Conclusion. Discriminative ability of the risk prediction models showed varying performance. The model by Lodise et al. appears to be most useful when a low risk level is deemed acceptable for failure rate, while at a moderate to high risk of missing a CRE case (20% and 30% FNR), the methods by Seligman and Vazquez-Guillamet et al. are most desirable as they minimize the chance of over-treatment. Additional work to increase sample size and to evaluate the models inter-rater reliability is currently on-going.

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1256. Clinical Response by Minimum Inhibitory Concentrations in Carbapenem-Resistant Pseudomonas aeruginosa Infections under Cefiderocol Commpassionate Use Program

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Session: P-72. Resistance Mechanisms

Background. Cefiderocol (CFDC) has been developed for the treatment of serious infections caused by drug-resistant aerobic Gram-negative pathogens, including carbapenem-resistant (CR) Pseudomonas aeruginosa (CRPA). The current CFDC susceptibility breakpoints for P. aeruginosa differ between US Food and Drug Administration (FDA) and Clinical and Laboratory Standards Institute (CLSI) (Table). Data characterizing the impact of CFDC minimum inhibitory concentrations (MICs) on the clinical responses of patients treated with CFDC for CRPA are sparse.

Methods. We reviewed patients treated with compassionate-use CFDC (2 g, q8h or renally adjusted dosages) for infections caused by CRPA with no alternative treatment options. CFDC minimum inhibitory concentrations (MICs) were evaluated according to CLSI guidelines in iron-depleted cation-adjusted Müller–Hinton broth for available CRPA isolates. We then assessed physician-reported clinical responses to CFDC therapy and stratified results by CFDC MIC.

Results. There were 71 patients overall with CRPA treated with CFDC. Treatment duration ranged from 1 to 132 days. For the subset of 33 patients for whom CFDC MIC values were available, the most common infection sites were the respiratory tract (n=15), blood (n=12), and urinary tract (n=4). Patients could have had an infection at ≥1 sites and in other locations. CFDC MIC range was ≤0.03– >64 µg/mL. The modal MIC value was 2 µg/mL (n=13; Table). CRPA isolates were susceptible to CFDC in 13/33 patients (39.4%) based on the FDA breakpoint (MIC ≤1 µg/mL) and in 31/33 patients (93.9%) based on the CLSI breakpoint (MIC ≤4 µg/mL). Clinical response was reported for 15/18 patients (83.3%) who had infections with CFDC MICs of 2–4 µg/mL, organisms that are considered susceptible by CLSI but not by FDA breakpoints (Table). Clinical response was reported in 6/13 patients (46.1%) with infections with CFDC MIC ≤1 µg/mL and in 1 of 2 patients (50.0%) with CFDC MIC ≥8 µg/mL (Table). 21 (63.6%) patients survived to Day 28 and there were no trends in mortality by CFDC MIC.

Conclusion. Clinical response rate was high for CRPA infections with CFDC MICs of 2–4 µg/mL, supporting the higher CLSI susceptibility breakpoint.

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1257. Re-Evaluation of Cefepime or Piperacillin-Tazobactam to Decrease Use of Carbapenems in ESBL-Producing Enterobacteriales Urinary Tract Infections (REDUCE-UTI)

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Session: P-72. Resistance Mechanisms

Background. Cefepime (CEF) and piperacillin-tazobactam (TZ) are commonly prescribed for urinary tract infections (UTIs) caused by ESBL-producing Enterobacteriales (TPs).

Methods. The study was conducted at 27 medical centers in the United States. Patients with ESBL-UTIs (≥10,000) were identified and their antibiotic use was evaluated. CEF and TZ were assigned to patients at participating hospitals. The primary outcome was the proportion of patients with ESBL-UTIs who received appropriate antibiotics and the secondary outcome was the proportion of patients who were cured.

Results. There were 10,131 ESBL-UTIs evaluated. The primary outcome was achieved in 6,941 (68.5%) patients with ESBL-UTIs treated with CEF or TZ. The proportion of patients who were cured was not significantly different between the two groups (85.6% vs 84.9% for CEF and TZ, respectively).

