(Other Financial or Material Support, Personal fees)**Grupo Biotoscana** (Other Financial or Material Support, Personal fees)**Janssen Pharmaceuticals** (Grant/Research Support)**Matinas** (Other Financial or Material Support, Personal fees)-**Medicines Company** (Grant/Research Support)**MedPace** (Grant/Research Support)**MedPace** (Other Financial or Material Support, Personal fees)**Melinta Therapeutics** (Grant/Research Support)**Menarini Ricerche** (Other Financial or Material Support, Personal fees)**Merck/MSD** (Other Financial or Material Support, Personal fees)**Merck/MSD** (Grant/Research Support)**Mylan Pharmaceuticals** (Consultant)**Nabriva Therapeutics** (Other Financial or Material Support, Personal fees)**Octapharma** (Other Financial or Material Support, Personal fees)**Paratek Pharmaceuticals** (Other Financial or Material Support, Personal fees)**Pfizer** (Other Financial or Material Support, Personal fees)**Pfizer** (Grant/Research Support)**PSI** (Other Financial or Material Support, Personal fees)**Rempex** (Other Financial or Material Support, Personal fees)**Roche Diagnostics** (Other Financial or Material Support, Personal fees)**Scynexis** (Other Financial or Material Support, Personal fees)**Scynexis** (Grant/Research Support)**Seres Therapeutics** (Other Financial or Material Support, Personal fees)**Tetraphase** (Other Financial or Material Support, Personal fees) **Philipp Koehler, MD**, **Akademie für Infektionsmedizin e.V.,** (Other Financial or Material Support, Personal fees)**Astellas Pharma GmbH** (Other Financial or Material Support, Personal fees)**Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases, University of Cologne, Cologne, Germany** (Other Financial or Material Support, Other)**Gilead Sciences GmbH** (Other Financial or Material Support, Personal fees)**GPR Academy Ruesselsheim** (Speaker's Bureau)**Miltenyi Biotec GmbH** (Other Financial or Material Support, Non-financial support)**MSD Sharp & Dohme GmbH** (Other Financial or Material Support, Personal fees)**Noxxon N.V.** (Speaker's Bureau)**University Hospital, LMU Munich** (Other Financial or Material Support, Personal fees) **Katrien Lagrou, n/a**, **FUJIFILM WAKO** (Speaker's Bureau)**Gilead** (Consultant, Speaker's Bureau)**MSD** (Consultant, Speaker's Bureau, Other Financial or Material Support, travel grant)**Pfizer** (Speaker's Bureau, travel grant)**SMB Laboratoires Brussels** (Consultant) **Zdenek Racil, n/a**, **Astellas** (Grant/Research Support, Speaker's Bureau, travel grant) **Blandine Rammaert, n/a**, **Gilead** (Speaker's Bureau, Other Financial or Material Support, travel grant)**Merck/MSD** (Speaker's Bureau)**Pfizer** (Other Financial or Material Support, travel grant) **Nikolay Klimko, n/a**, **Astellas** (Speaker's Bureau)**Gilead** (Speaker's Bureau)**Merck/MSD** (Speaker's Bureau)**Pfizer** (Speaker's Bureau) **Sung-Yeon Cho, MD**, **Gilead** (Grant/Research Support, Speaker's Bureau)**Merck Sharp & Dohme** (Grant/Research Support, Speaker's Bureau)**Pfizer** (Grant/Research Support, Speaker's Bureau)

1599. Clinical Outcomes for Patients Treated with Fluoroquinolones for Bacteremia Caused by Enterobacteriaceae Reclassified as Not Susceptible by Updated CLSI Breakpoints

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Antibiotic resistance remains a pressing public health challenge. Antibiotic susceptibility testing is crucial to identify resistance and predict which antibiotics are most likely to be effective. In vitro minimum inhibitory concentrations (MICs) are interpreted using MIC breakpoints set for the United States by The Clinical and Laboratory Standards Institute (CLSI). In 2019 CLSI updated fluroquinolone (FQ) breakpoints for Enterobacteriaceae. Previously any isolate with an MIC ≤ 1 μg/mL of ciprofloxacin would be considered susceptible but based largely on pharmacokinetic/pharmacodynamic simulations the susceptibility breakpoint was revised to ≤ 0.25 μg/mL. However, the clinical relevance of this decision remains unclear.

