**Session:** P-61. Novel Agents

**Background.** Gram negative (GN) bacterial infections are on the rise in patients with cancer and frequently require extended hospital stays that may lead to a major increase in healthcare cost. This study aimed to evaluate the in vitro activity of a novel oral carbapenem, tebipenem against recent gram-negative clinical isolates from our cancer patients.

**Methods.** All 173 clinical isolates from our cancer patients including 36 Extended Spectrum Beta-Lactamase (ESBL) isolates from blood cultures were tested against tebipenem and other comparators. Clinical and Laboratory Standards Institute (CLSI) approved broth microdilution method was used. Appropriate ATCC controls were included. MICs, MIC₅₀, MIC₉₀ and percent of susceptibility calculations were made using FDA breakpoints available. The tebipenem provisional susceptibility breakpoint for most GN organism is ≤ 0.125 mg/L.

**Results.** Tebipenem and comparators antibiotics susceptibility percent (S; %), and MIC₅₀ are shown in the table below. Tebipenem demonstrated highly potent activity against *Escherichia coli*, *Klebsiella pneumoniae* (including ESBL producing strains), *Enterobacter cloacae* and inhibited 90% of the *Enterobacter aerogenes* strains screened. MIC₉₀ ranged from 0.06-0.25 μg/mL for all tested *Enterobacteriaceae*. At a provisional breakpoints of 0.125 mg/L, the susceptibilities, MICs and ranges were comparable to meropenem, and ertapenem. Comparative study between Tebipenem and comparators for MIC90 (mg/L) and Susceptibility (%) results against Gram-Negative Bacteria Isolated from Patients with Cancer

**Conclusion.** Our data demonstrate that oral tebipenem has promising activity against clinically significant bacterial pathogens isolated from cancer patients, and it has similar activity to that of other tested carbapenem. Further clinical evaluation for oral carbapenem treatment of bacterial infections is warranted.

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

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**1070. In vitro Activity of PLG0206 Against Isolates Commonly Found in Periprosthetic Joint Infections (PJIs)**

David Huang, MD, PhD¹; Jonathan Stockbeck, PhD²; David Huganfel, BS¹; Bev Murray, BS²; David Huganfel, BS²; Chris Pillar, PhD²; Wessam Abdelhady, BS²; Arnold Bayer, MD, PhD²; Bev Murray, BS², Micromyx, Kalamazoo, Michigan

**Session:** P-61. Novel Agents

**Background.** PLG0206 is a novel engineered cationic antimicrobial peptide being evaluated for treatment of prosthetic joint infections. In this study, the activity of PLG0206 was evaluated by broth microdilution against 104 isolates of *Staphylococcus epidermidis*, 53 other coagulase-negative staphylococci (CoNS), 3 *S. aureus*, and 66 Gram-negative isolates consisting of Enterobacterales, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*.

**Methods.** Impenem, levofloxacin, tigecycline, linezolid, vancomycin, oxacillin, cefazidine, colistin, and amikacin were tested as comparators. Testing was conducted in accordance with guidelines from the Clinical and Laboratory Standards Institute (CLSI; M7 and M100). Test organisms consisted of reference strains from the American Type Culture Collection, the Centers for Disease Control Antibiotic Reference Bank and clinical isolates from the Micromyx repository. The media employed for testing in the broth microdilution MIC assay for all organisms were cation-adjusted Mueller Hinton Broth and for PLG0206 only included RPMI 1640 medium supplemented with 0.002% P-80.

**Results.** Activity of PLG0206 in RPMI against CoNS, *S. aureus*, and resistant Gram-negative pathogens are shown in Table. Activity of PLG0206 in RPMI against CoNS, *S. aureus* and resististant Gram-negative pathogens

<table>
<thead>
<tr>
<th>pathogen</th>
<th>MIC₅₀ (μg/mL)</th>
<th>MIC₉₀ (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. epidermidis</em></td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>MRSE (N=46)</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>CoNS (N=58)</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td><em>E. aerogenes</em> (N=59)</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**Conclusion.** PLG0206 was found to have potent antimicrobial activity when evaluated in RPMI against *S. epidermidis*, CoNS non-epidermidis, *S. aureus*, Enterobacterales, *P. aeruginosa*, and *A. baumannii*, including isolates with multi-drug resistance.

