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; Flamm, 2014; Sanchez, 2016]. Gepotidacin (GEP), a first-in-class, novel triazaacenaphthylene antibacterial 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 any currently approved human therapeutic agent, GEP warrants further study as a potential opportunity to address an unmet medical need by providing a new and effective oral 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 to 1.92 hours. Steady-state was attained by 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 urine 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.

Geometric mean (%CVb) [n] for key GEP plasma and urine PK parameters:

Plasma PK Parameter (unit)	Day 1	Day 4
AUCtau (µg•hr/mL)	20.3 (29.3) [20]	29.4 (31.9) [21]
Cmax (µg/mL)	5.89 (47.3) [20]	8.44 (38.0) [21]
Cτ (µg/mL)	-	0.851 (41.4) [21]
Urine PK Parameter (unit)	**Day 1**	**Day 4**
AUCtau (µg•hr/mL)	3742 (93.9) [16]	5973 (87.2) [18]
Cτ (µg/mL)	-	327 (248.7) [21]

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

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Background. Leptospirosis is the most widespread zoonotic disease in the world. In India, it is endemic in coast 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. Demographic, clinical and laboratory data were compared between the groups and analyzed. 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 vs. 42.99 ± 15.15 years) had longer hospital stay (9.04 ± 5.62 vs. 6.27 ± 3.27 days) had higher SOFA (7.97 ±2.9 vs. 3.37 ± 2.6) and APACHE 2 scores (14.37±5.93 vs. 4.66 ± 4.4), lower mean arterial pressure (84.01 ± 14.45 vs. 89.01 ± 10.63 mmHg; $P = 0.001$) lower serum bicarbonate level (21.70 ± 2.35 vs. 18.73 ± 3.78 mEq/dL; $P < 0.001$). Factors like serum lactate, AST, ALT had no significant difference between the groups. Serovar identification was done in 88 patients, of which 57 had AKI. *Australis* (16.7%), *Pyrogenes* (16.7%) and *Grippotyphosa* (11.1%) were the commonest serovars isolated. Serovar most commonly associated with AKI was *Pyrogenes* (17.5%)

Predictors for AKI were jaundice (*P* = **0**.01, OR 2.25; CI 1.21 –3.26), vomiting (*P* = 0.017, OR 1.9, CI 1.12- 3.26) Hypotension (*P* = 0.02, OR = 12.3, CI 1.85 – 107.2), tachypnea (*P* = 0.006, OR = 2.55, CI 1.11- 3.24), leukocytosis (*P* < 0.001, OR 5.45, CI 1.86- 4.89), thrombocytopenia (*P* < 0.001, OR 6.49, CI 2.33 – 6.75)

Conclusion. Identification of features like hypotension, tachypnea, acidosis, leukocytosis, thrombocytopenia, the occurrence of serovar *Pyrogenes* should alert the clinician on risk of developing AKI

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1482. Microbiological Analysis from a Phase II Study Evaluating Gepotidacin (GSK2140944) in the Treatment of Uncomplicated Urinary Tract Infections

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Background. Gepotidacin (GEP), a first in class novel triazaacenaphthylene bacterial topoisomerase 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. Susceptibility 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 ($\geq 10^5$ CFU/mL). Microbiological success was defined as culture-confirmed eradication (no growth, $<10^3$ 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. pneumoniae*, and 1 *C. koseri*) and were included in the micro-ITT. GEP MICs against the 8 qualifying uropathogens ranged from 0.06 to 4 µg/mL. 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 cefazolin. One additional *E. coli* isolate was ampicillin-resistant. Of the 8 participants in the micro-ITT, 7 (88%), and 6 (75%) were microbiological successes at the Test of Cure (TOC) and Follow-up Visits, respectively. The one microbiological failure at TOC (*E. coli*) was due to an unreportable (out of stability) urine specimen. For the 4 participants with available steady-state PK, qualifying Enterobacteriaceae uropathogens and who were microbiological successes at TOC, plasma fAUC24h/MICs ranged from 7 to 90.5 and urine AUC24h/MICs from 1292 to 121,698. The participant with the lowest plasma fAUC/MIC (7) and urine AUC24h/MIC (1292) had a *K. pneumoniae* with a gepotidacin MIC of 4 µg/mL.

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

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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, cefepime, and non-β-lactam agents). The primary outcome was clinical response, defined as resolution of signs and symptoms of UTI without requiring escalation of antimicrobial therapy after 48 hours of therapy initiation. Secondary outcomes include 30-day infection-related readmission, 30-day infection recurrence rate, 30-day all-cause mortality, and length of hospital stay. Patients with resistance to ceftriaxone were reviewed for β-lactam exposure (≥7 days) within the last month.

Results. One-hundred 56 patients were identified. Clinical response, 30-day infection-related readmission, 30-day infection recurrence, 30-day mortality rates, and median length of hospital stay were similar between the AmpC stable and AmpC susceptible groups (Table 1). Notably, 39.1% of patients with ceftriaxone resistance reported had recent β-lactam exposure vs. only 11.6% of patients without ceftriaxone resistance ($P = 0.0028$).

Conclusion. Based our data, there does not appear to be a difference in clinical response, 30-day-related readmission, 30-day infection recurrence, 30-day all-cause mortality rates, or length of stay in patients with UTIs treated with AmpC stable and AmpC susceptible agents. AmpC induction can be seen with at least 7 days of β-lactam use in the past 30 days as demonstrated by more frequent use of recent β-lactam agents in those with ceftriaxone resistance detected.

Table 1. Primary and Secondary Outcomes

Clinical Outcomes	AmpC Susceptible (n=56)	AmpC Stable (n=100)	P-value
Primary Outcomes			
Patients with clinical response to treatment, n (%)	55 (98.2)	95 (95.0)	0.4207
Secondary Outcomes			
30-d infection related readmission, n (%)	17 (30.4)	26 (26.0)	0.5793
30-d infection recurrence rate, n (%)	4 (7.1)	4 (4.0)	0.4588
30-d all-cause mortality, n (%)	3 (5.4)	4 (4.0)	0.7021
Length of hospital stay (d), median (IQR)	4.6 (2.6,9.0)	3.8 (2.7,5.1)	0.1699

Disclosures. **All authors:** No reported disclosures.