Smithson Valley, Texas, Department of Medicine, Division of Cardiology, Stanford University, Stanford, California, 2Department of Radiology, Department of Medicine, Stanford University, Stanford, California, 3Institute of Stem Cell Biology and Regenerative Medicine, Stanford University, Stanford, California, 4Centro de Pesquisas René Rachou, FIOCRUZ, Belo Horizonte, Brazil, 5Division of Infectious Diseases and Geographic Medicine, Stanford University, Stanford, California

Session: 144. Novel Agents
Friday, October 5, 2018: 12:30 PM

Background. Trypanosoma cruzi is the etiologic agent of Chagas disease, which can result in severe cardiomyopathy. Trypanosoma cruzi is endemic to the Americas, and of particular importance in Latin America. In the United States and other nonendemic countries, rising case numbers have been observed. The only drugs available so far are benznidazole and nifurtimox, which have limited efficacy during chronic infection. We repurposed iraconazole, originally an antifungal, in combination with amiodarone, an antiarrhythmic, with the goal to interfere with T. cruzi infection of Vero cells or HSIPC-CM. The combination of iraconazole and amiodarone was more potent than the single substances, or benznidazole at therapeutic concentrations, without affecting host cell metabolism. In addition to effects on infection, iraconazole, or amiodarone affected T. cruzi multiplication. Here, iraconazole/amiodarone on combination was more potent than either alone, both, in Vero cells, and HSIPC-CM.

Conclusion. Our in vitro data suggest that a combination of iraconazole and amiodarone might serve as an effective new treatment option for Chagas disease, particularly cardiac involvement, in human and animal patients.

Disclosures. All authors: No reported disclosures.

1358. In vitro Activity of Ceftazidime–Avibactam and Comparator Agents Against Pseudomonas aeruginosa Causing Intra-Abdominal, Lower Respiratory, and Urinary Tract Infections Collected in Latin America as Part of the INFORM Global Surveillance Program, 2012–2016
Mark Wise, PhD1; Krystyna Kamilczarek, PhD1; Gregory G. Stone, PhD1; and Dan Sahm, PhD1; 2IHMA, Inc., Schaumburg, Illinois, 3Pfizer, Inc., New York, New York, 4International Health Management Associates, Inc., Schaumburg, Illinois

Session: 144. Novel Agents
Friday, October 5, 2018: 12:30 PM

Background. The non-β-lactam β-lactamase inhibitor avibactam (AVI) is active against class A, C, and some class D β-lactamases, in combination with ceftazidime (CAZ) has been approved by the FDA and EMA for treatment of intra-abdominal infections (IAI), lower respiratory tract infections (LRTI), and urinary tract infections (UTI). This study reports on the in vitro activity of (CAZ-AVI) and comparators vs. P. aeruginosa collected from IAIAs, LRTIs, and UTIs in Latin America as part of the INFORM surveillance study from 2012 to 2016.

Methods. For INFORM surveillance over 2012–2016 in Latin America, 1,595 nonduplicate P. aeruginosa isolates linked to IAIAs, LRTIs, and UTIs were collected from 26 clinical sites in six countries. Susceptibility testing was done using broth microdilution according to CLSI guidelines and using CLSI 2018 breakpoints. CAZ was tested with AVI at a fixed concentration of 4 mg/mL. Meropenem (MEM) nonsusceptible organisms were screened for β-lactamase genes by PCR.

Results. Among the full collection of P. aeruginosa, CAZ-AVI showed consistently higher % susceptibilities than all comparators except for colistin (CST) for all infection sources. The addition of AVI to CAZ resulted in an increase in susceptibility ranging from 14.2% to 19.5% (IAI) against the non-metallo-β-lactamase (MBL) harboring subset, CAZ-AVI showed extremely potent activity (MIC90 8 mg/mL) for all infection sources. In this subset, the activity of CAZ-AVI approached that of colistin for IAIAs (susceptibility of 93.3% vs. 96.4%, respectively).

