28th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES
Madrid, Spain
21 – 24 April 2018

P1046 Global activity of imipenem-relebactam against P. aeruginosa from respiratory tract infections - SMART 2015-2016

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Background: Relebactam (MK-7655) is a β-lactamase inhibitor of class A and C β-lactamases in development in combination with imipenem. Relebactam can enhance imipenem's clinical activity against *P. aeruginosa* that demonstrate carbapenem resistance due to impermeability arising from porin loss combined with AmpC expression. In this report, we evaluated the activity of imipenem-relebactam against *P. aeruginosa*, including populations not susceptible to other key β-lactam agents, collected globally as part of the 2015-2016 SMART surveillance program.

Materials/methods: 178 hospitals in 53 countries each collected up to 100 consecutive, aerobic or facultative anaerobic, gram-negative pathogens from lower respiratory tract infections per year, for a total of 28,111 isolates. MICs were determined for 7,888 *P. aeruginosa* using CLSI broth microdilution. The percent susceptible was assessed using CLSI breakpoints; for comparison purposes the imipenem susceptible breakpoint of 2 mg/L was applied to imipenem-relebactam. Multidrug-resistance (MDR) was defined as non-susceptibility (intermediate or resistant) to any 3 or more antimicrobial agents of 8 sentinel drugs (amikacin, aztreonam, cefepime, ceftazidime, ciprofloxacin, colistin, imipenem, piperacillin-tazobactam).

Results: The proportion of *P. aeruginosa* among all gram-negative respiratory pathogens ranged from 24.3% in Latin America to 33.8% in United States/Canada. The proportion of MDR isolates among *P. aeruginosa* ranged from 16.7% in South Pacific to 35.5% in Asia and 35.3% in Latin America. Susceptibilities to imipenem-relebactam of *P. aeruginosa* and resistant phenotypes are shown below:

	% Imipenem-relebactam-susceptible (total no. of isolates)						
Phenotypes	**Africa**	**Asia**	**Europe**	**Latin America**	**Middle East**	**US/Canada**	**South Pacific**
All *P. aeruginosa*	85.9 (509)	89.1 (1601)	90.9 (2110)	84.1 (898)	93.1 (519)	92.9 (1657)	96.0 (594)
Ceftazidime-NS	53.0 (134)	68.1 (483)	73.1 (613)	54.6 (262)	75.8 (132)	80.0 (415)	81.6 (87)
Cefepime-NS	51.8 (137)	65.6 (451)	70.7 (591)	50.0 (258)	74.4 (125)	79.2 (467)	75.6 (82)
Imipenem-NS	65.9 (211)	65.1 (496)	75.1 (771)	60.2 (359)	82.6 (207)	75.4 (479)	76.0 (100)
Pip-tazo-NS	57.4 (155)	74.4 (573)	75.2 (738)	58.4 (320)	81.1 (175)	80.8 (521)	82.9 (111)
MDR	56.8 (162)	71.0 (569)	73.5 (717)	55.5 (317)	79.4 (175)	79.7 (531)	77.8 (99)

NS, non-susceptible; Pip-tazo, piperacillin-tazobactam; MDR, multi-drug resistant

Susceptibility rates to the tested cephalosporins, aztreonam, fluoroquinolones, piperacillin-tazobactam, and imipenem were typically between ~10 and 30 percentage points lower than imipenem-relebactam

for *P. aeruginosa* overall and between ~20 and 60 percentage points lower for populations not susceptible to β-lactams and MDR phenotypes.

Conclusions: Imipenem-relebactam showed strong activity against *P. aeruginosa* from respiratory tract infections, matched or exceeded only by amikacin and colistin. Susceptibility against isolates not susceptible to various β-lactams was 65 to 80% in most regions. Imipenem-relebactam could provide an important treatment option against *P. aeruginosa* isolates from respiratory tract infections that are not susceptible to several of the currently available β-lactam agents.