P0339
Paper Poster Session
Susceptibility trends for old and new antibiotics

Antimicrobial activity of ceftolozane/tazobactam from the PACTS programme tested against Enterobacteriaceae isolated from patients hospitalized in intensive care units from 20 European countries and Israel (2013-2014)

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Objective: To evaluate the activity of ceftolozane/tazobactam (TOL/TAZ) and comparator agents against Enterobacteriaceae isolated from patients in intensive care units (ICUs) in 20 European countries and Israel. TOL/TAZ was approved by the European Medicines Agency for complicated intra-abdominal infections (in combination with metronidazole), acute pyelonephritis, and complicated urinary tract infections, and is currently in clinical development in patients with ventilator-associated bacterial pneumonia.

Methods: A total of 1,258 Enterobacteriaceae isolates were consecutively collected from patients hospitalized in ICUs during 2013-2014, from 39 medical centres located in 21 countries (number of centres): Belgium (1), Czech Republic (1), Denmark (1), Finland (1), France (4), Germany (5), Greece (1), Ireland (2), Israel (1), Italy (4), Netherlands (1), Norway (1), Poland (1), Portugal (1), Russia (3), Spain (3), Sweden (1), Switzerland (1), Turkey (2), United Kingdom (3), and Ukraine (1). Susceptibility (S) testing was performed by reference broth microdilution methods and MIC interpretations for comparator agents were as published by EUCAST. Multidrug-resistant (MDR), extensively drug-resistant (XDR), and pandrug-resistant (PDR) bacteria were classified based on Magiorakos AP, et al. (2012). *Clin Microbiol Infect.* 18:268-81.

Results: Overall, 82.3% of 1,258 isolates were S to TOL/TAZ compared to S rates of 73.8, 70.8 and 95.2% for piperacillin/tazobactam (PIP/TAZ), ceftazidime (CAZ) and meropenem (MER), respectively (Table). Against 317 (25.2%) MDR/87 (6.9%) XDR Enterobacteriaceae, MER S was 81.0/41.9% followed by TOL/TAZ (46.1/9.2%), PIP/TAZ (28.4/5.8%) and then CAZ (20.5/4.6%). Ten isolates were PDR (Russia 3, Greece 2, Turkey 2, Italy 2, Poland 1); all 10 were R to MER, TOL/TAZ, PIP/TAZ and CAZ. TOL/TAZ was very active (96.4% S) against *Escherichia coli*, including extended spectrum beta-lactamase-phenotype (ESBL) strains (84.6% S), but less active against *Klebsiella pneumoniae* (KPN, 66.9% S). Only 36.5% of ESBL-KPN were S to TOL/TAZ, which increased to 52.6% in the MER-S-ESBL strains. TOL/TAZ S against 210 *Enterobacter* spp. isolates was 66.7% compared to 60.8, 58.1 and 97.1% for PIP/TAZ, CAZ and MER, respectively. *E. cloacae* (ECL; n=139) and *E. aerogenes* (EAE; n=67) were 71.2 and 58.2% S to TOL/TAZ, respectively. TOL/TAZ activity against presumptive AmpC phenotype (ceftazidime resistant and cefepime susceptible) was low (16.0 – 18.8%) but higher than CAZ (0.0%) and PIP/TAZ (4.0%) with all isolates S to MER.

Conclusion: TOL/TAZ demonstrated higher S rates than CAZ and PIP/TAZ, but not MER, against MDR and XDR Enterobacteriaceae (including *E. coli*, *K. pneumoniae*, *E. cloacae* and *E. aerogenes*) isolated from ICU patients in Europe and Israel during 2013 and 2014.

	TOL/TAZ	PIP/TAZ	CAZ	MER
Organism or phenotype (n)	**$MIC_{50/90}$/%S[a]**	**$MIC_{50/90}$/%S[a]**	**$MIC_{50/90}$/%S[a]**	**$MIC_{50/90}$/%S[a]**
E. coli (386)	0.25/0.5/96.4	2/32/83.6	0.25/16/78.8	≤0.06/≤0.06/100.0
ESBL-phenotype (91)	0.5/2/84.6	8/>64/60.4	16/>32/9.9	≤0.06/≤0.06/100.0
K. pneumoniae (329)	0.5/>32/66.9	8/>64/57.2	1/>32/50.2	≤0.06/8/84.1
ESBL-phenotype (170)	4/>32/ 36.5	>64/>64/21.9	>32/>32/3.5	0.06/>8/69.1
MER-S-ESBL phenotype (116)	1/>32/52.6	32/>64/32.2	16/>32/4.3	≤0.06/0.5/100.0
Enterobacter spp. (210)	0.5/8/66.7	4/>64/60.8	0.5/>32/58.1	≤0.06/0.12/97.1
E. cloacae (139)	0.5/8/71.2	4/>64/64.5	0.5/>32/61.9	≤0.06/0.12/97.8
CAZ-R and FEP-S[b] (16)	4/8/18.8	32/64/0.0	-	≤0.06/0.12/100.0
E. aerogenes (67)	1/8/58.2	8/64/53.7	1/>32/50.8	≤0.06/0.12/95.5
CAZ-R and FEP-S (25)	2/4/16.0	32/64/4.0	-	≤0.06/0.12/100.0

a. Susceptible (S), resistant (R) breakpoints established by EUCAST (2015).
b. CAZ-R and FEP-S = ceftazidime resistant and cefepime susceptible (presumptive AmpC phenotype).