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 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. Resistance breakpoints were based on 2017 CLSI breakpoints. As FEP/VNRX-5133 breakpoints have not yet been established, the FEP 2 µg/g ml susceptible dose-dependent (SDD) breakpoint of ≤8 µg/mL was considered for comparative purposes.

**Results.** FEP/VNRX-5133 showed potent post-treatment activity against drug-resistant subsets of Enterobacteriaceae, with MIC₅₀ 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 ≤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 therapy, development is warranted.


1361. Pharmacokinetics and Safety of Ridinilazole (RDZ), a Potential New Therapy for Closstridium 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 BID for 10 days. The Phase 2 enrolled 100 patients. Toxicology, 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.


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 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 Enterobacteriaceae (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 RenalSil Silicone Tubing were placed in the bladders of BALB/c female mice (n = 3/6/group). Approximately 1 × 10⁸ colony-forming units/mL. ESKEAPE 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-approval gels) or phosphate-buffered saline (placebo) was administered into the bladder. After 18 hours, animals were euthanized and colony-forming units in bladders and on catheters were determined, and histological analysis of bladder was performed.

**Results.** GML Gel was bactericidal against ESKEAPE 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. Schillert, Hennepin Life Sciences: Board Member, Consulting fee.

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

**Background.** Sulopenem is a thienopenem antibacterial with oral and parenteral formulation 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 coli and Klebsiella species. We evaluated the activity of sulopenem and amoxicillin–clavulanate against drug-resistant Enterobacteriaceae isolates from patients in North America with UTI or cIAI collected during 2016–2017. 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

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Susceptible (%)</th>
<th>%I</th>
<th>%R</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulopenem</td>
<td>75.6</td>
<td>0</td>
<td>24.4</td>
<td>0.25</td>
<td>1.0</td>
<td>0.03</td>
<td>0.25</td>
</tr>
<tr>
<td>Meropenem</td>
<td>99.6</td>
<td>0</td>
<td>0.4</td>
<td>0.3</td>
<td>1.0</td>
<td>0.03</td>
<td>0.05</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>75.8</td>
<td>7</td>
<td>24.2</td>
<td>0.008</td>
<td>0.03</td>
<td>0.03</td>
<td>0.06</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>68.7</td>
<td>32</td>
<td>31.6</td>
<td>12</td>
<td>4</td>
<td>1.5</td>
<td>6</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>96.3</td>
<td>3</td>
<td>3.4</td>
<td>2.2</td>
<td>1.0</td>
<td>53.9</td>
<td>2.8</td>
</tr>
</tbody>
</table>

The sulopenem MIC₅₀ values for Enterobacteriaceae were 0.03/0.25 µg/mL. For Enterococcus coli, Klebsiella species and Proteus mirabilis, the MIC₅₀ values 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.


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

**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

**Poster Abstracts • OFID 2018:5 (Suppl 1) • 5417**

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