Methods. All cases of Enterobacteriaceae bacteremia with isolates previously considered susceptible but reclassified as resistant (MIC = 1 μg/mL) in adults treated with FQs between 08/01/2018 and 07/31/2019 were identified. Demographics, clinical characteristics and outcomes were compared with an equal number of randomly selected isolates with an automated MIC reported as ≤ 0.5 μg/mL. Available stored isolates with a reported MIC of ≤ 0.5 μg/mL had manual E-testing performed to identify a more precise MIC.

Results. 29 cases with an MIC = 1 μg/mL were compared with 29 controls with a MIC of ≤ 0.5. Only 3 cases and 1 control received FQs as empiric therapy, the remaining patients in each group were transitioned to FQ after a median of 4 days of other antibiotics. No significant difference was found for predetermined outcomes including 30 day mortality, escalation after starting FQ, length of hospital stay, and readmission in 30 days (see Table). No primary outcome was thought to be related to antibiotic failure. E-testing found no isolates with an MIC = 0.5 μg/mL.

Table 1

	MIC = 1 (n = 29)	MIC ≤ 0.5 (n = 29)
30 day mortality	0	1 (3.4%)
Non-sterilization (w/FQ)	0	0
Escalation after starting FQ	1 (3.4%)	0
LOS	6.5 days	6.2 days
Readmission (30d)	6 (21%)	7 (24%)

Conclusion. Patients with Enterobacteriaceae bacteremia treated with FQs for isolates reclassified as resistant had similar outcomes to those with lower MICs. While FQs are generally not recommended as first line empiric antibiotics, FQs may still be safe to use as stepdown therapy for isolates with a ciprofloxacin MIC = 1 μg/mL, particularly if the only alternative may be IV antibiotics. A larger study is needed to confirm this.

Disclosures. Gregory Weston, MD MSCR, Allergan (Grant/Research Support)

1600. Closing the gap on moxifloxacin breakpoints for *Stenotrophomonas maltophilia*

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Moxifloxacin (MOX) has *in vitro* activity against Enterobacterales and *Stenotrophomonas maltophilia* (SM). Although MOX commonly displays lower minimum inhibitory concentration ($MIC_{50/90}$ values against SM when compared to levofloxacin, there are currently no established MOX breakpoints for treatment of SM. The Clinical and Laboratory Standards Institute (CLSI) has established interpretive categories and MIC breakpoints for levofloxacin (S ≤2μg/ml) against SM. The US Food and Drug Administration and European Committee on Antimicrobial Susceptibility Testing provide MOX breakpoints for Enterobacterales with susceptible MICs represented at ≤ 2 μg/mL and ≤ 0.25 μg/mL, respectively. The purpose of this study was to evaluate MOX MIC distribution against SM strains recovered from clinical specimens.

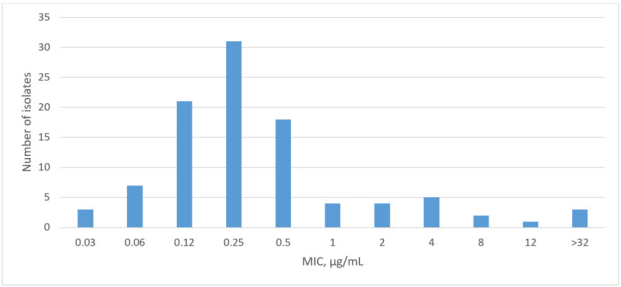
Methods. Clinical samples from patients with suspected infection during calendar year 2018 and 2019 were processed in the microbiology lab of Wake Forest Baptist Medical Center. After incubation, SM colonies were identified by MALDI-TOF system. MOX susceptibility testing was performed for these clinical isolates by gradient diffusion strip methodologies. Results were displayed as MIC (μg/mL) without interpretation. $MIC_{50/90}$ and susceptibility rates at potential breakpoints were calculated.

