Disclosures. All authors: No reported disclosures.

777. Combination Vancomycin/Cefazolin (VAN/CFZ) for Methicillin-Resistant Staphylococcus aureus (MRSA) Bloodstream Infections (BSI)
Trang D. Trinh, Pharm.D.1; Evan J. Zaowski, PharmD, BCPs2; Abdulhamid M. Lagin, MD3; Sathish Bhatia, B.S.4; Sorabh Dhar, MD4; Ryan Mynatt, PharmD5; Jason M. Pogue, PharmD6 and Michael J. Rybak, PharmD, MPH, PhD3. 1Anti-Infective Research Laboratory, Department of Pharmacy Practice, Wayne State University, Eugene Applebaum College of Pharmacy & Health Sciences, Detroit, Michigan, 2Detroit Medical Center, Detroit, Michigan, 3Detroit Medical Center / Wayne State University, Detroit, Michigan

Session: 76. Treatment of Resistant Infections - Clinical Analyses
Thursday, October 5, 2017: 12:30 PM

Background. VAN remains the standard for MRSA BSI but has been associated with treatment failures and resulted in prolonged BSI durations and recurrences. In vitro studies of VAN/CFZ against MRSA demonstrated synergy and prevention of VAN resistance. However, clinical use of VAN/CFZ has not been reported. The objective of this study was to compare patient outcomes treated with VAN/CFZ vs. VAN for MRSA BSI.

Methods. This was a retrospective, cohort, comparative-effectiveness study of hospitalized adults ≥18y with ≥1 MRSA blood culture and received VAN/CFZ combination for ≥24h or VAN alone initiated within 72h of index infection between 1/1/08 and 5/1/17. Patients who received ≥24h β-lactams other than CFZ, MRSA-active antibiotics other than VAN, with polymicrobial BSI, or had a second MRSA BSI episode during the study period were excluded. The primary composite failure outcome included: 30d mortality, MRSA BSI ≥7d, and 60d recurrence. Demographics were compared by X², Fisher’s exact, Student’s t, or Mann–Whitney U tests. Multivariable regression models compared outcomes between the two treatment groups. Covariates with p-values ≤0.2 in bivariate analyses were included in the model.

Results. A total of 101 patients were included (CFZ/VAN = 41, VAN = 60). Demographics were similar except VAN patients were older (mean ±SD) age 58 ±14 vs. 51 ±18 y, P = 0.04), had higher median (IQR) Charlson Comorbidity Index (3 (2-5) vs. 1 (0-4), P < 0.01), APACHE II scores (13 (8-18) vs. 11 (6-18), P = 0.2), and more endocarditis source (37% vs 20%, P = 0.06). After accounting for BSI source, VAN/CFZ (adjusted odds ratio [aOR], 95% confidence intervals [CI], 0.33, 0.13-0.83) and low APACHE II scores (aOR 1.07, 95% CI 1–1.15) were independently associated with fewer failures. Bivariate outcomes are in table below:

| Variable                  | n (%)         | CFZ/VAN | VAN | P value |
|---------------------------|---------------|---------|-----|---------|
| Composite failure         | 10 (24)       | 31 (52) |     | 0.006   |
| 30d mortality             | 3 (7.3)       | 5 (8.3) |     | 1       |
| BSI ≥7d                   | 6 (15)        | 21 (35) |     | 0.023   |
| 60d recurrence            | 3 (7.3)       | 9 (15)  |     | 0.351   |
| Failure switch            | 1 (2.4)       | 10 (17) |     | 0.026   |

Conclusion. In this cohort of MRSA BSI, patients treated with VAN/CFZ experienced fewer failures than with VAN alone, with shorter BSI durations. Additional studies are needed to confirm the role of VAN/CFZ combination treatment for MRSA BSI.

Disclosures. J. M. Pogue, Achaogen, Inc.: Consultant, Consulting fee. M. J. Rybak, Allergan: Scientific Advisor, Consulting fee.

778. Modeling Likelihood of Coverage for Narrow Spectrum Antibiotics in Patients Hospitalized with Urinary Tract Infections
Courtney Hebert, MD, MS1; Erin Hade, PhD2; Proteva Rahman, BS3; Mark Lustberg, MD, PhD4; Kurt Stevenson, MD, MPH, FSHEA1 and Preeti Pancholi, PhD5. 1Biomedical Informatics, The Ohio State University Wexner Medical Center, Columbus, Ohio, 2Biomedical Informatics, The Ohio State University, Columbus, Ohio, 3Division of Infectious Diseases, Department of Internal Medicine, The Ohio State University Wexner Medical Center, Columbus, Ohio, 4Division of Internal Medicine, Division of Infectious Diseases, The Ohio State University Wexner Medical Center, Columbus, Ohio, 5Clinical Microbiology, The Ohio State Univ Med Ctr, Columbus, Ohio

Session: 76. Treatment of Resistant Infections - Clinical Analyses
Thursday, October 5, 2017: 12:30 PM

Background. When prescribing empiric antibiotics, providers try to choose the narrowest spectrum antibiotic that will cover a patient's infection. To do this they must assess the likelihood of coverage of different regimens. We developed a model for cefazolin (or cephalexin) coverage for patients admitted to the hospital with urinary tract infections (UTI), to identify agroup of patients with a high likelihood of coverage by this first-line, narrow spectrum antibiotic. We also compared cefazolin coverage to the likelihood of coverage of other regimens. We developed a model for cefazolin coverage.

