Recently, ceftolozane/tazobactam and ceftazidime/avibactam became available to clinicians to meet the rising need for therapeutics to treat multidrug resistant (MDR) organisms.

Phase 3 clinical trials investigating efficacy of these agents compared to carbapenems in nosocomial pneumonia are currently in progress.

However, data regarding their role in treatment of pulmonary infections caused by Imipenem resistant Pseudomonas (Psa) is still lacking.

This report summarizes our early institutional experience.

**METHODS**

- We identified patients with Imipenem resistant Psa pneumonia. Each was treated with ceftolozane/tazobactam or ceftazidime/avibactam.
- Genetic analyses of Psa isolates were performed to understand the molecular basis for the emergence of this resistance phenotype in our institution.
- Patients’ characteristics, severity of illness and outcomes were reviewed.
- Multi locus sequence typing (MLST) was performed to evaluate Psa strain relatedness.
- PCR was done to screen for presence of blaKPC and metallo-beta-lactamase (MBL) genes. OprD genes was sequenced and analyzed. Exasy Swiss modeling server was used to construct models of OprD porin.

**RESULTS**

- Patient characteristics, treatment, and outcomes are summarized in Table 1. In all three cases microbiologic eradication was achieved. Two out of three patients survived.
- Psa isolates were not related by MLST typing and did not possess blaKPC or MBL genes. All isolates had mutations in the oprD gene resulting in early stop codons. Modelling of these OprD channels showed significantly truncated proteins.

**CONCLUSION**

- Our early experience demonstrates ceftazidime/avibactam and ceftolozane/tazobactam are promising therapeutic options for the treatment of Imipenem resistant non carbapenemase producing Psa pulmonary infections.
- Our genetic analysis indicates that Imipenem resistance in these isolates was partly mediated by OprD porin mutations, causing truncated, likely non-functional protein.
- Analysis of additional cases is needed to delineate the role of these novel cephalosporin/beta-lactamase inhibitor combinations in treatment of MDR Psa infections. As importantly, understanding the impact of mutations in OprD porins may lead to deeper insights of the mechanisms responsible for imipenem transport into Psa.