Disclosures. Leonard R. Duncan, PhD, AbbVie (formerly Allergan) (Research Grant or Support)Basilea Pharmaceutica International, Ltd. (Research Grant or Support)Cipla Therapeutics (Research Grant or Support)Cipla USA Inc. (Research Grant or Support)Department of Health and Human Services (Research Grant or Support, Contract no. HHSO10020160002C)Shionogi (Research Grant or Support)Kamal Hamed, MD, MPH, Basilea Pharmaceutica International, Ltd (Employee)Department of Health and Human Services (Research Grant or Support, Contract no. HHSO10020160002C)Jennifer Smart, PhD, Basilea Pharmaceutica International, Ltd. (Employee)Department of Health and Human Services (Research Grant or Support, Contract no. HHSO10020160002C)Michael A. Pflaletter, MD, Basilea Pharmaceutica International, Ltd. (Research Grant or Support)Cidara Therapeutics, Inc. (Research Grant or Support)Department of Health and Human Services (Research Grant or Support, Contract no. HHSO100201600002C)Melinta Therapeutics, LLC (Research Grant or Support)Nabriva Therapeutics (Research Grant or Support)Pfizer, Inc. (Research Grant or Support)Helio S. Sader, MD, PhD, FIDSA, AbbVie (formerly Allergan) (Research Grant or Support)Basilea Pharmaceutica International, Ltd. (Research Grant or Support)Cipla Therapeutics (Research Grant or Support)Cipla USA Inc. (Research Grant or Support)Department of Health and Human Services (Research Grant or Support, Contract no. HHSO10020160002C)Melinta Therapeutics, LLC (Research Grant or Support)Nabriva Therapeutics (Research Grant or Support)Pfizer, Inc. (Research Grant or Support)Shionogi (Research Grant or Support)Spero Therapeutics (Research Grant or Support)

1241. In Vivo Efficacy of Meropenem Against Metallo-
β-Lactamase (MBL)-Harboring Pseudomonas aeruginosa and Correlation to In Vitro Susceptibility Upon Addition of EDTA

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Session: P-72. Resistance Mechanisms

Background. Prior investigations evaluating the predictive value of zinc-depleted mICs for MBL susceptibility testing have focused on Enterobacteriales. Therein, bacterial killing observed with meropenem (MEM) in vivo was concordant with its pharmacodynamic profile using MIC values determined in zinc-depleted media compared with conventional cation-adjusted Mueller-Hinton broth (CAMHB). This study aims to evaluate the exposure-response relationship of MEM against VIM- and NDM-harboring P. aeruginosa (PA) using the murine thigh infection model and zinc-depleted MICs.

Methods. MBL-harboring PA isolates (VIM n=11; NDM n=10) were tested both in vivo (neutropenic murine thigh infection model) and in vitro (broth microdilution). The 24 h murine thigh study was conducted with treatment groups receiving a humanized MEM 2g q8h (3h infusion) dose. Six different zinc-limited media were prepared by the addition of EDTA at concentrations ranging from 3 to 300 mg/L to CAMHB. MEM MICs were determined in triplicate in conventional CAMHB and zinc-limited media. Time >MIC values (generated in each zinc-depleted media) were then plotted against the change in 24h bacterial density count in an Emass model.

Results. Average 0 h bacterial densities were 5.21 ± 0.40 and 5.13 ± 0.81 log10 CFU/mL for NDM and VIM isolates, respectively. MEM resulted in -0.89 CFU reduction to +3.69 CFU growth against NDM isolates. MEM resulted in -2.59 CFU reduction to +4.81 CFU growth against VIM isolates. All MEM MICs in conventional CAMHB were >64 µg/mL for NDM and ranged from 8 to >64 µg/mL for VIM isolates. Increasing EDTA concentrations resulted in several-fold MIC reductions and on average, a larger magnitude of reduction was observed among VIM (6-fold) compared with conventional CAMHB+EDTA (30 mg/L) (r=0.88) provided the highest correlation with MEM in vivo activity compared with CAMHB (r=0.55).

