combination therapy in 631 (43%) encounters, which most often included aminoglycosides, colistin or tigecycline. Mortality was 22% in the monotherapy and 25% in the combination therapy group ($P = 0.08$).

Conclusion. CAV use across US academic medical centers has increased modestly over 3 years. More than 40% of CAV prescriptions appear to be empiric and targeted therapy often occurs without ID consultation at academic centers.

Table 1: Demographics for Encounters Receiving Ceftazidime-avibactam

Variable	Encounters receiving ceftazidime-avibactam N = 2128 (%)
Age (median and IQR)	56 (27)
Sex	
Male	1254 (59)
Female	874 (41)
Race	
White	1358 (64)
African American	462 (22)
Other	240 (11)
Unknown	68 (3)
Comorbid condition	
Congestive heart failure	501 (24)
Diabetes mellitus	810 (38)
Transplant	141 (7)
Malignancy	86 (4)
Dialysis	202 (9)
Tracheostomy	423 (20)
Chronic kidney disease	667 (31)
Presumed site of infection#	
Abdominal	330 (16)
Bacteremia	100 (5)
Central nervous system	8 (0.4)
Central venous catheter	136 (6)
Respiratory	720 (34)
Skin/soft tissue	167 (8)
Urinary	557 (26)
Unknown/other	656 (31)
Admission APR DRG Severity of Illness assignment*	
Minor	12 (1)
Moderate	153 (8)
Major	669 (33)
Extreme	1204 (59)
Hospital Region	
Midwest	30 (33)
Northeast	27 (29)
South	21 (23)
West	14 (15)
Length of stay (median days and IQR)	19 (31)
ICU stay	862 (41)

#Not mutually exclusive
*1 Encounter missing APR DRG SOI data
APR DRG= All patients refined diagnosis related groups (provided by 3M™)

Figure 1A: Cumulative Increase in the Number of Hospital Prescribing Ceftazidime-avibactam within the Vizient Database (168 hospitals) by Quarter, 2015q1–2017q4

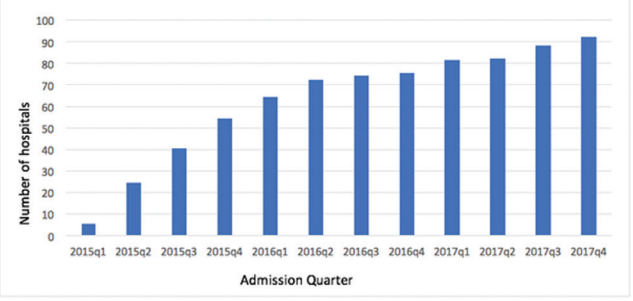
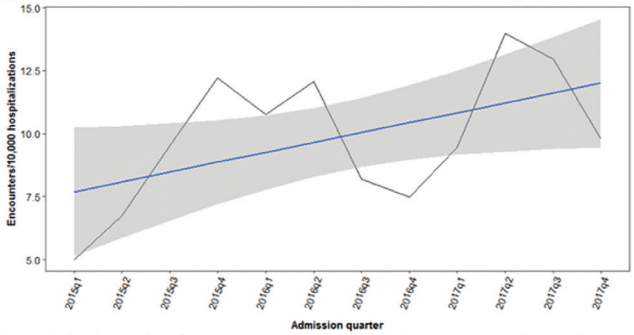
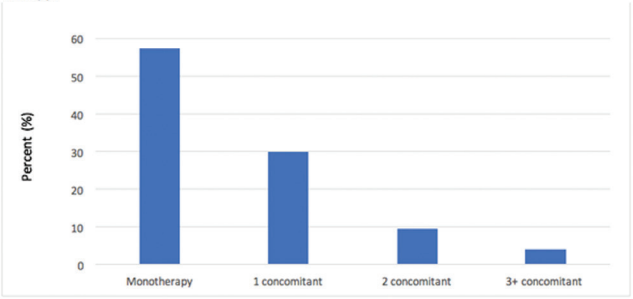


Figure 1B Trends in the Number of Encounters Prescribing Ceftazidime-Avibactam by Quarter



