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 urine cultures and antibiotics prior to non-urgent urological procedures.

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

1477. A Randomized Phase 2 Study of Cefepime Combined with the Novel Extended Spectrum β-Lactamase Inhibitor Enmetazobactam in Hospitalized Adults with Complicated Urinary Tract Infections (cUTI) Including Acute Pyelonephritis (AP)

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Background. Third-generation cephalosporin (3GC)-resistant *Enterobacteriaceae* has been classified as critical priority pathogens. The novel extended-spectrum β-lactamase (ESBL) inhibitor enmetazobactam (formerly AAI101; EMT) in combination with cefepime (FEP) is currently being developed as a carbapenem-sparing treatment of serious Gram-negative infections in settings with a high prevalence of 3GC-resistant *Enterobacteriaceae*. We report here the results from a phase 2 study that assessed safety, tolerability, and pharmacokinetics of FEP-EMT in patients with cUTI/AP.

Methods. Forty-five patients were enrolled in a randomized, multicenter, double-blind study of hospitalized adults with cUTI/AP. Patients received dosing regimens of FEP or FEP-EMT IV therapy q8h by 2 hours infusion (table) for 7 to 10 days with a 28-day follow-up. Efficacy was evaluated in the microbiological-modified ITT (μMITT) population. Safety was monitored in patients who received at least 1 dose of study drug. Clinical cure was designated as the resolution of cUTI symptoms present at study entry. Plasma and urine PK were determined from all patients.

Results. The study drugs were well tolerated in each cohort, with similar % adverse events and no new or unexpected safety concerns (table). Two discontinuations were due to allergic 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.

1478. Efficacy and Safety of a Booster Dose of the MenACWY-TT Vaccine Administered 10 Years After Primary Vaccination with MenACWY-TT or MenACWY-PS

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Background. The quadrivalent meningococcal ACWY polysaccharide tetanus toxoid conjugate vaccine (MenACWY-TT; Nimenrix) is licensed in various countries to prevent disease caused by meningococcal serogroups A, C, W, and Y. In a previous study (NCT00464815), subjects aged 11–17 years received a primary dose of MenACWY-TT or a quadrivalent polysaccharide vaccine (MenACWY-PS). Here, we report the long-term antibody persistence of the primary dose and the immunogenicity and safety of a booster dose given 10 years after primary vaccination of subjects.

Methods. Participants were enrolled from the Philippines and received a booster dose of MenACWY-TT at 10 years postvaccination. Antibody persistence 10 years postprimary vaccination and immunogenicity 1 month after the booster dose were evaluated by serum bactericidal activity assays using rabbit complement (rSBA) to assess the percentages of subjects with titers ≥1:8 and ≥1:128 and geometric mean titers (GMTs) for each serogroup. Safety was assessed for the booster dose.

Results. Of 229 subjects enrolled in this extension study, 169 and 58 subjects in the MenACWY-TT and MenACWY-PS groups, respectively, completed the booster phase. The percentages of primary MenACWY-TT recipients with prebooster rSBA titers ≥ 1:8 and ≥ 1:128 at year 10 ranged from 71.6%–90.7% and 64.8%–85.2% for all serogroups, respectively, compared with 43.1%–82.4% and 25.5%–76.5% of primary MenACWY-PS recipients; rSBA GMTs for all serogroups were higher in the MenACWY-TT group than in the MenACWY-PS group at year 10. For the MenACWY-TT and MenACWY-PS groups, respectively, the MenACWY-TT booster dose elicited rSBA titers ≥1:8 in 100% and ≥98.0% of subjects (figure); 100% and ≥96.1% of all subjects had titers ≥1:128. For all serogroups, rSBA GMTs at 1 month after the booster dose were higher than before the booster dose. No new safety signals were observed during the booster phase.

Conclusion. Functional antibody responses elicited by MenACWY-TT persisted 10 years after primary vaccination; the booster dose was well tolerated and elicited robust immune responses.

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Table. Safety and Efficacy Outcomes in Patients with cUTI/AP in the Phase 2 Study Following Treatment with Cefepime or Cefepime-Enmetazobactam

Parameter	Cohort 1		Cohort 2		Total
	FEP 1 g/EMT 0.5 g	FEP 1 g	FEP 2 g/EMT 0.75 g	FEP 2 g	
Safety population, n	15	7	15	8	45
AEs, no. patients (%)	9 (60.0)	3 (42.9)	4 (26.7)	3 (37.5)	19 (42.2)
Serious AEs, no. patients (no. events)	0 (0)	0 (0)	2[a] (2)	0 (0)	2 (2)
Drug-related TEAEs, no. patients (no. events)	2 (9)	1 (1)	2 (2)	2 (2)	7 (14)
Discontinuations due to drug-related TEAEs, no. patients (no. events)	0 (0)	0 (0)	2[b] (2)	0 (0)	2 (2)
Death, n	0	0	0	0	0
Efficacy (μMITT), n	13	7	11	8	39
% Microbiological eradication (n)/ %Clinical cure (n)					
Test of cure	76.9 (10)/100 (13)	100 (7)/100 (7)	90.9(10)/90.9 (10)	50.0 (4)/87.5 (7)	NR

Abbreviations: FEP, cefepime; EMT, enmetazobactam; AEs, adverse events; μMITT, microbiological modified intent to treat; TEAE, treatment-emergent adverse event; NR, not reported.
[a]Colorectal cancer and nephrolithiasis not related to study drug.
[b]Two discontinuations due to allergic dermatitis

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

1479. Clinical Efficacy and Safety Analysis Evaluating Oral Gepotidacin (GSK2140944) from a Phase IIa 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. GEP presents an opportunity to address an unmet medical need and warrants study as a potential new and effective oral treatment for acute cystitis.

Methods. This Phase IIa 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 PK 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 CFU's (see microbiology abstract). Safety Endpoint: Most common AEs involved the GI tract (diarrhea (18/22 [82%] and nausea 17/22 [77%]). 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.

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1480. Plasma and Urine Pharmacokinetic Analysis of Gepotidacin (GSK2140944) Following BID Oral Dosing in a Phase IIa Study for Treatment of Uncomplicated Urinary Tract Infections

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