ceftriaxone or their combination. The valves were then washed from any planktonic cells and the biofilm biomass was established by CFU enumeration.

**Conclusion.** This study demonstrates that a proper in vitro testing is essential in the treatment of PVE with phages. As seen here, the phage-antibiotic combination intended for treatment should be drawn according to their efficacy on suitable models, simulating the clinical settings, with the specific pathogen, the valve material, and the used phages taken into consideration.

**Disclosures.** Ran Nir-Paz, MD, BiomX (Consultant); Technophage (Scientific Research Study Investigator, Advisor or Review Panel member)

1062. Analysis of Resistance to Oral Standard of Care Antibiotics for Urinary Tract Infections Caused by Escherichia coli and Staphylococcus saprophyticus Collected Worldwide between 2019-2020

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Session: P-61. Novel Agents

**Background.** Gepotidacin (GSK2140944) is a novel triazaaacenaphthyline bacterial type II topoisomerase inhibitor under development for the treatment of gonorrhea and uncomplicated urinary tract infections (UTI). This study reports on the in vitro activity of gepotidacin and other oral antibiotics when tested against contemporary Escherichia coli and Staphylococcus saprophyticus clinical isolates collected from patients with UTIs for a gepotidacin uUTI global surveillance study as part of the SENTRY Antimicrobial Surveillance Program.

**Methods.** A total of 3,562 E. coli and 344 S. saprophyticus isolates were collected between 2019 and 2020 from 92 medical centers located in 25 countries. Most isolates were tested after urine specimens collected from patients seen in ambulatory, emergency, family practice, and outpatient medical services. Bacterial identifications were confirmed by MALDI-TOF. Isolates were tested for susceptibility by CLSI methods at a central laboratory (JMI Laboratories). MIC results for oral antibiotics licensed for the treatment of uUTI and drug-resistant subsets were interpreted per CLSI guidelines.

**Results.** Gepotidacin (MIC < 4 mg/L) displayed good activity against 3,562 E. coli isolates, with 98.0% of all observed gepotidacin MICs ≤ 4 mg/L (Table). Susceptibility (S) rates for the other oral agents tested against these isolates were: amoxicillin-clavulanate (79.6% S), ampicillin (72.5% S), amoxicillin, ceftriaxone, or their combination. The β-lactam antibiotic is in black.

**Conclusion.** Gepotidacin demonstrated potent in vitro activity against contemporary E. coli and S. saprophyticus urine isolates. This activity was largely unaffected among isolates demonstrating drug-resistance to other oral standard of care antibiotics.

**Table.**

**Disclosures.** S. J. Ryan Arends, PhD, AbbVie (formerly Allergan) (Research Grant or Support); GlaxoSmithKline, LLC (Research Grant or Support); Melinta Therapeutics, LLC (Research Grant or Support); Sero Therapeutics (Research Grant or Support); Deborah Butler, n/a, GlaxoSmithKline, LLC (Employee); Nicole Scangarella-Oman, MS, GlaxoSmithKline, LLC (Employee) Lindsey Paustian, BS (ASCp), GlaxoSmithKline, LLC (Research Grant or Support); Jennifer M. Streit, BS, GlaxoSmithKline, LLC (Research Grant or Support); Shionogi (Research Grant or Support); Rodrigo E. Mendes, PhD, AbbVie (Research Grant or Support); AbbVie (formerly Allergan) (Research Grant or Support); Cipla Therapeutics (Research Grant or Support); Cipla USA Inc. (Research Grant or Support); ContraFect

Corporation (Research Grant or Support); GlaxoSmithKline, LLC (Research Grant or Support); Melinta Therapeutics, LLC (Research Grant or Support); Shionogi (Research Grant or Support); Pfizer, Inc. (Research Grant or Support)

1063. ARGONAUT-V: Susceptibility of Multidrug Resistant (MDR) Pseudomonas aeruginosa to Cefepime-Taniborbactam

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Session: P-61. Novel Agents

**Background.** P. aeruginosa is a Gram-negative pathogen responsible for many serious infections. MDR, both intrinsic and acquired, presents major clinical challenges. Taniborbactam (formerly VNRX-5133; Fig 1) is a β-lactamase inhibitor (BLI) characterized by a bicyclic boronate, uniquely possessing activity toward all four Amber classes of β-lactamas, both serum and metallo, with the exception of class B IMP β-lactamas. The β-lactam-BLI (BL-BLI) combination cefepime-taniborbactam (FTB; Fig 1) is currently in phase 3 clinical trials.

