1521. Heterogeneity of Recent Phase 3 cUTI Clinical Trials with New Antibiotics
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Background. For new antibiotics to treat Gram-negative infections, one regulatory pathway includes complicated urinary tract infections (cUTI) clinical trials. Although individual cUTI clinical trials comply with regulatory guidelines, they may differ substantially in design and execution. Six recent cUTI trials that supported or are likely to support FDA regulatory review were compared to determine variables that impacted patient selection and outcome parameters.

Methods. cUTI trials for six new antibiotics developed to treat multi-drug-resistant Gram-negative infections were obtained from publicly disclosed information including FDA documents, publications, or presentations at scientific meetings. Antibiotics included were: ceftolozane-tazobactam (CTZ-TAZ), ceftazidime–avibactam (CTZ-AVI), meropenem–vaborbactam (MER-VAB), cefiderocol, plazomicin, and fosfomycin. Comparison variables included: mITT sample size, age, % female patients, % acute pyelonephritis, % E. coli and other pathogens at baseline, switch to PO antibiotic, and the non-inferiority margin. Other variables as well as the microbiologic eradication, clinical response, and the combined outcomes will be included in the poster.

Results. mITT (n) Non-inferiority margin (%) Age, years (mean) % female Acute pyelonephritis (%) E. coli (%) (V-to-PO) 800 810 374 371 388 362 4.2 10 10 15 15 10 62 59.4 62 59.4 62 52.8 Not Reported 62 72 59 27 42 53 78.6 73.8 64.7 62.3 69.6 73.4

Conclusion. Study design and eligibility criteria significantly influence patient characteristics. The proportion of acute pyelonephritis varied greatly and influenced population demographics (age, gender) and baseline microbiology. Studies with a smaller proportion of acute pyelonephritis resulted in an older patient population, fewer females and less E. coli. Larger sample size did not impact outcomes.

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1522. Initial Clinical Response of Children with Extended-Spectrum Cephalosporin-Resistant Urinary Tract Infections (ESC-R UTIs) Started on Discardant Antibiotics
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Background. ESC-R UTIs in children are often resistant to common empiric regimens. Our objective was to describe the initial clinical response of children with ESC-R UTIs while on discardant antibiotics.

Methods. We conducted a multicenter retrospective chart review of children <18 years with ESC-R UTIs presenting to an acute care setting of 5 children's hospitals and a large managed care organization from 2012 to 2017.ESC-R UTI was defined as having a urinalysis with positive leukocyte esterase or >5 white cells per high-power field and a urine culture with ≥100,000 colony-forming units per milliliter of E. coli or Klebsiella spp. nonsusceptible to ceftriaxone. Children were included if they received initial discardant antibiotic (an agent to which their isolate was nonsusceptible) and had phone or in-person follow-up when urine culture susceptibilities resulted. Children with urologic surgery, immunosuppression and nonrenal chronic conditions were excluded. Outcomes were: (1) Escalation of care, defined as an emergency room visit, hospital admission or intensive care unit (ICU) transfer while on discardant therapy and (2) clinical response at the time of follow-up, classified as improved (complete or partial resolution of presenting symptoms) or not improved (persistence of symptoms) and assessed by a second reviewer in 20% of charts to determine inter-rater reliability.

Results. Of 253 children with ESC-R UTIs, 76% were female, median age was 2 years (interquartile range [IQR] 0.5–6.5) and 88% were started on cephalosporins. Median time to follow-up was 3 days (IQR 2–3). Nine children (4%) had escalation of care without ICU transfer. Follow-up records with clinical response information were available for 187 children (74%); 154 (83%) were improved and 33 (17%) were not improved (s = 0.80). Figure 1 shows improvement by symptom. In children with repeat urine testing while on discardant therapy, pyuria improved in 12/15 and urine cultures sterilized in 10/13.

Conclusion. Most children with ESC-R UTIs experienced initial clinical improvement while on discardant antibiotics. Future studies should prospectively evaluate the in vitro and clinical effect of discardant therapy in children to assess the need for modified urine-confirmed broad-spectrum treatment.

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1523. Antimicrobial Activity of Ceftazidime–Avibactam and Comparator Agents Tested Against Gram-Negative Organisms Isolated from Complicated Urinary Tract Infections: Results from the National Network for Optimized Resistance Monitoring (INFORM) Program
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Background. Urinary tract infections (UTIs) are among the most frequent healthcare-associated infections and represent a major source of Gram-negative (GN) bactemia. We evaluated the antimicrobial susceptibility (S) of GN bacteria isolated from patients with complicated UTIs (cUTIs) in United States medical centers.