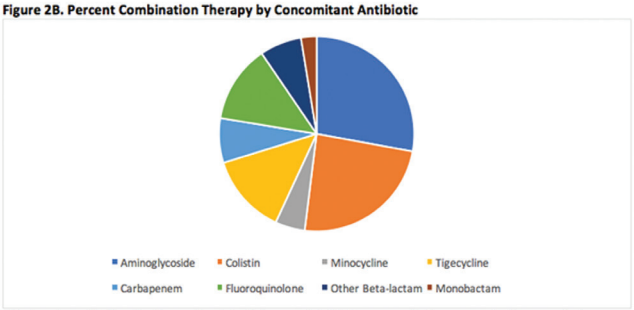
*Rate calculated as number of encounters receiving CA per total admissions in hospitals prescribing ceftazidime-avibactam by quarter.
**Quarterly Percent Change: 2.1 [0.7-3.6], (p=0.004)

Figure 2A. Percent of Targeted Therapy Encounters that Received Monotherapy versus Combination Therapy.



*Concomitant antibiotic was any of the select gram-negative active antibiotics (see below) prescribed for 3 consecutive days in addition to ceftazidime-avibactam, except for aminoglycosides which could be prescribed on day 1 and day 3 of the overlap period

Figure 2B. Percent Combination Therapy by Concomitant Antibiotic



*Aminoglycoside (amikacin, gentamicin, tobramycin), Carbapenem (ertapenem, doripenem, imipenem, meropenem), Fluoroquinolone (ciprofloxacin, levofloxacin), Other β-lactam (piperacillin-tazobactam, ampicillin-sulbactam, ceftazidime, cefepime), Monobactam (aztreonam)
#Reserve agents include: aminoglycosides, colistin, and tigecycline
** Funding Source: Division of Intramural Research, NIAID, NIH and NCI Contract No. HHSN261200800001E

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

2399. β-Lactam Therapy for Potential AmpC-Producing Organisms: A Cohort Study and an Updated Systematic Review and Meta-Analysis

Matthew P. Cheng, MD[1]; Robyn Lee, PhD[2]; Alexandre P. Cheng, BSc[3]; Samuel De L'Étoile-Morel, MD[4]; Koray Demir, MDCM Candidate[5]; Cedric Yansouni, MD[6]; Patrick Harris, MBBS FRACP FRCPA[7]; Emily Mcdonald, MDCM, MSc[8] and Todd C. Lee, MD, MPH[8]; [1]Harvard Medical School, Boston, Massachusetts, [2]Harvard School of Public Health, Boston, Massachusetts, [3]École Polytechnique de Montréal, Montréal, QC, Canada, [4]McGill University, Montreal, QC, Canada, [5]McGill University Faculty of Medicine, Montreal, QC, Canada, [6]Infectious Diseases, McGill University, Montreal, QC, Canada, [7]Central Pathology, Pathology Queensland, Brisbane, Australia, [8]Clinical Practice Assessment Unit, McGill University, Montréal, QC, Canada

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

Background. Certain organisms, including *Serratia, Providentia, Acinetobacter, Citrobacter, Enterobacter*, and *Morganella* species (SPACE-M) may possess an inducible broad-spectrum β-lactamase, AmpC, which is not inhibited by most β-lactamase inhibitors. Our objective was to determine whether treating SPACE-M bloodstream infections (BSI) with potentially hydrolyzable β-lactams was associated with increased risk of 30-day mortality.

Methods. A retrospective cohort study was performed including all adult cases of bacteremia attributed to SPACE-M species between April 2010 and June 2015 at the McGill University Health Centre (Montreal, Canada). We used multivariable logistic regression to estimate the odds ratio (OR) of death or recurrence within 30 days for potentially hydrolyzable β-lactams vs. other therapies. We then updated a systematic review and meta-analysis comparing carbapenems to β-lactam/β-lactamase inhibitors (BL/BLIs). We included studies published up to December 31, 2017 and calculated the unadjusted OR for mortality within 30 days comparing BL/BLI vs. carbapenems as definitive therapy.

Results. Over the 5-year period, there were 173 BSI involving SPACE-M organisms at our center. After adjusting for patient comorbidities and severity of the initial illness, the use of hydrolyzable β-lactams as definitive therapy was not associated with an increased risk of death or recurrence when compared with other antimicrobial agents (OR 1.20, 95% CI 0.40–3.62). The meta-analysis further suggested that patients treated with BL/BLI therapy have similar outcomes to those treated with carbapenems (30-day mortality OR 1.13, 95% CI 0.58–2.20).

