Background. Uncomplicated urinary tract infections (uUTIs) are very common, with approximately 11% of women <18 years of age experiencing at least 1 episode of acute cystitis per year [Foxman, 2000]. Multidrug resistance has now emerged at the community level and has made treatment approaches for UTIs more difficult [Hooton, 2012; Flemm, 2014; Sanchez, 2014]. Gepotidacin (GEP), a first-in-class, novel triazacena- cyclohexylene antibiotic, has demonstrated in-vitro activity against uropathogens, including E. coli. With its unique ability to selectively inhibit bacterial DNA replication by a means not utilized by currently approved human therapeutic agent, GEP warrants further study as a potential opportunity to address an unmet medical need by providing a new uropathogen (non-β-lactam) treatment option for acute cystitis.

Methods. All participants received oral GEP 1500 mg BID for 5 days (total of 10 doses) and PK sampling was performed on Days 1–5.

Results. GEP was rapidly absorbed with median Tmax values of 1.50 ± 1.92 hours. Steady-state plasma exposure on Day 3 with moderate accumulation in plasma following BID dosing (1.4 fold), which is consistent with an effective elimination half-life of 6.6 hours. Steady-state trough levels were high and remained above an MIC of 4 µg/mL over 12 hours. Approximately 20% of the dose was excreted in urine over the 12-hour dosing interval on Day 1, which increased to 31% on Day 4. Urinary AUC24hr (11945 µg hours/mL) was higher than the free plasma AUC24hr (39.4 µg hours/mL). Slightly higher GEP plasma and urine exposures were observed in uUTI patients compared with Phase I healthy subjects.

Conclusion. Oral dosing of 1500 mg BID produces urine GEP exposures that exceed free plasma exposures by ~300-fold. Urine concentrations were also higher than the GEP MIC90 values for common UTI pathogens, such as E. coli (MIC90 = 4 µg/mL), suggesting that GEP warrants further clinical study for the treatment of uUTI.

Disclosures. All authors: No reported disclosures.

1483. Comparison of Outcomes in Urinary Tract Infections Caused by SPICE Organisms Treated with Non-Carbapenem-β-lactams vs. Non-β-lactam Agents

Julia Sapaohnikov, PharmD; Angela Huang, PharmD, BCIDP; Kelsey Powell, PharmD; Allison Gibble, PharmD; Froedtert and the Medical College of Wisconsin, Buffalo Grove, IL

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Friday, October 4, 2019: 12:15 PM

Background. The “SPICE organisms” intrinsically produce low levels of a chromosomally encoded β-lactamase enzyme, AmpC. When SPICE organisms are exposed to certain antimicrobial agents, they can select for de-repressed mutants and induce the AmpC gene. No study to date has determined the optimal treatment of lower inoculum infections such as urinary tract infections (UTIs) caused by SPICE organisms.

Methods. This study is a single-center, retrospective observational review of adult hospitalized patients with a UTI caused by a SPICE organism from November 2012 to November 2015. The objective of this study was to compare outcomes amongst patients with UTIs caused by select SPICE organisms treated with drugs susceptible to AmpC hydrolysis (penicillins, cephalosporins except cefepime, and monobactams) vs. drugs stable against AmpC (carbapenems, cepofam, and non-β-lactam agents).

Conclusion. Our data, there does not appear to be a difference in clinical response, 30-day infection-related readmission, 30-day infection-related mortality, 30-day all-cause mortality, and length of hospital stay. Patients with resistance to ceftriaxone were treated with β-lactam exposure (27 days) within the last month.

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Table 1. Primary and Secondary Outcomes

| Clinical Outcomes | AmpC Susceptible | AmpC Stable | P-value |
|-------------------|-----------------|-------------|---------|
| Patients with clinical response to treatment, n (%) | 50 (91.1) | 85 (94.6) | 0.4207 |
| Secondary Outcomes |                 |             |         |
| 30-d infection related readmission, n (%) | 13 (14.5) | 26 (28.9) | 0.5767 |
| 30-d infection recurrence rate, n (%) | 3 (3.4) | 4 (4.4) | 0.6588 |
| 30-d all-cause mortality, n (%) | 3 (3.4) | 4 (4.4) | 0.7021 |

