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Paper Poster Session VI

New data on new cephalosporin/beta-lactamase inhibitor combinations

Antimicrobial activity of ceftolozane/tazobactam and comparator agents tested against *Pseudomonas aeruginosa* isolates from 15 European countries and Israel (2013)

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Objective: To evaluate the anti-*P. aeruginosa* activity of ceftolozane/tazobactam, ceftazidime, meropenem and other comparator agents against isolates from 15 European (EU) countries and Israel. Ceftolozane is a novel oxyimino-aminothiazolyl cephalosporin with potent anti-pseudomonal activity. Tazobactam, a penicillanic acid-sulfone, is a well-established β-lactamase inhibitor that extends the spectrum of β-lactam agents. Ceftolozane/tazobactam is currently being investigated for treatment of ventilator-associated bacterial pneumonia, intra-abdominal infections and urinary tract infections.

Methods: A total of 1266 *P. aeruginosa* isolates were consecutively collected during 2013 from 34 medical centres located in 15 EU countries, including Turkey, Russia and Ukraine, plus Israel. Susceptibility testing was performed by CLSI broth microdilution methods and MIC interpretations for comparator agents were as published by EUCAST and CLSI. Ceftolozane/tazobactam was tested at a fixed 4 mg/L concentration of tazobactam.

Results: The number of isolates per country varied from 11 in Ukraine to 197 in Spain. Ceftolozane/tazobactam (overall $MIC_{50/90}$, 0.5/4 mg/L) was generally four-fold more active than ceftazidime ($MIC_{50/90}$, 2/>32 mg/L) and inhibited 93.4% and 91.5% of all isolates, at MIC values of ≤8 mg/L and ≤4 mg/L, respectively. In contrast, susceptibility to ceftazidime was 75.4%. Similarly, susceptibility to meropenem was 71.0% overall. The highest combined susceptibility observed for ceftazidime and meropenem were 90.5%/90.5% (Sweden) and 91.3%/82.6% (Ireland), respectively. Susceptibility (by EUCAST criteria) to both ceftazidime and meropenem were extremely low (≤50%) in Belgium and Poland and below 70% in Portugal and Russia. Overall susceptibility rates (by EUCAST criteria) to piperacillin/tazobactam, doripenem, ciprofloxacin and amikacin were 69.2, 66.1, 65.6 and 86.1%, respectively. MDR rates (26.0% overall) varied widely, ranging from 9.5% in Sweden to 64.8% in Poland (Ukraine 0.0% but only 11 isolates). XDR rates were >30% in Belgium, Poland, Portugal and Russia. Only two PDR isolates were found (in Italy).

Conclusion: Antimicrobial susceptibility, MDR and XDR of *P. aeruginosa* varied widely among EU countries. MDR, XDR and resistance rates to ceftazidime and meropenem were generally elevated and particularly high in some EU nations. At a MIC of ≤8 mg/L, ceftolozane/tazobactam had higher susceptibility rates than β-lactams currently available for treatment of *P. aeruginosa* infections.

Country (no. tested)	Ceftolozane/tazobactam $MIC_{50/90}$ (% at ≤8 mg/L)	Ceftazidime $MIC_{50/90}$ (% at ≤8 mg/L)[a]	Meropenem $MIC_{50/90}$ (% at ≤2 mg/L)[a]	%MDR/%XDR/ %PDR[b]
Belgium (40)	1/>32 (72.5)	8/>32 (50.0)	4/>8 (41.0)	52.5/35.0/0.0
Czech Republic (22)	0.5/4 (100.0)	1/>32 (81.8)	0.5/8 (63.6)	27.3/18.2/0.0
France (76)	0.5/2 (100.0)	2/32 (77.6)	0.5/4 (88.2)	14.5/9.2/0.0
Germany (168)	0.5/2 (99.4)	2/32 (85.7)	0.5/8 (74.4)	17.9/10.7/0.0
Greece (44)	0.5/8 (90.9)	2/16 (88.6)	0.5/8 (84.1)	15.9/9.1/0.0
Ireland (46)	0.5/2 (100.0)	2/8 (91.3)	0.5/4 (82.6)	15.2/4.4/0.0
Israel (66)	0.5/4 (98.5)	4/>32 (72.7)	0.5/>8 (71.2)	31.8/19.7/0.0
Italy (160)	0.5/4 (94.4)	4/>32 (71.9)	0.5/>8 (72.3)	31.9/25.6/1.3
Poland (71)	2/16 (85.9)	16/>32 (46.5)	8/>8 (22.5)	64.8/53.5/0.0
Portugal (60)	1/32 (73.3)	2/>32 (60.0)	2/>8 (51.7)	38.3/36.7/0.0
Russia (71)	1/>32 (73.2)	8/>32 (52.1)	1/>8 (63.4)	40.9/33.8/0.0
Spain (197)	0.5/4 (96.5)	2/32 (80.7)	0.5/8 (78.7)	18.3/14.2/0.0
Sweden (42)	0.5/2 (100.0)	2/8 (90.5)	0.25/2 (90.5)	9.5/2.4/0.0
Turkey (111)	1/4 (95.5)	2/32 (82.9)	0.5/>8 (73.6)	23.4/13.5/0.0
UK (81)	0.5/2 (100.0)	2/32 (84.0)	0.5/>8 (75.3)	13.6/6.2/0.0
Ukraine (11)	0.5/2 (100.0)	4/32 (63.6)	0.25/0.5 (100.0)	0.0/0.0/0.0
Overall (1266)	**0.5/4 (93.4)**	**2/>32 (75.4)**	**0.5/>8 (71.0)**	**26.0/18.6/0.2**

a. Susceptible breakpoint established by EUCAST (2014).

b. Multidrug-resistant (MDR), extensively drug-resistant (XDR), and pandrug-resistant (PDR) bacteria were classified according to Magiorakos AP, et al. (2012). *Clin Microbiol Infect.* 18:268-81.