Methods. We developed a model for cefazolin coverage. The final model had an area under the receiver operating curve (AUC) of 69% (95% CI: 67%, 71%) in the test and 70%, (66%, 74%) in the validation set. Overall 49/65 (75%) in the highest estimated decile of cefazolin coverage had a UTI that would have been covered; only 13/66 (20%) in the lowest decile would have been covered. Of the 49/65 patients in the highest decile of coverage, 48/65 (74%) were covered by the actual empiric regimen given, however, 35/65 (54%) of those regimens consisted of multiple antibiotics, and of those patients who would have been covered by cefazolin, 36/69 (53%) were empirically treated with broader spectrum antibiotics.

Results. A total of 3,456 patients with an eligible UTI were included. Six hundred and Ninety-one (691) were held out for validation. Cefazolin covered 49% of the UTIs. The final model had an area under the receiver operating curve (AUC) of 69% (95% CI: 67%, 71%) in the test and 70%, (66%, 74%) in the validation set. Overall 49/65 (75%) in the highest estimated decile of cefazolin coverage had a UTI that would have been covered; only 13/66 (20%) in the lowest decile would have been covered. Of the patients in the highest decile of cefazolin coverage, 48/65 (74%) were covered by the actual empiric regimen given, however, 35/65 (54%) of those regimens consisted of multiple antibiotics, and of those patients who would have been covered by cefazolin, 36/69 (53%) were empirically treated with broader spectrum antibiotics.
Conclusion. Our findings suggest that the model can reasonably identify patients whose infections would be likely to be covered by ceftazolin. Further, the majority of patients would have been covered by a narrower spectrum antibiotics than what they received.

Research reported in this publication was supported by the National Institute of Allergy, and Infectious Diseases of the NIH under Award Number R01AI16975.

Disclosures. All authors: No reported disclosures.

779. Therapeutic efficacy of isavuconazole in experimental Aspergillus fumigatus endophthalmitis

John Guest, BS; Pawan Kumar Singh, PhD; Sanjay G. Revankar, MD; Pranatharthi H. Chandra sekhar, MD; and Ashok Kumar, PhD

University, Detroit, Michigan, 1Department of Ophthalmology, Kresge Eye Institute, Wayne State University School of Medicine, Detroit, Michigan, 2Division of Infectious Disease, Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan, 2Department of Anatomy and Cell Biology, Wayne State University School of Medicine, Detroit, Michigan, 3Department of Microbiology, Immunology, and Biochemistry, Wayne State University School of Medicine, Detroit, Michigan

Session: 76. Treatment of Resistant Infections - Clinical Analyses

Thursday, October 5, 2017: 12:30 PM

Background. Fungal endophthalmitis remains a significant cause of vision impairment and blindness with poor prognosis, in part, due to delay in diagnosis and limited availability of antifungal agents without ocular toxicity. Thus, it is imperative to evaluate the therapeutic efficacy of newer antifungal agents such as Isavuconazole in fungal endophthalmitis.

Methods. Aspergillus fumigatus (AF) endophthalmitis was induced by intravitreal (IVT) injection of AF spores in C57BL/6 mice eyes. Therapeutic efficacy of isavuconazole was evaluated by administering the drug in five treatment groups (1) oral gavage, (2) IVT injections, (3) intravenous, (4) IVT injection followed by oral gavage, and (5) IVT injection followed by intravenous. In all treatment groups, isavuconazole therapy was started at 6 h post infection and continued daily for a maximum of three day post infection (dpi). Disease progression was monitored by daily eye exam and the assessment of retinal function using the electroretinogram (ERG) diagnostic test. Encuclated eyes were used for histology and the determination of fungal burden and inflammatory cytokines.

Results. In comparison to placebo, isavuconazole treatment significantly (P < 0.001) retained retinal function in all treatment groups. This coincided with preservation of retinal architecture (histology analysis) and reduction in fungal burden and intraocular inflammation. Among various treatment groups, daily oral administration of isavuconazole alone was as effective as IVT alone, as evidenced by significant (P < 0.0001) inhibition of inflammatory cytokine levels (TNF-α, IL-1β, IL-6), drastic (P < 0.0001) reduction in fungal burden and retinal tissue damage, culminating in significant (P < 0.001) retention of retinal function (ERG response). Moreover, oral isavuconazole combined with single IVT injection also seems to be highly effective in comparison with IVT+ intravenous delivery of the drug.

