

**Session:** 250. Treatment of AMR Infections  
*Saturday, October 6, 2018: 12:30 PM*

**Background.** The increasing prevalence of multidrug-resistant (MDR) Gram-negative bacteria (GNB) represents an urgent public health threat. Ceftazidime-avibactam (CZA) is a novel cephalosporin/ $\beta$ -lactamase inhibitor with activity against MDR GNB including carbapenem-resistant Enterobacteriaceae (CRE). Real-world experience with CZA in the treatment of MDR GNB is accumulating but remains limited by the small number of patients thus far described. We sought to build upon prior reports by describing the clinical characteristics and outcomes of a diverse cohort of patients with MDR GNB infections treated with CZA.

**Methods.** Retrospective, multicenter, cohort study of patients treated with CZA ( $\geq 72$  h) for suspected or confirmed MDR GNB (resistant to  $\geq 1$  antibiotic in  $\geq 3$  classes) infections between 2015 and 2018. The primary outcome was clinical failure defined as a composite of 30-day mortality, 30-day recurrence, or worsening signs and symptoms while on CZA. Independent predictors of clinical failure were sought through multivariable logistic regression analysis.

**Results.** A total of 114 patients were included. The median (IQR) age was 65 (53, 74), the median Charlson Comorbidity Index was 4 (2, 6), and the median APACHE II score was 20 (14, 28). CRE and MDR *Pseudomonas aeruginosa* were isolated in 74 (66%) and 31 (28%) of cases, respectively. The predominant sources were respiratory (40%) and urinary tract (20%). Blood cultures were positive in 10% of cases. Combination therapy ( $\geq 48$  h) was used in 40%. Among carbapenem-resistant *Klebsiella pneumoniae* ( $n = 34$ ), 97% were susceptible to CZA. The resistant isolate was positive for NDM and OXA. Clinical failure, 30-day mortality, and recurrence were 28%, 13% and 5%, respectively. Independent predictors of clinical failure were immune compromise (aOR 6.25, 95% CI 1.30, 30.11), Glasgow Coma scale  $\leq 12$  (aOR 3.76, 95% CI 1.30, 10.88), primary bacteremia or respiratory source (aOR 2.96, 1.07–8.17) and age less than 65 (aOR 2.87, 95% CI 1.09, 7.61).

**Conclusion.** The use of CZA was associated with a clinical failure rate of 28% which compares favorably with historical controls of MDR GNB infections. Future investigations evaluating long-term outcomes and comparative studies are needed to more precisely define the role of CZA in MDR GNB infections.

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### 2380. Healthcare Resource Utilization for High-Risk Patients Treated With Dalbavancin in Physician Office Infusion Centers (POICs)

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**Background.** Medicare beneficiaries and patients (patients)  $\geq 65$  years comprise the highest risk for utilization of healthcare resources including emergency department (ED) visits and hospitalizations (hosp). Dalbavancin (DAL) is a long-acting lipopeptide approved for treatment of bacterial skin and skin structure infections, well suited for outpatient therapy due to a 1–2 dose regimen. We investigated the use of healthcare resources following DAL with associated costs compared with national data.

**Methods.** A multi-center, retrospective chart review was conducted of all high-risk patients receiving DAL during 2017 at participating sites. Data included demographics, diagnosis, Charlson index, prior/post-IV therapies, DAL regimen, and adverse drug reactions (ADRs). ED visits and hosp within 30 days post-DAL were assessed and compared with Healthcare Cost and Utilization Project Nationwide Inpatient Sample and Nationwide Emergency Department Sample stratified by diagnosis. The inpatient length of stay (LOS) was used to calculate hospital charges.

