

**O0282 Extended-spectrum beta-lactamases and resistance to ceftazidime-avibactam and ceftolozane-tazobactam combinations in *Escherichia coli* and *Pseudomonas aeruginosa***José Manuel Ortiz De La Rosa<sup>1</sup>, Patrice Nordmann<sup>1</sup>, Laurent Poirel\*<sup>1</sup><sup>1</sup> University of Fribourg, Fribourg, Switzerland

**Background:** Ceftazidime-avibactam (CZA) and ceftolozane-tazobactam (C/T) are recent  $\beta$ -lactam- $\beta$ -lactamase inhibitor combinations that are efficient against multidrug-resistant *Escherichia coli* and *Pseudomonas aeruginosa* isolates. Although the most commonly identified ESBLs encountered in *E. coli* are CTX-M-type enzymes, along with TEM- and SHV derivatives, those mainly encountered in *P. aeruginosa* are SHV-, VEB-, GES-, and PER-like enzymes, although BEL-, TEM-, and CTX-M-like enzymes have been rarely identified. We recently showed that production of GES-6 in *P. aeruginosa* was the source of acquired resistance to C/T while not affecting the susceptibility to CZA. This result prompted us to evaluate the relative impact of a series of ESBLs on susceptibility to C/Z and to CZA, either in *E. coli* or *P. aeruginosa* backgrounds.

**Materials/methods:** A series of fourteen ESBL-encoding genes was cloned and expressed in *E. coli* or *P. aeruginosa* recipient strains. Those ESBLs were derivatives of  $bla_{TEM}$ ,  $bla_{SHV}$ ,  $bla_{CTX-M}$ ,  $bla_{VEB}$ ,  $bla_{PER}$ ,  $bla_{GES}$ , and  $bla_{BEL}$ . In addition, the two carbapenemase genes  $bla_{KPC-2}$  and  $bla_{VIM-2}$  were added. *P. aeruginosa* PAO1 and *E. coli* TOP10 were used as recipient strains. MIC values were determined by E-test (AB bioMérieux; Solna, Sweden) or broth microdilution.

**Results:** Expression of the ESBL genes in *E. coli* TOP10 gave variable MIC value of CZA, that remained in the susceptibility range. However, the MIC of CZA of the  $bla_{PER-1}$ -positive recombinant strain was at 8  $\mu$ g/ml that actually corresponds to the breakpoint value. MICs of C/Z for those recombinant *E. coli* strains were also variable, but noteworthy several values were in the resistance range. Expression of the ESBL genes in *P. aeruginosa* PU21 did not confer resistance to CZA except for the PER-1 producer. Several ESBLs of the GES-, PER- and BEL-types conferred resistance to C/T in *P. aeruginosa*.

**Conclusions:** ESBL production in *P. aeruginosa* mainly affected the efficacy of C/T, although susceptibility to CZA was preserved in the majority of the strains. Noteworthy, resistance to both CZA and C/T was observed for only two types of isolates, namely those producing CTX-M-2 and PER-1. This is of concern in particular for PER-1-producing *P. aeruginosa* isolates that often identified in many Asian and European countries.

