a. According to CLSI breakpoints. b. % inhibited at ≤8 mg/L (high dose, CLSI).