Methods. Unique patient isolates were consecutively collected from patients with cUTIs in 83 medical centers in 2015–2017, and the GN organisms (n = 9,403) were S tested against CAZ-AVI and comparators by reference broth microdilution ( broth microdilution). Cefepime-tazobactam (CTZ-TAZ) was tested in 2017 only. Enterobacteriaceae (ENT) with an extended-spectrum β-lactamase (ESBL) phenotype was evaluated by whole genome sequencing for the presence of genes encoding β-lactamases.

Results. The most common organisms were E. coli (EC; 53.2%), K. pneumoniae (KPN; 12.5%), E. faecalis (6.0%), P. mirabilis (PM; 5.5%), and P. aeruginosa (PA; 4.9%). An ESBL phenotype was observed among 13.2, 13.4 and 7.0% of EC, KPN, and PM, respectively. CAZ-AVI inhibited >99.9% of all ENT, including all EC, PM and E. cloacae (ECL) isolates, at the S breakpoint of 8 µg/mL (table). CAZ-AVI was also highly active against KPN, including ESBL-phenotype (MIC50, 0.25/µg/mL; 99.5%) and meropenem (MEM)-non-S isolates (MIC50, <2 µg/mL; 98.0%). In contrast, only 72.9 and 73.1% of ESBL-phenotype KPN isolates were S to CTZ and MEM, respectively. Only one ENT isolate was CAZ-AVI-resistant, a KPN with a CAZ-AVI MIC of 16 µg/mL that produced a KPC-2 and an SHV-12 and exhibited decreased activity against CAZ (99.5%S) and meropenem (MEM)-non-S isolates (MIC50, <2 µg/mL; 98.0%).

Discussion. All authors: No reported disclosures.
1524. Are Providers Shifting from NTF to Fosfomycin for Inpatient UTI? Big Data Reveals Small Shifts
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Background. Fosfomycin (fosf) and NTF (ntf) are IDSA guideline approved drugs for acute cystitis in women. However, their activity against multi-drug-resistant Gram-negatives may be driving increased use among inpatients with more complicated UTI. We evaluated trends in inpatient prescribing of these UTI-specific agents in the predominantly male population of the national VA system over a 7-year period.

Methods. All inpatient bar-coded administrations for fosf and NTF at every VA facility nationwide from 2011 to 2017 were captured through a data analytics platform which extracts data from the VA Data warehouse. Antibiotic days of therapy and rates per 1,000 patient-days (DOT/1,000CD) were extracted by year and compared using Mantel-Haenszel chi square for linear trend (MH OR). Demographics were captured via administrative data.

Results. Prescriptions from over 65 million patient-days spanning 7 years and all inpatient units in 129 VA facilities were included. Approximately 90% of patients were male with a mean age range of 55–64 years. FOS use increased from 128 prescriptions in 2011 to a high of 1,230 in 2016 and 1,003 in 2017 (figure). At the maximum in 2016, prescription rates increased almost 10-fold compared with 2011 (MH OR 9.8, P < 0.001). NTF prescriptions declined from 26,590 in 2011 to 19,343 in 2017. Rates decreased 25% from 2.8 to 2.1, MH OR 0.75, P < 0.001. In 2017, FOS and NTF usage rates were highest in rehabilitation/spinal cord units (table). Conclusion. In this large nationwide cohort, FOS use increased almost 10-fold among predominantly male inpatients while NTF use declined slightly. NTF is still used orders of magnitude more than FOS, even after adjusting for extended days of activity of FOS. Both agents retain activity against many MDR GNRs but differences in efficacy, tissue penetration, familiarity and availability likely influence the choice for oral UTI-specific treatment.

| 2017 Data | ICU | MEDSURG | NH | PSYCH | REHAB/GCI |
|-----------|-----|---------|----|-------|-----------|
| FOS DOT/1,000CD | 0.06 | 0.15 | 0.07 | 0.03 | 0.73 |
| NTF DOT/1,000CD | 0.56 | 1.46 | 2.41 | 2.55 | 9.35 |
| FGs | 28 | 392 | 292 | 58 | 28 |
| NTF days | 251 | 3,699 | 7,826 | 2,634 | 4,013 |

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1525. Evaluation of Clinical Outcomes With Fosfomycin for E. coli and Non-E. coli Enterobacteriaceae Urinary Tract Infections
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Background. Fosfomycin is a broad-spectrum oral antibiotic increasingly used for the treatment of uncomplicated and complicated urinary tract infections (UTIs). The Clinical and Laboratory Standards Institute (CLSI) does not support fosfomycin susceptibility testing on urinary isolates outside of Enterococcus faecalis and Escherichia coli. This is in light of building evidence and concern for the presence of chromosomal fmoA gene in non-E. coli Enterobacteriaceae. Regardless, clinicians have continued to test and use fosfomycin for these pathogens due to multidrug resistance or intolerance to other agents without ample data on clinical implications.

