Introduction

Relebactam (MK-7655) (REL) is a β-lactamase inhibitor of class A and class C β-lactamases that is in development in combination with imipenem. REL restores the activity of IMI against 95.7% E. cloacae isolates. 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 caused by Enterobacteriaceae, K. pneumoniae, Serratia, ESBL E. cloacae, and facultative gram-negative pathogens from lower respiratory tract infections in Europe - SMART 2015. A total of 1,949 non-Proteeae strains were tested for β-lactamase content.

Materials & Methods

46 hospitals in 17 countries collected up to 100 consecutive aerobic and facultative gram-negative pathogens from lower respiratory tract infections. MICs were determined for IMI and amikacin and 19 non-Proteeae Enterobacteriaceae (NPE) (using CLSI broth microdilution [2,12]) were evaluated due to clinical need. Non-susceptible phenotypes were defined as those resistant for MICs >2 mg/L for imipenem, >8 mg/L for meropenem, >1 mg/L for amikacin, or >64 mg/L for piperacillin-tazobactam. Multiple isolates within the same species were tested.

Results

• Among 1,065 P. aeruginosa, the modal IMI MIC dropped from >32 to ≤0.5 µg/ml in the presence of REL (Figure 2), and 79% of isolates were rendered susceptible.

• Among the 116 IMI-NS NPE isolates, the modal MIC dropped from >16 to ≤1 µg/ml in the presence of REL (Figure 2), and 58.9% of isolates were rendered susceptible.

• Of the 68 NPE isolates that were rendered IMI-NS in the presence of REL, >70% carried KPC; the 11 OXA-48-positive isolates showed an IM MIC decrease of only one dilution.

• Of the IMI-NS NPE isolates, 92% carried IMI and/or OXA-48 carbapenemases.

Conclusions

Relebactam exhibited strong potential for restoring the in vitro activity of IMI against gram-negative pathogens otherwise non-susceptible to carbapenems. Further development of this compound could provide a valuable therapeutic option to treat these resistant infections caused by resistant gram-negative bacilli.

References and Acknowledgments:


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