therapeutic options include combinations of aztreonam (ATM), which is resistant to hydrolysis by MBLs, plus ceftazidime/avibactam (CZA) or meropenem/vaborbactam (M/V) for coverage of relevant SBLs. However, these selections add a level of complexity to clinical management compared with administration of a single antibiotic as monotherapy.

Methods. Minimum inhibitory concentrations (MICs) of WCK 5222 (cefepime/zidebactam), ATM, CZA, and M/V were determined with Liofilchem MIC Test Strips against SBL- and MBL-positive CRE (N = 15). The gradient diffusion strip (GDS) cross method was used to assess the activities of CZA+ATM and M/V+ATM. Additive interactions as defined by fractional inhibitory concentration indices ≤ 1 would be predicted based upon the known genotypic profiles; thus, the relative activities of the combination regimens were compared with the "zone of hope" (ZOH) test. The size of the ZOH (the zone of inhibited growth) was quantitated by multiplying the observed length of inhibited growth (in mm) adjacent to each GDS from the point of intersection. The Mann–Whitney rank-sum test was used to assess differences.

Results. All isolates (N = 15) contained one MBL and ≥1 SBL, and were resistant to ATM, CZA, and M/V with the exception of one isolate intermediate to M/V (MIC=8 mg/L). The WCK 5222 MIC_{50} (range) was 1 (0.19–2) mg/L. The median (interquartile range) ZOH product for CZA+ATM and M/V+ATM was 75.4 (62.8–93.7) and 23.5 (14.1–60.4), respectively (P = 0.002). In strains that produced OXA-type carbapenemases (n = 6), the median ZOH product for CZA+ATM and M/V+ATM was 78.1 and 20.7, respectively (P = 0.004). In the remaining 9 strains with a single carbapenemase (i.e., the MBL),the median ZOH product for CZA+ATM and M/V+ATM was 73.8 and 25.6, respectively (P = 0.052).

Conclusion. WCK 5222 displayed potent *in vitro* activity against SBL- and MBL-positive CRE, warranting further pre-clinical *in vivo* evaluation as a monotherapy option. When considering the co-expression of SBL and MBL, CZA+ATM appears to offer enhanced coverage compared with M/V+ATM.

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686. Evaluation of Contezolid Activity to Anaerobic and Gram-positive-cocci Isolates from a Phase 3 Acute Bacterial Skin and Skin Structure Infection Clinical Trial (MRX-I-06)

Yang Yang, Master of Medicine[1,2]; Demei Zhu, Bachelor[1]; [1]Institute of Antibiotics, Huashan Hospital, Fudan University, Shanghai, China (People's Republic), [2]Key Laboratory of Clinical Pharmacology of Antibiotics, National Health and Family Planning Commission, Shanghai, China (People's Republic)

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Contezolid (MRX-I) is an oxazolidinone in development for the treatment of acute bacterial skin and skin structure infections (ABSSSIs). In this study, *in vitro* susceptibility (S) for Contezolid and comparator agents for Gram-positive (GP) and anaerobic isolates from Phase 3 ABSSSI clinical trials were determined.

Methods. 313 isolates were collected from 65 participated sites and sent to a central laboratory for MIC testing. Clinical isolates included 34 anaerobes (15 *Finegoldia magna*, 8 *Actinomyces* spp., 4 *Prevotella* spp., 3 *Propionibacterium avidum*, 2 *Peptostreptococcus* spp., 1 *Veillonella* spp. and 1 *Bacteroides fragilis*), 187 *S. aureus* (59.7%). 12 *S. pyogenes*, 5 *Enterococcus*, and 75 other Gram-positive organisms. Broth micro-dilution method was used to determine the MIC of contezolid, linezolid, and other comparators to facultative isolates. Agar dilution was carried out for the anaerobes.