**Disclosures.** David Huang, MD, PhD, Peptilogics (Employee) Jonathan Stockbeck, PhD, Peptilogics (Employee) Chris Pillar, PhD, Micromyx (Employee) Bev Murray, BS, Micromyx (Employee) David Huganfel, BS, Micromyx (Employee) Dean Shinabanger, PhD, Micromyx (Employee)

**1071. Efficacy of Anti-Staphylococcal Lysin, LSVT-1701, in Combination with Daptomycin in Experimental Left-Sided Infective Endocarditis (IE) Due to Methicillin-Resistant *Staphylococcus aureus* (MRSA)**

David Huang, MD, PhD¹; Eric Gaulkel, BS¹; Mary Borruto-Enda, PhD²; Yan Xiong, PhD²; Vessam Abdelhady, BS²; Arnold Bayer, MD, PhD²; Lysovant, Houston, Texas; ²The Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center, Torrance, California

**Session:** P-61. Novel Agents

**Background.** Anti-staphylococcal phage lysins, such as LSVT-1701, represent important candidate adjunctive agents against invasive MRSA infections because of both their microbicidal and anti-biofilm properties. We, thus, sought to examine the in vivo efficacy of LSVT-1701 combination with daptomycin, a standard-of-care anti-MRSA agent with proven efficacy against bacteremia and IE in humans.

**Methods.** We utilized the rabbit model of aortic valve infective endocarditis (using the prototype MRSA strain, MW2) to examine the combined efficacy of LSVT-1701 plus daptomycin. We examined microbiologic outcomes in distinct target tissues (cardiac vegetations, spleen and kidney) in this model, as well as the pharmacokinetic importance of both their microbicidal and anti-biofilm properties. We, thus, sought to examine the in vivo efficacy of LSVT-1701 combination with daptomycin, a standard-of-care anti-MRSA agent with proven efficacy against bacteremia and IE in humans.

**Results.** The Table below shows all LSVT-1701 regimens in combination with daptomycin significantly reduced MRSA burdens in all target tissue as compared to untreated controls. The reduction in MRSA counts was statistically significant in instances of both increasing LSVT-1701 dose level (i.e., single doses of 32.5 mg/kg vs 32.5 mg/kg iv), as well as increased numbers of lysin doses (i.e., four daily doses vs a single-dose or two daily-doses) in combination with daptomycin. Of note, both the LSVT-1701 50 mg/kg and 32.5 mg/kg daily dose strategies given for four days in combination with daptomycin sterilized all target tissues (i.e., quantitative cultures ≤ the lower limit of detection of 1 log₁₀ CFU/g, tissue).

**Session:** P-61. Novel Agents

**Background.** Gram-negative isolates, such as *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* have shown increased resistance to existing antibiotic therapies. As such, new therapeutic options are urgently needed. The Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center, Torrance, California

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MRSA bio-burden in blood, vegetables, kidneys and spleen in rabbit IE model

**Conclusion.** LSVT-1701 administered at 32.5 or 50 mg/kg in a 4 d daily regimen in combination with daptoycin resulted in microbiologic sterilization of all target organs in this MRSA IE model. These data support further clinical development of LSVT-1701 for the treatment of MRSA endovascular infections including IE.