**Results.** Gepotidacin (MIC < 4 mg/L) displayed good activity against 3,562 E. coli isolates, with 98.0% of all observed gepotidacin MICs ≤ 4 mg/L (Table). Susceptibility (S) rates for the other oral agents tested against these isolates were: amoxicillin-clavulanate (79.6% S), ampicillin (45.6% S), ceftriaxone, or their combination. The β-lactam antibiotic is in black.

**Conclusion.** Gepotidacin demonstrated potent in vitro activity against contemporary E. coli and S. saprophyticus urine isolates. This activity was largely unaffected among isolates demonstrating drug-resistance to other oral standard of care antibiotics.

**Table.**

**Disclosures.** S. J. Ryan Arends, PhD, AbbVie (formerly Allergan) (Research Grant or Support); GlaxoSmithKline, LLC (Research Grant or Support); Melinta Therapeutics, LLC (Research Grant or Support); Sero Therapeutics (Research Grant or Support); Deborah Butler, n/a, GlaxoSmithKline, LLC (Employee); Nicole Scangarella-Oman, MS, GlaxoSmithKline, LLC (Employee) Lindsey Paustian, BS (ASCp), GlaxoSmithKline, LLC (Research Grant or Support); Jennifer M. Streit, BS, GlaxoSmithKline, LLC (Research Grant or Support); Shionogi (Research Grant or Support); Rodrigo E. Mendes, PhD, AbbVie (Research Grant or Support); AbbVie (formerly Allergan) (Research Grant or Support); Cipla Therapeutics (Research Grant or Support); Cipla USA Inc. (Research Grant or Support); ContraFect

Corporation (Research Grant or Support); GlaxoSmithKline, LLC (Research Grant or Support); Melinta Therapeutics, LLC (Research Grant or Support); Shionogi (Research Grant or Support); Pfizer, Inc. (Research Grant or Support)
Disclosures.

Conclusion.

Left panel. Mean relative abundance taxonomic class level at timepoints for participants in PUNCH CD3 before and after RBX2660 treatment. For doses of RBX2660 administered in PUNCH CD3, the four taxonomic classes that change most from before to after treatment are shown with the mean and confidence intervals based on fitting OTU data to a Dirichlet multinomial distribution. Right panel, MHI biomarker for the same time points and investigational product groups, shown as median (red) and individual samples. A previously calculated threshold of MHI = 7.2 is shown (dotted line). The majority of responders’ MHI values shifted from a range common to antibiotic dysbiosis to a range common in healthy populations.

Figure 1

Background.

Several investigational microbiota-based live biotherapeutics are in clinical development for reducing recurrence of *Clostridioides difficile* infection (rCDI), including RBX2660 a liquid suspension of a broad consortium of microbiota, which includes Bacteroides and Firmicutes. RBX2660 has been evaluated in >600 participants in 6 clinical trials. Here we report that RBX2660 induced significant shifts to the intestinal microbiota of treatment-responsive participants in PUNCH CD3—a Phase 3 randomized, double-blinded, placebo-controlled trial.

Methods.

PUNCH CD3 participants received a single dose of RBX2660 or placebo between 24 to 72 hours after completing rCDI antibiotic treatment. Clinical response was the absence of CDI recurrence at eight weeks after treatment. Participants voluntarily submitted stool samples prior to blinded study treatment (baseline), 1, 4 and 8 weeks, 3 and 6 months after receiving study treatment. Samples were extracted and sequenced using shallow shotgun methods. Operational taxonomic unit (OTU) data were used to calculate relative taxonomic abundance, alpha diversity, and the Microbiome Health Index (MHI)—a biomarker of antibiotic-induced dysbiosis and restoration.

Results.

Clinically, RBX2660 demonstrated superior efficacy versus placebo (70.4% versus 58.1%). From before to after treatment, RBX2660-treated clinical responders exhibited microbiome divergence shifted significantly (Mann-Whitney), and did not microbiome composition (Generalized Wald Test). Post-treatment changes were characterized by increased Bacteroidia and Clostridia and decreased Gammaproteobacteria and Bactilli, and changes were durable to at least 6 months. Repeated measures analysis confirmed that shifts were greater among RBX2660 responders compared to placebo responders (DMRepeat). The majority of responders’ MHI values shifted from a range common to antibiotic dysbiosis to a range common in healthy populations.