**Results.** DAL was administered to 124 patients (mean age:  $71 \pm 10$  years, mean Charlson index of 4.6, 55% male) in 10 POICs. Most patients (92%) received a 1-dose regimen. Diagnoses included cellulitis (32%), abscess (22%), diabetic foot infection (15%), osteomyelitis (10%), surgical site infections (9%), prosthetic device infection (9%), and musculoskeletal infections (3%). 55% were treated from the community. IV therapy with other agents was provided prior to DAL in 58% and following DAL in 6%. Moderate to severe ADRs were seen in 12 patients (10%) with 4 admitted to the ED

and 3 hosp. Median onset of ADRs was 5 days post DAL. All cause ED visits were 10 (8%), compared with a national rate of 10.6% based on diagnosis and age  $\geq 65$ . All cause 30-day hosp admissions were 11.3% (14/124) compared with a national rate of 16.1% based on diagnosis. Mean inpatient LOS was 4.9 days compared with 5.3 days, resulting in healthcare resource cost savings of \$97,014.

**Conclusion.** Use of DAL in high-risk, comorbid patients treated in POICs was associated with lower usage of both healthcare resources and corresponding costs than national estimates for respective diagnoses. AEs contributed to healthcare resource use. DAL provides a convenient outpatient treatment option for high-risk patients that may save use of healthcare resources.

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### 2381. Ceftolozane/Tazobactam in the Treatment of Experimental *Pseudomonas aeruginosa* Pneumonia in Persistently Neutropenic Rabbits: Impact on Strains With Genetically Defined Resistance

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**Background.** *Pseudomonas pneumonia* is a life-threatening infection with high mortality, particularly in neutropenic patients. The efficacy of current antimicrobial therapy with extended spectrum penicillins (ESPs) and anti-pseudomonal cephalosporins (ASCs) is limited by emergence of resistance. Ceftolozane/tazobactam is a novel cephalosporin with *in vitro* activity against isolates of *Pseudomonas aeruginosa* that are resistant to ESPs and ASCs. In order to assess the antimicrobial effect of ceftolozane/tazobactam in treatment of *Pseudomonas pneumonia*, we investigated this new agent in the treatment of experimental *Pseudomonas pneumonia* in persistently neutropenic rabbits infected with different strains of genetically defined mechanisms of resistance.

**Methods.** *Pseudomonas pneumonia* was established in a rabbit model by direct endotracheal inoculation of *P. aeruginosa*  $1 \times 10^8$ – $10^9$  CFUs for tracheobronchial colonization that evolves into bronchopneumonia. Four treatment groups were studied: ceftolozane/tazobactam, ceftazidime (CTZ), piperacillin/tazobactam (TZP), and untreated controls (UC). Rabbits were dosed IV to achieve humanized doses of ceftolozane/tazobactam 3g (2g/1g) Q8h, CTZ 2g Q8h, and TZP 4.5g Q8h. Four isolates of *P. aeruginosa* were studied: pan-susceptible (PS), OPRD porin loss (OPRDPL), efflux pump expression (EPE), and AmpC hyperexpression (ACHE). Profound, persistent neutropenia was maintained with cytosine arabinoside and methylprednisolone. Treatment was continued for 12 days.

**Results.** Treatment with ceftolozane/tazobactam resulted in  $\geq 10^5$  reduction in residual pulmonary bacterial burden caused by all 4 strains ( $P \leq 0.01$ ). This antibacterial activity coincided with reduction of lung weight ( $P < 0.05$ ), which is a marker of organism-mediated pulmonary injury. CTZ was less active in ACHE-infected rabbits, while TZP had less activity in EPE, ACHE, and OPRDPL strains. Survival was prolonged in ceftolozane/tazobactam and CTZ treatment groups in comparison to that of TZP and UC ( $P < 0.001$ ).

**Conclusion.** Ceftolozane/tazobactam is highly active in treatment of experimental *P. aeruginosa pneumonia* in persistently neutropenic rabbits, including infections caused by strains with the most common resistant mechanisms.

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### 2382. Ceftolozane/Tazobactam for the Treatment of Multidrug-Resistant *Pseudomonas aeruginosa* Infections in Immunocompromised Patients: A Multi-Center Study

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