Methods. 929 ABC isolates, including 698 *A. baumannii*, 13 *A. calcoaceticus*, 54 *A. nosocomialis*, and 164 *A. pittii*, were collected in 2018 from geographically diverse medical centers in the United States, Europe, Latin America, Israel and the Asia-Pacific region. Susceptibility testing was performed according to CLSI guidelines. Data analysis was performed using CLSI and EUCAST breakpoint criteria where available. Select isolates were subjected to whole genome sequencing with an Illumina MiSeq V2 instrument and analysis using CLCBio Genomics Workbench v6.5.

Results. In surveillance of 929 global isolates from 2018, the SUL-DUR MIC_{90} was 2 mg/L compared with 64 mg/L for SUL alone. This level of potency was consistent across species, regions, source of infection and subsets of resistance phenotypes. Fifty percent of the isolates were non-susceptible to carbapenems. Only 7 isolates (0.75%) had SUL-DUR MIC values >4 mg/L. Whole genome sequencing of these 7 isolates revealed that they either encoded the metallo-β-lactamase NDM-1, which DUR does not inhibit, or single amino acid substitutions near the active site of PBP3, the primary target of SUL.

Conclusion. SUL-DUR demonstrated potent antibacterial activity against recent, geographically diverse clinical isolates of ABC, including MDR isolates. These data support the potential utility of SUL-DUR for the treatment of antibiotic-resistant infections caused by ABC.

Disclosures. Sarah McLeod, PhD, Entasis Therapeutics (Employee) Samir Moussa, PhD, Entasis Therapeutics (Employee) Alita Miller, PhD, Entasis Therapeutics (Employee)

1255. *In Vitro* Activity of Vancapticin against Methicillin-Resistant *Staphylococcus aureus* from Periprosthetic Joint Infection

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Session: P-58. Novel Agents

Background. The vancapticins are modified vancomycin derivatives developed by adding membrane targeting motifs to the *C*-terminus of vancomycin. We determined the *in vitro* activity of a lead vancapticin candidate against periprosthetic joint infection-associated methicillin-resistant *Staphylococcus aureus* (MRSA) in the planktonic and biofilm states, and the effect of adding 0.002% polysorbate 80 (P-80; Sigma-Aldrich) on vancapticin susceptibility testing.

Methods. Thirty-seven clinical isolates of MRSA collected at Mayo Clinic (Rochester, Minnesota) were studied. Vancapticin minimum inhibitory concentrations (MICs) were determined using Clinical and Laboratory Standards Institutes guidelines. Minimum biofilm bactericidal concentrations (MBBCs) were determined using a pegged lid microtiter plate assay. Vancapticin MIC and MBBC values were assessed with and without P-80. Vancapticin, vancomycin, and dalbavancin biofilm time-kill assays were performed using biofilms formed by 10 MRSA isolates on Teflon coupons.

Results. Vancapticin MICs with and without P-80 ranged from 0.015 to 0.12 μg/mL and 0.25 to 1 μg/mL, respectively. Vancapticin MBBCs with and without P-80 ranged from 0.25 to 4 μg/mL and 1 to 8 μg/mL, respectively. Reductions of biofilm bacterial densities on Teflon coupons after 8 and 24 hours of incubation with vancapticin, vancapticin with P-80, vancomycin, or dalbavancin with P-80 were less than 3-$\log_{10}$ cfu/cm^2 for all isolates tested.

Conclusion. Vancapticin has promising *in vitro* activity against planktonic MRSA and MRSA in a pegged lid biofilm assay, but was not bactericidal against biofilms on Teflon coupons. P-80 decreased vancapticin MICs and MBBCs.

Disclosures. **Mark A. Blaskovich, PhD**, **MAB Consulting** (Consultant)**The University of Queensland** (Employee, Grant/Research Support, Other Financial or Material Support, Inventor on patent) **Robin Patel, MD**, **Accelerate Diagnostics** (Grant/Research Support)**CD Diagnostics** (Grant/Research Support)**Contrafect** (Grant/Research Support)**Curetis** (Consultant)**GenMark Diagnostics** (Consultant)**Heraeus Medical** (Consultant)**Hutchison Biofilm Medical Solutions** (Grant/Research Support)**Merck** (Grant/Research Support)**Next Gen Diagnostics** (Consultant)**PathoQuest** (Consultant)**Qvella** (Consultant)**Samsung** (Other Financial or Material Support, Dr. Patel has a patent on Bordetella pertussis/parapertussis PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued.)**Selux Dx** (Consultant)**Shionogi** (Grant/Research Support)**Specific Technologies** (Consultant)

1256. *In Vivo* Activity and Structural Characterization of a New Generation γ-Lactam Siderophore Antibiotic Against Multidrug-Resistant Gram-Negative Bacteria and *Acinetobacter* spp.

