metals β-lactamases (Amler Classes A, B, C, and D). In this analysis, we evaluated the activity of cephalazin (CEP) in combination with VNRX-5133 and comparators against 1,120 recent Enterobacteriaceae clinical isolates, including carbapenem-resistant strains.

**Methods.** MICs of CEP in combination with VNRX-5133 fixed at 4 µg/mL (CEP/VNRX-5133) were determined following CLSI M7-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 CEP/VNRX-5133 breakpoints have not yet been established, the CEP 2 g qh susceptible dose-dependent (SDD) breakpoint of ≤8 µg/mL was considered for comparative purposes.

**Results.** CEP/VNRX-5133 showed potent in vitro drug-resistant subsets of Enterobacteriaceae, with MIC₅₀ values ranging from 1 µg/mL against ceftazi-
dime, levofloxacin, or piperacillin–tazobactam-non-susceptible isolates, to 8 µg/mL against meropenem-non-susceptible isolates. CEP/VNRX-5133 inhibited >93% of all resistant subsets at ≤8 µg/mL.

**Conclusion.** Cephalazin 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 therapy development is warranted.

**Disclosures.** M. Hackel, IHMA, Inc., Employee, Salary. VenatoRx: Consultant, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant.

1361. Pharmacokinetics and Safety of Ridinilazole (RDZ), a Potential New Therapy for Clostridium difficile infection (CDI): From Animal Models to Patients

**Background.** CDI is the leading cause of nosocomial diarrhea associated with 29,000 deaths p.a. in the United States. RDZ is a novel oral drug highly selective for *C. difficile* limiting collateral damage to the gut microbiota. Here we present a combined analysis of all pharmacokinetic (PK) and tolerability data obtained throughout the development of RDZ from animal models to Phase 2, including new human PK data.

**Methods.** RDZ levels were measured in plasma and in the GI tract of infected hamsters after a single oral dose at 25 mg/kg. Quantitative whole-body autoradiography (QWBA) and excretion mass balance studies were performed in rats following a single 50 mg/kg oral dose of 14C RDZ. In GLP toxicity studies, RDZ was administered orally for 28 days to dogs and rats at 1,000 mg/kg/day. Toxicokinetic, clinical pathology, and histopathology analysis were performed. The Phase 1 study enrolled 56 healthy male subjects receiving single ascending doses from 2 to 2,000 mg, or 200 or 500 mg RDZ for 10 days. The Phase 2 enrolled 100 subjects at doses ranging from 150 mg to 300 mg RDZ twice daily for 14 days. Both clinical trials quantified RDZ in plasma and feces, and assessed safety and tolerability.

**Results.** In all animal studies, plasma levels of RDZ were below or at the limit of quantification (LOQ, 0.1 ng/mL). In the GI tract of hamsters, RDZ levels were highest in the cecum and colon, the site of infection; >99% of radioactivity was excreted in feces and no radioactivity was detected systemically. 28 days repeat dosing in dog and rat resulted in no observations from treatment, histopathology or in-life parameters. In Phase 1 and 2 studies, RDZ plasma levels were generally near or below the LOQ (0.1 ng/mL). Concomitant medications, CDI severity and age had no impact on exposure. In Phase 1, AEs were mild with no dose-dependent relationship, occurring and at a similar incidence to placebo. No significant findings from clinical laboratory, ECGs or other assessment were observed. RDZ was well tolerated in Phase 2 with the incidence of AEs and SAEs similar in both RDZ and VANN groups.

**Conclusion.** In both clinical and nonclinical studies to date, RDZ has been well tolerated and associated with low systemic absorption. Further assessment of safety, tolerability, and PK in Phase 3 studies is warranted.

**Disclosures.** E. Duperchy, Summitt Therapeutics: Employee, Salary, S. Chowdhury, Summitt Therapeutics Inc.: Employee and Shareder, Salary and Shareholder. R. Vickers, Summitt Therapeutics: Employee, Salary and Stock options. N. Robinson, Summitt Therapeutics: Consultant, Consulting fee.

1362. A Novel Intravesical Antimicrobial for CAUTIs

**Background.** As many as 1.5 million people reside in long-term care facilities in the United States. Nearly all of these patients will develop catheter-associated uri-
nary tract infections (CAUTIs) within a month of catheterization. These infections collectively cost the healthcare system billions of dollars each year. In addition, the emergence of multi-drug-resistant ESKEPA (Enterobacter species, *Staphylococcus aureus, Klebsiella species, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterococcus species*) pathogens affects the severity of infections, increasing both morbidity and mortality. Our research group is exploring a novel, dual-acting, antimicro-
bial, glycerol monolaurate (GML)-containing gel to prevent and treat CAUTIs.

**Methods.** Pieces (7 mm in length) of Renafilm Silicone Tubing were placed in the bladders of BALB/c female mice (n = 5/ group). Approximately 1 × 10⁸ colony-forming units/mL (CFU/mL) of *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* were instilled into the bladder. Animals were returned to cages for 18 hours. One hundred microliters of 2.5% GML Gel (50:50 mix of saline and human-approved glycols) or phosphate-buffered saline (PBS) was administered into the bladder. After 18 hours, animals were euthanised and colony-forming units in bladders and on catheters were determined, and histological analysis of bladders was performed.

**Results.** GML Gel was bactericidal against ESKEPA pathogens at 2 hours post-treatment. Subsequent histological analysis of bladders from infected and non-
infected mice showed that GML Gel was not toxic to bladder tissue.

**Conclusion.** Our results in this murine catheter infection model indicate that the newly formulated GML Gel may be useful in prevention and treatment of CAUTIs.

**Disclosures.** M. Peterson, Hennepin Life Sciences: Board Member, Consulting fee. M. Kilgore, Hennepin Life Sciences: Employee, Salary. P. Schlievert, Hennepin Life Sciences: Board Member, Consulting fee.

1363. Sulopenem Activity Against Enterobacteriaceae Isolates From Patients With Urinary Tract Infection or Intra-Abdominal Infection

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**Session.** 144. Novel Agents

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**Background.** Sulopenem is a thiopenem antibacterial with oral and parenteral for-
mulations being developed for the treatment of urinary tract infection (UTI) or compli-
cated 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 *Escherichia coli* 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.** and other antimicrobial agents were tested for in vitro activity against 1,008 recent (2016–2017) consecutive Enterobacteriaceae isolates col-
lected through the SENTRY Antimicrobial Surveillance Program from patients in North America with UTI (906 isolates) or cIAI (102 isolates). Reference broth microdi-
fusion 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