Methods. This retrospective study included patients who received fosfomycin for the treatment of a UTI caused by any Enterobacteriaceae for which fosfomycin testing was performed from March 2016 through April 2018. We separated patients who received fosfomycin for the treatment of UTIs caused by E. coli from those caused by other Enterobacteriaceae for comparison. The primary outcome is the rate of clinical success at 48-hours, defined as the absence of UTI symptoms and normalization of vital signs. The secondary outcome is the rate of recurrent UTIs caused by the same pathogen within 30 days of the index infection.

Results. There were 28 separate episodes of E. coli UTIs in 24 patients and 25 separate episodes of non-E. coli UTIs in 26 patients included in this study. Patients were mostly balanced between the two groups and were on average about 64 years old, mostly females (61%), and had an average Charlson Comorbidity Index of 5. All E. coli isolates were susceptible to fosfomycin, while only 82.8% non-E. coli isolates were fosfomycin-susceptible. The rates of clinical success were similar between the E. coli and non-E. coli groups (89.3% vs. 88.5%). There was a higher rate of recurrence of the same UTI with E. coli (15.4%) than with non-E. coli (4.8%). Conclusion. Findings from this small study suggest favorable outcomes with use of fosfomycin for non-E. coli Enterobacteriaceae. Despite recommendations against testing and use of fosfomycin in these pathogens, it appears that in vitro resistance does not always correlate with clinical response.

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1526. Oral Fosfomycin Use for Urinary Tract Infections and Its Clinical Impact on Hospital Stay
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Background. Oral fosfomycin is a treatment option for urinary tract infections (UTI) caused by multi-drug-resistant organisms (MDRO). The objective of the study was to describe the prescribing pattern of fosfomycin and determine its role in (1) preventing hospital admissions for patients seen in the emergency department or (2) promoting earlier discharges for admitted patients.

Methods. This retrospective chart review evaluated adults that received at least one dose of fosfomycin during the period 2014–2017. Information was collected using electronic medical records (e.g., demographics, symptoms, dose/duration of fosfomycin, urine culture results, length of stay, and hospital readmission). Statistical analysis was performed using descriptive statistics.

Results. Forty-three patients were included (60.5% females). Nearly half of the population (48.4%) had a history of recurrent UTIs. Patients received fosfomycin for cystitis (58.1%), pyelonephritis (34.9%), and asymptomatic bacteriuria (7%). Only two patients received >1 dose. Empiric use of fosfomycin was seen in only 9.3%. Of those treated based on culture results, 84.6% of patients had MDROs (2 ESBL, 2 VRE, 1 KPC, 1 resistant-Pseudomonas). None of the isolates had fosfomycin susceptibilities performed. In 72% of the time, patients had no other oral options. In 74.3% of the time, fosfomycin was used as step-down therapy from intravenous (IV) antibiotics (e.g., carbapenem 69%, ceftaxime 13.8%). Infectious Diseases was consulted on 81.4% of cases. Seven percent of patients had documented allergies to the preferred agent. Treatment success was seen in 93% of patients, while three patients failed treatment requiring readmission for IV therapy. Fosfomycin use resulted in earlier discharge in 75.8% of cases (range of 1–6 days, mean 2.92 hospital days avoided per patient). For those who received fosfomycin as part of their emergency visit, 90% (9 of 10) were able to avoid hospitalization.

Conclusion. In our study, fosfomycin was used in UTI caused by MDROs, with treatment success demonstrated in a majority of patients. Fosfomycin allowed for patients to avoid hospitalization or promote earlier discharge, on average for patients days sooner than anticipated. Use of fosfomycin should be considered in appropriate patients in an effort to decrease length-of-stay or altogether avoid hospitalization.

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1527. The Prevalence of Enterobacteriaceae (ENT) Resistant to All Major Classes of Oral Antibiotics from Outpatient Urine Cultures in the United States and Effect of Clinical Outcomes
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Background. Oral fosfomycin is a treatment option for urinary tract infections (UTI) in the United States are treated with either a quinolone, β-lactam, trimethoprim-sulfamethoxazole (T/S) or nitrofurantoin (NHF). Resistance to all classes of antibiotics is now