**Disclosures.** David Huang, MD, PhD, Lysovant (Consultant) Eric Gaukel, BS, Lysovant (Employee) Katyna Borrotto-Eloda, MD, Lysovant (Consultant) Arnold Bayer, MD, PhD, Lysovant (Grant/Research Support)

1072. In Vitro Antibacterial Susceptibility Testing of Sulopenem Against Category A and B Bio Threat Bacterial Pathogens

Michael Dunne, MD; Steven I. Aronin, MD; Stephanie A. Halasohoris, n/a; Lisa M. Pyrs, BS; Sanee Lembirik, BS; James M. Meinig, PhD; Iterum Therapeutics, Old Saybrook, Connecticut; US Army Medical Research Institute of Infectious Disease, Ft. Detrick, Maryland; US Army Medical Research Institute of Infectious Diseases, Ft. Detrick, Maryland

**Session:** P-61. Novel Agents

**Background.** Sulopenem is a thienopenem β-lactam antibiotic being developed for the treatment of infections caused by multi-drug resistant bacteria. Sulopenem possesses potent activity against species of the Enterobacteriales that encode ESBLs or AmpC-type β-lactamases that confer resistance to third generation cephalosporins. It has also demonstrated good in vitro microbiological activity against a range of bacterial pathogens including penicillin resistant S. pneumoniae, β-lactamase-producing H. influenzae and M. catarrhalis. Sulopenem is available as intravenous and oral pro-drug formulations, and its activity aligns with the most urgent drug-resistant antimicrobial threats defined by the CDC.

**Methods.** Bacterial inoculums were prepared by suspending colonies into cation adjusted Mueller Hinton broth (CAMHB) from 18-24 h (B. anthracis, B. pseudomallei and B. mallei plates incubated at 35°C); or 36-48 h (F. tularensis and Y. pestis plates incubated at 35°C and 28°C, respectively). Sheep blood agar plates were used for B. anthracis and Y. pestis. Chocolate agar plates were used for F. tularensis, B. pseudomallei and B. mallei. Suspended cultures were diluted with CAMHB to achieve a turbidity equivalent to 0.5 McFarland standard. MICs were determined by the microdilution method-in 96-well microplates according to CLSI guidelines (Clinical and Laboratory Standards Institute, 2020). Antibiotic ranges used for sulopenem were 0.03 - 64 μg/mL and 0.004 - 8 μg/mL for the diversity strains of B. mallei, F. tularensis, Y. pestis, B. mallei, and B. pseudomallei, based on a final well volume of 100 μL after inoculation.

**Results.** A summary of sulopenem MIC₅₀ results versus bio-threat bacterial pathogens in presented in the table. Criteria for down selection into mice was met for all pathogens except F. tularensis.

**Conclusion.** Sulopenem is active in vitro against a number of bio-threat pathogens at concentrations likely to be achieved after oral dosing in humans and meets criteria to be tested in the murine model of B. anthracis, Y. pestis, B. mallei, and B. pseudomallei.

**Disclosures.** Michael Dunne, MD, Iterum Therapeutics (Board Member, Consultant, Shareholder) Steven I. Aronin, MD, Iterum Therapeutics (Employee, Shareholder)

1073. Sulbactam-Durabactam Has Potent Activity Against Multidrug-Resistant Acinetobacter baumannii Clinical Isolates From Thai Patients With Chronic Infections

Dhamnna Leshan Wannigama, MD, PhD; Paul G. Higgins, PhD; Cihan Yavuzer, PhD; Shuichi Abe, MD; Parichat Hengsong, MD, PhD; Sirirat Luk-In, PhD; Naris Kueakulpattana, MSc; Mathima Laowanisri, MSc; Chanikan Tanasatitchai, MD; Sukrit Srisakul, MSc; Anthony Kicic, PhD;

**Conclusion.** Sulbactam-Durabactam (SUL-DUR) may be an important new therapeutic option for the treatment of MDR Acinetobacter baumannii chronic infections with accompanying considerable morbidity and mortality, it is imperative to find effective novel treatments. Durabactam (DUR) is a potent broad-spectrum inhibitor of Ambler classes A, C and D serine β-lactamases that effectively restores sulbactam (SUL) activity against MDR A. baumannii isolates. SUL-DUR is currently in late-stage development for the treatment of infections caused by Acinetobacter spp., including drug resistant isolates. In this study, we sought to evaluate potency of SUL-DUR against MDR A. baumannii isolates collected from Thai patients with chronic infections.