Conclusion. Results indicate that MIC values generated in conventional CAMHB do not appropriately characterize the in vitro efficacy of meropenem against MBL-harboring PA, and addition of EDTA (30 mg/L) to CAMHB appears to be a viable option for in vitro testing of these organisms.

Disclosures. David P. Nicolau, PharmD, Abbvie, Cepheid, Merck, Paratek, Pfizer, Wockhardt, Shionogi, Tetraphase (Other Financial or Material Support, Contract no. HHSO10020160002C)

1242. Efficacy and Safety of Intravenous Fosfomycin for the Treatment of Multi-resistant Gram Negative Infections

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Session: P-72. Resistance Mechanisms

Background. To describe the clinical use, efficacy and safety of intravenous (IV) fosfomycin in the treatment of infections caused by Gram-negative bacteria (GNB).

Methods. Hospitalized patients who received ≥48 hours of IV fosfomycin therapy during September 27, 2017 thru January 31, 2020 were included. The primary outcome was the proportion of subjects with clinical improvement at the end of IV fosfomycin therapy; defined as resolution of baseline signs and symptoms of infection.

Results. Thirty patients were included, of which 19 (63.3%) were males, and the median age was 63.5 years (interquartile range 46–73). Frequent risk factors for GNB infection included hospitalization (23, 76%), receipt of broad-spectrum antibiotics (15, 50%), and surgery (10, 33%), all within the preceding 90 days. Urinary tract infection (17, 56.7%) was the most common indication for use of IV fosfomycin, followed by bacteremia (4, 13.3), and skin and soft tissue infections (4, 13.3%). K. pneumoniae (17, 56.7%), E. coli (7, 23.3%) and P. aeruginosa (4, 13.3%) were the most common target pathogens. Almost all target pathogens (29, 96.7%) were resistant in vitro to ≥1 agent from ≥3 different antimicrobial classes. The primary outcome was achieved in 22 (73.3%) patients. The most frequently observed adverse events were hypokalemia (13, 43.3%) and hypernatremia (7, 23.3%). However, the majority of adverse events were classified as Grade 1 or Grade 2 severity.

Microbiological characteristics

| Organism        | E. Coli | Klebsiella pneumoniae | Pseudomonas aeruginosa | Other | MRDO |
|-----------------|---------|----------------------|-----------------------|-------|------|
|                 | 7       | 17                   | 19                    | 2     | 29   |
| Antibiotic resistance | MERO    | Coletin              | Grade 2               | AG    | Bacteremia |
|                 | 22      | 6                    | 27                    | 7     | 6    |
| Documented clearance | Yes    | No                   | Not applicable        | Yes   | No   |
|                 | 12      | 14                   | 11                    | 5     | 14   |
|                 | 40%     | 46.6%                | 36.7%                 | 16%   | 14%  |

The table describes microbiological characteristics of the isolated organism species, resistance pattern, development of fosfomycin resistance Management outcomes and safety profile.

1243. Eravacycline in Bacteremia: A Case Series

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Session: P-72. Resistance Mechanisms

Background. Eravacycline (ERV) is FDA-approved for the treatment of complicated intra-abdominal infections, but there is limited experience for non-FDA approved indications.

Methods. We present five cases that utilized ERV for treatment of bacteremia.

Results. Patient 1 in septic shock (SS) started on vancomycin (VAN) and cefazolin (CZA). On day 9, gram-positive cocci in chains in BC grew and VAN was added. BCPS finalized to VRE to CZA. On day 27, meropenem (CZA). Blood culture (BC) finalized to +4.81 CFU growth against VIM isolates. All MEM MICs in conventional CAMHB and zinc-limited media. Time >MIC values (generated in each zinc-depleted media) were then plotted against the change in 24h bacterial density count in an Emass model.

Conclusion. IV fosfomycin is a potentially effective and safe option for the treatment of patient with GNB infections.

Disclosures. All Authors: No reported disclosures

1244. Fosfomycin in the Treatment of complicated intra-abdominal infections.

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