Results. For both 33 MRSA and 154 MSSA $MIC_{50/90}$ values of contezolid and linezolid were 2 mg/L. One *E. faecalis* showed decreased susceptibility to oxazolidinones (both MIC = 4). 1 mg/L contezolid and linezolid could inhibit 12 *S. pyogenes*. 2 mg/L contezolid and linezolid could inhibit 15 *Finegoldia magna*. 0.5 mg/L contezolid and linezolid could inhibit *8 Actinomyces* spp. To one *Bacteroides fragili,* two *Prevotella bivia* and one *Leuconostoc lactis* (Intrinsic resistant to vancomycin) the MIC of contezolid were 4 or 8 mg/L. In general, Contezolid had lower or equal $MIC_{50/90}$ values against both GP and ANA species compared with linezolid for all organisms.

Conclusion. Contezolid demonstrated potent *in vitro* antibacterial activity against Gram-positive and anaerobic isolates tested. These data suggest that contezolid might be a beneficial supplement to the arena against MDR Gram-positive infection.

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

687. *In vitro* Activity of a New Generation Oxopyrazole Antibiotic Against *Acinetobacter* spp.

Joel Goldberg, MD, PhD[1]; Christopher Bethel, MS[2]; Andrea M. Hujer, BS[3]; Kristine Hujer, BS[1]; Steven Marshall, MS[4]; Krisztina M. Papp-Wallace, PhD[1,2]; Federico Perez, MD, MS[1]; Elizabeth Spencer, MS[5]; Denton Hoyer, PhD[5]; Mark Plummer, PhD[5]; Robert A. Bonomo, MD[6]; [1]Case Western Reserve University, Cleveland, Ohio; [2]Louis Sokes Cleveland VA Medical Center, Cleveland, Ohio; [3]Louis Stokes VA Medical Center, Cleveland, Ohio; [4]Louis Stokes Cleveland Medical Center, Cleveland, Ohio; [5]Yale University, West Haven, Connecticut; [6]Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio

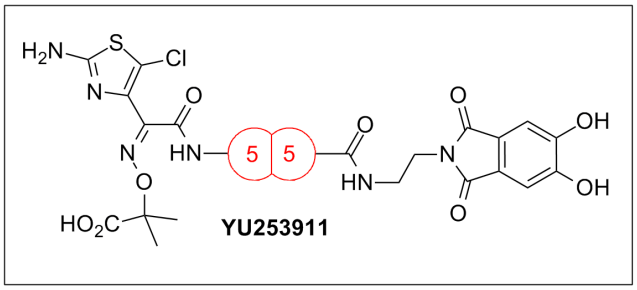
Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. *Acinetobacter* spp. resistant to common antibiotics have become a worrying cause of hospital-acquired infections and represent a critical need for innovative antibacterial development. New oxopyrazole agents targeting penicillin-binding proteins (PBPs) based on a non-β-lactam core and incorporating a siderophore moiety (figure) which facilitates transport to the periplasm are being developed which show promise against Gram-negative organisms including *Acinetobacter* spp.

Methods. YU253911, an example of this new class of antibacterials, was characterized *in vitro*. Minimum inhibitory concentrations (MICs) were determined by broth microdilution against a collection of 200 previously described (whole-genome sequencing) *Acinetobacter* isolates including 98 carbapenem-resistant *A. baumannii* strains. YU253911's antimicrobial activity was also evaluated in combination with complementary PBP agents and β-lactamase inhibitors by MIC and disc diffusion testing. All studies were performed according to current Clinical and Laboratory Standards Institute (CLSI) guidelines using iron-depleted media. Breakpoints for ceftazidime were arbitrarily chosen as reference.

Results. Using ceftazidime (breakpoint ≤8 μg/mL) as a comparator, 175 of the 200 Acinetobacter isolates were susceptible to YU253911, which possessed an MIC_{50} of 0.5 μg/mL and an MIC_{90} of 16 μg/mL. This compared favorably to all previously tested β-lactams including penicillins, cephalosporins, monobactams and carbapenems (MIC_{50}s 2 to >16 μg/mL). Against the subset of carbapenem-resistant *A. baumannii* isolates, YU253911's potency was similar with an MIC_{50} of 1 μg/mL. Genetic analysis showed β-lactamase genes, including OXA-23 and other carbapenemases, were common in both YU253911-resistant and susceptible strains.

