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ePoster Viewing
New and old beta-lactamase inhibitors

CEFTOLOZANE/TAZOBACTAM ACTIVITY AGAINST GRAM-NEGATIVE BACTERIA CAUSING URINARY TRACT INFECTIONS IN EUROPEAN HOSPITALS (2011-2012): A REPORT FROM AN INTERNATIONAL ANTIMICROBIAL SURVEILLANCE PROGRAM

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Objectives: Ceftolozane/tazobactam (TOL/TAZ) is a novel antibacterial with activity against common Gram-negative pathogens, including most extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and *Pseudomonas aeruginosa*, as well as drug-resistant strains, and is currently under Phase 3 clinical development. As part of the Program to Assess Ceftolozane/Tazobactam Susceptibility (PACTS), this study evaluated the activity of TOL/TAZ and comparator agents against a collection of clinically isolated Gram-negative organisms obtained from patients with urinary tract infections (UTIs) in European hospitals.

Methods: During 2011-2012 a total of 1727 unique bacterial isolates were collected consecutively from patients with UTIs in 31 hospitals in 11 European countries, plus Russia, Turkey, Ukraine and Israel. Susceptibility testing for TOL/TAZ and other antibacterial agents (including levofloxacin [LEV], piperacillin/tazobactam [PIP/TAZ], ceftazidime [CAZ], meropenem [MEM] and colistin) commonly used to treat patients with UTIs in Europe was performed using broth microdilution methodology according to CLSI M07-A9 document. Antimicrobial susceptibility (S) rates of Gram-negative organisms were based on EUCAST (2013) interpretative criteria. A proposed TOL/TAZ susceptible breakpoint of 8 mg/L was used. TOL/TAZ was tested at a fixed 4 mg/L concentration of TAZ.

Results: The distribution of organisms in these UTI specimens was 55% *Escherichia coli* (15.3% ESBL-phenotype), 11.1% *Klebsiella pneumoniae* (42.2% ESBL-phenotype) and 8.2% *P. aeruginosa* (42.6% classified as multidrug resistant [MDR]). Against *E. coli*, including ESBL–phenotype isolates, the S rate to TOL/TAZ was 100% (Table). Against *K. pneumoniae,* overall susceptibility to MEM was high (94.3%), and TOL/TAZ was more active than LEV, PIP/TAZ and CAZ (87.0% S), including against ESBL–phenotype isolates (69.1% S). Against *P. aeruginosa*, with the exception of colistin (data not shown), TOL/TAZ was the most active agent tested (88.7% S), including against MDR isolates (73.3% S). The activities of LEV, PIP/TAZ, CAZ and MEM were limited against MDR *P. aeruginosa*. A per-country analysis showed that S to TOL/TAZ was >95% in Enterobacteriaceae isolates obtained from UTI patients in all countries except 3 (Russia, Israel and Poland). S to TOL/TAZ by *P. aeruginosa* isolates varied widely by country, with MICs >8 mg/L found in Belgium (1), Greece (1), Poland (3), Portugal (10) and Turkey (1) and 100% S in isolates obtained from patients in France, Germany, Ireland, Italy, Spain, Sweden and the UK.
Conclusion: Antimicrobial S varied among European countries. At an MIC of <=8 mg/L TOL/TAZ demonstrated greater *in vitro* activity than several antibacterials (LEV, PIP/TAZ and CAZ) commonly used to treat Gram-negative pathogens causing UTIs in European hospitals (2011-2012) and could represent a valuable treatment option for these pathogens.

	MIC_{50}/MIC_{90} (mg/L)/%Susceptible				
Organism	**TOL/TAZ[a]**	**LEV[b]**	**PIP/TAZ[b]**	**CAZ[b]**	**MEM[b]**
E. coli (n = 950)	0.25/0.5/100	≤0.12/>4/72.6	2/8/90.0	0.12/4/86.1	≤0.06/≤0.06/100
E. coli ESBL-phenotype (n = 145)	0.5/1/100	>4/>4/26.2	8/64/63.4	8/>32/9.0	≤0.06/≤0.06/100
K. pneumoniae (n = 192)	0.5/32/87.0	0.25/>4/67.2	4/>64/67.2	0.5/>32/59.9	≤0.06/≤0.06/94.3
K. pneumoniae ESBL-phenotype (n = 81)	2/>32/69.1	4/>4/37.0	32/>64/35.8	32/>32/4.9	≤0.06/>8/86.4
P. aeruginosa (n = 141)	0.5/32/88.7	0.5/>4/61.7	8/>64/59.6	4/32/69.5	0.5/>8/73.8
P. aeruginosa MDR[c] (n = 60)	2/>32/73.3	>4/>4/20.0	64/>64/11.7	16/>32/28.3	4/>8/43.3

[a]Proposed susceptible breakpoint of 8 mg/L of TOL/TAZ used for comparative purposes.

[b]Susceptible breakpoint established by EUCAST (2013).

[c]MDR bacteria were classified according to Magiorakos AP, et al. *Clin Microbiol Infect.* 2012;18:268-281.