Conclusion. MEM/NAC combination shows excellent in vitro activity against current clinical EB isolates and the potential to extend MEM activity to MDR, MEM nonsusceptible and CAZ/AVI-resistant isolates, which supports the continued clinical development of MEM/NAC for infections caused by CREs. This project has been funded in part under HHS BARDA Contract HHSO100201600038C.

Disclosures. R. Okuayya, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Employee, Salary. F. Garcia-Alcalde, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Employee, Salary. C. Zampaloni, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Employee. S. Magnet, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Research Contractor, Contracting fee to IHMA. S. Magnet, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Research Contractor, Contracting fee to IHMA. N. Kothari, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Research Contractor, Contracting fee to IHMA. I. Harding, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Research Contractor, Contracting fee to Micron. K. Bradley, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland; Employee, Salary.

1360. Antimicrobial Activity of Cefepime in Combination with VNRX-5133 Against a Global Collection of Enterobacteriaceae Including Resistant Phenotypes
Matthew L. Hackel, PhD1; and Dan Sahm, PhD1; 2IHMA, Inc., Schaumburg, Illinois, 3International Health Management Associates, Inc., Schaumburg, Illinois

Session: 144. Novel Agents
Friday, October 5, 2018: 12:30 PM

Background. VNRX-5133 is a novel cyclic boronate-based broad-spectrum β-lactamase inhibitor with potent and selective direct inhibitory activity against both serine- and...
metals β-lactamases (Ambler Classes A, B, C, and D). In this analysis, we evaluated the activity of cephalosporin (FEP) in combination with VNRX-5133 and comparators against 1,120 recent Enterobacteriaceae clinical isolates, including carbapenem-resistant strains. **Methods.** MICs of FEP in combination with VNRX-5133 fixed at 4 µg/mL (FEP/VNRX-5133) were determined following CLSI M07-A10 guidelines against 1,120 Enterobacteriaceae from community and hospital infections collected globally in 2012–2013. Resistant phenotypes were based on 2017 CLSI breakpoints. As FEP/VNRX-5133 breakpoints have not yet been established, the FEP 2 µg/mL susceptible dose-dependent (SDD) breakpoint of ≤8 µg/mL was considered for comparative purposes. **Results.** FEP/VNRX-5133 showed potent activity against drug-resistant subsets of Enterobacteriaceae, with MIC90 values ranging from 1 µg/mL against ceftazidime, levofloxacin, or pipéracillin–tazobactam-nonsusceptible isolates, to 8 µg/mL against meropenem-nonsusceptible isolates. FEP/VNRX-5133 inhibited >93% of all resistant subsets at ≤5 µg/mL. **Conclusion.** Cephalosporin in combination with VNRX-5133 demonstrated potent in vitro activity against Enterobacteriaceae, including cephalosporin-, fluoroquinolone-, and carbapenem-resistant (CRE) isolates. Because this drug combination exhibited substantial potential for the treatment of infections caused by isolates often resistant to first-line treatment, further development is warranted. **Disclosures.** M. Hackel, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant, and **and**0.03 **and**0.03 **82.8 **128 **2.2 **7.7 **, Summit Therapeutics: Employee, Salary. **0.6 **, Hennepin Life Sciences: Board Member, Consulting fee. **14.0 **0.25 **99.6 **0.03 **Enterobacter **MIC **50/90 **63.8 **1.5 **, Iterum Therapeutics: Employee. **4 **>8 **, Allergan: **49x84**nary tract infections (CAUTI) within a month of catheterization. These infections are a major contributing cause of nosocomial bloodstream infection (BSI) and are clinically important in the United States. Nearly all of these patients will develop catheter-associated urinary tract infection (cUTI) or complicat ed intra-abdominal infection (cIAI). The activity of sulopenem aligns with the most urgent drug-resistant antimicrobial threats defined by the Centers for Disease Control (CDC, Including ESBL-producing strains of Enterococcus and Klebsiella species. We evaluated the in vitro antibacterial activity of sulopenem against clinical Enterobacteriaceae isolates from patients in North America with UTI or cIAI collected during 2016–2017. **Methods.** Sulopenem and other antimicrobial agents were tested for in vitro activity against 1,008 recent (2016–2017) consecutive Enterobacteriaceae isolates collected through the SENTRY Antimicrobial Surveillance Program from patients in North America with UTI (906 isolates) or cIAI (102 isolates). Reference broth microdilution susceptibility testing was conducted using frozen-form panels produced by JMI Laboratories according to CLSI (M07, 2018) guidelines using cation-adjusted Mueller–Hinton broth. Quality control (QC) and interpretation of results were performed in accordance with CLSI M100 (2018) guidelines. **Results.** Table 1. Activity of sulopenem and comparator antimicrobial agents against 1,008 Enterobacteriaceae North American isolates **Antibiotic** | %S | %I | %R | MIC (µg/mL) | MIC (µg/mL) | CLSI | Sulopenem | – | – | 0.03 | 0.25 | Meropenem | 99.6 | 0.1 | 0.3 | 0.03 | 0.06 | Ertapenem | 99.3 | 0.3 | 0.4 | ≤0.008 | 0.03 | Pipéracillin–tazobactam | 87.2 | 0.0 | 12.1 | ≤0.008 | >8 | Pipéracillin–tazobactam | 96.3 | 2.2 | 1.5 | 2 | 8 | Amoxicillin–clavulanate (2:1) | 75.8 | 7.7 | 16.5 | 4 | 64 | Levoﬂoxacin | 82.8 | 1.8 | 15.4 | 0.06 | 16 |Nitrofurantoin | 63.8 | 22.2 | 14.0 | 22 | 128 | The sulopenem MIC susceptibility values for Enterobacteriaceae were 0.03/0.25 µg/mL. For Enterococcus coli, Klebsiella species and Proteus mirabilis, the MIC susceptibility results were 0.03/0.03 µg/mL, 0.03/0.06 µg/mL, and 0.12/0.25 µg/mL, respectively. **Conclusion.** Sulopenem demonstrated potent in vitro activity against organisms commonly implicated in UTI and cIAI. These data support the further clinical development of sulopenem for Gram-negative infections. **Disclosures.** S. Puttagunta, Iterum Therapeutics: Employee and Shareholder. Salary. S. Aronin, Iterum Therapeutics: Employee and Shareholder, Salary. M. Huband, JMI Labs: Research Contractor, Grant recipient. R. K. Flamm, Allergan: Employee, Research support. M. Dunne, Iterum Therapeutics: Employee and Shareholder, Salary. 1363. Sulopenem Activity Against Enterobacteriaceae Isolates From Patients With Urinary Tract Infection or Intra-Abdominal Infection