Conclusion. YU253911 demonstrates promising *in vitro* potency against a collection of *Acinetobacter* isolates and compares favorably to β-lactam antibiotics. Understanding interactions with PBP agents and β lactamase inhibitors is being explored as well as further studies on the mechanism of resistance.



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688. *In Vitro* Activity of Eravacycline, a New Tetracycline Analog, and Comparators Against the Six Most Commonly Isolated Ribotypes of *Clostridioides difficile*

Eugenie Basseres, PhD; Julie Miranda, MPH; Anne J. Gonzales-Luna, PharmD; Travis J. Carlson, PharmD; Tasnuva Rashid, MD, PhD, MPH; M. Jahangir Alam, PhD; Kevin W. Garey, PharmD, MS, FASHP; University of Houston College of Pharmacy, Houston, Texas

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Eravacycline is a novel, tetracycline class antibacterial indicated for the treatment of complicated intra-abdominal infections in adults. In clinical trials, patients given eravacycline had a low likelihood of developing *Clostridioides difficile* infection (CDI). We hypothesized this was likely due, in part, to the *in vitro* susceptibility of eravacycline to *C. difficile*. The purpose of this study was to test the *in vitro* susceptibility of eravacycline vs. comparators on contemporary clinical isolates representing common ribotypes, including isolates with decreased susceptibility to metronidazole and vancomycin.

Methods. Two hundred and thirty-four isolates from our biobank were selected from the six most common ribotypes (F001, F002, F014-020, F027, F106, and F255). Minimum inhibitory concentrations (MIC) at 24 hours were measured according to CLSI guidelines for eravacycline, vancomycin, metronidazole and fidaxomicin. MICs results were tabulated and are presented as the geometric mean by ribotype.

Results. Geometric MIC results are shown in Table 1. Eravacycline was the most potent antimicrobial tested followed by fidaxomicin, metronidazole, and vancomycin. Results were consistent amongst all ribotypes, including isolates with reduced susceptibility to vancomycin and metronidazole.

Conclusion. Eravacycline displayed potent *in vitro* activity against a large collection of clinical *C. difficile* isolates. These data provide insight into why patients given eravacycline had a low likelihood of developing CDI and support further research to better understand the use of eravacycline to prevent or potentially treat patients with CDI.

	MIC (mg/L) geometric mean by ribotype					
Drug	**F001**	**F002**	**F014-020**	**F027**	**F106**	**F255**
Eravacycline	0.01	0.01	0.01	0.01	0.01	0.01
Vancomycin	1.52	1.58	1.66	1.71	1.70	1.70
Metronidazole	0.23	0.25	0.25	0.24	0.24	0.25
Fidaxomicin	0.02	0.03	0.03	0.03	0.03	0.03

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689. Therapeutic Efficacy of CB-012, a Novel Cloudbreak Antiviral Fc-Conjugate (AVC) in Lethal Mouse Models of Influenza A (H1N1) and Influenza B (Victoria)

James Levin, PhD; Allen Borchardt, PhD; Thanh Lam, PhD; Wanlong Jiang, PhD; Zhi-Yong Chen, PhD; Joanne Fortier, BSc; Suzanne Akers-Rodriguez, BSc; Karin Amundson, BSc; Joanna Donatelli, BSc; Simon Döhrmann, PhD; Jason Cole, PhD; Les Tari, PhD; Cidara Therapeutics, San Diego, California

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. In 2018, the World Health Organization estimated up to 650,000 influenza-related respiratory deaths occur annually. Cidara therapeutics is developing a novel class of potent, long-acting antiviral Fc-conjugates (AVCs) against influenza that in a single molecule combine a surface-acting antiviral agent with the Fc domain of a human IgG1 antibody. AVCs function by inhibiting viral replication while simultaneously engaging the immune system, providing a multimodal mechanism of action. Here we present efficacy data on an AVC development candidate against influenza A and B.

