Conclusion. Our findings suggest that the model can reasonably identify patients whose infections would be likely to be covered by cefazolin. 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 R01AI116975.

Disclosures. **All authors:** No reported disclosures.

779. Therapeutic efficacy of isavuconazole in experimental *Aspergillus fumigatus* endophthalmitis

John Guest, BS[1]; Pawan Kumar Singh, PhD[2]; Sanjay G. Revankar, MD[3]; Pranatharthi H. Chandrasekar, MD[3] and Ashok Kumar, PhD[2,4,5]; [1]Ophthalmology, Wayne State University, Detroit, Michigan, [2]Department of Ophthalmology, Kresge Eye Institute, Wayne State University School of Medicine, Detroit, Michigan, [3]Division of Infectious Disease, Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan, [4]Department of Anatomy and Cell Biology, Wayne State University School of Medicine, Detroit, Michigan, [5]Department 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 starting at 6 h post *AF*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. Enucleated 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 be potentially 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

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

Maroun Sfeir, MD, MPH[1,2]; Gülce Askin, MPH[2] and Paul Christos, Dr.PH, MS[2]; [1]Medicine/ Division of Infectious Disease, New York-Presbyterian Hospital/ Weill Cornell Medicine, New York, New York, [2]Healthcare 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 reported 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≤ 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.

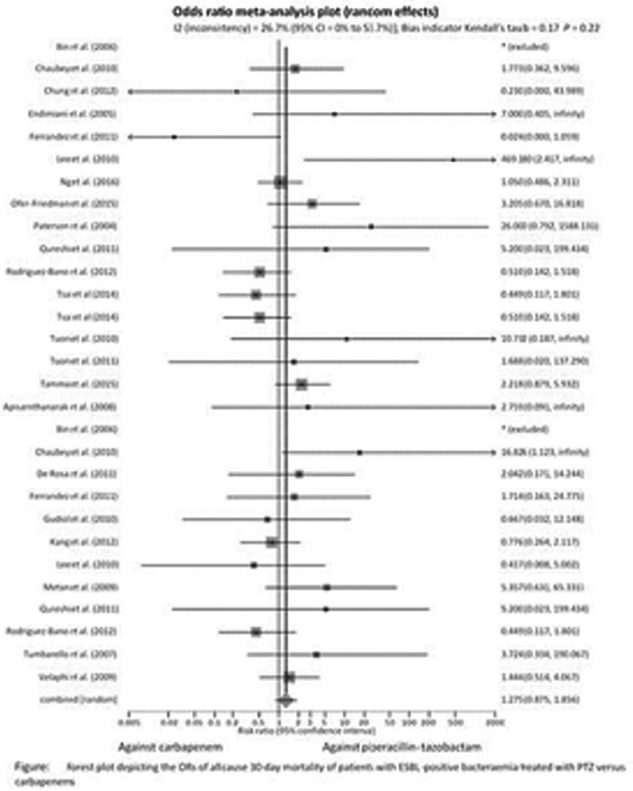

Figure: Forest plot depicting the ORs of all-cause 30-day mortality of patients with ESBL positive bacteriamia treated with PTZ versus carbapenems

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, MBA[1]; Alyssa P. Gould, PharmD[2]; Julie Ann Justo, PharmD, MS, BCPS-AQ ID[3]; Stella Okoye, MD[4]; David P. Nicolau, PharmD, FCCP, FIDSA[5] and P. Brandon Bookstaver, PharmD, FCCP, FIDSA, BCPS, AAHIVP, AAHIVP[3]; [1]Clinical Pharmacy and Outcomes Sciences, South Carolina College of Pharmacy, Columbia, SC, [2]Palmetto Health Richland, Columbia, South Carolina, [3]Department of Clinical Pharmacy and Outcomes Sciences, University of South Carolina College of Pharmacy, Columbia, South Carolina, [4]University of South Carolina School of Medicine, Columbia, South Carolina, [5]Center 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* LVAD 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 at 6, 12, 18, 24, and 48 hours after initiating CI. The samples were

centrifuged at 2,500 rpm for 10 minute and stored at -80°C until assayed. Ceftolozane and tazobactam concentrations were quantified using previously validated high-performance liquid chromatography (HPLC) methods.