Conclusion. In this first proof-of-principle study, we show that isavuconazole can potentially be used for the treatment of fungal (Aspergillus) endophthalmitis. Moreover, the better efficacy of oral administration alone may avoid the need for an invasive procedure (IVT injection) to deliver antifungal agents into the eye.

Disclosures. A. Kumar, Astellas Pharma Global Development, Inc.; Grant Investigator, Research grant

870. Piperacillin-tazobactam vs. carbapenem for treating blood stream infections due to extended spectrum β-lactamase producing bacteria: Systematic review and meta-analysis

Marou Sfeir, MD, MPH1; Gulce Akins, MPH2 and Paul Christos, Dr.PH, MS3

1Medicine: Division of Infectious Disease, New York-Presbyterian Hospital/ Weill Cornell Medicine, New York, New York, 2Healthcare Policy & Research, Weill Cornell Medicine, New York, New York

Session: 76. Treatment of Resistant Infections - Clinical Analyses

Thursday, October 5, 2017: 12:30 PM

Background. Infections due to extended-spectrum β-lactamases-producing Enterobacteriaceae (ESBL-PE) pose a major public health threat due to poor outcomes and high mortality rates. Given the lack of randomized trials comparing PTZ to carbapenem in treating infections due to ESBLPE, we aimed to conduct a systematic review and meta-analysis to investigate the impact of PTZ on mortality of patients with ESBLPE bloodstream infections (BSI) compared with carbapenem.

Methods. MEDLINE, EMBASE, Scopus, and the Cochrane library were searched electronically for studies between 1950 and January 15, 2017 that have provided data for mortality and addressed the terms “extended spectrum β-lactamases or ESBL” and “PTZ or β-lactam/β-lactamase inhibitor” and “carbapenem”. We also searched the reference sections of included studies looking for possible missed pertinent studies. Data extraction regarding study design, characteristics of the population, intervention, comparator, and outcomes was performed. The random-effects meta-analysis was performed with the use of StatsDirect statistical software (Version 3.0.190).

Results. Twenty-nine cohort or case–control studies were included and analyzed; 12 evaluated definitive treatment and 17 studied empiric therapy. PTZ was associated with a non-statistically significant higher 30-day mortality than carbapenem [odds ratio (OR) 1.28, 95% CI 0.88–1.86] for ESBLPE BSI treatment (Figure). No statistically significant differences in mortality were found between PTZ and carbapenem administered as definitive (OR 2.46, 95% 0.93–6.54) or empirical (RR 1.12, 95% CI 0.76–1.66) treatment. A subgroup analysis that included 3 studies that randomized mortality based on PTZ MIC revealed that PTZ MIC >1/4 but ≤ 4/4 is associated with a non-significantly higher mortality compared with carbapenem with OR 1.33, 95% CI 0.29–6.03. All 17 patients who had a PTZ MIC of ≤ 0.5/4 survived after they were treated with PTZ, but the difference with carbapenem could not be estimated.

Conclusion. PTZ was not significantly associated with higher overall 30-day mortality compared with carbapenem in treating EBLPE BSI. It may be considered as alternative treatment, especially if PTZ MIC is ≤ 0.5/4. There is a need for randomized controlled trials to better guide clinical practice and limit the use of carbapenem.

Disclosures. All authors: No reported disclosures.

781. Pharmacokinetic Assessment of Continuous Infusion Ceftolozane/Tazobactam for Drug-Resistant Pseudomonas aeruginosa Left Ventricular Assist Device Driveline Infection

Rachel Foster, PharmD, MBA1; Alyssa P. Gould, PharmD2; Julie Ann Justo, PharmD, MS, BCPS-AQ ID3; Stella Okoye, MD, MD1; David P. Nicolau, PharmD, FCCP, FIDSA4 and P Brandon Bookstaver, PharmD, FCCP, FIDSA, BCPS, AAHIVP, AAHIVP5

1Clinical Pharmacy and Outcomes Sciences, South Carolina College of Pharmacy, Columbia, South Carolina, 2Department of Clinical Pharmacy and Outcomes Sciences, University of South Carolina College of Pharmacy, Columbia, South Carolina, 3Department of Microbiology, Wayne State University School of Medicine, Detroit, Michigan, 4Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, Connecticut

Session: 76. Treatment of Resistant Infections - Clinical Analyses

Thursday, October 5, 2017: 12:30 PM

Background. Pseudomonas aeruginosa is a common pathogen in left ventricular assist device (LVAD) infections. Ceftolozane/tazobactam (C/T) is a β-lactam/β-lactamase inhibitor with activity against P. Aeruginosa, including multi-drug-resistant (MDR) isolates. We describe the novel use of continuous infusion (CI) C/T with therapeutic drug monitoring in a 70-year-old man who developed a MDR P. Aeruginosa VAD driveline infection.

Methods. The patient received CI C/T 6g IV over 24 hours to facilitate long-term outpatient therapy after receipt of five days of intermittent infusion (3g IV every 8 hours over 1 hour). Blood samples were collected in heparinized tubes immediately prior to and 6, 12, 18, 24, and 48 hours after initiating CI. The samples were