Methods. Efficacy studies were conducted in female BALB/c mice (6–8 weeks) challenged intranasally with 3x the LD_{95} of influenza A/Puerto Rico/8/1934 (H1N1) or B/Malaysia/2506/04. CB-012 or CB-012b (CB-012 with slightly modified Fc) was administered as a single intravenous (IV) dose 2 hours after challenge. Oseltamivir was dosed orally, twice daily for 5 days in the influenza A study. Vehicle and appropriate Fc controls were included. Body weights (BW) and mortality were monitored for 2 weeks; animals with 20% BW loss, or moribund, were scored as a death.

Results. In an initial study of CB-012 against influenza A, a single IV dose of 0.4 mg/kg was fully protective and statistically significant compared with the Fc control (P = 0.0027). In contrast, mice treated with oseltamivir at 5 mg/kg twice daily for 5 days were not protected; only the higher 20 mg/kg dose was fully protective. Importantly, mice treated with CB-012 (0.4 mg/kg) showed a transient BW loss of 1% compared with 14% in mice of the oseltamivir (20 mg/kg) group, although treatment was initiated at the same time. In a second study against influenza B, CB-012b was fully protective with a single IV dose at 0.3 mg/kg (P = 0.0027). In contrast, vehicle and Fc control groups reached mortality by day 6. BW loss in the CB-012b 0.3 mg/kg group was transient and <4% overall during the study.

Conclusion. The novel AVCs CB-012 and CB-012b demonstrated robust efficacy in multiple influenza models. In conjunction with previous findings against influenza A (H3N2), the data on CB-012 support its potential as a candidate against seasonal influenza. The continued development of CB-012 for the prevention and treatment of influenza is warranted.

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690. Activity of a Novel Polymyxin Analog, QPX9003, Tested Against Resistant Gram-Negative Pathogens, Including Carbapenem-Resistant *Acinetobacter*, *Enterobacterales*, and *Pseudomonas*

Mariana Castanheira, PhD[1]; Jill Lindley[1]; Holly Huynh[1]; Rodrigo E. Mendes, PhD[1]; Olga Lomovskaya, PhD[2]; [1]JMI Laboratories, North Liberty, Iowa; [2]Qpex Biopharma, San Diego, California

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Multidrug resistance (MDR) among Gram-negative (GN) organisms and the limited active therapeutic options against these pathogens are matters of worldwide concern. Polymyxins are cationic peptides that act on the bacterial cell membrane and have good activity against GN organisms, including MDR strains. We evaluated the activity of QPX9003, a novel polymyxin analog with an improved safety profile over current polymyxins, against a large collection of resistant GN isolates collected worldwide.

Methods. Susceptibility testing was performed by reference microbroth dilution against 2,518 GN organisms for QPX9003, colistin (COL), levofloxacin, tigecycline, gentamicin, amikacin, meropenem, cefepime, piperacillin–tazobactam, and ceftazidime–avibactam. Isolates included 1,000 *Pseudomonas aeruginosa* (PSA) enriched for MDR, 503 carbapenem-resistant *Acinetobacter baumannii* (CRAB), and 1,105 *Enterobacterales* (ENT).

Results. QPX9003 had potent activity against PSA isolates enriched for resistance against β-lactam/β-lactamase inhibitor combinations and was 4-fold more potent than COL ($MIC_{50/90}$, 0.25/0.25 mg/L vs. $MIC_{50/90}$ of 1/1 mg/L). QPX9003 was also more potent than COL against the panel of CRAB with $MIC_{50/90}$ of 0.125/1 mg/L and 0.5/4 for QPX9003 and COL, respectively. QPX9003 had a modal MIC of 0.06 mg/L against a large collection of ENT isolates resistant to cephalosporins and/or carbapenems ($MIC_{50/90}$, 0.06/16 mg/L). QPX9003 activity was identical against 508 carbapenem-resistant *Enterobacterales* (CRE; $MIC_{50/90}$, 0.06/16 mg/L) isolates and 511 *Klebsiella pneumoniae* isolates ($MIC_{50/90}$, 0.06/16 mg/L) in this collection. *Escherichia coli* isolates were considerably more sensitive to QPX9003 ($MIC_{50/90}$, 0.06/0.12 mg/L) compared with *K. pneumoniae* isolates. Activity of QPX9003 and COL was similar against ENT. Other comparator agents had limited activity against PSA, CRAB, and CRE isolates.