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Session: P-58. Novel Agents

Background. Multidrug-resistant (MDR) *A. baumannii* presents a critical need for innovative antibacterial development. We have identified a new series of γ-lactam (oxopyrazole) antibiotics that target penicillin binding proteins (PBPs) and incorporate a siderophore moiety to facilitate periplasmic uptake. YU253911, an advanced iteration of this class shows potent *in vitro* activity against clinically relevant Gram-negative organisms including *Acinetobacter* spp.

Methods. Minimum inhibitory concentrations (MICs) for YU253911 were determined using broth microdilution against a 198-member panel of clinical isolates of *Acinetobacter* spp. Resistant strains were further evaluated for susceptibility to YU253911 in combination with sulbactam. The antibiotic's target protein was evaluated by binding studies with Bocillin™, a fluorescent penicillin analogue, and modeled in the PBP active site. YU253911 was evaluated *in vivo* in a mouse soft tissue infection model.

Results. MIC testing for YU253911 revealed an MIC_{50} of 0.5 μg/mL and an MIC_{90} of 16 μg/mL, which compared favorably to all tested β-lactam antibiotics including penicillins, cephalosporins, monobactams and carbapenems (MIC_{50} = 2 to > 16 μg/mL). Combination with sulbactam augmented the activity of the agent. There was no apparent correlation between YU253911-resistance and the presence of specific β-lactamase genes, and incubation with representative β-lactamase proteins (KPC-2, OXA-23, OXA-24, PER-2, PDC-3, NDM-1, VIM-2, and IMP-1) showed negligible hydrolysis of the agent. YU253911 showed promising preclinical pharmacokinetics in mice with a 15 h half-life from intravenous administration and demonstrated a dose-dependent reduction in colony forming units from 50 and 100 mg/kg q6h dosing in a mouse thigh infection model using *P. aeruginosa*.

Conclusion. YU253911, a new generation γ-lactam antibiotic effective against MDR *A. baumannii* demonstrated promising in *in vitro* potency and favorable pharmacokinetics which correlated with *in vivo* efficacy.

Disclosures. **Krisztina M. Papp-Wallce, PhD**, **Entasis** (Grant/Research Support)**Merck** (Grant/Research Support)**Venatorx** (Grant/Research Support) **Robert A. Bonomo, MD**, **Entasis, Merck, Venatorx** (Research Grant or Support)

1257. A phase II Prospective Randomized Study to Assess Ceftolozane-Tazobactam in the Management of Febrile Neutropenia in Patients with Hematological Malignancies

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Session: P-58. Novel Agents

Background. Despite the implementation of successful antibiotic stewardship programs, antibiotic resistance continue to emerge particularly against gram-negative bacteria. With the increase use of antibiotics in high risk patients with hematological malignancies, the empiric therapy with standard antibiotic could be inappropriate. New antibiotics may be useful to cover potential resistant pathogens. We evaluated the role of a new cephalosporin /β-lactamase inhibitor ceftolozane-tazobactam (C/T) in comparison to standard of care (SOC) antibiotics in the empiric treatment of febrile neutropenic cancer patients with hematological malignancies.

Methods. We conducted a prospective randomized open label comparative study to evaluate the safety and efficacy of C/T vs SOC antibiotics consisting of cefepime, piperacillin-tazobactam or meropenem when used in combination with gram positive antibacterial agents. Between May 2018 and March 2020, we enrolled 88 febrile neutropenic patients with hematological malignancies who presented to our emergency center. Patients received at least 72 hours of intravenous study drugs and were followed through end of IV therapy and for up to 42 days.

