evaluating outcomes of patients who received combination therapy compared to those receiving monotherapy for CRO infections is limited.

Methods. This retrospective analysis was completed across 7 campuses at AdventHealth Orlando (AHO) from March 2018-October 2019. AHO implemented CRO PCR testing in March 2018, to identify carbapenemase producing CROs (CP-CROs). Inclusion criteria were hospitalization, age ≥ 18 years, culture with CP-CRO detected by PCR, and ≥ 72 hours of either monotherapy or combination therapy. Primary outcome was clinical success, defined as resolution of signs and symptoms of infection and absence of recurrent infection. Secondary outcomes included mean length of therapy, mean length of stay, inpatient mortality, adverse reactions and 30-day all cause readmissions.

Results. CRO was isolated 68 times in 59 unique patients (56% male, mean age 62 years). Most common sources included urine (41%), sputum (24%) and wound (22%). Commonly isolated organisms include *K. pneumoniae* (44%) and *E. cloacae* (29%). Thirty infections (44%) were polymicrobial and 28 patients (41%) had a secondary source of infection. Forty-three patients (63%) received definitive treatment therapy with a single antibiotic. Monotherapy treated patients had higher rates of treatment success (79% vs 68%, p=0.39), lower in-hospital mortality (4% vs 9%, p=0.066), less nephrotoxicity (6% vs 10%, p=0.084), shorter length of therapy (9.6 vs 13.4 days, p=0.034) and shorter hospital stay (20 vs 34 days, p=0.056). All-cause readmission rates were higher in the monotherapy group (18% vs 9%, p=0.78). Minimum inhibitory concentrations (MIC) were reported in 97% of patients.

Conclusion. Treatment with a single antibiotic for carbapenem-resistant infections can lead to treatment success, while minimizing adverse events, compared to utilizing combination therapy.

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

1602. Comparative Activity of Ceftolozane-Tazobactam (C/T) and Ceftazidime-Avibactam (CZA) against *Pseudomonas aeruginosa* (PSA) from Patients with Cystic Fibrosis (CF)

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Acute pulmonary exacerbations (APE) are a frequent cause of hospitalization for patients with CF. PSA is among the most common pathogen implicated in CF APE. Due to repetitive antibiotic courses, multidrug resistance (MDR) must be considered leaving few available intravenous antibiotic options. CZA and C/T are newer anti-PSA antibiotics that have been used to treat CF APE, but little data are available to compare their *in vitro* activity.

Methods. Non-duplicate, contemporary, clinical PSA (n=105) isolates were acquired from 85 patients during CF APE from 3 US hospital systems. MICs were assessed in at least triplicate by reference broth microdilution for C/T, CZA, aztreonam (ATM), cefepime (FEP), ceftazidime (CAZ), ciprofloxacin (CIP), levofloxacin (LVX), meropenem (MEM), piperacillin/tazobactam (TZP), and tobramycin (TOB). Current CLSI breakpoints were used to define susceptibility. Activity was further assessed in MDR, CAZ and MEM non-susceptible (NS) phenotypes.

Results. The mean patient age at isolate retrieval was 31 years (IQR: 21-43), and 20% were under 18 years. Mucoid morphology was observed in 48 (46%) isolates, and MDR defined in 41 (39%). Rates of susceptibility (MIC_{50}/MIC_{90}/%S) were: C/T (1/4/92%), CZA (2/8/90%), CAZ (4/64/68%), TZP (8/256/67%), TOB (2/32/63%), MEM (1/32/58%), ATM (8/64/57%), FEP (8/≥128/50%), CIP (2/8/27%), and LVX (4/16/24%). A mucoid phenotype did not alter %S (non-mucoid vs. mucoid) for C/T (93 vs. 92%) or CZA (91 vs. 88%). Among the 41 MDR PSA, activity was 2/16/83% and 4/16/76% for C/T and CZA, respectively. C/T, CZA, and MEM %S was 77, 69, and 23% for the 35 CAZ-NS isolates. C/T, CZA, and CAZ %S was 84, 77, and 39% for MEM-NS isolates.

Conclusion. These contemporary PSA from patients with CF displayed low susceptibility rates to most β-lactams, fluoroquinolones, and tobramycin, and MDR was common. C/T and CZA retained similarly high susceptibility against these isolates, including MDR strains and CAZ-NS/MEM-NS phenotypes. These data justify that both CT and CZA may be considered for CF APE due to PSA non-susceptible to current standard of care treatment options.

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1603. Comparison of Ceftolozane/Tazobactam, Ceftazidime/Avibactam, and Meropenem/Vaborbactam Activity Against *P. aeruginosa*: A Multicenter Evaluation

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Recent data have shown high rates of resistance and co-resistance of *P. aeruginosa* (PsA) to traditional first-line β-lactam antibiotics (piperacillin/tazobactam, ceftazidime, cefepime, and meropenem), with < 45% susceptibility to the others when resistance to one agent is present, driving a large medical need for newer agents. We compared the in vitro activity of newer Gram-negative antibiotics ceftolozane/tazobactam (CT), ceftazidime/avibactam (CA), and meropenem/vaborbactam (MV) against a global collection of PsA isolates.

