

### Antimicrobial activity of ceftolozane/tazobactam and comparator agents tested against *Pseudomonas aeruginosa* isolates from 14 European countries and Israel

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**Objective:** To evaluate the anti-*P. aeruginosa* (PSA) activity of ceftolozane/tazobactam (TOL/TAZ), ceftazidime (CAZ), meropenem (MER) and other comparator agents against isolates from 14 European (EU) countries and Israel. TOL (formerly CXA-101) is a novel oxyimino-aminothiazolyl cephalosporin with potent anti-PSA activity. TOL/TAZ is currently under clinical development for treatment of ventilator associated bacterial pneumonia, intra-abdominal infections and urinary tract infections. **Methods:** A total of 991 PSA isolates were consecutively collected in 2011 from 31 medical centres located in 14 EU countries, including Russia and Turkey, plus Israel. Susceptibility (S) testing was performed by CLSI broth microdilution methods and MIC interpretations for comparator agents were as published by EUCAST and CLSI. TOL/TAZ was tested at a fixed 4 mg/L concentration of TAZ. **Results:** The number of isolates per country varied from 11 in Sweden and 29 in Belgium to 130 in Spain and 158 in France. TOL/TAZ (overall MIC<sub>50</sub>, 1 mg/L) was generally four-fold more active than CAZ (MIC<sub>50</sub>, 4 mg/L) and inhibited >94% of isolates at MIC of ≤8 mg/L in eight countries. In contrast, the highest S observed for CAZ and MER was 85.4% (Ireland) and 85.7% (United Kingdom [UK]), respectively and was 64.9% overall (Table). Resistance (R) to CAZ and MER were extremely high (>60% non-S isolates) in Poland, Russia and Ukraine mainly due to the widespread of VIM-producing strains, and TOL/TAZ showed more limited activity against PSA from these countries as well. S to CAZ and MER was below 70% in Belgium, Portugal and Turkey; and ≥80% only in Ireland, Italy and UK. Overall S (by EUCAST criteria) to piperacillin/TAZ, doripenem, ciprofloxacin and amikacin was 60.7, 59.8, 57.7 and 78.3%, respectively, below TOL/TAZ at ≤8 mg/L (82.3%). **Conclusions:** Antimicrobial S of PSA varied widely among EU countries. R to CAZ and MER was generally elevated and particularly high in some Eastern EU nations. At a MIC of ≤8 mg/L, TOL/TAZ provides greater coverage than beta-lactams currently available for treatment of PSA infections and could represent a valuable addition to the armamentarium for this pathogen.

Country (no. tested)	Ceftolozane/tazobactam MIC <sub>50/90</sub> (% at ≤8 mg/L)	Ceftazidime MIC <sub>50/90</sub> (% at ≤8 mg/L) <sup>a</sup>	Meropenem MIC <sub>50/90</sub> (% at ≤2 mg/L) <sup>a</sup>
Belgium (29)	2/>32 (72.4)	8/>32 (51.7)	8/>8 (41.4)
France (158)	1/4 (97.5)	2/>32 (76.0)	0.5/>8 (76.6)
Germany (47)	1/2 (95.7)	4/32 (78.7)	0.5/8 (76.6)
Greece (39)	0.5/>32 (74.4)	2/>32 (74.4)	0.5/>8 (64.1)
Ireland (48)	1/1 (100.0)	2/16 (85.4)	0.5/8 (85.4)
Israel (62)	1/4 (95.2)	2/>32 (74.2)	0.5/8 (75.8)
Italy (121)	0.5/4 (94.2)	2/32 (82.6)	0.5/8 (81.0)
Poland (45)	>32/>32 (17.8)	32/>32 (15.6)	>8/>8 (22.2)
Portugal (35)	1/>32 (85.7)	4/32 (62.9)	2/>8 (54.3)
Russia (85)	32/>32 (37.7)	32/>32 (21.2)	8/>8 (24.7)
Spain (130)	0.5/2 (99.2)	2/32 (75.4)	0.5/8 (73.9)
Sweden (11)	0.5/1 (100.0)	4/>32 (72.7)	2/>8 (72.7)
Turkey (94)	1/>32 (86.2)	4/>32 (67.0)	2/>8 (54.3)
UK (35)	0.5/4 (97.1)	2/>32 (80.0)	0.5/8 (85.7)
Ukraine (52)	>32/>32 (40.4)	32/>32 (21.2)	4/>8 (38.5)
<b>Overall (991)</b>	<b>1/&gt;32 (82.3)</b>	<b>4/&gt;32 (64.9)</b>	<b>1/&gt;8 (64.1)</b>

a. Susceptible breakpoint established by EUCAST (2012) and CLSI (2012).