Conclusion. QPX9003 had activity against this collection of highly resistant GN isolates and was particularly active against the PSA and CRAB isolates. QPX9003 is a promising new-generation polymyxin agent.

	% of isolates at MIC								MIC (mg/L)	
Organisms (no. tested)	0.03	0.06	0.12	0.25	0.5	1	2	4	50%	90%
Enterobacterales (1,015)	16.8	67.7	79.5	80.6	81.4	82.1	82.6	83.6	0.06	16
K. pneumoniae (511)	19.2	73.6	78.1	79.1	80.2	80.8	81.6	83.0	0.06	16
E. coli (297)	9.1	67.3	96.6	97.3	97.3	98.3	98.3	99.3	0.06	0.12
CRE (508)	21.3	68.9	74.4	75.8	77.0	77.8	78.5	79.9	0.06	16
P. aeruginosa (1,000)	1.0	5.1	29.8	95.1	99.0	99.5	99.6	99.6	0.25	0.25
Carbapenem-resistant *A. baumannii* (503)	0.4	3.6	56.5	81.5	89.7	92.4	94.6	95.0	0.12	1

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

691. Activity of TNP-2092 Against Biofilms Formed by Prosthetic Joint Infection-Associated Staphylococci

Cody Fisher[1]; Suzannah Schmidt-Malan, MS[1]; Ying Yuan, PhD[2]; Shijie He[2]; Zhenkun Ma, PhD[2]; Robin Patel, MD[1]; Robin Patel, MD[1]; [1]Mayo Clinic, Rochester, Minnesota; [2]TenNor Therapeutics, Suzhou Industrial Park, Jiangsu, China (People's Republic)

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Infection occurs in ~1–2% of prosthetic joint replacement surgeries, with staphylococci being the most common cause. TNP-2092 is an investigational drug composed of rifamycin and quinolizinone pharmacophores conjugated via a stable linker. Here, we determined TNP-2092's *in vitro* activity against biofilms formed by staphylococci associated with prosthetic joint infection and compared activity to that of ciprofloxacin and rifampin alone and in combination, as well as to daptomycin and vancomycin.

Methods. A total of 80 staphylococcal isolates (40 *Staphylococcus aureus* and 40 *Staphylococcus epidermidis*) were studied. Planktonic state minimum inhibitory concentrations (MICs) of TNP-2092, ciprofloxacin, rifampin, ciprofloxacin + fixed concentration (1 mg/mL) rifampin, daptomycin and vancomycin were determined following CLSI guidelines. Tween-80 (0.002%) was added to TNP-2092 to prevent drug binding to plastic plates. Minimum biofilm inhibitory concentrations (MBICs) and minimum biofilm bactericidal concentration (MBBCs) were determined as follows. Bacteria were grown in TSB to logarithmic phase and adjusted to a turbidity of 0.5 McFarland; 150 µL aliquots were transferred to individual wells of 96-well flat-bottom plates and the plates covered with 96-pegged lids. Plates were incubated on a shaker for 5 hours at 37°C. Pegged lids were rinsed using 200 µL PBS/well and placed into a microtiter plate containing serial 2-fold drug dilutions in CAMHB Plates were incubated for 20–24 hours at 37°C and MBICs read by visual turbidity. Pegged lids were rinsed with PBS and placed into plates filled with 200 µL CAMHB/well and incubated for 20–24 hours at 37°C after which MBBCs were determined by assessing visual turbidity.

Results. Results shown in the table.