Conclusion. The use of β-lactam/β-lactamase inhibitors may remain a viable carbapenem-sparing option for patients with potential AmpC-producing organisms.

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

2400. Activity of a Long-Acting Echinocandin, Rezafungin, Tested Against Invasive Fungal Isolates Collected Worldwide

Michael A. Pfaller, MD; Shawn A. Messer, MS-MT; Paul R. Rhomberg, BS; Beth A. Schaefer, BS and Mariana Castanheira, PhD; JMI Laboratories, Inc., North Liberty, Iowa

Session: 250. Treatment of AMR Infections

Saturday, October 6, 2018: 12:30 PM

Background. Echinocandins are important agents for treating invasive fungal infections. We evaluated the activity of rezafungin (RZF; previously CD101), an echinocandin with extended half-life, and comparators using CLSI broth microdilution methods against 719 invasive fungal isolates collected worldwide during 2017.

Methods. Susceptibility tests were conducted on 616 *Candida* spp. (6 species), 25 *C. neoformans* (CNEO), 18 *A. flavus* (AFL), and 60 *A. fumigatus* (AFU) for RZF, anidulafungin, caspofungin, micafungin, and azoles. CLSI clinical breakpoint (CBP) and epidemiological cutoff value (ECV) interpretive criteria were applied.

Results. RZF inhibited 100.0% of *C. albicans* (CA) isolates, 96.3% of *C. tropicalis* (CT), 93.4% of *C. glabrata* (CG), 100.0% of *C. krusei*, and 100.0% of *C. dubliniensis* at ≤0.12 µg/mL. All but 2 (116/118 [98.3%]) *C. parapsilosis* (CP) isolates were inhibited by RZF at ≤2 µg/mL. Resistance to fluconazole was detected among 10.7% of CG, 10.2% of CP, 1.9% of CT, and 0.7% of CA. The activity of RZF against these 6 *Candida* spp. was similar to that of the other echinocandins, the vast majority of which were susceptible/wild type (WT) using CBP/ECV. Fluconazole and other triazoles displayed good activity against CNEO whereas echinocandins, including RZF, displayed limited activity against CNEO isolates (MIC90 >8 µg/mL). Echinocandins displayed good activity against ASF and AFL, and RZF activity was similar to that of anidulafungin, caspofungin, and micafungin. All isolates displayed WT MIC values for the mold-active azoles.

Conclusion. Rezafungin was as active as other echinocandins against common fungal organisms recovered from invasive fungal infections. The extended half-life and stability of rezafungin is very desirable for prevention and treatment, especially in patients who could be discharged on outpatient therapy.

	MIC/MEC$_{50/90}$ (µg/mL)			
Organism (no. tested)	Rezafungin	Anidulafungin	Caspofungin	Micafungin
C. albicans (267)	0.03/0.06	0.015/0.06	0.015/0.03	0.015/0.015
C. glabrata (121)	0.06/0.12	0.06/0.12	0.03/0.06	0.015/0.03
C. parapsilosis (118)	1/2	2/2	0.25/0.5	1/1
C. tropicalis (54)	0.03/0.12	0.03/0.06	0.03/0.06	0.03/0.06
C. dubliniensis (28)	0.06/0.12	0.03/0.12	0.03/0.03	0.015/0.03
C. krusei (28)	0.03/0.12	0.06/0.12	0.12/0.25	0.06/0.12
A. fumigatus (60)	0.015/0.015	0.015/0.03	0.03/0.03	≤0.008/0.015
A. flavus (18)	0.015/0.015	0.015/0.03	0.03/0.03	0.015/0.03

Disclosures. **M. A. Pfaller**, Cidara Pharmaceuticals: Research Contractor, Research support. **S. A. Messer**, Cidara Pharmaceuticals: Research Contractor, Research support. **P. R. Rhomberg**, Cidara Pharmaceuticals: Research Contractor, Research support. **B. A. Schaefer**, Cidara Pharmaceuticals: Research Contractor, Research support. **M. Castanheira**, Cidara Pharmaceuticals: Research Contractor, Research support.