Sallia Puttagunta, MD1; Steven Aronin, MD2; Michael Huband, BS2; Robert K. Flamm, MD2 and PhD1; Iterum Therapeutics, Old Saybrook, Connecticut, 1JMI Laboratories, North Liberty, Iowa, 2JMI Laboratories, Inc., North Liberty, Iowa

**Session:** 144. Novel Agents

**Friday, October 5, 2018: 12:30 PM**

**Background.** Sulopenem is a thienopenem antibacterial with oral and parenteral formulations being developed for the treatment of urinary tract infection (UTI) or complicated intra-abdominal infection (cIAI). The activity of sulopenem aligns with the most urgent drug-resistant antimicrobial threats defined by the Centers for Disease Control (CDC), including ESBL-producing strains of Enterococcus and Klebsiella species. We evaluated the in vitro antibacterial activity of sulopenem against clinical Enterobacteriaceae isolates from patients in North America with UTI or cIAI collected during 2016–2017.

**Methods.** Sulopenem and other antimicrobial agents were tested for in vitro activity against 1,008 recent (2016–2017) consecutive Enterobacteriaceae isolates collected through the SENTRY Antimicrobial Surveillance Program from patients in North America with UTI (906 isolates) or cIAI (102 isolates). Reference broth microdilution susceptibility testing was conducted using frozen-form panels produced by JMI Laboratories according to CLSI (M07, 2018) guidelines using cation-adjusted Mueller–Hinton broth. Quality control (QC) and interpretation of results were performed in accordance with CLSI M100 (2018) guidelines.

**Results.** Table 1. Activity of sulopenem and comparator antimicrobial agents against 1,008 Enterobacteriaceae North American isolates