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 ana-
lysis 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 CLC Bio Genomics Workbench v6.5.

Results. In surveillance of 929 global isolates from 2018, the SUL-DUR MIC was 2 μg/mL compared with 64 μg/mL for SUL alone. This level of potency was consistent across a range of resistance phenotypes. Fifty percent of the isolates were non-susceptible to carbapenems. Only 7 isolates (0.75%), had SUL-DUR MIC values >4 μg/mL. Whole genome sequencing of these 7 isolates revealed that they either encoded the metallo-β-lactamase NDM-1, which does not interact, 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 infec-
tions caused by ABC.

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

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

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Session: P-58. Novel Agents

Background. The vancapticin derivatives 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 methylcin-resistant Staphylococcus aureus (MRSA) in the plank-tonic and biofilm states, and the effect of adding 0.002% polyborate 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 concentra-
tions (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 1 μg/mL and 1 to 8 μg/mL, respectively. Reductions of biofilm bacter-
torial densities on Teflon coupons after 8 and 24 hours of incubation with vancapticin, vancomycin, or dalbavancin with P-80 were less than 3-log cfu/cm² for all isolates tested.

Conclusion. Vancapticin has promising in vitro activity against planktonic MRSA and S. aureus 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) 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, Patent) Dr. Patel has a patent on Bordetella pertussis/parapertussis PCR issued, a patent on a device/method for sonication with royalties paid by Symbioz to Mayo Clinic, and a patent on an anti-biofilm substance issued. Seul Do (Consultant) Shionogi (Grant/Research Support) Specific Technologies (Consultant)

1256. In Vitro 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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Background. Multidrug-resistant (MDR) A. baumannii presents a critical need for novel antibacterial development. We have identified a new series of γ-lactam (oxoacyclopyrazolidinone) antibiotics that target penicillin binding proteins (PBPs) and incor-
porate a sidechain 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 19-member panel of clinical isolates of Acinetobacter spp. Resistant strains were further evaluated for susceptibility to YU253911 in combination with sublicam. The antibiotic’s target protein was evalu-
ated 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 of 0.5 μg/mL and an MIC of 16 μg/mL, which compared favorably to all tested β-lactam antibiotics including penicillins, cephalosporins, monobactams and carbapenems (MIC0 = 2 to >16 μg/mL). Combination with sublicam 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 >15 h half-life and tissue distribution 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 vitro potency and favorable pharmacokinetics which correlate 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 of antibiotics in high risk patients with hematological malignancies, the empirical 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 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 ceftazidime/tazobactam (CUT) in comparison to standard of care (SOC) antibiotics in the empiric treatment of febrile neutropenic patients with hematological malignancies.

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 re-
sponse 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 eradi-
cation was similar in both groups. Drug-related adverse events that led to drug dis-
continuation was similar in both groups (7%). Similarly overall mortality was similar in both groups (1.3%).

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

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