Length of hospital stay (d), median (IQR): 4.6 (2.6–9.0) vs. 3.8 (2.7–5.1)

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1482. Microbiological Analysis from a Phase II Study Evaluating Gepotidacin (GS2K149044) in the Treatment of Uncomplicated Urinary Tract Infections

Nicole Scangarella-Olam, MD; Mohammad Hassan, PhD; Timothy Tiemeyer Jr, BS; Caroline R. Perry, PhD; Courtney Tiffany, BSc; Aparna Rayachaudhuri, MD; Etienne Dumont, MD; GloxoSmithKline Pharmaceuticals, Collegville, Pennsylvania; GloxoSmithKline, Collegville, Pennsylvania; PPFD, Highland Heights, Kentucky

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Background. Gepotidacin (GEP), a first in class novel triazacenacyclohexylene bacteriophage-sensitive inhibitor, inhibits bacterial replication and has in vitro activity against key pathogens, including drug-resistant strains, associated with a range of infections.

Methods. This phase IIa single-center study evaluated the safety, tolerability, pharmacokinetics, and efficacy of oral GEP 1,500 mg BID for 5 days in female subjects with acute cystitis. Clean catch mid-stream urine specimens were obtained for quantitative culture by standard methods. Sensitivity testing by CLSI broth microdilution and gradient diffusion (fosfomycin only) was conducted. Inclusion in the microbiological intent-to-treat population (micro-ITT) required growth of a qualifying baseline uropathogen. The primary endpoint was clinical success defined as cultures-concordant eradication (no growth, <1,000 CFU/mL) of the qualifying baseline uropathogen.

Results. Of 22 participants, 8 (36%) had a baseline qualifying uropathogen (5 E. coli, 1 S. saprophyticus, 1 K. pneumoniiae, and 1 C. koseri) and were included in the microbiological analysis. Negative cultures consisted of 2 E. coli; All 8 patients were negative for uropathogens after 7 days. Two E. coli isolates were multidrug-resistant (defined as resistance to >3 antibiotic classes) due to resistance to ampicillin, trimethoprim-sulfamethoxazole and ciprofloxacin/levofloxacin or ceftazolin. One additional E. coli isolate was ampicillin-resistant. Of the 8 patients in the micro-ITT, 7 (88%) and 6 (75%) were microbiological successes at the Test of Cure (TOC) and Follow-up Visits, respectively.

Conclusion. This first report of microbiological efficacy in the treatment of acute cystitis supports further clinical study of GEP as a first-in-class, novel mechanism of action antibacterial.

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1481. A Study for Risk Factors of Acute Kidney Injury in Leptospirosis in a Tertiary Health Center in South India

Bhavarna Suraparadage, MBBS; Murdahhar Varma, MBBS, MD; Shashidhar V, MBBS, MD; Kasturba Hospital, Manipal, Karnataka, India

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Background. Leptospirosis is the most widespread zoonotic disease in the world. In India, it is endemic in coastal lined states. Renal failure is a severe complication with mortality approaching 22%, early recognition of which helps clinicians in acting fast. This study aimed to investigate the predictors of Acute Kidney Injury (AKI) in Leptospirosis.

Methods. This is a prospective, case-control study done in a tertiary care center in Southern India carried out between October 2017 and December 2018. Patients with confirmed Leptospirosis as per CDC 2013 and Faine’s criteria (2012) having AKI as per KDIGO criteria were defined as cases. Subjects without AKI were controls. Logistic regression was performed to analyze the possible risk factors associated with AKI in Leptospirosis.

Results. A total of 329 subjects met the inclusion criteria of the study; 187 patients with AKI (CASES) and 142 patients without AKI (CONTROLS) were studied. Patients with AKI were older, (mean age: 46.99 ± 13.21 v 42.99 ± 15.15 years) had longer hospital stay (9.04 ± 5.62 vs. 6.27 ± 3.27 days) and higher SOFA (7.97 ± 2.9 vs. 7.15 ± 1.9) when compared to the groups and analyzed. Logistic regression was performed to analyze the possible risk factors associated with AKI in Leptospirosis. Patients with AKI had older age, higher SOFA scores and higher serum lactate, AST, ALT and creatinine levels.

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