Conclusion. TNP-2092 has promising *in vitro* activity against prosthetic joint infection-associated staphylococcal biofilms.

Antimicrobial Agent	*Staphylococcus* species	Planktonic Susceptibility (µg/mL)		Biofilm Susceptibility (µg/mL)			
		MIC_{50}/ MIC_{90}	MIC Range	$MBIC_{50}$/ $MBIC_{90}$	MBIC Range	$MBBC_{50}$/$MBBC_{90}$	MBBC Range
TNP-2092	*aureus*	≤0.0075/ 0.015	≤0.0075/ 0.125	≤0.0075/ 0.03	≤0.0075/ 0.06	0.5/ 2	≤0.0075/ 4
	epidermidis	≤0.0075/ 0.015	≤0.0075/ 8	≤0.0075/ 0.06	≤0.0075/ 0.25	0.06/ 0.25	≤0.0075/ 1
Rifampin	*aureus*	0.0075/ 0.015	≤0.004/ 0.25	0.0075/ 0.03	≤0.004/ 0.25	>4/ >4	0.03/ >4
	epidermidis	0.0075/ 0.125	≤0.004/ >4	≤0.004/ 0.25	≤0.004/ >4	0.125/ >4	≤0.004/ >4
Ciprofloxacin	*aureus*	8/ >128	0.25/ >128	8/ >128	0.25/ >128	>128/ >128	2/ >128
	epidermidis	2/ >128	0.25/ >128	2/ >128	0.5/ >128	>128/ >128	0.5/ >128
Ciprofloxacin* +1 µg/ml Rifampin	*aureus*	≤0.125/ ≤0.125	≤0.125/ ≤0.125	≤0.125/ ≤0.125	≤0.125/ 0.125	>128/ >128	≤0.125/ >128
	epidermidis	≤0.125/ ≤0.125	≤0.125/ 128	≤0.125/ ≤0.125	≤0.125/ 128	≤0.125/ >128	≤0.125/ >128
Daptomycin	*aureus*	0.25/ 0.5	≤0.125/ 4	1/ 2	≤0.125/ 2	8/ 16	0.03/ 64
	epidermidis	0.25/ 0.5	≤0.125/ 2	0.5/ 1	≤0.125/ 2	2/ 6	≤0.125/ >128
Vancomycin	*aureus*	1/ 2	0.25/ 4	2/ 4	0.06/ 0.25	>128/ >128	2/ >128
	epidermidis	2/ 4	0.06/ 4	2/ 4	0.03/ 0.5	64/ >128	0.06/ >128

*Ciprofloxacin concentration shown

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692. *In Vitro* Antibacterial Activity of Cefiderocol Against a Multi-national Collection of Carbapenem-Nonsusceptible Gram-Negative Bacteria From Respiratory Infections: SIDERO-WT-2014–2017

Sonia N. Rao, PharmD[1]; Sean T. Nguyen, PharmD[1]; Melinda M. Soriano, PharmD[1]; Jennifer M. Hayes, PharmD[1]; Meredith M. Hackel, PhD[2]; Daniel F. Sahm, PhD, D(ABMM), FAAM [2]; Glenn S. Tillotson, PhD[3]; Roger Echols, MD[4]; Masakatsu Tsuji, PhD[5]; Yoshinori Yamano, PhD[5]; [1]Shionogi Inc., Florham Park, New Jersey; [2]International Health Management Associates, Inc., Schaumburg, Illinois; [3]GST Micro LLC, Henrico, Virginia; [4]Infectious Disease Drug Development Consulting LLC, Easton, Connecticut; [5]Shionogi & Co., Ltd., Osaka, Japan

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Cefiderocol (CFDC) is a new siderophore cephalosporin with potent *in vitro* activity against a broad range of Gram-negative (GN) pathogens, including carbapenem-nonsusceptible (Carb-NS) strains. We evaluated the *in vitro* activity of CFDC and comparator agents against recent clinical Carb-NS GN respiratory isolates collected from North America and Europe as part of the multi-national SIDERO-WT surveillance program.