of stay was reduced by 0.65 days and 1.37 in the CAZ-AVI arms of the MDRE and MDRPA analyses, respectively.

Conclusion. CAZ-AVI is a cost-effective alternative to meropenem in the treatment of HAP/VAP caused by MDRE or MDRPA in China.

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1605. Differences in Clinical Characteristics of Third Generation Cephalosporin Resistance and Treatment Outcomes in *Escherichia coli* and *Klebsiella pneumoniae* Bacteremia in Patients with Liver Cirrhosis

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. This study aimed to identify characteristics of third-generation cephalosporin (3GC) resistance in *Escherichia coli* bateremia (ECB) and *Klebsiella pneumoniae* bacteremia (KPB) in patients with liver cirrhosis (LC), and to investigate the effects of appropriateness of empirical antibiotic treatment on outcomes.

Methods. We retrospectively collected demographic, clinical and microbiological information on all ECB and KPB episodes in LC patients ≥ 18 years of age hospitalized to a tertiary-care teaching hospital in South Korea from 2007 to 2018. Clinical characteristics associated with 3GC resistance and treatment failure were analyzed using a multivariate logistic regression model. Treatment failure was defined as persistent bacteremia for ≥ 7 days, or relapsed bacteremia ≤ 30 days, or all-cause mortality ≤ 30 days.

Results. 3GC resistance rates of *E. coli* were 30.3% overall and increased significantly during the study period (*P*=0.001), while the rates of *K. pneumoniae* were not changed (24.3% overall) (P=0.994). Of total 356 ECB and KPB episodes, 112 were caused by 3GC resistant strains. The factor associated with 3GC resistance was isolation of 3GC resistant strain ≤ 1 year in both ECB (OR, 7.754; 95% CI, 2.094~28.716) and KPB (OR, 2.774; 1.318~5.838). In ECB, beta-lactam or fluoroquinolone treatment ≤ 30 days was another factor associated with 3GC resistance (OR, 2.774; 95% CI, 1.318~5.838), but not in KPB. The factor associated with treatment failure was high MELD score in both ECB (OR, 1.193 at 1 increase; 95% CI, 1.118~1.272) and KPB (OR, 1.163; 95% CI 1.083~1.250). Additionally, in ECB, non-alcoholic LC (OR 3.262; 95% CI 1.058~10.063), high Charlson Comorbidity Index (OR, 1.285; 95% CI 1.066~1.548), and inappropriate empirical antibiotic treatment (OR, 3.194; 95% CI 1.207~8.447) were associated with treatment failure.

Conclusion. During the study period, 3GC resistance increased in ECB, but not in KPB. In ECB, the severity of the underlying disease and the appropriateness of empirical antibiotics were associated with treatment failure, but there was no correlation in KPB. In ECB of LC patients, the appropriateness of empirical antibiotics was a factor associated with treatment outcome, and is the only correctable factor in the clinical setting.

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1606. Distinct Effectiveness of Oritavancin Against Tolerance-Induced Staphylococcus aureus

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Within a sufficiently large bacterial population, some members will naturally adopt an alternate, metabolically-active state that favors small molecule synthesis over cell division. In *Staphylococcus aureus* this process can be sharply accelerated by multiple factors present during infection including nutrient limitation, host cationic peptide exposure and polymorphonuclear neutrophil internalization. These isogenic "tolerant" subpopulations have variable responses during antibiotic exposure and can remain viable in the presence of typically bactericidal concentrations. Survivors of antibiotic exposure can restart cell division upon cessation of antibiotics and cause relapse or recurrent infection. In this study we determine the ability of typical and atypical antistaphylococcal therapies to reduce the viability of tolerant *Staphylococcus aureus* bacteria.

Methods. *S. aureus* strain ATCC29213 as well as four clinical isolates (two MSSA, two MRSA) were selected for analysis. Overnight cultures were diluted in pre-warmed broth (MHB50) to 1×10^6 cfu/mL. Tolerance was induced by exposure to mupirocin (low [0.032 µg/mL] or high [3.2 µg/mL]) for 30 min. Tolerant cultures were exposed to vancomycin (35 µg/mL), cefazolin (25 µg/mL), daptomycin (7 µg/mL), telavancin (10 µg/mL), dalbavancin (6 µg/mL) or oritavancin (14 µg/mL) and viability was assessed by dilution plating at pre-defined time points (0, 2, 6, 24, 48 h). The minimum duration for 3-log viability reduction from baseline ($MDK_{99.9}$) and culture viability at 48h were calculated independently for each of three biological replicates.

