resistance mechanisms, including difficult to treat CRE isolates and MBL producers. Further development of QPX with various orally- and IV-available BL agents appears warranted.

Table

Antimicrobial agent	MIC50/MIC90 values (mg/L) for antimicrobial agents: Agent alone	with QPX7728 at fixed 4 mg/L	with QPX7728 at fixed 8 mg/L
Aztreonam	64 / >64	≤0.03 / 0.25	≤0.03 / 0.12
Cefepime	64 / >64	≤0.03 / 0.5	≤0.03 / 0.25
Ceftolozane with tazobactam at fixed 4 mg/L	8 / >64	0.12 / 32	0.06 / 4
Piperacillin with tazobactam at fixed 4 mg/L	128 / >128	1 / 4	0.25 / 2
Meropenem	0.5 / >64	≤0.03 / 0.12	≤0.03 / 0.06
Ceftibuten	16 / >64	≤0.03 / 2	N/A
Cefdinir	>64 / >64	0.12 / 4	N/A
Tebipenem	0.5 / >64	≤0.03 / 0.5	N/A

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1054. Activity of a Anti-staphylococcal Lysin, LSVT-1701: *In vitro* Susceptibility of *Staphylococcus aureus* and Coagulase-Negative Staphylococci (CoNS) Global Clinical Isolates (2002 to 2019)

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Session: P-61. Novel Agents

Background. LSVT-1701, formerly SAL200, is a novel, recombinantly-produced, bacteriophage-encoded lysin that specifically targets staphylococci via cell wall enzymatic hydrolysis. We reported the *in vitro* activity of LSVT-1701 against clinical isolates of *S. aureus* and coagulase-negative staphylococci (CoNS) collected worldwide.

Methods. LSVT-1701 and comparators were tested against 415 *S. aureus* (n=315) and CoNS (n=100) clinical isolates expressing various resistance phenotypes. The isolates were collected in 2002-2019 from medical centers located in the United States (50 medical centers; 174 isolates; 41.9% overall), Europe (37 medical centers; 140 isolates; 33.7% overall), Asia-Pacific region (15 medical centers; 55 isolates; 13.3% overall), and Latin America (12 medical centers; 46 isolates; 11.1% overall). These isolates originated mostly from the year 2019 (n=323).The isolates were susceptibility tested by the CLSI broth microdilution method. MIC interpretations were based on CLSI and EUCAST criteria where available.

Results. LSVT-1701 was highly active against *S. aureus* and CoNS isolates with MIC_{90} values of 2 mg/L for all *S. aureus*, methicillin-susceptible *S. aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), and CoNS (Table). The highest LSVT-1701 MIC values were 4 and 8 mg/L among *S. aureus* and CoNS, respectively. LSVT-1701 retained potent activity against *S. aureus* isolates showing resistance or decreased susceptibility to oxacillin, vancomycin, teicoplanin, telavancin, linezolid, daptomycin, ceftaroline, or lefamulin; MIC50 values ranged from 0.5 to 1 mg/L and MIC_{90} values ranged from 1 to 4 mg/L among *S. aureus* resistant subsets.

Table Summary of LSVT-1701 activity against *S. aureus*, CoNS and resistant subsets

Organism/resistant subset (no. of isolates)	Cumulative % of isolates inhibited at LSVT-1701 MIC (mg/L) of: 0.12	0.25	0.5	1	2	4	8	>8	MIC50	MIC90
S. aureus										
MSSA (102)		0.0	25.5	77.5	98.0	100.0			1	2
MRSA (102)		0.0	24.5	83.3	97.1	100.0			1	2
Vancomycin-resistant (11)		0.0	45.5	63.6	90.9	100.0			1	2
Vancomycin MIC of 2 mg/L (14)		0.0	28.6	78.6	100.0				1	2
Teicoplanin MIC ≥4 mg/L (11)	0.0	18.2	27.3	72.7	90.9	100.0			1	2
Telavancin MIC ≥0.12 mg/L (12)	0.0	16.7	66.7	91.7	100.0				0.5	1
Linezolid-resistant (22)	4.5	31.8	86.4	100.0					0.5	1
Daptomycin-non-susceptible (18)	0.0	11.1	38.9	77.8	88.9	100.0			1	4
Ceftaroline MIC of 4 mg/L (12)	0.0	8.3	58.3	91.7	100.0				0.5	1
Lefamulin-non-susceptible (11)	9.1	27.3	63.6	100.0					0.5	1
CoNS (100)	2.0	7.0	41.0	75.0	92.0	97.0	99.0	100.0	1	2

Summary of LSVT-1701 activity against S. aureus, CoNS and resistant subsets

Conclusion. LSVT-1701 demonstrated potent *in vitro* activity against contemporary clinical isolates of *S. aureus* and CoNS collected from medical centers worldwide and against resistant *S. aureus* isolates with uncommon resistance phenotypes. The results of this study support further clinical development of LSVT-1701 to treat staphylococcal infections.

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1055. ARGONAUT-IV: Susceptibility of Carbapenem-resistant *Klebsiellae* to Ceftibuten/VNRX-5236

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Session: P-61. Novel Agents

Background. Carbapenem resistance in *Klebsiellae* spp. arises through mutational and acquired mechanisms and is considered an "urgent threat" by the CDC. VNRX-5236 is a bicyclic boronate β-lactamase inhibitor (BLI) that combines oral bioavailability (via etzadroxil prodrug VNRX-7145; Figure 1) and activity against all three Ambler classes of serine β-lactamases. VNRX-7145 is currently in development with the oral cephalosporin, ceftibuten (CTB) (Figure 1).