Results. A total of 88 patients were analyzed of whom 42 received C/T and 46 SOC antimicrobial agents. The rate of documented bloodstream infections was similar in both groups (CE-TZ 21% vs SOC 26%, p=0.61). Favorable clinical response at end of IV therapy was significantly better in the C/T arm compared to SOC therapy (88% vs 72%, p=0.039), at test of cure (21 days), and last follow-up (42 days). In patients with documented infections, the rate of microbiological eradication was similar in both groups. Drug-related adverse events that led to drug discontinuation was similar in both groups (7%). Similarly overall mortality was similar in both groups.

Conclusion. The empiric use of C/T to cover gram negative organisms in high risk febrile neutropenic patients with hematological malignancies is safe and associated with better clinical outcome than SOC antimicrobial agents. The emergence of resistant pathogens should be further evaluated.

Disclosures. **Issam I. Raad, MD**, **Citius** (Other Financial or Material Support, Ownership interest)**Cook Medical** (Grant/Research Support)**Inventive Protocol** (Other Financial or Material Support, Ownership interest)**Novel Anti-Infective Technologies** (Shareholder, Other Financial or Material Support, Ownership interest)

1258. Activity of a Series of Investigational Compounds Tested Against Invasive Fungal Isolates

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Session: P-58. Novel Agents

Background. Fox Chase Chemical Diversity Center (FCC) is developing non-peptide analogs of host defense proteins for the treatment of invasive fungal infections mainly caused by *Candida* (CAN) and *Aspergillus* (ASP). We evaluated the activity of 6 novel compounds and 2 comparators against 150 isolates from 15 fungal groups.

Methods. Susceptibility testing was performed per CLSI broth microdilution methods for investigational compounds and comparators against 70 CAN and 40 ASP isolates in addition to 10 *Cryptococcus* spp. (CRYP), 10 *Fusarium* spp. (FUS), 10 Mucorales, and 10 *Scedosporium* spp. (SCED) isolates from recent (2017-2019) clinical infections. MIC results were determined as ≥ 50% reduction at 24 and 72 hours for CAN and CRYP respectively, and 100% reduction at 24, 72, and 48 hours for Mucorales, SCED, and other moulds, respectively. CLSI clinical breakpoint (CBP) and epidemiological cutoff value (ECV) interpretive criteria were applied for comparators.

Results. Compounds FC10790, FC11083, FC11212, and FC11275 had MIC_{50} results at ≤ 0.015 mg/L and MIC_{90} results at ≤ 0.015 to 0.12 mg/L against CRYP, ASP, and FUS isolates. Compounds FC5096 and FC11022 were 2- to 4-fold less active while demonstrating MIC_{50} and MIC_{90} results of 0.03 to 0.5 mg/L against CAN, CRYP, ASP, and FUS isolates. The Mucorales isolate set showed the widest range of MIC results for FC compounds. FC10790 exhibited the greatest potency with a $MIC_{50/90}$ at 0.5/2 mg/L. FC compounds showed potent activity against SCED with MIC_{90} results of 0.03 to 0.25 mg/L. Fluconazole showed a wide range of MIC results, from 0.06 to >64 mg/L, but the highest results observed were for *Candida auris* ($MIC_{50/90}$, 64/ > 64 mg/L) and *Candida krusei* ($MIC_{50/90}$; 16/32 mg/L). Itraconazole was active against all ASP ($MIC_{50/90}$, 1/1 mg/L), but showed poor activity against FUS ($MIC_{50/90}$, > 8/ > 8 mg/L). Amphotericin B showed a narrow range of MIC results (0.5 to 2 mg/L) for all isolates except 1 ASP and most SCED.

Conclusion. Novel FCC compounds showed equal or greater activity than comparators against most CAN, ASP, SCED, and FUS. FC10790, FC11212, and FC11275 showed the greatest activity against all tested fungal isolates. development of this series of compounds for clinical studies.

Table 1

Compound	Organism group $MIC_{50/90}$ (mg/L)					
	Candida spp.	*Cryptococcus* spp.	*Aspergillus* spp.	*Fusarium* spp.	Mucorales	*Scedosporium* spp.
FC 5096	0.06/0.5	0.03/0.03	0.03/0.12	0.03/0.06	1/>8	0.12/0.25
FC 10790	≤0.015/1	≤0.015/≤0.015	≤0.015/0.06	≤0.015/≤0.015	0.5/2	0.03/0.03
FC 11022	0.06/0.25	0.03/0.03	0.06/0.12	0.06/0.06	2/8	0.25/0.25
FC 11083	≤0.015/8	≤0.015/≤0.015	≤0.015/0.12	≤0.015/0.03	>8/>8	0.12/0.12
FC 11212	≤0.015/1	≤0.015/≤0.015	≤0.015/0.06	≤0.015/0.03	2/>8	0.03/0.03
FC 11275	≤0.015/1	≤0.015/≤0.015	≤0.015/0.06	≤0.015/≤0.015	0.25/>8	0.03/0.06
Amphotericin B	1/1	0.5/1	1/2	2/2	1/1	4/>4
Fluconazole	0.25/64	2/4	--/--	--/--	--/--	--/--
Itraconazole	-- / --	-- / --	1/1	>8/>8	2/8	4/4

