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; Flam, 2014; Sanchez, 2016]. Gepotidacin (GEP), a first-in-class, novel triazaceneacenaphthylene bacteriophage topomerase 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 eradication (no growth, <10^6 CFU/mL) of the qualifying baseline uropathogen.

Results. Of 22 participants, 8 (36%) had a baseline qualifying uropathogen (E. coli, S. saprophyticus, K. pneumoniae, and C. koseri) and were included in the micro-ITT (67%) and all of the qualifying uropathogens had MIC of ≤ 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 AUC24h/MICs ranged from 7 to 90.5 and urine AUC24h/MICs from 1292 to 121.698. The participant with the lowest plasma AUC/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.

Disclosures. All authors: No reported disclosures.

1483. Comparison of Outcomes in Urinary Tract Infections Caused by SPICE Organisms Treated with Non-Carbapenem β-lactamants vs. Non-β-lactam 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 cepixime, and monobactams) vs. drugs stable against AmpC (carbapenems, cetopenem, 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 (≥3 days) within the last month.

Results. One-hundred 56 patients were identified. Clinical response, 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 (≥3 days) within the last month. Patients with AmpC-stable and AmpC susceptible agents. AmpC induction can be seen 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.

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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) | 0.5937 |
| 30-d infection recurrence rate, n (%) | 7 (1.1) | 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) | 0.1999 |

Disclosures. All authors: No reported disclosures.