Results. Ceftolozane and tazobactam concentrations are shown in Table 1. The susceptibility profile (VITEK® 2) demonstrated the following minimum inhibitory concentrations (MICs): gentamicin ≤ 1 mcg/mL, cefepime = 32 mcg/mL, ciprofloxacin ≥ 4 mcg/mL, meropenem = 8 mcg/mL. Colistin, polymyxin B, and C/T MICs were confirmed via E-test (2 mcg/mL, 2 mcg/mL, and 1.5 mcg/mL, respectively). The patient clinically improved with resolution of signs and symptoms of infection after 6 weeks with CI C/T. Suppressive therapy was continued indefinitely in lieu of source control. A subjective increase in gout pain was reported, but no other major adverse events were noted during therapy.

Conclusion. Adequate systemic drug concentrations of C/T well above the MIC were achieved when administered as a CI of 6g over 24 hours. Based on serum ceftolozane concentrations, dose modification of CI may be possible with future evaluation. Continuous infusion represents a potentially well-tolerated delivery for C/T and warrants further study.

Table 1. Ceftolozane and tazobactam drug concentrations.

Collection Time	Ceftolozane Concentration (µg/ml)	Tazobactam Concentration (µg/ml)
Intermittent Infusion		
Trough, steady state	97.83	25.62
Continuous Infusion		
6 hour	55.12	16.91
12 hour	47.49	13.32
18 hour	39.36	9.31
24 hour	39.90	10.92
48 hour	40.64	19.64

Disclosures. **D. P. Nicolau**, Merck: Investigator and Speaker's Bureau, Research support. **P. B. Bookstaver**, Rock Pointe: Content Developer, Consulting fee

782. Antimicrobial resistance patterns of colonizing *Streptococcus pneumoniae* among young child-mother pairs in the rural highlands of the Peruvian Andes

Leigh Howard, MD, MPH[1]; Kathryn Edwards, MD, FIDSA[2]; Marie Griffin, MD, MPH[3]; Ana Gil, MS[4]; Gina Minaya, Licensed auxiliary nurse[5]; Erik Mercado, BS[6]; Theresa Ochoa, MD[6]; Claudio Lanata, MD, MPH[4] and Carlos G. Grijalva, MD, MPH[7]; [1]Pediatrics, Vanderbilt University Medical Center, Nashville, TN, [2]Department of Pediatrics, Division of Pediatric Infectious Diseases, Vanderbilt University School of Medicine, Nashville, TN, [3]Vanderbilt University Medical Center, Nashville, TN, [4]Instituto de Investigacion Nutricional, Lima, Peru, [5]Instituto de Investigación Nutricional, Lima, Peru, [6]Universidad Peruana Cayetano Heredia, Lima, Peru, [7]Department of Health Policy, Vanderbilt University Medical Center, Nashville, TN

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

Background. Despite widespread use of pneumococcal conjugate vaccines (PCVs), *Streptococcus pneumoniae* (pneumococcus) remains an important cause of pneumonia. Prior to widespread PCV use, we found a high prevalence of nasopharyngeal (NP) colonization with pneumococcus resistant to multiple antibiotic classes among young children in the rural highlands of Peru. We sought to confirm contemporary resistance profiles among young children, their mothers, and animal contacts in the post-PCV era.

Methods. We enrolled eligible members of Peruvian households whose children had participated in our previous study. Mothers were questioned about antibiotic use for themselves and their children age <3 years. NP samples were collected from children, mothers, and their animal contacts including cows, guinea pigs, and dogs, when available. Samples were cultured for pneumococcus using standard methods and routine disk antibiotic susceptibility testing was performed. Drinking water and milk samples were tested, when available, for the presence of β-lactam and tetracycline residues (IDEXX B-Tetra testing kit; Westbrook, ME).

Results. Members of 47 households were enrolled, including 50 children and 47 mothers (3 sibling pairs). The median (IQR) age of children was 1.2 years (0.6-2.2) and number of household members was 5 (4-6). Sixteen of 50 (32%) children and 7/47 (15%) mothers had received antibiotics in the prior 6 months (**Fig 1**). Pneumococcus was detected in 31/50 (62%) children, 9/47 (19%) mothers, and 1/31 (3%) guinea pigs. Pneumococci were not detected in dogs (n = 29) or cows (n = 7). Resistance to multiple classes of antibiotics, including TMP-SMX, tetracyclines, and β-lactams, was common among children and adults (**Fig 2**). No antibiotic residues were detected in water (n = 41) or milk (n = 7) samples.

Conclusion. Pneumococcal colonization was common among young children, less prevalent among adults, and rare among animals. Resistance to macrolides and tetracyclines was common despite very little reported use of these antibiotics in people. Additional studies should evaluate whether this high prevalence of resistance is a result of local prescribing practices or unintentional environmental exposures.

