Medical Center (Individual(s) Involved: Self): Research Grant or Support; Universite de Sherbrooke (Individual(s) Involved: Self): Research Grant or Support; University of Iowa (Individual(s) Involved: Self): Research Grant or Support; University of Iowa Hospitals and Clinics (Individual(s) Involved: Self): Research Grant or Support; University of Wisconsin (Individual(s) Involved: Self): Research Grant or Support; UNT System College of Pharmacy (Individual(s) Involved: Self): Research Grant or Support; URMC (Individual(s) Involved: Self): Research Grant or Support; UT Southwestern (Individual(s) Involved: Self): Research Grant or Support; VenatoRx (Individual(s) Involved: Self): Research Grant or Support; Viosera Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Wayne State University (Individual(s) Involved: Self): Research Grant or Support

201. Frequency of *Pseudomonas aeruginosa* (PA) Discrete Inner Colonies and Comparison of Minimal Inhibitory Concentration (MIC) Values between Parent and Inner Colony Isolates Following Fosfomycin Disk Diffusion (DD) Testing

Dina Zheng[1]; Morgan L. Bixby, BS[1]; Elizabeth C. Smith, BS[1]; Jadyn C. Anderson[1]; Phillip J. Bergen, BSc, BPharm (Hons), PhD, GCAP[2]; Cornelia B. Landersdorfer, BPharm, PhD[2]; Elizabeth B. Hirsch, PharmD[1]; [1]University of Minnesota College of Pharmacy, Minneapolis, MN; [2]Monash University Centre for Medicine Use and Safety, Melbourne, Victoria, Australia

Session: O-40. What's New in Antimicrobial Resistance

Background. Fosfomycin combination therapy is a potential approach for treatment of multidrug-resistant (MDR) PA infections despite a lack of approved susceptibility breakpoints for this organism. While DD testing is commonly used for fosfomycin, growth of discrete inner colonies (IC) within the zone of inhibition has been observed for multiple organisms following DD. Criteria recommended by CLSI and EUCAST are contradictory for interpreting these inner colonies. We therefore sought to determine the frequency of inner colonies and MIC differences between PA parent-inner colony pairs from an international isolate collection.

Methods. A convenience collection of 198 clinical PA isolates from three U.S institutions (n = 82), two Australian institutions (n = 72), and the CDC & FDA Antibiotic Resistance Isolate Bank (n = 44) were included. Fosfomycin MIC values were determined in duplicate on separate days by DD and broth microdilution (BMD) testing. For parent isolates with discrete IC observed during DD, IC isolates were subcultured and MIC values were determined and then compared to their corresponding parent isolates. MIC values were interpreted using CLSI *Escherichia coli* (EC) breakpoints (susceptible: MIC ≤ 64 µg/mL, intermediate: MIC = 128, resistant: MIC ≥ 256 µg/mL).

Results. Parent isolate BMD MIC values ranged from < 4 to > 256 µg/mL while IC isolate BMD MIC values ranged from 128 to > 1024 µg/mL. $MIC_{50/90}$ values were 128/256 µg/mL and > 1024/ > 1024 µg/mL for the parent and IC isolates, respectively. A high frequency of 45% (89/198) of parent isolates displayed discrete IC which also demonstrated a higher frequency of resistance (97.8%) compared to the parent isolates (23.7%).

Conclusion. IC MIC values were higher overall compared to parent MIC values, with an average fold difference of ~18 between the parent-inner colony pairs. The frequency of IC found in this study (45%) is considerably higher than previously observed in EC clinical isolates. These data highlight the need to further investigate the importance of these IC and warrant caution for extrapolation of EC breakpoints for fosfomycin susceptibility testing against PA.

