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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/l-β-lactamide 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 (2/572) for suspected confirmed MDR GNB (Treated to ≥2 antibiotic in ≥2 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 45 (39%) of cases, respectively. The predominant pathogens were respiratory (40%) and urinary tract (20%). Blood cultures were positive in 10% of cases. Combination therapy (≥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 ≤ 12 (aOR 3.76, 95% CI 1.30, 10.88), primary bacteremia or respiratory source (aOR 2.96, 1.07–8.17) and age ≤ 65 (aOR 3.87, 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) ≥65 years comprise the highest risk for utilization of healthcare resources including emergency department (ED) visits and hospitalizations (hosps). Dalbavancin (DAL) is a long-acting lipoglycopeptide 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 treated with 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 ± 10 years, mean Charlson index of 4.6, 45% male) in 10 POICs. Most patients (92%) received a 1-dose regimen. Diagnoses included cellulitis (32%), abscess (22%), diabetic foot infection (13%), osteomyelitis (10%), sarcoma (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% (compared with a national rate of 10.6% based on diagnosis and age 265). 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 the use of healthcare resources.

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2381. Ceftolozane/Tazobactam in the Treatment of Experimental Pseudomonas aeruginosa Pneumonia in Persistently Neutropenic Rats: Impact on Strains With Genetically Defined Resistance
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Background. Pseudomonas aeruginosa is a life-threatening infection with high mortality, particularly in neutropenic patients. The efficacy of current antimicrobial therapies 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 aerugi- nosa that are resistant to ESPs and ASCs. In order to assess the antimicrobial effect of ceftolozane/tazobactam in treating experimental Pseudomonas pneumonia, we investigated this new agent in the treatment of experimental Pseudomonas pneumonia in persistently neutropenic rats infected with different strains of genetically defined mechanisms of resistance.

Methods. Pseudomonas aeruginosa pneumonia was established in a rabbit model by direct endotracheal inoculation of P. aeruginosa ≥10^6 CFUs for tracheobronchial colonization that evolves into bronchopneumonia. Four treatment groups were studied: ceftolozane/tazobactam, ceftazidime (CTZ), piperacillin/tazobactam (TZP), and untreated controls (UC). Rats were dosed IV to achieve humanized doses of ceftolo- zane/tazobactam 3g (2g) /Q8h, CTZ 2g Q8h, and TZP 4.5g Q8h. Four isolates of P. aeruginosa were studied: pan-susceptible (PS), OPRD porin loss (OPRDP), efflux pump expression (EPE), and AmpC hyperexpression (ACHE). Prolonged, persistent neutropenia was maintained with cytosine arabinoside and methylprednisolone.

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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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