2401. Risk Factors for Antimicrobial Resistance in Invasive Pneumococcal disease (IPD) in Toronto, Canada, 2012–2017

Thomas Fear, MD[1]; Karen Green, MSc, RN[2]; Agron Plevneshi, BSc[2]; Jeff Li, BSc[2]; Wallis Rudnick, MSc[2]; Sarah Nayani, PhD[3]; Allison McGeer, MD, MSc[4] and Toronto Invasive Bacterial Diseases Network; [1]Internal Medicine, University of Toronto, Toronto, ON, Canada, [2]Mount Sinai Hospital, Toronto, ON, Canada, [3]Microbiology, Sinai Health System, Toronto, ON, Canada, [4]Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada

Session: 250. Treatment of AMR Infections

Saturday, October 6, 2018: 12:30 PM

Background. Several studies have documented factors predictive of antimicrobial resistance (AMR) in invasive pneumococcal disease(IPD). However, the implementation of routine pediatric PCV programs, antimicrobial stewardship, and increasing immunocompromised in populating might be expected to change such factors. We report on predictive factors for AMR in IPD from 2012 to 2017.

Methods. TIBDN performs population-based surveillance for IPD in Toronto/Peel (pop 4.5M). IPD cases are reported to a central office and one isolate/case is serotyped and has antimicrobial susceptibility testing performed by broth microdilution to CLSI standards.

Results. 2459 cases of IPD were identified from January 2012 to December 2017. Overall rates of resistance to penicillin, macrolides, fluoroquinolones, and TMP-SMX were relatively stable over the course were stable over the study. Risk factors for infection with resistant to penicillin at meningitis breakpoints as opposed to penicillin- susceptible pneumococci were current residence at nursing home (odds ratio [OR], 2.30; $P < 0.001$), immune compromised status (OR, 1.41; $P = 0.012$), HIV infection (OR 2.13, P = 0.016), history of receiving PPV23 vaccine (OR 1.38; $P = 0.007$). Infection with TMP-SMX-resistant pneumococci was associated with HIV infection (OR, 3.2; $P = 0.001$) and current residence in a nursing home (OR 2.4, $P = 0.002$). Infection with macrolide-resistant isolates was associated with any use of macrolide 3 months prior to infection (OR, 3.24; $P < 0.001$), or macrolide treatment failure of the current episode (OR, 6.64; $P = 0.003$). Infection with levofloxacin-resistant pneumococci was associated with current residence in a nursing home (OR, 13.7; $P < .001$), and fluorquinolone treatment failure of the current episode (OR 49.4, $P = 0.0034$).

Conclusion. Previous same class antibiotic exposure remains a major predictive factor for macrolide resistance. History of treatment failure is a predictive factor for macrolide and fluoroquinolone failure. HIV infection and immune compromise are risk factors for IPD infection with penicillin resistant pneumococci. Hospital acquisition of infection is no longer a risk factor for fluoroquinolone resistance.

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

2402. Daptomycin Pulmonary Eosinophilia: Review of Cases and New Hyperacute Syndromic Presentation

Katelyn West, MS[1]; Kimberly Mackay, PharmD[2] and Graeme N. Forrest, MBBS, FIDSA[3,4]; [1]VA Portland Healthcare System, Portland, Oregon, [2]Pharmacy, VA Portland Healthcare System, Portland, Oregon, [3]Division of Infectious Disease, Veterans Affairs Portland Health Care System, Portland, Oregon, [4]Section of Infectious Disease, Department of Medicine, Oregon Health & Science University, Portland, Oregon

Session: 250. Treatment of AMR Infections

Saturday, October 6, 2018: 12:30 PM

Background. Daptomycin pulmonary eosinophilia (DPE) has been described as a rare event. Since the Food and Drug Administration (FDA) first described the syndrome which occurs about 3 weeks after starting the drug, it continues to be a miss diagnosed. Most outpatient antibiotic treatment (OPAT) programs focus on screening for CPK elevations. We describe an unusual increase in DPE at our center including acute reactions on re-exposure to daptomycin.

Methods. Retrospective review from local VA pharmacy and OPAT database of adverse drug events (ADE) with daptomycin from 2010 to April 2018. Data evaluated include, age, gender, weight, body mass index (BMI), daptomycin dosing, indication for use, duration of therapy, time to symptom onset, Creatinine clearance, white cell count (WCC), %eosinophilia (%eos), admission to intensive care unit (ICU), and clinical outcomes or interventions.