Disclosures. Paul R. Rhomberg, n/a, Cidara Therapeutics (Research Grant or Support)Fox Chase Chemical Diversity Center (Research Grant or Support)Merck (Research Grant or Support) Shawn A. Messer, PhD, Amplyx Pharmaceuticals (Research Grant or Support)Fox Chase Chemical Diversity Center (Research Grant or Support) Richard W. Scott, PhD, Fox Chase Chemical Diversity Center (Employee) Simon DP Baugh, PhD, Fox Chase Chemical Diversity Center (Employee) Michael A. Pfaller, MD, Amplyx Pharmaceuticals (Research Grant or Support)Basilea Pharmaceutica International, Ltd (Research Grant or Support)Cidara Therapeutics (Research Grant or Support)Cidara Therapeutics (Research Grant or Support) Department of Health and Human Services (Research Grant or Support)Fox Chase Chemical Diversity Center (Research Grant or Support)Paratek Pharma, LLC (Research Grant or Support) Mariana Castanheira, PhD, 1928 Diagnostics (Research Grant or Support)A. Menarini Industrie Farmaceutiche Riunite S.R.L. (Research Grant or Support)Allergan (Research Grant or Support)Allergan (Research Grant or Support)Amplyx Pharmaceuticals (Research Grant or Support)Cidara Therapeutics (Research Grant or Support)Cidara Therapeutics (Research Grant or Support) Cipla Ltd. (Research Grant or Support)Cipla Ltd. (Research Grant or Support)Fox Chase Chemical Diversity Center (Research Grant or Support)GlaxoSmithKline (Research Grant or Support)Melinta Therapeutics, Inc. (Research Grant or Support) Melinta Therapeutics, Inc. (Research Grant or Support)Melinta Therapeutics, Inc. (Research Grant or Support)Merck (Research Grant or Support)Merck (Research Grant or Support)Merck & Co, Inc. (Research Grant or Support)Merck & Co, Inc. (Research Grant or Support)Paratek Pharma, LLC (Research Grant or Support) Pfizer (Research Grant or Support)Qpex Biopharma (Research Grant or Support) Cecilia G. Carvalhaes, MD, PhD, A. Menarini Industrie Farmaceutiche Riunite S.R.L. (Research Grant or Support)Allergan (Research Grant or Support)Cidara Therapeutics (Research Grant or Support)Cipla Ltd. (Research Grant or Support)Fox Chase Chemical Diversity Center (Research Grant or Support)Melinta Therapeutics, Inc. (Research Grant or Support)Merck (Research Grant or Support)Merck (Research Grant or Support)Merck & Co, Inc. (Research Grant or Support)Pfizer (Research Grant or Support)

1259. Activity of eravacycline against staphylococci isolated from periprosthetic joint infections

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Session: P-58. Novel Agents

Background. Perirosthetic joint infections (PJIs) are costly and difficult to treat. The most common causes of PJIs are *Staphylococcus aureus* and *Staphylococcus epidermidis*. Eravacycline is a newer tetracycline with promising activity against Gram-positive and negative bacteria which is approved for treatment of complicated intraabdominal infections. Here, the *in vitro* activity of eravacycline was assessed against bacteria associated with PJI.