**Methods.** Non-duplicate clinical strains were isolated during 2016-2019 from 200 chronically infected patients in different medical wards with a variety of different infections at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Susceptibility testing of SUL-DUR and comparator agents was performed according to CLSI guidelines. SUL-DUR potency was tested on a background of imipenem (IPM) therapy (SUL-IPM titrated at a 1:1 ratio plus DUR fixed at 4 μg/mL). Data analysis was performed using CLSI and EUCAST breakpoint criteria where available.

**Results.** This collection of isolates was 92% sulbactam-resistant (using a breakpoint of 4 μg/mL), 91% carbapenem-resistant, 74% amikacin resistant, and 59% colistin resistant. In contrast, the SUL-DUR MIC₅₀ was 4 μg/mL compared with 64 μg/mL for sulbactam alone. SUL-DUR was equally potent across antibiotic-resistant subsets. Only 6 isolates (3%) had SUL-DUR MIC values >4 μg/mL. Interestingly, addition of imipenem to SUL-DUR showed similar potency as SUL-DUR alone, with an MIC₅₀ of 2 μg/mL.

**Conclusion.** SUL-DUR showed potent in vitro activity against contemporary clinical isolates from a hospital in Bangkok, Thailand. If successfully developed, SUL-DUR may be an important new therapeutic option for the treatment of MDR Acinetobacter baumannii infections.

**Disclosures.** Alita Miller, PhD, Entasis Therapeutics (Employee)

1074. The Relationship Between the Patient's Body Mass Index and Dalbavancin's Efficacy in the Treatment of Invasive Gram-Positive Infections

Adamchick, M.D., Claire Sessa, PharmD, BCPS, BCIDP; Barnaby, PhD; Hongsing, M.D; Miller, M.D.

**Session:** P-61. Novel Agents

**Background.** Dalbavancin is a long-acting lipoglycopeptide antibiotic used in the treatment of invasive gram-positive infections. There is a lack of published research on the effect of obesity on dalbavancin's pharmacokinetics. The primary objective was to determine if obesity correlates to clinical failure at 90 days for patients with gram-positive infections treated with dalbavancin.

**Methods.** This retrospective observational study reviewed the use of dalbavancin from 1/1/2015- 3/31/2021 at 2 community hospitals. Patients were included if ≥ 18 years and received at least one dose of dalbavancin as an inpatient or at an outpatient infusion center. Patients were excluded if inpatient infusion stopped within 90 days or had an infection lasting ≥ 90 days. Covariates included patient demographic information, weight, BMI, pre-dose albumin, and infection source control.

**Results.** A total of 81 patients received dalbavancin with 19 patients excluded for lack of follow up. Patient demographics: mean age (SD) 45.3 (15.8) years, 50% male; CCM 2.6 (3.1). Indications included osteomyelitis n=22, endovascular n=12, diabetic foot/skin soft tissue n=9, septic joint n=8, other n=11. A total of 29 (47%) of patients were intolerant, hospital readmission for same indication, need for additional surgery/debridement, or death. Clinical cure (CC) was defined as not meeting the criteria for failure, hospital readmission for same indication, need for additional surgery/debridement, or death. Clinical cure (CC) was defined as not meeting the criteria for failure, hospital readmission for same indication, need for additional surgery/debridement, or death.

**Conclusion.** CF was compared with weight, BMI, CCM, albumin and source control. CF . Patient demographics, BMI, indication, achievement of source control, Charlson comorbidity index (CCI), and other factors were compared with clinical failure (CF) and clinical cure (CC) using Chi-square tests. A total of 29 (47%) of patients were intolerant, hospital readmission for same indication, need for additional surgery/debridement, or death. Clinical cure (CC) was defined as not meeting the criteria for failure, hospital readmission for same indication, need for additional surgery/debridement, or death. Clinical cure (CC) was defined as not meeting the criteria for failure, hospital readmission for same indication, need for additional surgery/debridement, or death.

**Disclosures.** David Huang, MD, PhD, Lysovant (Consultant) Eric Gaukel, BS, Lysovant (Employee) Katyna Borrotto-Eloda, MD, Lysovant (Consultant) Arnold Bayer, MD, PhD, Lysovant (Grant/Research Support)