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

Methods. MICs of FEP 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 g q8h susceptible dose-dependent (SDD) breakpoint of ≤8 μg/mL was considered for comparative purposes.

Results. FEP/VNRX-5133 showed potent *in vitro* activity against drug-resistant subsets of *Enterobacteriaceae*, with MIC_{90} values ranging from 1 μg/mL against ceftazidime-, levofloxacin-, or piperacillin–tazobactam-nonsusceptible isolates, to 8 μg/mL against meropenem-nonsusceptible isolates. FEP/VNRX-5133 inhibited >93% of all resistant subsets at ≤8 μg/mL.

		Cefepime/VNRX-5133			
		MIC (μg/mL)			
Resistance Phenotype	N	MIC_{50}	MIC_{90}	%≤8 μg/mL	%>8 μg/mL
Cefepime NS	328	0.25	2	97.0	3.1
Meropenem NS	134	0.5	8	93.3	6.7
Piperacillin-tazo NS	445	0.12	1	97.8	2.3
Ceftazidime NS	483	0.12	1	98.1	1.9
Levofloxacin NS	407	0.12	1	98.3	1.7

Conclusion. Cefepime 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, further development is warranted.

Disclosures. **M. Hackel**, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant, Consulting fee. **D. Sahm**, IHMA, Inc.: Employee, Salary. VenatoRx: Consultant, Consulting fee.

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

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

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 hamster 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 ^{14}C RDZ. In GLP toxicology 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 BID for 10 days. The Phase 2 enrolled 100 patients assigned 1:1 to 10 days oral RDZ 200 mg BID or VAN 125 mg QID treatment. 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, 1.0 ng/mL). In the GI tract of hamsters, RDZ levels were highest in the colon. QWBA and excretion studies showed RDZ accumulated 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 VAN 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**, Summit Therapeutics: Employee, Salary. **S. Chowdhury**, Summit Therapeutics Inc.: Employee and Shareholder, Salary and Shareholder. **R. Vickers**, Summit Therapeutics: Employee, Salary and Stock options. **N. Robinson**, Summit Therapeutics: Consultant, Consulting fee.

1362. A Novel Intravesical Antimicrobial for CAUTIs

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Friday, October 5, 2018: 12:30 PM

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 urinary 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 ESKAPE (*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, antimicrobial, glycerol monolaurate (GML)-containing gel to prevent and treat CAUTIs.

Methods. Pieces (7 mm in length) of RenaSil Silicone Tubing were placed in the bladders of BALB/c female mice ($n = 5$/group). Approximately 1×10^8 colony-forming units/mL ESKAPE pathogens (50 μL) were inoculated into the bladder, and 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 (placebo) was administered into the bladders. After 2 hours, animals were euthanized and colony-forming units in bladders and on catheters were determined, and histological analysis of bladders was performed.

Results. GML Gel was bactericidal against ESKAPE pathogens at 2 hours post-treatment. Subsequent histological analysis of bladders from infected and noninfected 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. **S. 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
Friday, October 5, 2018: 12:30 PM

Background. Sulopenem is a thiopenem 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 *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. 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

	CLSI				
Antibiotic	%S	%I	%R	MIC_{50}	MIC_{90}
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
Ceftriaxone	87.3	0.6	12.1	≤0.06	>8
Piperacillin–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	32	128

The sulopenem $MIC_{50/90}$ values for *Enterobacteriaceae* were 0.03/0.25 μg/mL. For *Escherichia coli*, *Klebsiella* species and *Proteus mirabilis*, the $MIC_{50/90}$ 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.

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1364. Efficacy of Omadacycline Against Molecularly Characterized Gram-Positive and Gram-Negative Pathogens Causing Infections in the Phase 3 CABP and ABSSSI Clinical Trials

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Background. Omadacycline (OMC) is a once-daily agent with IV and oral formulations. One Phase 3 trial for community-acquired bacterial pneumonia (CABP; OPTIC) and two Phase 3 trials for acute bacterial skin and skin structure infections