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Paper Poster Session
Cefepime-tazobactam

Antimicrobial activity of WCK 4282 (high-dose cefepime-tazobactam) tested against Gram-negative organisms from medical centres located in Europe and the Asia-Pacific region

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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 spectrum of activity of WCK 4282 (cefepime-tazobactam) tested against contemporary Gram-negative isolates collected as part of the SENTRY Antimicrobial Surveillance Program.

Material/methods: A total of 4,326 unique patient isolates, including 2,926 from Europe (EU; 44 centers in 19 nations), 983 from Asia-Pacific (APAC; 15 centers in 8 nations) and 417 from China (10 centers), were susceptibility tested against cefepime-tazobactam (tazobactam at fixed 8 mg/L) and comparators by reference broth microdilution method. The isolates were collected in 2014, except China (2013).

Results: The most common infection types were pneumonia (31.8%), bacteremia (31.6%) and skin/soft tissue (15.5%). Against Enterobacteriaceae, cefepime-tazobactam inhibited 93.8-98.7% of strains at ≤8 mg/L [high dose, CLSI; see Table] and 92.6-97.8 at ≤2 mg/L [low dose, CLSI]), and showed activity similar to that of meropenem (94.2-98.6% S). Further, cefepime-tazobactam was more active than piperacillin-tazobactam (84.2-89.2% susceptible [CLSI]) against Enterobacteriaceae [79.3-85.0% by EUCAST]. Extended-spectrum β-lactamase (ESBL)-phenotype rates were (EU/APAC/China) 19.3/18.8/66.3% among *E. coli*; and 44.8/28.7/41.7% among *Klebsiella* spp.; 100.0 and 71.8% of ESBL-phenotype *E. coli* and *Klebsiella* spp. from EU were inhibited at cefepime-tazobactam MIC of ≤8 mg/L, respectively. Cefepime-tazobactam inhibited 97.4-100.0% of *Enterobacter* spp. (EBS) at ≤8 mg/L; and exhibited good activity against ceftazidime-non-susceptible isolates ($MIC_{50/90}$, 0.25/2 mg/L and 95.5% inhibited at ≤8 mg/L in EU). When tested against *P. aeruginosa*, cefepime-tazobactam activity ($MIC_{50/90}$ of 4/16 mg/L and 79.8% inhibited at ≤8 mg/L in EU) was similar to that of cefepime ($MIC_{50/90}$ of 4/32 mg/L and 78.3% susceptible in EU), and greater than ceftazidime and meropenem (73.1-73.9% susceptible in EU). Cefepime-tazobactam and all β-lactams showed limited activity against *Acinetobacter* spp.

Conclusions: WCK 4282 demonstrated potent activity against Enterobacteriaceae, including ESBL-phenotype *E. coli* and ceftazidime-non-susceptible EBS strains, and *P. aeruginosa* isolated in hospitals from EU, APAC and China. WCK 4282 may represent a valuable option for the treatment of serious infections caused by Gram-negative bacilli, including some multidrug-resistant isolates.

	Cefepime-tazobactam MIC_{50}/MIC_{90} (% inhibited at ≤8 mg/L [high dose, CLSI])		
Organism (n: EU/APAC/China)	**EU**	**APAC**	**China**

Enterobacteriaceae (2351/693/243)	≤0.03/0.5 (95.8)	≤0.03/0.25 (98.7)	0.06/0.5 (93.8)
E. coli (883/325/104)	≤0.03/0.12 (100.0)	≤0.03/0.06 (99.7)	0.06/0.25 (96.2)
Klebsiella spp. (737/230/72)	0.06/32 (87.4)	≤0.03/0.25 (96.5)	0.06/64 (86.1)
Enterobacter spp. (228/68/38)	0.06/0.5 (98.7)	0.06/1 (100.0)	0.06/1 (97.4)
Citrobacter spp. (132/15/6)	≤0.03/0.25 (99.2)	≤0.03/0.25 (100.0)	0.12/-- (100.0)
S. marcescens (93/25/11)	0.06/0.25 (100.0)	0.06/0.12 (100.0)	0.06/0.25 (100.0)
P. aeruginosa (391/197/84)	4/16 (79.8)	2/16 (85.8)	4/32 (73.8)
Acinetobacter spp. (184/93/90)	64/>64 (18.5)	>64/>64 (18.3)	>64/>64 (15.6)