Conclusion. This study demonstrated no increased risk of post-operative infection in patients with a positive urinalysis or urine culture with bacteriuria prior to intervention. There was a high use of broad-spectrum antibiotic as a reflex to positive urinalyses alone highlighting an avenue for improved anti-microbial stewardship. More research is needed to guide clinicians on the role of urines culture and antibiotics prior to non-urgent urological procedures.

Disclosures. All authors: No reported disclosures.

1477. A Randomized 2 Phase Study of Cefpodoxime with the MenACWY-TT and MenACWY-PS groups, respectively, completed the booster to assess the percentages of subjects with titers of ≥1:8 and ≥1:128 at 10 years postvaccination. Antibody persistence 10 years after primary vaccination was evaluated in a microbiological-method of TTT (gMBTT) population. Safety was monitored in patients who received at least 1 dose of study drug. Clinical cure was designated as the resolution of CTT symptoms present at study entry. Plasma and urine PK were determined from all subjects.

Methods. Forty-five patients were enrolled in a randomized, multicenter, double-blind study of hospitalized adult patients with cUTI/AP. Patients received dosing regimens of FEP or FEP-EMT IV therapy q2 h by 2 hours infusion (table) for 7 to 10 days with a combination of FEP and EMT. Efficacy was evaluated in a microbiological-method of TTT (gMBTT) population. Safety was monitored in patients who received at least 1 dose of study drug. Clinical cure was designated as the resolution of CTT symptoms present at study entry. Plasma and urine PK were determined from all subjects.

Results. The drugs were well tolerated in each cohort, with similar % adverse events and no new or unexpected safety concerns (table). Two discontinuations were due to adverse dermatitis. The microbiological- and clinical responses at test-of-cure for the combined FEP-EMT group were 83.3% (20/24) and 95.8% (23/24) compared with responses in the combined FEP group of 73.3% (11/15) and 93.3% (14/15), respectively (table). The most common baseline pathogens were Escherichia coli (66.7%) and Klebsiella pneumoniae (23.1%): 28.2% of isolates produced ESBLs with eradication rates for the combined FEP-EMT group of 85.7% (6/7) and for the combined FEP group of 75.0% (3/4). FEP and EMT PK were best described by a 2-compartment linear PK model. Both agents exhibited half-lives of 2.3 hours. Creatinine clearance had a significant covariate effect on FEP and EMT, consistent with predominant renal excretion of both agents.

Conclusion. Results from this phase 2 study justify advancement to phase 3 studies to evaluate the safety and efficacy of FEP-EMT in patients with cUTI/AP.

Disclosures. All authors: No reported disclosures.

1479. Clinical Efficacy and Safety Analysis Evaluating Oral Gepotidacin (GSK2140994) in a Phase Ia Study in the Treatment of Uncomplicated Urinary Tract Infections.

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Background. Urinary tract infections (UTIs) are very common, with approximately 11% of women >18 years of age experiencing at least 1 episode of acute cystitis per year. Multidrug resistance, typically associated with nosocomial infections, has now emerged at the community level making treatment options for UTIs more difficult. Gepotidacin (GEP), a first-in-class, novel triazaacenaphthylene antibacterial has demonstrated in vitro activity against uropathogens including E. coli and provides high and sustained urine concentrations. It selectively inhibits bacterial DNA replication through a unique mechanism not utilized by any currently approved antibacterial. Gepotidacin presents an opportunity to address an unmet medical need and warrants a study as potential new and effective oral treatment for acute cystitis.

Methods. This Phase Ia single-center study was designed primarily to evaluate plasma and urine pharmacokinetics (PK) of gepotidacin in female participants with acute cystitis. Safety data and clinical and microbiological efficacy of gepotidacin were also assessed as secondary and exploratory endpoints. All participants received oral gepotidacin 1,500 mg BID for 5 days (total of 10 doses) during clinic confinement. Pretreatment and posttreatment CR collections were performed together with safety, efficacy, microbiological, and exploratory assessments throughout the study.

Results. Summary of Exploratory Endpoints (ITT Population). Clinical Efficacy: All subjects had significant improvement of clinical symptoms (dysuria, frequency, urgency, lower abdominal pain) within 24 to 48 hours of treatment. Most subjects, (20/22; 90.9%) achieved symptom resolution at test of cure (ToC) and follow-up (F/U). Microbiological eradication was achieved independent of baseline CFUs (see microbiology abstract). Safety Endpoint: Most common AEs involved the GI tract (diarrhea, nausea, vomiting, abdominal discomfort) in 20/22 (90.9%) of subjects. Per investigator observation, tolerance to nausea was observed with repeat dosing. No withdrawal due to AE. There were no clinically relevant trends in safety laboratories, ECG, or vital signs.

Conclusion. This first report of efficacy and safety in the treatment of acute cystitis supports further study of the clinical use of GEP in this indication.