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

202. Comparative Activity of Ceftazidime-Avibactam, Imipenem-Relebactam and Meropenem-Vaborbactam Tested Against Carbapenem-Nonsusceptible *Enterobacterales* that Are Carbapenemase-Negative

Mariana Castanheira, PhD[1]; Mariana Castanheira, PhD[1]; Rodrigo E. Mendes, PhD[1]; Helio S. Sader, MD, PhD, FIDSA[1]; [1]JMI Laboratories, North Liberty, IA

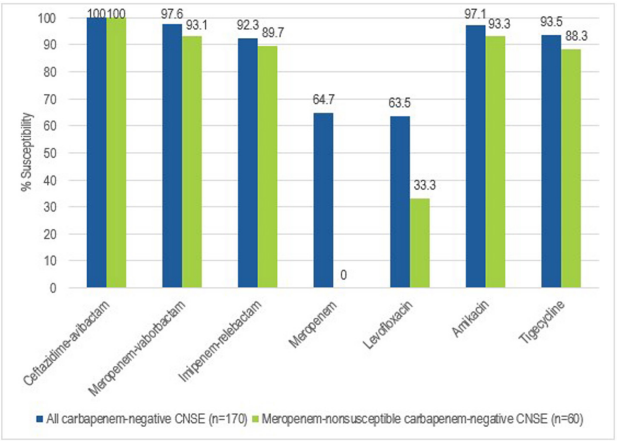
Session: O-40. What's New in Antimicrobial Resistance

Background. Most carbapenem-nonsusceptible *Enterobacterales* (CNSE) produce carbapenemases, but some isolates do not carry these enzymes. Ceftazidime-avibactam (CAZ-AVI), meropenem-vaborbactam (MBV), and imipenem-relebactam (IMR) have activity against CNSE isolates producing serine-carbapenemases, but these agents might have variable activity against isolates that do not produce these enzymes. We evaluated the activity of these agents against a collection of 170 carbapenemase-negative CNSE collected during 5 years in US hospitals.

Methods. *Enterobacterales* isolates (n=47,858) collected in US hospitals from 2016-2020 were susceptibility (S) tested by reference broth microdilution methods. Results were interpreted using CLSI 2020 breakpoints. CNSE displayed nonsusceptible (NS) MICs for imipenem or meropenem. CNSE isolates were screened for carbapenemase genes using whole genome sequencing.

Results. Among 685 (1.4% of the isolates) CNSE, 170 (24.8% of the CNSE) isolates did not produce carbapenemases. Most of these isolates were *K. aerogenes* (n=42), *K. pneumoniae* (32), and *E. cloacae* (32), but 13 other species also were carbapenemase negative. CAZ-AVI inhibited all carbapenemase-negative CNSE isolates (Figure). MBV and IMR inhibited 97.6% and 92.3% of the isolates. Amikacin (AMK) and tigecycline (TIG) inhibited 97.1% and 93.5%, while levofloxacin and meropenem (MEM) inhibited 63.5% and 64.7%. A total of 141 (82.9%) isolates were nonsusceptible (NS) to imipenem. When MEM NS isolates (n=60) were analysed separately, the S rates were lower for all agents except CAZ-AVI. CAZ-AVI inhibited all MEM NS carbapenemase-negative CNSE isolates. MBV and IMR inhibited 93.1% and 89.7% of these isolates, respectively. AMK and TIG inhibited 93.3% and 88.3%, respectively. Only 8.3% of the isolates were resistant to colistin.

Conclusion. CAZ-AVI displayed good activity against carbapenemase-negative CNSE isolates, including all MEM NS that displayed greater resistance rates against all comparator agents. High-risk patients with infections caused by CNSE have an increased mortality rate compared to isolates susceptible to these agents. Implementation of appropriate therapy for these isolates is critical.