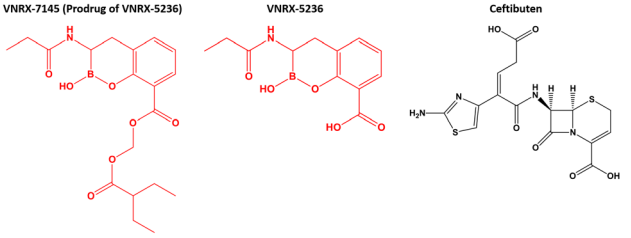

Figure 1. Structures of VNRX-7145, VNRX-5236, and ceftibuten. The β-lactamase inhibitors are in red and the β-lactam antibiotic is in black.

Methods. The activity of CTB/VNRX-5236 against 200 carbapenem-resistant *Klebsiellae* from the Consortium on Resistance against Carbapenems in *Klebsiella* (CRACKLE) was assessed in this study. Among these, 193 expressed class A KPC enzymes, one expressed a class B NDM enzyme, and six expressed a class D OXA-48 or variant enzyme. Minimum inhibitory concentrations (MIC) were determined by broth microdilution (CLSI M07 Ed. 11) using the ThermoFisher Sensititre system with custom assay panels. MICs were interpreted using CLSI M100 Ed. 30, except the EUCAST breakpoint for CTB (S≤1 µg/mL) was used for CTB and was applied for comparative purposes to CTB/VNRX-5236 MICs where VNRX-5236 was fixed at 4 µg/mL. American Type Culture Collection strains were used for quality control.

Results. 92.5% of stains studied in this CRACKLE collection were provisionally susceptible to CTB/VNRX-5236. In comparison, strains were 95.5% and 98% susceptible to meropenem-vaborbactam (MVB) and ceftazidime-avibactam (CZA), respectively. MIC_{50}s were in the susceptible range for CZA, MVB, and CTB/VNRX-5236; and resistant for CTB, ceftazidime (CAZ) and meropenem (MEM). MIC_{90}s were in the susceptible range for CZA, MVB, and CTB/VNRX-5236 and resistant range for CAZ, MEM, and CTB (Table 1). One of four CZA-resistant and three of nine MVB non-susceptible strains were provisionally susceptible to CTB/VNRX-5236.

	AMK	CST	CAZ	CZA	FEP	MEM	MVB	CTB	CTB/VNRX-5236	TGC
CLSI Susceptible Breakpoint	≤16	≤2*	≤4	≤8/4	≤2	≤1	≤4/8	≤1**	≤1/4***	≤2
MIC_{50}	16	0.5	>16	1	>32	>4	≤ 0.03	16	≤0.12	1
MIC_{90}	32	>4	>16	2	>32	>4	1	>16	1	4
%S	60	77	1	98	1.5	2.5	95.5	4.5	92.5***	88.5

MIC_{50} and MIC_{90} values (µg/mL) and percent susceptibility for Klebsiella pneumoniae strains (n=200). AMK, amikacin; CST, colistin; CAZ, ceftazidime; CZA, ceftazidime-avibactam; FEP, cefepime; MEM, meropenem; MVB, meropenem-vaborbactam; CTB, ceftibuten; TGC, tigecycline. * The breakpoint for CST is intermediate, as no susceptible breakpoint is available. ** The CTB breakpoint is valid only for urinary tract isolates. *** The breakpoint for CTB was provisionally used for CTB/VNRX-5236, where VNRX-5236 was fixed at 4 µg/mL.

MIC50 and MIC90 values (µg/mL) and percent susceptibility for Klebsiella pneumoniae strains (n=200). AMK, amikacin; CST, colistin; CAZ, ceftazidime; CZA, ceftazidime-avibactam; FEP, cefepime; MEM, meropenem; MVB, meropenem-vaborbactam; CTB, ceftibuten; TGC, tigecycline. * The breakpoint for CST is intermediate, as no susceptible breakpoint is available. ** The CTB breakpoint is valid only for urinary tract isolates. *** The breakpoint for CTB was provisionally used for CTB/VNRX-5236, where VNRX-5236 was fixed at 4 µg/mL.

Conclusion. The addition of VNRX-5236 enhanced the activity of CTB against the 200 *Klebsiella* isolates tested, reaching a total of 92.5% susceptibility. The prodrug (VNRX-7145) allows for oral administration, making it a potential option for step-down therapy. Importantly, VNRX-5236 has a broader spectrum of activity than existing oral BLIs, opening new treatment options for resistant infections as a key addition to the existing antibiotic arsenal.

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1056. Safety and Tolerability of Dalbavancin in Vancomycin Allergic Patients – A Case Series

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Session: P-61. Novel Agents

Background. VVancomycin and dalbavancin, both in the glycopeptide class of antibiotics, are used in the treatment of Gram-positive infections, including methicillin-resistant *Staphylococcus aureus*. Antibiotics in this class contain a heptapeptide core that has potential for cross-sensitivity. Due to this risk, dalbavancin carries a warning in the package insert for use in patients with a glycopeptide allergy. Dalbavancin, a semi-synthetic derivative of vancomycin, has lipophilic side chains which reduce the risk of cross-sensitivity to vancomycin. This case series evaluated patients with a listed vancomycin allergy in their electronic health record who received dalbavancin as an outpatient infusion.

Methods. This study was a non-randomized, retrospective chart review of adult patients who had a documented vancomycin allergy and received dalbavancin between February 2016 and February 2021 for any indication in the outpatient setting. The primary objective was to evaluate dalbavancin tolerability in patients allergic to vancomycin. Patient characteristics and the specifics of dalbavancin infusion – dose, volume, infusion rate, intravenous line access, and receipt of premedication before infusion – were collected on each patient.

Results. 559 unique patients received dalbavancin over the time frame. Of these, ten had a documented, subjective vancomycin allergy. Patient-reported allergic