Results. The rate of bacterial killing ($MDK_{99.9}$) was reduced for all study antibiotics by the addition of mupirocin in a dose-dependent manner. In contrast to all other regimens, including lipoglycopeptide comparators, oritavancin was the only antimicrobial agent that maintained a similar extent of bacterial killing against tolerant staphylococci.

Conclusion. Antimicrobial tolerant staphylococci exhibit a decreased rate of killing by antistaphylococcal agents. However, oritavancin remained effective at maintaining a similar extent of killing. Further studies to investigate the role of otritavancin against recurrent or relapse staphylococcal infection is warranted.

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1607. Dual Therapy with Aztreonam & Ceftazidime/Avibactam Against Multi-Drug Resistant *Stenotrophomonas maltophilia* on Tricuspid Valve Endocarditis

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Antimicrobial resistance in *Stenotrophomonas maltophilia* is one of the most complex among Gram-negatives. Presence of regulating non-specific antimicrobial class efflux pumps and chromosomal encoded L1 metallo-betalactamase (Ambler Class B) and L2 betalactamase (Ambler Class A) are responsible for few clinically active antimicrobials and pan-drug resistant strains.

Methods. A 38 year old male with a history of IV drug use, chronic hepatitis C, and recent MSSA endocarditis was admitted with sepsis. Workup revealed tricuspid valve endocarditis with pulmonary septic emboli due to *S. maltophilia*. Initial antibiotics were levofloxacin (LVX), metronidazole, and piperacillin-tazobactam (TZP) followed by LVX and minocycline (MIN). He had valve replacement on day 6. Repeat blood cultures and valve tissue culture revealed pan-resistant *S. maltophilia* (resistant: ceftazidime (CAZ), LVX, MIN, TMP/SMX, chloramphenicol; intermediate: MIN; eravacycline MIC 8 µg/mL; tigecycline MIC 16 µg/mL). Microbiology Department was consulted for additional antimicrobial options. *In vitro* testing for aztreonam (ATM) with ceftazidime/avibactam (CZA) was recommended.

Results. Synergy testing between ATM and CZA was performed by positioning ATM strip over the area where CZA had been previously been placed and removed after 10 minutes of incubation. The interception of the growth with the ATM strip was read. In presence of avibactam, ATM MIC was 4 µg/mL, 6 two-fold dilutions lower than ATM without CZA. MIC for ATM (256 µg/mL), CAZ (256 µg/mL) and CZA (32 µg/mL) were tested individually. ATM with CZA was recommended as a salvage treatment based on *in vitro* result. Patient completed 6 weeks of ATM with CZA along with MIN. He achieved microbiologic clearance and clinical recovery from infection. At the end of treatment, he experienced episodes of refractory ascites. With complex comorbidities, patient was not a transplant candidate and transitioned to hospice two weeks later.

Conclusion. Although the surgical excision was key, treatment with ATM and CZA provided effective antimicrobial treatment in the setting of persistent positive blood culture. ATM with CZA should be considered for cases of pan-drug resistant *S. maltophilia* with limited treatment options.

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1608. Efficacy of Ceftolozane/Tazobactam for Multidrug-Resistant Gram-Negative Infections in Multiple Urban Hospitals

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Ceftolozane/tazobactam (C/T) is a novel cephalosporin/beta-lactamase inhibitor combination developed for use against multidrug-resistant (MDR) Gram-negative infections, particularly *Pseudomonas aeruginosa* (PA). C/T is approved for complicated urinary tract and intraabdominal infections as well as hospital-acquired/ventilator-associated bacterial pneumonias. However, comprehensive clinical characterization of patients treated with C/T in non-FDA-approved indications is limited.

Methods. Patients ≥18 years who received C/T for ≥48 hours while hospitalized in 9 acute care centers in Houston, TX from January 2016 through September 2018 were included. Demographic, microbiologic, treatment and clinical outcome data were retrospectively collected by chart review. In patients who received multiple inpatient courses of C/T, only the first course with C/T was assessed.

