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P1190 Activity of ceftolozane/tazobactam against a collection of *Escherichia coli* and *Klebsiella pneumoniae* isolated from bloodstream infections that are non-susceptible to ceftriaxone

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Background: Ceftolozane/tazobactam is a novel beta-lactam/beta-lactamase inhibitor combination that may provide an alternative to carbapenems for third-generation cephalosporin (3GC) non-susceptible *E. coli* and *K. pneumoniae*. In this study, we tested the *in-vitro* activity of ceftolozane/tazobactam against bloodstream isolates collected from an international randomised trial, with genome sequencing used to characterise the resistome. In particular, as oxacillinase enzymes are known to elevate minimum inhibitory concentrations (MICs) of other beta-lactam/beta-lactamase inhibitor (BLBI) combinations, we sought to determine their effect on ceftolozane/tazobactam MICs.

Materials/methods: The MERINO trial was a randomised, open-label study comparing meropenem to piperacillin/tazobactam for treatment of 3GC non-susceptible *E. coli* and *K. pneumoniae* bloodstream infections. Bloodstream isolates were collected from enrolled patients and tested by broth microdilution (BMD) against ceftolozane/tazobactam using custom made Sensititre plates (Thermo Fisher). Isolates were assessed as susceptible based upon EUCAST (v8.0; ≤ 1 µg/mL) and CLSI (M100-ED28:2018; ≤ 2 µg/mL) breakpoint tables. Resistome analysis was performed using Illumina sequencing and antibiotic resistance genes were detected using Abricate (v0.8). Beta-lactamase enzymes were grouped as any combination of ESBL, plasmid ampC, oxacillinase profiles.

Results: 302 isolates were available for BMD, with 263 *E. coli* and 39 *K. pneumoniae* isolates sequenced for genotypic resistome correlation. 95% and 97% of *E. coli* and 87% and 92% of *K. pneumoniae* strains tested susceptible according to EUCAST and CLSI breakpoints respectively. When pooled together, plasmid ampC producers and isolates harbouring oxacillinase enzymes had higher geometric MICs than ESBLs (0.67 and 0.46 versus 0.38 µg/ml), but all still fell below the EUCAST breakpoint (≤ 1 µg/ml).

Conclusions: Alternative treatment to carbapenems for multidrug resistant Enterobacteriaceae is a key strategy for protecting their activity as last line agents. This study demonstrates high *in-vitro* activity against 3GC non-susceptible *E. coli* and *K. pneumoniae*, including those harbouring ESBLs, plasmid ampCs and oxacillinase enzymes.