

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* matching 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 triazaacenaphthylene 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 a 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 (68%) tested were cultured from 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_{50/90} 2/2 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), ciprofloxacin (72.5% S), fosfomicin (99.0% S), mecillinam (94.1% S), nitrofurantoin (97.3% S), and trimethoprim-sulfamethoxazole (68.2% S). When tested against the drug-resistant subsets, gepotidacin maintained similar MIC_{50/90} values (2/4 mg/L), except against isolates resistant to fosfomicin (2/8 mg/L). Against *S. saprophyticus* isolates, gepotidacin (MIC_{50/90} 0.06/0.12 mg/L) inhibited all isolates at ≤0.25 mg/L. Most oral agents showed S results of >97% against *S. saprophyticus* isolates, except for penicillin (3.5% S).

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

Organism (No. isolates)	No. and cumulative % of isolates inhibited at a gepotidacin MIC (mg/L) of:											MIC ₅₀	MIC ₉₀
	≤0.25	0.5	1	2	4	8	16	32	MIC ₅₀	MIC ₉₀			
<i>E. coli</i> (3,562)	47	190	1218	1780	255	48	19	5	2	2			
AMX-CLA-R (202)	1.3	6.7	40.8	90.8	99.3	99.9	100				2	4	
AMP-R (1,914)	29	135	682	852	160	33	18	5	2	4			
FQ-R (902)	34	100	311	338	92	16	8	3	2	4			
FOS-R (25)	0	3	7	7	4	3	1				2	8	
MEC-R (151)	4	8	39	78	17	3	2				2	4	
NIT-R (46)	1	11	24	24	7	1	0	1	2	4			
TMP-SMX-R (1,130)	19	87	421	468	95	31	9	4	2	4			

Abbreviations: -R, resistant per CLSI 2021; AMX-CLA, amoxicillin-clavulanate; AMP, ampicillin; FQ, fluoroquinolones; FOS, fosfomicin; MEC, mecillinam; NIT, nitrofurantoin; and TMP-SMX, trimethoprim-sulfamethoxazole.

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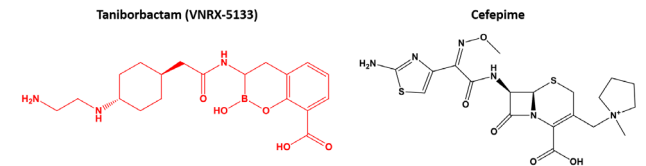
Corporation (Research Grant or Support)GlaxoSmithKline, LLC (Research Grant or Support)Melinta Therapeutics, Inc. (Research Grant or Support)Melinta Therapeutics, LLC (Research Grant or Support)Nabriva Therapeutics (Research Grant or Support)Pfizer, Inc. (Research Grant or Support)Shionogi (Research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

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

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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 as a bicyclic boronate, uniquely possessing activity toward all four Ambler classes of β-lactamases, both serine and metallo, with the exception of class B IMP β-lactamases. The β-lactam-BLI (BL-BLI) combination cefepime-taniborbactam (FTB; Fig 1) is currently in phase 3 clinical trials.



Structures of taniborbactam and cefepime. The β-lactamase inhibitor is in red and the β-lactam antibiotic is in black.

Methods. The activity of FTB was tested against 197 well-characterized clinical *P. aeruginosa* isolates that were part of PRIMERS (Platforms for Rapid Identification of MDR-Gram-negative bacteria and Evaluation of Resistance Studies). Nearly 58% of these strains were reported as carbapenem-non-susceptible. Porin changes, efflux pumps, and/or the presence of acquired class A or class B carbapenemases were previously reported. Broth microdilution minimum inhibitory concentrations (MICs) were determined by CLSI M07 Ed. 11 methods with custom Sensititre frozen panels and interpreted using CLSI M100 Ed. 30 breakpoints. American Type Culture Collection strains were used for quality control. FEP breakpoints were provisionally used for FTB, where taniborbactam was fixed at 4 μg/mL.

Results. Percent susceptibility to BL agents alone was 45.2% for imipenem (IPM), 55.8% for meropenem (MEM), 60.9% for ceftazidime (CAZ), and 67.0% for FEP. The addition of BLI to BL increased % susceptibility for MEM-vaborbactam (MVB), 56.9%; ceftolozane-tazobactam (C/T), 77.7%; CAZ-avibactam (CZA), 79.7%, and FTB, 82.7%. MIC₅₀s were in the susceptible range for all drugs except IPM, which was intermediate, and all MIC₉₀s were in the resistant range (Table 1). Taniborbactam reduced FEP MIC by 2-fold in 32% of isolates and ≥ 4-fold in 13% of isolates. Against carbapenem-non-susceptible strains, % susceptibilities were: FTB, 68.5%, CZA, 63.0%, C/T, 59.3%; and MVB, 21.3% (Table 2).

	AMK	ATM	C/T	CAZ	CZA	FEP	FTB	IPM	MEM	MVB	TZP	TOB
CLSI Breakpoint	≤16	≤8	≤4/4	≤8	≤8/4	≤8	≤8*	≤2	≤2	*	≤16/4	≤4
MIC ₅₀	4	8	0.5	4	2	4	4	4	1	1	8	0.5
MIC ₉₀	>32	>16	>8	>16	>8	>16	>8	>4	>4	>4	>64	>8
%S	87.3	53.8	77.7	60.9	79.7	67.0	82.7*	45.2	55.8	56.9	56.9	78.7

MIC₅₀ and MIC₉₀ values (μg/mL) and percent susceptibility (%S) for all *P. aeruginosa* strains (n=197). AMK, amikacin; ATM, aztreonam; C/T, ceftolozane-tazobactam; CAZ, ceftazidime; CZA, ceftazidime-avibactam; FEP, cefepime; FTB, cefepime-taniborbactam; IPM, imipenem; MEM, meropenem; MVB, meropenem-vaborbactam; TZP, piperacillin-tazobactam; TOB, tobramycin. *The breakpoints for FEP and MEM alone were provisionally applied to FTB and MVB, respectively. Tazobactam, avibactam, and taniborbactam were fixed at 4 μg/mL, while vaborbactam was fixed at 8 μg/mL. Breakpoints from CLSI M100, 31st ed. 2021.

MIC₅₀ and MIC₉₀ values (μg/mL) and percent susceptibility (%S) for all *P. aeruginosa* strains (n=197). AMK, amikacin; ATM, aztreonam; C/T, ceftolozane-tazobactam; CAZ, ceftazidime; CZA, ceftazidime-avibactam; FEP, cefepime; FTB, cefepime-taniborbactam; IPM, imipenem; MEM, meropenem; MVB, meropenem-vaborbactam; TZP, piperacillin-tazobactam; TOB, tobramycin. *The breakpoints for FEP and MEM