Results. 210 patients met inclusion criteria: 58% were non-white, 35% were female and 13% were immunocompromised. Median age was 61 years (IQR, 48 to 69). Median Charlson comorbidity index was 5 (IQR, 2 to 6). At the onset of the index episode, a significant proportion of patients required intensive care unit admission (44%), mechanical ventilation (37%) and pressor support (22%). Respiratory sources were the most common (50%) followed by urine (15%). Positive cultures were documented in 93% of the cases and PA was found in 86%. Majority (95%) of PA which were MDR. C/T use was guided by susceptibility testing of the index isolate in ca. 52%. In 5.7% of cases, C/T was used to escalate therapy without any documented C/T-susceptible organism. Half (51%) of the cohort received initial dosing appropriate for renal function while 36% receiving a lower than recommended dose. Clinical success (i.e., recovery from infection-related signs and symptoms) occured in 77%. The in-hospital mortality rate in our cohort was 15% with 26 of 31 deaths deemed infection-related.

Conclusion. We report a large multicenter observational cohort that received C/T. A 77% clinical success with the use of C/T was documented. These data support the use of C/T in critically ill patients infected with MDR PA.

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1609. Epidemiology and Susceptibility to Imipenem/Relebactam of Gram-Negative Pathogens from Patients with Lower Respiratory Tract Infections – SMART United States 2017-2018

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Relebactam (REL) inhibits class A and C β-lactamases and was approved in the US combined with imipenem (IMI) and cilastatin for complicated urinary tract and intraabdominal infections. Using isolates collected as part of the global SMART surveillance program in the US, we evaluated the activity of IMI/REL against gram-negative pathogens (GNP) from patients with lower respiratory tract infections (LRTI), including a comparison of isolates from ICU and non-ICU wards.

Methods. In 2017-2018, 27 US hospitals each collected up to 100 consecutive aerobic or facultative GNP from LRTI patients per year. MICs were determined using CLSI broth microdilution and breakpoints.

Results. Among 3878 GNP isolates from LRTI, the most common species collected were *P. aeruginosa* (*Psa*, 33.3%), *K. pneumoniae* (10.9%), *E. coli* (10.4%), and *S. marcescens* (6.9%). Susceptibility of GNP is shown in the table.

IMI/REL inhibited 93% of *Psa* and Enterobacterales, which included 174 isolates of *Morganellaceae* that are not expected to be susceptible to IMI or IMI/REL. *S. marcescens* also showed low susceptibility to IMI, with improved but still reduced activity upon addition of REL. IMI/REL inhibited 83% of all GNP combined, 7-18 percentage points higher than the comparator β-lactams. Of the tested comparators, only amikacin exceeded the activity of IMI/REL.

Only *Psa* showed substantial differences in susceptibility between isolates from ICU (n=486) and non-ICU wards (n=611), with 63.4% and 70.2%, respectively, susceptible to IMI, 71.6/78.7% to cefepime, and 64.2/73.3% to piperacillin/tazobactam (P/T). Susceptibility to IMI/REL was high in both settings (91.4/93.6%). Among Enterobacterales, susceptibility was generally similar in ICU and non-ICU wards (IMI/REL, 92.5% in both settings; IMI, 86.3 and 87.1%, respectively; cefepime, 89.9/89.0%; P/T, 88.7/87.4%).

Table

	% Susceptible[a]							
Species (n)	IMI/REL	IMI	FEP	CAZ	ATM	P/T	CIP	AMK
All Enterobacterales (2036)	92.7	87.0	89.1	83.0	83.4	87.9	76.4	99.2
K. pneumoniae (422)	99.5	95.7	83.4	80.8	82.5	86.3	79.2	99.3
E. coli (404)	100	99.5	81.9	81.7	80.7	90.8	56.2	98.8
S. marcescens (269)	84.4	69.5	94.8	92.9	91.1	94.8	71.8	98.9
Psa (1292)	92.9	67.0	75.2	75.2	62.4	68.7	67.6	96.6
Enterobacterales + *Psa* (3328)	92.8	79.3	83.7	80.0	75.2	80.4	72.9	98.2
All GNP[b] (3878)	83.3	73.2	75.3	76.1	64.8	73.2	66.7	89.1

*Results for colistin are not shown because Enterobacterales and *Psa* are no longer considered susceptible to colistin per CLSI 2020 guidelines, as clinical and PK/PD data demonstrated limited clinical efficacy.
[a]Calculated using breakpoints appropriate for each species and assuming 0% susceptible for species with no breakpoints for any given drug.
IMI, imipenem; REL, relebactam; FEP, cefepime; CAZ, ceftazidime; ATM, aztreonam; P/T, piperacillin/tazobactam; CIP, ciprofloxacin; AMK, amikacin; *Psa, P. aeruginosa*; GNP, gram-negative pathogens

Conclusion. Although resistance rates have frequently been reported to be higher in ICU than non-ICU wards, this pattern was seen in the current study only among *Psa* isolates. IMI/REL showed activity >90% against both Enterobacterales and *Psa* from both ward types. These *in vitro* data suggest that IMI/REL could provide an important treatment option for patients with LRTI in the US, including those in ICUs.

