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P1047 Potentiation of imipenem by relebactam for Pseudomonas aeruginosa from bacteraemia and respiratory isolates

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Background: Resistance to imipenem in *Pseudomonas aeruginosa* largely arises by loss of the 'carbapenem-specific' porin OprD. This mechanism requires functional AmpC beta-lactamase, whether inducible or derepressed, and is abrogated if this enzyme is lost or inhibited. More rarely, imipenem resistance reflects acquired carbapenemases. Relebactam is a developmental diazabicyclooctane beta-lactamase inhibitor with a spectrum including pseudomonal AmpC. We investigated its effects on imipenem MICs for *P. aeruginosa* isolates submitted to The British Society for Antimicrobial Chemotherapy Resistance Surveillance Programme.

Materials/methods: Consecutive *P. aeruginosa* isolates causing bacteraemia or hospital-onset lower respiratory tract infections (LRTI) at participating laboratories (n=24-38) throughout the UK and Ireland were tested. Bacteraemia isolates were collected Jan 2015-Dec 2016, whereas respiratory isolates were collected Oct 2014-Sept 2016. MICs were determined centrally by BSAC agar dilution with relebactam at a fixed concentration of 4 mg/L. Beta-lactamase genes were identified by PCR.

Results: 851 *P. aeruginosa* isolates were tested: 433 from bacteraemia and 418 from LRTI. For most (726/759, 95.6%) imipenem-susceptible *P. aeruginosa* the MIC values of imipenem alone were 0.5-2 mg/L and were decreased to 0.25-0.5 mg/L by relebactam, with a 4-fold decrease in modal MIC. For the great majority (82/92, 89%) of imipenem-non-susceptible *P. aeruginosa*, the imipenem MIC values were 8-16 mg/L, and were reduced to 1-2 mg/L by relebactam. Two further imipenem-resistant isolates had VEB or PER ESBLs (which do not themselves confer imipenem resistance); in these cases the imipenem MICs were reduced from 8 and 16 mg/L to 2 and 4 mg/L, respectively. Five *P. aeruginosa* had VIM or NDM metallo-carbapenemases (MBL). For these, the MICs of imipenem were 32 - >256 mg/L and remained at 16 - >256 mg/L with relebactam.

Conclusions: Relebactam reduces MICs of imipenem for almost all *P. aeruginosa*, putatively reflecting its inhibition of endogenous AmpC. MICs for the great majority of imipenem-resistant isolates, where resistance reflects the interplay of AmpC with loss of OprD, imipenem MICs were restored to the clinical range. MBL-associated resistance was seen in <1% of this collection and was not overcome by relebactam.