Disclosures. All authors: No reported disclosures.

1480. Plasma and Urine Pharmacokinetic Analysis of Gepotidacin (GSK2140994) Following BID Oral Dosing in a Phase Ia Study for Treatment of Uncomplicated Urinary Tract Infections.

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Background. Urinary tract infections (UTIs) are very common, with approximately 11% of women >18 years of age experiencing at least 1 episode of acute cystitis per year. Multidrug resistance, typically associated with nosocomial infections, has now emerged at the community level making treatment options for UTIs more difficult. Gepotidacin (GEP), a first-in-class, novel triazaacenaphthylene antibacterial has demonstrated in vitro activity against uropathogens including E. coli and provides high and sustained urine concentrations. It selectively inhibits bacterial DNA replication through a unique mechanism not utilized by any currently approved antibacterial. Gepotidacin presents an opportunity to address an unmet medical need and warrants a study as potential new and effective oral treatment for acute cystitis.

Methods. This Phase Ia single-center study was designed primarily to evaluate plasma and urine pharmacokinetics (PK) of gepotidacin in female participants with acute cystitis. Safety data and clinical and microbiological efficacy of gepotidacin were also assessed as secondary and exploratory endpoints. All participants received oral gepotidacin 1,500 mg BID for 5 days (total of 10 doses) during clinic confinement. Pretreatment and posttreatment CR collections were performed together with safety, efficacy, microbiological, and exploratory assessments throughout the study.

Results. Summary of Exploratory Endpoints (ITT Population). Clinical Efficacy: All subjects had significant improvement of clinical symptoms (dysuria, frequency, urgency, lower abdominal pain) within 24 to 48 hours of treatment. Most subjects, (20/22; 90.9%) achieved symptom resolution at test of cure (ToC) and follow-up (F/U). Microbiological eradication was achieved independent of baseline CFUs (see microbiology abstract). Safety Endpoint: Most common AEs involved the GI tract (diarrhea, nausea, vomiting, abdominal discomfort) in 20/22 (90.9%) of subjects. Per investigator observation, tolerance to nausea was observed with repeat dosing. No withdrawal due to AE. There were no clinically relevant trends in safety laboratories, ECG, or vital signs.

Conclusion. This first report of efficacy and safety in the treatment of acute cystitis supports further study of the clinical use of GEP in this indication.

Disclosures. All authors: No reported disclosures.
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 triazacennazolylbencosine-p-halogenated phenylalanine (TzNpH) antibacterially active in vitro 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 unmet medical need by providing a new 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 1.5 to 1.92 hours. Steady-state pharmacokinetics were established 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 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. Oral dosing of 1500 mg BID produces urine GEP exposures that exceed the 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.

Table 1. Primary and Secondary Outcomes

| Clinical Outcomes | AmpC Susceptible (n=56) | AmpC Stable (n=100) | P-value |
|-------------------|-------------------------|---------------------|---------|
| Patients with clinical response to treatment, n (%) | 55 (98.2) | 95 (95.0) | 0.4207 |
| 30-d infection related readmission, n (%) | 17 (30.4) | 26 (26.0) | 0.5793 |
| 30-d infection recurrence, 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.

1482. Microbiological Analysis from a Phase II Study Evaluating Gepotidacin (GSK2149049) in the Treatment of Uncomplicated Urinary Tract Infections Nicole Scangarella-Oman, MBBS; Mohammad Hossain, PhD; Timothy Tiemeyer Jr, BS; Caroline R. Perry, PhD; Courtney Tiffany, BSc; Aparna Raychaudhuri, PhD; Etienne Dumont, MD; GlaxoSmithKline Pharmaceuticals, Collegville, Pennsylvania; GlaxoSmithKline, Collegville, Pennsylvania; PPD, Highland Heights, Kentucky

Background. Gepotidacin (GEP), a first in class novel triazacennazolylbencosine-p-halogenated phenylalanine (TzNpH) antibacterially active in vitro 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 in 5 days in female subjects with acute cystitis. Clean-catch mid-stream urine specimens were obtained for quantitative eradication by standard methods. Susceptibility testing by CLSI broth microdilution and gradient diffusion (Isonamycin only) was conducted. Inclusion in the microbiological intent-to-treat population (micro-ITT) required growth of a qualifying baseline uropathogen(s) (≥10^7 CFU/mL). Microbiological success was defined as culture-con

Table 1. Secondary Outcomes

| Outcome | n (%) | P-value |
|---------|-------|---------|
| 30-d infection related readmission | 17 (30.4) | 0.5793 |
| 30-d infection recurrence | 4 (7.1) | 0.4588 |
| 30-d all-cause mortality | 3 (5.4) | 0.7021 |
| Length of hospital stay (d) | 4.6 (2.6-9.0) | 0.1699 |

Disclosures. All authors: No reported disclosures.