Results. There were 363 unique initiations of Daptomycin in the time period. There were 17 DPE (5%) and 3 CPK (0.6%) events in that time period. The medians for all DPE was; Age 68 years (range 55–95), BMI 29 m/kg^2 (range 21–49.5), daptomycin dose 500 mg (>7 mg/kg), baseline CrCl 35.5 mL/minute, eosinophilia at onset of DPE 9% (8–44%), and duration of therapy to onset was 21 days (1–33). All recovered on removal of daptomycin, but 5 patients required adjunctive corticosteroid therapy. Four patients had a severe and novel hyperacute DPE within 48 hours of a new initiation of daptomycin therapy. All 4 patients had prior exposure to daptomycin in the last 12 months. They presented with hypoxic respiratory failure, abnormal chest x-rays and/or CT chest scans, with preceding systemic fevers and fatigue after the first dose. All had low grade %eos (3–5%) on prior use, and all recovered rapidly with discontinuation of daptomycin.

Conclusion. DPE may be underreported and is associated with doses of 500 mg or >7 mg/kg, with CrCl <35 mL/minute and older age. Of concern are the new cases of hyperacute DPE within 48 hours of re-exposure to daptomycin that we have seen, who had prior low-grade eosinophilia. Close monitoring of these factors may be warranted in at risk individuals.

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

2403. Comparison of Daptomycin Combination Therapy With Ceftaroline or Oxacillin Against Methicillin-Resistant *Staphylococcus aureus* (MRSA) Isolates Causing Persistent Bacteremia

Jeannette Bouchard, PharmD[1]; Chelsea Jones, BA[2]; Ellen Kline, MS[2]; Louise-Marie Oleksiuk, PharmD[1] and Ryan K. Shields, PharmD[3]; [1]UPMC Presbyterian Shadyside, Pittsburgh, Pennsylvania, [2]University of Pittsburgh, Pittsburgh, Pennsylvania, [3]University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania

Session: 250. Treatment of AMR Infections

Saturday, October 6, 2018: 12:30 PM

Background. Increasing evidence suggests that daptomycin (DAP) demonstrates *in vitro* synergy in combination with other anti-staphylococcal agents, including ceftaroline (CPT) and oxacillin (OXA), against MRSA. Nevertheless, optimal combinations remain undefined. Here, our objective was to compare DAP in combination with CPT or OXA against MRSA bloodstream isolates collected from patients with persistent bacteremia despite >7 days of vancomycin treatment.

Methods. Minimum inhibitory concentrations (MICs) for DAP, CPT, and OXA were determined in duplicate by reference broth microdilution methods. We used time-kill analyses (TKA) to test free peak concentrations (fC_{max}) of DAP (8 µg/mL), CPT (16 µg/mL), and OXA (4 µg/mL) alone and in combination against 1×10^8 CFU/mL to simulate high-inocula infections. Bactericidal and synergistic activity were defined as a ≥3-$\log_{10}$ decrease in CFU/mL and >2-$\log_{10}$ decrease in CFU/mL in combination compared with the most active single agent, respectively, at 24 hours.

Results. A representative isolate was selected from 12 patients with persistent MRSA bacteremia. Median (range) MICs were 0.5 (0.5–1), 0.5 (0.5–1), and 64 (64–≥128) µg/mL for DAP, CPT, and OXA, respectively. By TKA ($n = 5$ isolates), median log-kills were −3.81, −1.90, and +1.99 $\log_{10}$CFU/mL for DAP, CPT, OXA, respectively. Corresponding rates of bactericidal activity were 80%, 20%, and 0%, respectively. In combination, median log-kills were −7.83 and −4.82 $\log_{10}$CFU/mL for DAP+CPT and DAP+OXA, respectively ($P = 0.111$; Figure 1). DAP was synergistic in combination with CPT or OXA against 80% and 60% of isolates, respectively. Median log-kills in combination with CPT or OXA were higher than DAP alone ($P = 0.003$ and $P = 0.0497$, respectively). At 24 hours, colony counts were below the lower limit of detection (50