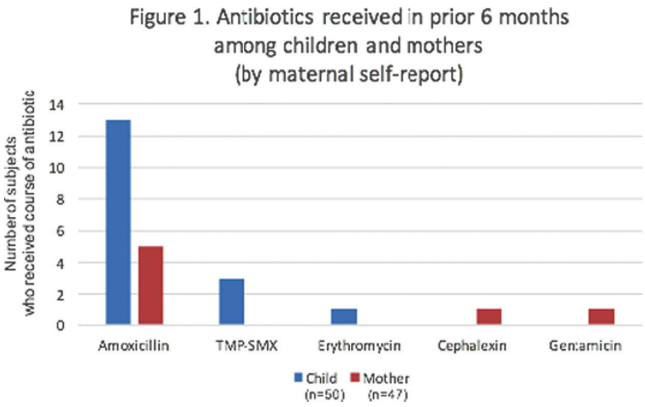

Figure 2. Prevalence of antimicrobial susceptibility among pneumococcal isolates in children and adults

	Children (n=31)		Adults (n=9)	
	I/R n (%)	S n (%)	I/R n (%)	S n (%)
TMP-SMX	26 (84)	5 (16)	6 (67)	3 (33)
Oxacillin	23 (74)	8 (26)	3 (33)	6 (67)
Erythromycin	16 (52)	15 (48)	2 (22)	7 (78)
Azithromycin	15 (48)	16 (52)	2 (22)	7 (78)
Tetracycline	10 (32)	21 (68)	4 (44)	5 (56)
Clindamycin	5 (16)	26 (84)	1 (11)	8 (89)
Rifampicin	1 (3)	30 (97)	0 (0)	9 (100)
Vancomycin	1 (3)	30 (97)	0 (0)	9 (100)
Levofloxacin	0 (0)	31 (100)	0 (0)	9 (100)
Chloramphenicol	0 (0)	31 (100)	0 (0)	9 (100)

* TMP-SMX, trimethoprim-sulfamethoxazole; I/R, intermediate/resistant; S, susceptible

ADDIN EN.REFLIST

Disclosures. **K. Edwards**, Novartis: Grant Investigator, Research grant. **M. Griffin**, MedImmune: Grant Investigator, Grant recipient. **C. Lanata**, Takeda: Scientific Advisor, Consulting fee. **C. G. Grijalva**, Pfizer: Consultant, Consulting fee.

783. Associations Between Timeliness of Therapy and Clinical and Economic Outcomes Among Patients With Serious Infections Due to Gram-negative Bacteria (GNB): How Much Does Delayed Appropriate Therapy (DAT) Matter?

Nicole G. Bonine, PhD, MPH[1]; Ariel Berger, MPH[2]; Arman Altincatal, MS[2]; Rosa Wang, MHA[2]; Tarun Bhagnani, MS[2]; Patrick Gillard, PharmD[1] and Thomas Lodise, PharmD, PhD[3]; [1]Allergan plc, Irvine, California, [2]Evidera, Waltham, MA, [3]Albany College of Pharmacy and Health Sciences, Albany, New York

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

Background. Patients with serious GNB infections who receive DAT have worse outcomes. Most studies that have examined this issue include both antibiotic-resistant and susceptible pathogens. It is difficult to assign causality as DAT is correlated with resistance, which is associated with poorer prognosis. Our objective was to assess association between DAT and outcomes among patients with GNB infection, stratified by antibiotic susceptibility status.

Methods. Hospitalized adults between 7/2011–9/2014 were identified from Premier Hospital Database. Patients were diagnosed with complicated urinary tract infection, complicated intra-abdominal infection, hospital-associated pneumonia, or bloodstream infection, and had a positive culture for GNB from a site consistent with infection type (date of culture draw was index date). Patients were required to receive antibiotics on this date or ≤2 days after. Delayed therapy was defined as no receipt of an antibiotic with microbiologic activity during this period. Patients were stratified by antibiotic-resistant GNB (Third-generation cephalosporin-resistant Enterobacteriaceae, carbapenem-resistant (CR) Enterobacteriaceae, CR *Pseudomonas sp.*, or multi-drug-resistant *Pseudomonas sp.*) vs. antibiotic-susceptible GNB counterparts. Inverse probability weighting and multivariate regression analyses were used to estimate the association between DAT and outcomes. Logistic models were used for composite mortality (in-hospital death or discharge to hospice) and discharge to home. Generalized linear models were used for post-index duration of antibiotic therapy, hospital length of stay (LOS), and costs.