Conclusion. CEF or TZ is a cost-effective option for the treatment of ESBL-UTIs and should be considered as an alternative to carbapenems.
Achromobacter, and 80% of carbapenem-resistant Enterobacteriaceae spp., Ceftriaxone-susceptible (CRO-S) and piperacillin-tazobactam nonsusceptible Enterobacteriaceae isolates.  

Session: P-72. Resistance Mechanisms  

Background. Carbenapens (CBP) are considered first-line for infections caused by extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E). However, recent literature suggests that cepfime (FEP) and piperacillin-tazobactam (TZP) may produce similar outcomes vs. CBPs for the treatment of ESBL-E urinary tract infections (UTIs). The goal of this study was to determine if non-carbenapen (NCBP) therapy with FEP or TZP is as effective as CBPs for the treatment of ESBL-E UTIs.  

Methods. This was a retrospective observational study of patients admitted to the hospital from January 1st, 2016 to June 30th, 2020 with a urine culture positive for ESBL-E. Patients were included if they received a study antibiotic (meropenem, ertapenem, TZP, or FEP). Patients were excluded if they had any of the following: absence of pyuria, prior receipt of study antibiotic, CBP-resistant organism isolated in urine culture, polymicrobial urine culture, end-stage renal disease, or concomitant gram-negative infection. The primary outcome was clinical cure defined as complete resolution of signs and symptoms of infection. Secondary outcomes included in-hospital mortality, recurrence within 30 days, and resistance within 30 days.  

Results. A total of 133 patients were included based on definitive therapy received; 69 (52%) received CBP and 64 (48%) received NCBP therapy. Of the total patient population, 17 (13%) were admitted to the intensive care unit, 84 (63%) had a complicated UTI, and 64 (48%) had pyelonephritis. Baseline characteristics were similar between the two groups. There was no difference in clinical cure between the CBP and NCBP therapy groups (96% vs. 97%, p = 1.0). Additionally, no differences in secondary outcomes were observed. Subgroup analyses were performed in patients with specific pathogens, uncontrolled genitourinary source, complicated UTI, and pyelonephritis. These analyses did not reveal any differences in primary or secondary outcomes between the two groups.  

Conclusion. FEP or TZP may be reasonable CBP-sparing alternatives for the treatment of ESBL-E UTIs as clinical and microbiological outcomes were similar with these NCBP agents vs. CBPs in this study population.  

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1258. Antibiotic Resistant Nontyphoidal Salmonella Infection Following International Travel — United States, 2018  

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Session: P-72. Resistance Mechanisms  

Background. Antibiotic resistance in nontyphoidal Salmonella can limit treatment options for patients requiring antibiotic therapy.  

Methods. We assessed the contribution of international travel to resistance among nontyphoidal Salmonella infections.  

Results. Among 3,238 nontyphoidal Salmonella infections, 356 (11%) were in patients who traveled internationally in the 7 days before symptom onset. Of these, 109/356 (31%) had isolates resistant to first-line antibiotics, compared with 308/2882 (11%) non-travelers. Resistance was more likely following travel, after adjusting for age and sex (OR 3.7, 95% CI 2.9–4.8). Nine genes or mutations conferred resistance to first-line antibiotics among travel-associated isolates. The risk of resistance varied by region and was highest after travel to the Middle East (OR 7.5, 95% CI 4.7–12.0). Overall, 17.1% (95% CI 12.2–21.7%) of genetic resistance to first-line antibiotics was attributable to international travel.  

Conclusion. For patients with nontyphoidal Salmonella infections, international travel is associated with approximately three-fold increased risk that first-line agents could be ineffective. The estimated 17% of resistance to first-line antibiotics attributable to travel is encoded by relatively few genes and mutations. Investigation of the major sources of resistant strains could help target prevention efforts. Travel region should be considered when treating empirically; treatment should be adjusted based on results from susceptibility testing.  

