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. MIC_{50}, MIC_{90}, MIC ranges and percent of susceptibility calculations ware made using FDA breakpoints when available. The tebipenem provisional susceptibility breakpoint for most GN organism is ≤ 0.125 mg/L.

Results. Tebipenem and comparators antibiotics susceptibility percent (S: %), and MIC_{90} 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. MIC_{90}s ranged from 0.06-0.25 mg/L 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

Isolates	Tebipenem MIC_{90} (S: %)	Cefepime MIC_{90} (S: %)	Meropenem MIC_{90} (S: %)	TMP/SMX MIC_{90} (S: %)	Levofloxacin MIC_{90} (S: %)	Amikacin MIC_{90} (S: %)	Ertapenem MIC_{90} (S: %)
Non-ESBL *Escherichia coli*	0.015 (100%)	2 (90%)	0.015 (100%)	>32/608 (56%)	32 (47%)	4 (100%)	0.06 (100%)
Non-ESBL *Klebsiella pneumonie*	0.015 (100%)	0.125 (100%)	0.03 (100%)	32/608 (86%)	1 (94%)	1 (100%)	0.03 (100%)
ESBL *Escherichia coli*	0.125 (100%)	>32 (44%)	0.125 (100%)	>32/608 (44%)	>32 (22%)	8 (100%)	0.5 (100%)
ESBL *Klebsiella pneumonie*	0.125 (100%)	>32 (5.5%)	0.125 (100%)	>32/608 (5.5%)	16 (22%)	4 (100%)	0.25 (100%)
Proteus mirabilis	0.06 (100%)	0.06 (100%)	0.03 (100%)	0.25/1.2 (90%)	0.5 (100%)	8 (100%)	0.06 (100%)
Enterobacter aerogenes	0.06 (90%)	0.5 (90%)	0.06 (90%)	0.5/2.4 (90%)	0.125 (90%)	4 (90%)	1 (80%)
Enterobacter cloacae	0.125 (100%)	4 (87%)	0.125 (100%)	4/76 (87%)	0.25 (93%)	2 (100%)	1 (80%)
Klebsiella oxytoca	0.06 (100%)	4 (80%)	0.06 (100%)	>32/608 (87%)	16 (80%)	8 (100%)	0.125 (100%)
Achromobacter species	4 (NA)	>32 (NA)	>4 (NA)	8/152 (NA)	16 (NA)	>64 (NA)	>4 (NA)
Acinetobacter species	>4 (NA)	32 (80%)	>4 (80%)	4/76 (80%)	0.5 (90%)	2 (100%)	>4 (NA)

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.

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

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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. Imipenem, levofloxacin, tigecycline, linezolid, vancomycin, oxacillin, ceftazidime, 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 resistant Gram-negative* pathogens

	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)
All *S. epidermidis* (N=104)	0.12	0.12
MSSE (N=46)	0.12	0.12
MRSE (N=58)	0.12	0.12
CoNS non-*epidermidis* (N=53)	0.06	0.06
S. aureus (N=3)	0.12	0.12
Enterobacterales (N=22)	0.5	0.5
P. aeruginosa (N=20)	1	1
A. baumannii (N=24)	0.25	0.25

Abbreviations: MSSE, methicillin-sensitive *Staphylococcus epidermidis;* MRSE, methicillin-resistant *Staphylococcus epidermidis*

*Approximately 90% of the Gram-negative isolates tested were carbapenem-resistant.

Activity of PLG0206 in RPMI against CoNS, S. aureus and resistant Gram-negative* pathogens

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 Steckbeck, 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)

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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 and pharmacodynamic drivers and target attainment values most predictive of treatment outcomes. LSVT-1701 was given at two dose-regimens (32.5 mg/kg and 50 mg/kg) with different dose-durations (single dose vs daily dose for 2 d vs daily dose for 4 d); daptomycin was administered in combination with daptomycin at a sub-lethal daily dose of 4 mg/kg for 4 d to maximize potential synergistic interaction outcomes.

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 50 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 $\log_{10}$ CFU/g. tissue).