Results. A total of 211 isolates were tested, 112 from 2018 and 99 from 2019. MOX MIC_{50} and MIC_{90} for all isolates was 0.25 μg/mL and 2 μg/mL, respectively. The range of MIC distribution was ≤ 0.006 μg/mL to ≥ 64 μg/mL. Percent susceptibilities at incremental MICs, including established MOX breakpoints against Enterobacterales and established levofloxacin breakpoints against SM, are represented in Table 1. MIC distribution was plotted in Figure 1.

Table 1. Susceptibility rates of S. maltophilia to moxifloxacin at theoretical breakpoints

Breakpoint (μg/mL)	Percent Susceptible		
	All (n=211)	2018 (n=112)	2019 (n=99)
≤ 0.25	69%	75%	63%
≤ 1	88%	90%	85%
≤ 2	93%	97%	89%

Figure 1. Moxifloxacin MIC Distribution against All S. maltophilia Isolates



Conclusion: With no established breakpoint, these data represent one of the largest samples of MOX MICs against SM in the United States. Using the CLSI breakpoint for levofloxacin in SM (MIC of ≤2ug/ml) the overall susceptibility rate is 93%. This finding highlights the importance of performing susceptibility testing to this agent by the microbiology laboratory and the critical need for MOX breakpoints in SM.

Disclosures. **Tyler J. Stone, PharmD**, **Paratek** (Research Grant or Support) **John Williamson, PharmD**, **Paratek** (Research Grant or Support) **Elizabeth Palavecino, MD**, **Paratek** (Grant/Research Support)**Paratek** (Grant/Research Support)

1601. Combination Therapy versus Monotherapy for Carbapenem-resistant Organisms: Is More Really Better?

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Carbapenem-resistant organisms (CROs) represent an urgent public health threat and associated with mortality rates up to 60%. Pharmacotherapy for these infections remain challenging and historically included multiple agents. Meropenem/vaborbactam and ceftazidime/avibactam are options to treat CRO infections as monotherapy; however, combination therapy is still frequently utilized. Data

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.

Disclosures. **David P. Nicolau, PharmD**, **Cepheid** (Other Financial or Material Support, Consultant, speaker bureau member or has received research support.)**Merck & Co., Inc.** (Consultant, Grant/Research Support, Speaker's Bureau)**Wockhardt** (Grant/Research Support) **Joseph L. Kuti, PharmD**, **Allergan** (Speaker's Bureau)**bioMérieux** (Research Grant or Support, Other Financial or Material Support, Speaker Honorarium)**Melinta** (Research Grant or Support)**Merck & Co., Inc.** (Research Grant or Support)**Paratek** (Speaker's Bureau)**Summit** (Other Financial or Material Support, Research funding (clinical trials))

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*.

Disclosures. Pamela Moise, PharmD, Merck & Co., Inc. (Employee, Shareholder) C. Andrew DeRyke, PharmD, Merck & Co., Inc. (Employee, Shareholder) Marcela Gonzalez, MD, MSD (Employee, Shareholder) Irina Alekseeva, MD, PhD, MSD (Employee, Shareholder) Diego Lopez, MD, MSD (Employee, Shareholder) Brune Akrich, MD, MSD (Employee, Shareholder) Daniel F. Sahm, PhD, IHMA (Employee) Pfizer, Inc. (Consultant)Shionogi & Co., Ltd. (Independent Contractor) Katherine Young, MS, Merck & Co., Inc. (Employee, Shareholder)Merck & Co., Inc. (Employee, Shareholder) Mary Motyl, PhD, Merck & Co, Inc (Employee, Shareholder)

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