Disclosures. **Mariana Castanheira, PhD**, **AbbVie (formerly Allergan)** (Research Grant or Support)**Bravos Biosciences** (Research Grant or Support)**Cidara Therapeutics, Inc.** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**GlaxoSmithKline** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Qpex Biopharma** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Mariana Castanheira, PhD**, Affinity Biosensors (Individual(s) Involved: Self): Research Grant or Support; Allergan (Individual(s) Involved: Self): Research Grant or Support; Amicrobe, Inc (Individual(s) Involved: Self): Research Grant or Support; Amplyx Pharma (Individual(s) Involved: Self): Research Grant or Support; Artugen Therapeutics USA, Inc. (Individual(s) Involved: Self): Research Grant or Support; Astellas (Individual(s) Involved: Self): Research Grant or Support; Basilea (Individual(s) Involved: Self): Research Grant or Support; Beth Israel Deaconess Medical Center (Individual(s) Involved: Self): Research Grant or Support; BIDMC (Individual(s) Involved: Self): Research Grant or Support; bioMerieux Inc. (Individual(s) Involved: Self): Research Grant or Support; BioVersys Ag (Individual(s) Involved: Self): Research Grant or Support; Bugworks (Individual(s) Involved: Self): Research Grant or Support; Cidara (Individual(s) Involved: Self): Research Grant or Support; Cipla (Individual(s) Involved: Self): Research Grant or Support; Contrafect (Individual(s) Involved: Self): Research Grant or Support; Cormedix (Individual(s) Involved: Self): Research Grant or Support; Crestone, Inc. (Individual(s) Involved: Self): Research Grant or Support; Curza (Individual(s) Involved: Self): Research Grant or Support; CXC7 (Individual(s) Involved: Self): Research Grant or Support; Entasis (Individual(s) Involved: Self): Research Grant or Support; Fedora Pharmaceutical (Individual(s) Involved: Self): Research Grant or Support; Fimbrion Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Fox Chase (Individual(s) Involved: Self): Research Grant or Support; GlaxoSmithKline (Individual(s) Involved: Self): Research Grant or Support; Guardian Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Hardy Diagnostics (Individual(s) Involved: Self): Research Grant or Support; IHMA (Individual(s) Involved: Self): Research Grant or Support; Janssen Research & Development (Individual(s) Involved: Self): Research Grant or Support; Johnson & Johnson (Individual(s) Involved: Self): Research Grant or Support; Kaleido Biosceinces (Individual(s) Involved: Self): Research Grant or Support; KBP Biosciences (Individual(s) Involved: Self): Research Grant or Support; Luminex (Individual(s) Involved: Self): Research Grant or Support; Matrivax (Individual(s) Involved: Self): Research Grant or Support; Mayo Clinic (Individual(s) Involved: Self): Research Grant or Support; Medpace (Individual(s) Involved: Self): Research Grant or Support; Meiji Seika Pharma Co., Ltd. (Individual(s) Involved: Self): Research Grant or Support; Melinta (Individual(s) Involved: Self): Research Grant or Support; Menarini (Individual(s) Involved: Self): Research Grant or Support; Merck (Individual(s) Involved: Self): Research Grant or Support; Meridian Bioscience Inc. (Individual(s) Involved: Self): Research Grant or Support; Micromyx (Individual(s) Involved: Self): Research Grant or Support; MicuRx (Individual(s) Involved: Self): Research Grant or Support; N8 Medical (Individual(s) Involved: Self): Research Grant or Support; Nabriva (Individual(s) Involved: Self): Research Grant or Support; National Institutes of Health (Individual(s) Involved: Self): Research Grant or Support; National University of Singapore (Individual(s) Involved: Self): Research Grant or Support; North Bristol NHS Trust (Individual(s) Involved: Self): Research Grant or Support; Novome Biotechnologies (Individual(s) Involved: Self): Research Grant or Support; Paratek (Individual(s) Involved: Self): Research Grant or Support; Pfizer (Individual(s) Involved: Self): Research Grant or Support; Prokaryotics Inc. (Individual(s) Involved: Self): Research Grant or Support; QPEX Biopharma (Individual(s) Involved: Self): Research Grant or Support; Rhode Island Hospital (Individual(s) Involved: Self): Research Grant or Support; RIHML (Individual(s) Involved: Self): Research Grant or Support; Roche (Individual(s) Involved: Self): Research