

Session: P020 Carbapenemases - here, there and everywhere

**Category: 3b. Resistance surveillance & epidemiology: Gram-negatives**

22 April 2017, 15:30 - 16:30  
P0406

## Nationwide epidemiology of carbapenem-resistant *Klebsiella pneumoniae* isolates from Greek hospitals, in regards to plazomicin and aminoglycoside resistance

Irene Galani<sup>\*1</sup>, Konstantina Nafplioti<sup>2</sup>, Panagiota Adamou<sup>2</sup>, Ilias Karaiskos<sup>3</sup>, Helen Giamarellou<sup>3</sup>, Maria Souli<sup>4</sup>

<sup>1</sup>National and Kapodistrian University of Athens, Faculty of Medicine; 4th Dept Internal Medicine, Infectious Diseases Laboratory

<sup>2</sup>National and Kapodistrian University of Athens, School of Medicine; 4th Dept of Internal Medicine, Infectious Diseases Laboratory

<sup>3</sup>Hygeia General Hospital; 6th Dept. of Internal Medicine

<sup>4</sup>University of Athens, School of Medicine; Attikon General Hospital; 4th Dept of Internal Medicine

**Background:** Plazomicin is a next-generation aminoglycoside that was developed to overcome common aminoglycoside-resistance mechanisms. Plazomicin contains structural modifications that allow it to maintain activity in the presence of aminoglycoside modifying enzymes (AMEs) and is being developed for the treatment of patients with difficult to treat infections caused by multidrug-resistant Enterobacteriaceae, including ESBL producing and carbapenem-resistant Enterobacteriaceae. We evaluated the *in vitro* activities of plazomicin and comparator aminoglycosides and elucidated the underlying carbapenem and aminoglycoside resistance mechanisms among carbapenemase-producing *K.pneumoniae* (CPKp) isolates collected during a nationwide surveillance study in Greek hospitals.

**Material/methods:** 300 CPKp consecutive clinical strains obtained from unique patients at 14 hospitals in Greece, between November 2014 and August 2016, were studied. Susceptibility testing was performed using the CLSI broth microdilution method, with MICs interpreted per EUCAST breakpoints. All isolates were characterized by PCR for the presence of genes encoding carbapenemases and common AMEs (*aac(6′)-Ib*, *aac(3′)-IIa*, *aac(3′)-Ia*, *aac(3′)-IV*, *ant(2′)-Ia*, *ant(3′)-I*) while isolates highly resistant ( $\geq 128$ mg/L) to all clinically relevant aminoglycosides were characterized for genes encoding 16SrRNA methylases (RMTs).

**Results:** Of the 300 isolates tested (KPC, n=200; NDM, n=50; OXA-48, n=13; VIM, n=21; KPC & VIM, n=13; KPC & OXA, n=1; and NDM & OXA, n=2), 24 (8%) were PDR, 73 (24.3%) XDR, 203 (67.7%) MDR and had MIC<sub>50</sub>/MIC<sub>90</sub> ≥64mg/L to carbapenems. The isolates had an MIC<sub>50</sub>/MIC<sub>90</sub> to netilmicin, tobramycin, amikacin and gentamicin being 128/>256, 32/256, 32/128 and 4/>256mg/L, respectively. Plazomicin MICs ranged from 0.125 to >256mg/L, with MIC<sub>50</sub> and MIC<sub>90</sub> of 0.5 and 8mg/L, respectively. Of note, 84.7% and 89.3% of the isolates were inhibited by plazomicin at ≤2mg/L and ≤4mg/L, respectively. Twenty-three (7.7%) isolates (16 KPC-, 6 VIM- and one KPC & OXA-48-producers) exhibited MICs ≥64mg/L to all 4,6-disubstituted aminoglycosides tested including plazomicin, and harbored *rmtB* (n=22) or *armA* (n=1) 16S rRNA methylases. Among non-RMT positive isolates plazomicin exhibited MIC<sub>50</sub>/MIC<sub>90</sub> values of 0.5/2mg/L, while gentamicin 4/128mg/L. In our collection, AAC(6′)-Ib was the most common AME, identified in 57.3% of the isolates, followed by ANT(3′)-Ia in 51.3% and AAC (3)-IIa in 20.3% of the isolates. AAC(6′)-Ib and AAC (3)-IIa were co-produced by 12% of the isolates while AAC(6′)-Ib, AAC (3)-IIa and ANT(3′)-Ia were co-produced by only 3.3% of the isolates.

**Conclusions:** Plazomicin retains activity against most CPKp, with MICs consistently lower than those of the other aminoglycosides, even in the presence of AMEs. None of the NDM-producing isolates of our collection harbored an RMT gene, as reported in isolates from other countries, whereas 28.6% and 8% of VIM- and KPC-producers, respectively, carried an RMT gene, mostly *rmtB*. Additional studies examining the role of efflux pumps and outer membrane permeability alterations will likely elucidate the mechanisms responsible for plazomicin MIC of 4-8mg/L in 7.6% of our isolates.