Session: P060 News on relebactam and vaborbactam

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

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**Activity of imipenem-relebactam against Enterobacteriaceae and Pseudomonas aeruginosa from respiratory tract infections in Europe, SMART 2015**

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**Background:** Relebactam (MK-7655) (REL) is a β-lactamase inhibitor of class A and class C beta-lactamases that is in development in combination with imipenem. REL restores the in vitro activity of imipenem (IMI) against *Enterobacteriaceae*, including those producing KPCs, and *Pseudomonas aeruginosa*. In this study we evaluated the ability of REL to restore IMI susceptibility to a collection of gram-negative isolates from lower respiratory tract infections in European countries participating in the 2015 SMART surveillance program.

**Material/methods:** 45 hospitals in 17 countries each collected up to 100 consecutive aerobic and facultative gram-negative pathogens from lower respiratory tract infections. MICs were determined for 1065 *P. aeruginosa* and 1949 non-Proteae *Enterobacteriaceae* (NPE) using CLSI broth microdilution. Proteae were excluded due to intrinsic non-susceptibility to IMI. REL was tested at a fixed concentration of 4 mg/L in combination with IMI. The percent susceptible was assessed using EUCAST breakpoints. IMI S breakpoints of ≤2 mg/L (NPE) and ≤4 mg/L (*P. aeruginosa*) were applied to IMI/REL. All IMI non-susceptible isolates were tested for the presence of genes encoding β-lactamases using published multiplex PCR assays, followed by full-gene DNA sequencing.

**Results:** The cumulative percent of isolates at each IMI and IMI/REL MIC is shown in the table.
Among 1065 *P. aeruginosa*, 68.9% (734) were susceptible to IMI; of the 331 non-susceptible isolates, 79.8% (264) were rendered susceptible by the addition of REL, for a final 93.7% susceptible. The majority of the remaining IMI/REL non-susceptible *P. aeruginosa* isolates carried metallo-β-lactamases (MBLs) or GES carbapenemases (with 13 of the 15 GES-carbapenemase-positive isolates found in one hospital). Among 1949 NPE, 94.0% (1833) were susceptible to IMI; of the 116 non-susceptible isolates, 58.6% (68) were rendered susceptible by the addition of REL, for a final 97.5% susceptible. The majority of the isolates that remained IMI/REL non-susceptible carried MBLs. Isolates carrying OXA-48 carbapenemases were found in both subsets.

**Conclusions:** Relebactam exhibited strong potential for restoring the *in vitro* activity of IMI against many pathogens otherwise non-susceptible to carbapenems. Further development of this compound could provide a valuable therapeutic option for treating lower respiratory tract infections caused by resistant gram-negative bacilli.