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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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.

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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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