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Abstract (poster session)

Anti-mutant potentials of doripenem, imipenem and ciprofloxacin against *Pseudomonas aeruginosa* examined using an in vitro dynamic model

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Objectives: To compare the abilities of doripenem (DOR), imipenem (IMP) and ciprofloxacin (CIP) to restrict the amplification of resistant *P. aeruginosa*, their pharmacokinetics were simulated in vitro mimicking multiple antibiotic dosing. **Methods:** A clinical isolate of CIP-resistant *P. aeruginosa* (MIC of DOR 1 mg/L, MIC of IMP 2 mg/L, MIC of CIP 4 mg/L) was exposed to thrice-daily DOR or IMP and twice-daily CIP for three days at comparable ratios of the 24-hour area under the concentration-time curve (AUC) to the MIC (50-170 h with DOR, 30-140 h with IMP and 55-180 h with CIP). Given the mutant prevention concentrations (MPCs) of DOR (8 mg/L), IMP (1024 mg/L) and CIP (32 mg/L), the respective times inside the mutant selection window varied from 39 to 46% (DOR), from 41 to 66% (IMP) and from 77 to 90% (CIP) of the dosing interval. Based on daily population analyses (bacterial growth in the presence of 2×, 4×, 8× and 16×MIC of DOR, IMP or CIP), 72-hour areas under the bacterial mutant concentration – time curves (AUBCm)s were calculated. **Results:** DOR-, IMP- and CIP-resistant mutants were enriched in all simulations, except those at the highest AUC/MIC ratio with DOR. With each antibiotic, an increase in the simulated AUC/MIC ratio led to a systematic decrease in the AUBCm. A specific AUC/MIC relationship with AUBCm was established for each antibiotic. With DOR and IMP, the AUC/MIC plots of the AUBCm were lower than the CIP plot. At a given AUC/MIC ratio the effects of DOR and IMP on mutants resistant to 2× and 4×MIC were more pronounced than CIP. Less clear AUC/MIC relationships with resistance were seen with mutants resistant to 8× and 16×MIC of the antibiotics. The different AUBCm-AUC/MIC relationships observed with DOR, IMP and CIP were in concordance with the differences in mutant growth after the end of treatment: numbers of mutants resistant to 2×, 4×, 8× and 16×MIC of DOR were smaller than those resistant to IMP and, especially, to CIP. **Conclusions:** These data demonstrate greater abilities of DOR and IMP to restrict the enrichment of resistant *P. aeruginosa* compared to CIP.