Methods. Data were collected from multiple US hospitals as part of the SMART Surveillance Program (2019). Susceptibility testing (MIC, mg/L) was performed by broth microdilution, with susceptibility determined by CLSI breakpoints except for MV where EUCAST breakpoints were applied due to CLSI offering no susceptibility breakpoint criteria.

Results. 865 clinical *P. aeruginosa* isolates (one unique initial isolate per patient) were submitted from 21 US medical centers in 2019. 32% were from ICU patients; 71% were from lower respiratory tract infections. The phenotypic β-lactam susceptibility profile in this population was piperacillin/tazobactam (79%), ceftazidime (82%), cefepime (83%), and meropenem (78%). The table provides the comparative susceptibility rates. Co-resistance between commonly prescribed first line β-lactam antibiotics was common. CT, CA and MV were more active than traditional β-lactams, with CT having higher in vitro activity regardless of phenotype, followed by CA and then MV.

Table. Probability of Coverage for P. aeruginosa when Non-Susceptibility or Resistance to a Given First Line β-lactam Antibiotic

Susceptibility Phenotype (NS = Non-Susceptible; R = Resistant)	Ceftolozane/ Tazobactam (n, %S)	Ceftazidime/ Avibactam (n, %S)	Meropenem/ Vaborbactam (n, %S)	Pip/Tazo (n, %S)	Meropenem (n, %S)	Ceftazidime (n, %S)	Cefepime (n, %S)
All *P. aeruginosa* (n=865)	832 (96%)	818 (95%)	789 (91%)	687 (79%)	674 (78%)	709 (82%)	722 (83%)
Pip/Tazo NS (n=178)	150 (84%)	134 (75%)	116 (65%)	0	72 (40%)	46 (26%)	59 (33%)
Meropenem NS (n=191)	166 (87%)	154 (81%)	115 (60%)	85 (45%)	0	106 (55%)	101 (53%)
Ceftazidime NS (n=156)	123 (79%)	109 (70%)	104 (67%)	24 (15%)	71 (46%)	0	38 (24%)
Cefepime NS (n=143)	112 (78%)	97 (68%)	88 (62%)	24 (17%)	53 (37%)	25 (17%)	0
Pip/Tazo R (n=95)	73 (78%)	60 (63%)	61 (64%)	0	35 (37%)	3 (3%)	6 (6%)
Meropenem R (n=137)	116 (85%)	103 (75%)	61 (45%)	47 (34%)	0	60 (44%)	57 (42%)
Ceftazidime R (n=117)	85 (73%)	74 (63%)	80 (68%)	9 (8%)	52 (44%)	0	15 (13%)
Cefepime R (n=66)	39 (59%)	30 (45%)	35 (53%)	8 (12%)	22 (33%)	3 (5%)	0

Conclusion: To our knowledge, this is the largest multicenter head to head comparison of the activities of ceftolozane/tazobactam, ceftazidime/avibactam and meropenem/vaborbactam among *P. aeruginosa* with varying resistant phenotypes. Among the newer agents, ceftolozane/tazobactam demonstrated the most reliable in vitro activity against *P. aeruginosa* with resistance to traditional first-line β-lactams. Further studies are needed to translate the potential clinical relevance of these findings in different practice settings with varying rates of antimicrobial resistance among *P. aeruginosa*.

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1604. Cost-Effectiveness of Ceftazidime-Avibactam for Patients with Hospital-Acquired Pneumonia Caused by Multi-Drug Resistant Enterobacteriaceae or Pseudomonas in China

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. To estimate the cost-effectiveness of ceftazidime-avibactam (CAZ-AVI) for the treatment of hospital-acquired pneumonia (HAP) including ventilator-associated pneumonia (VAP) caused by multi-drug resistant enterobacteriaceae (MDRE) or MDR pseudomonas aeruginosa (MDRPA) in China.

Methods. A previously published patient-level simulation model was localized to China to estimate the cost-effectiveness of first-line CAZ-AVI compared to meropenem from a healthcare perspective. Patients flowed through the model which evaluates resistance status, response, and adverse events (AEs), which can all lead to a treatment switch. Second-line therapy of colistin plus high dose meropenem was used for both arms. Resistance rates were 0.7% (CAZ-AVI) and 7.6% (meropenem) for MDRE, and 10.7% (CAZ-AVI) and 35.5% (meropenem) for MDRPA. Effectiveness rates for CAZ-AVI and meropenem were based on a randomized, double-blind, phase 3 clinical trial. All cost data, including drugs, AEs, and hospitalization were localized to China. Utility values were based on response and sourced from the literature. Costs and benefits were discounted at 5% over the five year time horizon.

Results. At a cost-effectiveness threshold of three-times GDP per capita, CAZ-AVI was cost-effective compared to meropenem for HAP/VAP caused by both MDRE and MDRPA with ICERs of ¥147,500 and ¥30,496, respectively. Specifically, CAZ-AVI had ¥13,699 and 0.09 additional total costs and QALYs, respectively, within MDRE; ¥5,207 and 0.17 additional total costs and QALYs, respectively, within MDRPA. Length

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.

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

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.