Methods. 185 staphylococcal isolates, including 38 methicillin-resistant *S. aureus* (MRSA), 64 methicillin-susceptible *S. aureus* (MSSA), 62 methicillin-resistant *S. epidermidis* (MRSE) and 21 methicillin-susceptible *S. epidermidis* (MSSE) strains were studied. Minimum inhibitory concentrations (MICs) were determined according to Clinical and Laboratory Standards Institute guidelines (range of 0.06-64 µg/ml tested). Results were analyzed using susceptible breakpoints from EUCAST (≤0.25 µg/ml) and the FDA (≤0.06 µg/ml). Minimum biofilm bactericidal concentrations (MBBCs) were determined using a modification of the Calgary biofilm method. Briefly, biofilms were formed on pegged lids in trypticase soy broth, after which the pegged lids were rinsed in phosphate buffered saline (PBS), transferred to a plate containing dilutions of eravacycline in cation-adjusted Mueller Hinton broth (CAMHB) and incubated for 20-24h. Finally, the pegged lids were again rinsed in PBS and transferred to a plate containing CAMHB and incubated for 24h. The MBBC was the lowest concentration with no visible growth.

Results. $MIC_{50/90}$ (range) in µg/ml for MRSA, MSSA, MRSE, and MSSE were 0.125/0.125 (≤0.06-0.25), ≤0.06/0.125 (≤0.06-0.25). 0.125/1 (≤0.06-2), and 0.25/1 (≤0.06-1), respectively. Using the EUCAST susceptible breakpoint, 100% of isolates would be considered susceptible, whereas only 54% would be considered susceptible using the FDA breakpoint. $MBBC_{50/90}$ (range) in µg/ml for MRSA and MSSA were both 8/16 (4-16); for MRSE and MSSE, the values were 4/16 (2-32) and 8/16 (2-32), respectively.

Conclusion. Our data suggest that the FDA susceptible breakpoint may need re-evaluation. Eravacycline has low anti-staphylococcal biofilm activity.

Disclosures. Robin Patel, MD, Accelerate Diagnostics (Grant/Research Support) CD Diagnostics (Grant/Research Support)Contrafect (Grant/Research Support) Curetis (Consultant)GenMark Diagnostics (Consultant)Heraeus Medical (Consultant) Hutchison Biofilm Medical Solutions (Grant/Research Support)Merck (Grant/Research Support)Next Gen Diagnostics (Consultant)PathoQuest (Consultant)Qvella (Consultant)Samsung (Other Financial or Material Support, Dr. Patel has a patent on Bordetella pertussis/parapertussis PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued.)Selux Dx (Consultant)Shionogi (Grant/Research Support)Specific Technologies (Consultant)

1260. Activity of Manogepix (APX001A) against 2,669 Fungal Isolates from the SENTRY Surveillance Program (2018-2019) Stratified by Infection Type

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Session: P-58. Novel Agents

Background. Existing antifungal agents are active against many common fungal pathogens; however, breakthrough fungal infections occur and often involve less frequently encountered yeast and mould isolates. These rarer isolates tend to exhibit diminished susceptibility to current agents. Manogepix (MGX, APX001A) is a novel inhibitor of the fungal Gwt1 enzyme. The prodrug (fosmanogepix), is being evaluated in Phase 2 clinical trials for invasive candidiasis/candidemia, *Candida auris* infections, and invasive aspergillosis. In this study, we evaluated the *in vitro* activity of MGX and comparators against 2,669 clinical fungal isolates collected worldwide (2018-2019) and stratified by infection type.

Methods. Fungal isolates were collected from medical centers located in North America (34 sites; 42.3%), Europe (30 sites; 37.9%), Asia-Pacific (11 sites; 12.3%), and Latin America (7 sites; 7.6%). Isolates were collected from bloodstream infections (BSI; 51.7%), pneumonia in hospitalized patients (PIHP; 21.1%), skin and skin structure infections (SSSI; 5.5%), urinary tract infections (UTI; 2.3%), intraabdominal infections (IAI; 1.9%), and other infection types (17.5%).

Results. MGX demonstrated potent *in vitro* activity against 1,887 *Candida* spp. isolates from BSI, PIHP, SSSI, and all infection types ($MIC_{50/90}$, 0.008/0.03-0.06 mg/L) outperforming all comparator agents (Table). Similarly, MGX was equally active against 578 *Aspergillus* spp. isolates ($MEC_{50/90}$, 0.015/0.03 mg/L), regardless of infection type. MGX was active against *Cryptococcus neoformans* var. *grubii* isolates from BSI and ALL infection types with $MIC_{50/90}$ values of 0.5/2 mg/L. *Scedosporium* spp. isolates from PIHP and all infection types were inhibited by low concentrations of MGX ($MEC_{50/90}$, 0.03/0.03 mg/L).