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1610. Epidemiology and Treatment Heterogeneity in *Acinetobacter baumanii* Infections

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. *Acinetobacter baumannii* is known as a highly resistant organism causing serious infections in intensive care populations. However, the epidemiology of infections caused by *Acinetobacter baumannii* and approaches to treatment are not well described in a national healthcare system.

Methods. Our retrospective cohort study included patients with positive *Acinetobacter baumannii* cultures collected from any source during hospitalizations at Veterans Affairs (VA) medical centers nationally from January 2010 to April 2019. We evaluated patient characteristics and utilized exposure mapping to identify treatment patterns, including treatment heterogeneity. Heterogeneity was defined as patterns of antibiotic treatment (drug and duration) not shared by any other patient.

Results. Our study included 7,551 admissions with positive *Acinetobacter baumannii* cultures. The mean age was 66.7 years (±12.1) and 97.4% were male. Most patients were admitted from other healthcare facilities (59.2%) and 20.8% were in intensive care during the admission. Most patients had their culture collected on the day after admission and the median time to culture completion was 4 days (interquartile range 3-5). *Acinetobacter baumannii* cultures were most commonly obtained from urine (33.6%), followed by skin and soft tissue (25.3%), lung (21.8%), blood (9.2%), and bone/joint (5.0%). The median length of hospital stay was 11 days, with inpatient mortality and 30-day mortality rates of 11.6% and 12.5%, respectively.

Treatment heterogeneity was high, with 88.5% of admissions having different antibiotic treatment patterns (drug and duration), with a median time to first change of 1 day and median of 3 changes. Only 2% of the admissions were treated with polymyxins and 3.0% with colistin. Carbapenems were used in 18.9% of the admissions and extended-spectrum cephalosporins in 31.7% of the admissions.

Conclusion. In VA hospitals, *Acinetobacter baumannii* infections are observed in both critical and non-critical patient populations, mostly among patients with healthcare exposures. *Acinetobacter baumannii* infections were found to have various sources of infection, mostly from urine and skin and soft tissue, and approaches to treatment were highly varied.

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1611. Evaluating Clinical Outcomes and Efficacy of Daptomycin in Combination with a Beta-Lactam for the Treatment of Vancomycin-Resistant *Enterococcus* (VRE) Bacteremia

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. In-vitro studies have shown synergistic bactericidal activity with daptomycin (DAP) plus β-lactam antimicrobials against vancomycin resistant enterococci (VRE). There is a paucity of data regarding clinical outcomes with this combination in VRE bloodstream infections (BSI). The purpose of this study was to assess the efficacy of DAP plus a β-lactam with in-vitro activity vs. other therapies for treatment of VRE BSI.

Methods. IRB-approved, single-center, retrospective study of patients with VRE BSI from 01/2018-09/2019. Patients were excluded if < 18 years old, pregnant, or incarcerated. The primary outcome was time-to-microbiological clearance. Secondary outcomes included infection-related mortality, 30-day all-cause mortality, and incidence of recurrent BSI within 30 days of index culture. Targeted DAP doses were ≥ 8mg/kg and based on MIC. Factors associated with significance for outcomes, via univariate analysis, were evaluated with multivariable logistic regression (MLR), removed in a backward-step approach.

Results. A total of 85 patients were included, 23 of which received DAP plus a β-lactam. The comparator arm included linezolid or DAP monotherapy. Patients with combination therapy had significantly higher Charlson Comorbidity Index (CCI) (p=0.013) and numerically higher Pitt Bacteremia scores (PBS) (p=0.087) (Table 1). There was no difference seen in the primary outcome (Table 2). Secondary outcomes are provided in Table 2. The presence of polymicrobial infection and higher PBS were significantly associated with infection-related mortality (p=0.008 and p=0.005, respectively) by MLR. A Mann Whitney U test indicated that presence of infection-related