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1259. Carbenapens Versus Non-carbenapen Beta-Lactams for the Treatment of Ceftriaxone-Resistant and Piperacillin-Tazobactam-Resistant Enterobacteriales Isolates  

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Session: P-72. Resistance Mechanisms  

Background. Ceftriaxone-susceptible (CRO-S) and piperacillin-tazobactam (PWC)-sensitive enterobacteriales isolates have become a frequently isolated phenotype emerging in practice. The genotypic profile is still not clearly elucidated, although prior genotypic sequencing data of these isolates with this phenotypic profile suggests that they are not extended-spectrum beta-lactamase (ESBL) producers. Due to the unfamiliarity with this phenotype and the potential for overuse of broad-spectrum antibiotics, we investigated the clinical outcomes of CRO-S/TZP-NS isolates with carbenapen versus non-carbenapen beta-lactam (NCBL) therapy.  

Methods. This was a retrospective chart review of patients with a diagnosed infection caused by a CRO-S/TZP-NS Enterobacteriales isolate admitted to any of the three NYU hospitals: Long Island, Tisch, or Brooklyn campuses, treated with a beta-lactam (BL) antibiotic from October 2015 to October 2020. The primary outcome was treatment failure defined as an escalation of antibiotics due to clinical worsening, 30-day all-cause mortality, or relapse of infection with the same genus and species. Patients who received ≥ 72 consecutive hours of BL antibiotics were considered to be definitively on BL.  

Results. A total of 111 patients were included in this study, 9 in the carbenapen group and 102 in the NCBL group. There was no statistically significant difference in the clinical failure rate between the two groups (0% vs 10.8% respectively; P=0.56). A univariate analysis assessed the association of clinical failure with TZP, CRO, cefpodoxime, ceftazidime, and 3rd generation cephalosporins grouped. There were no statistically significant increases in 30-day treatment failure in any of the individual categories.  

Conclusion. There were no statistically significant differences in 30-day failure with use of carbenapen vs NCBL antibiotics. No individual BLs or classes were associated with an increased risk of clinical failure. This study suggests that there is a role for NCBL antibiotics for Enterobacteriales isolates with this phenotypic presentation and supports prior data that they are less likely to be ESBL producers. Prospective studies are warranted to confirm these findings.  

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1260. In Vitro Activity of Eravacycline Against Clinically Significant Bacteria Isolated from Patients with Cancer  

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Session: P-72. Resistance Mechanisms  

Background. Bacterial infections are common in patients with cancer (PWC). Many bacteria have developed resistance to currently used antibiotics, posing therapeutic challenges, we evaluated the in vitro activity of eravacycline (a novel fluoroacycline) against clinical bacteria recently (2018-2019) isolated from PWC.  

Methods. All 565 isolates tested were from blood cultures. CLSI approved broth microdilution method was used. Appropriate ATCC controls were included. MIC₅₀, MIC₉₀, MIC₉₀ percent susceptibility calculations were made using research FDA breakpoints when available. Eravacycline susceptibility breakpoint for most Gram-positive organisms (GPO) is ≤ 0.06 mg/L and for Enterobacteriales is ≤ 0.5 mg/L.  

Results. Eravacycline had potent activity against Staphylococcus aureus (methicillin-susceptible and resistant strains), oxacillin-susceptible coagulase-negative staphylococci (CoNS) including Staphylococcus lugdunensis, viridans group streptococci, beta-hemolytic streptococci, Streptococcus pneumoniae, Bacillus spp., Corynebacterium spp., and Micrococcus spp. It was slightly less active against oxacillin-resistant CoNS, and vancomycin-susceptible Enterococcus faecalis (MIC₅₀, 0.125 mg/L respectively) and was moderately active against vancomycin-resistant Enterococcus faecium (MIC₅₀, 0.06, and MIC₉₀ 0.25 mg/L). Eravacycline had potent activity against Escherichia coli (including ESBL producing strains), Citrobacter spp., and non-ESBL Klebsiella spp. Eravacycline inhibited 83% of ESBL positive K. pneumoniae, 83% of Enterobacter cloacae, and 80% of carbapenem-resistant Enterobacteriales (CRE) isolates ≤ 0.5 mg/L. The presence of ESBLs increased MIC₉₀ value no more than 2 fold. Eravacycline was also active against many non-fermenting (NFP) such as Acinetobacter spp., Achromobacter spp., Pseudomonas aeruginosa, and Stenotrophomonas maltophilia).