to first therapeutic trough and mean number of days treated were significantly higher in IVDU versus non-IVDR samples (65.9 vs. 50.2 hours, \(P = 0.044\) and 5.4 vs. 12.3 days, \(P = 0.017\), respectively). There was no detectable difference in rates of AKI and vancomycin failure.

**Conclusion.** Vancomycin use in patients with IVDU resulted in significantly lower steady state troughs compared to patients who were non-IVDU. These patients also had a longer time to first therapeutic trough. Patient populations who are IVDU may require additional consideration as a special population for future development of vancomycin pharmacokinetic models.

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

---

**1097. A Comparison of Area-Under Curve (AUC)-Guided vs Trough-Guided Monitoring of Vancomycin and Its Impact on Nephrotoxicity: A Systematic Review and Meta-analysis**

Ashley Shiyuan Lim, PharmD; Jun Jie Benjamin Seng, MD; Tao Tao Magdeline Ng, PhD; Hui Ting Chng, PhD; Zhe Han, PharmD; KK Women’s & Children’s Hospital, Singapore, Singapore; Ministry of Health Holdings, Singapore, Singapore, Not Applicable, Singapore; National University of Singapore, Singapore, Not Applicable, Singapore

**Session:** P-62. PK/PD Studies

**Background.** Trough levels have been used for Vancomycin (VAN) therapeutic drug monitoring (TDM) historically due to its practicality. A paradigm shift towards the use of area under curve (AUC)-guided dosing TDM has been made due to availability of advanced pharmacokinetics software, variability between trough levels and AUC values and the potential for reducing toxicity. This review aims to evaluate the impact of AUC-guided vs trough-guided vancomycin TDM on nephrotoxicity-related outcomes.

**Methods.** A systematic review was conducted using PubMed, Embase, Web of Science, Cochrane library up till 1st January 2021 and was reported according to the PRISMA checklist. Studies which evaluated AUC-guided or trough-guided VAN TDM and vancomycin-associated nephrotoxicity were included. Random effects models were used to compare differences in nephrotoxicity between trough level or AUC based vancomycin TDM due to expected heterogeneity in study designs.

**Results.** Of 1191 records retrieved, 57 studies were included. Majority of studies included adult and elderly patients (n=47, 82.5%). The pooled prevalence of nephrotoxicity was lower using the AUC-guided TDM (6.2%, 95% confidence interval (CI): 2.9 – 9.5%) compared to trough-guided TDM (17.0%, 95% CI: 14.7 – 19.2%). The risk of nephrotoxicity was lower with the AUC-guided approach as compared with the trough-guided approach (OR: 0.53, 95% CI: 0.32–0.89). AUC thresholds correlated with risk of nephrotoxicity only for the first 96 hours of therapy. A frequency analysis of significant multivariable factors showed that concomitant use of nephrotoxins, VAN trough levels and duration of VAN therapy were most commonly associated with nephrotoxicity.

**Conclusion.** Vancomycin use in patients with IVDU resulted in significantly lower steady state troughs compared to patients who were non-IVDU. These patients also had a longer time to first therapeutic trough. Patient populations who are IVDU may require additional consideration as a special population for future development of vancomycin pharmacokinetic models.
Pooled nephrotoxicity rates from trough-guided monitoring

Conclusion. The AUC-guided approach appeared to have lower risk of nephrotoxicity which supports the updated American Society of Health-System Pharmacists recommendations. More studies should be performed to evaluate the optimal derivation of AUC and clinical utility of repeated measurements of vancomycin AUC and trough levels.

Disclosures. All authors: No reported disclosures

1098. A Phase 1 Safety and Tolerability of Single Ascending Doses of a Novel Engineered Cationic Peptide, PLG0206, in Healthy Subjects

David Hwang, MD, PhD;2 Despina Dobbins, BS;3 Parviz Ghahramani, PhD, PharmD, MSc, MBA;1 Jonathan Stockbeck, PhD;1 Peptilogics, Houston, Texas;3 Innceleres, Jersey City, New Jersey

Session: P-62. PK/PD Studies

Background. PLG0206 is a novel engineered cationic antimicrobial peptide being evaluated for treatment of prosthetic joint infections (PJIs). This abstract presents the results from the first in human study to evaluate the safety, tolerability and pharmacokinetic (PK) profile of PLG0206 when administered as an intravenous (IV) infusion.

Methods. 6 cohorts of 8 participants were planned to receive escalating single 1-hour IV infusions of PLG0206 at 0.05, 0.125, 0.25, 0.5, 1, 2, and 3 mg/kg dose or placebo. Participants were randomized to receive either PLG0206 (6 per cohort) or placebo (2 per cohort). At each dose level, there were 2 sentinel participants (1 active, 1 placebo) who were dosed at least 48 hours in advance of the other participants in their group. Serial pharmacokinetic samples were taken prior to infusion and up to 48 post infusion. Safety and tolerability was assessed throughout the study. There was at least a 7-day period after dosing at each of the dose levels before dose escalation.

Results. PLG0206 was safe and well tolerated when administered to healthy volunteers across doses ranging from 0.05 to 1 mg/kg. Therapeutic exposures were achieved at 1 mg/kg. The 2 and 3 mg/kg cohorts were not studied. The incidence of treatment emergent adverse events related to study drug administration was low and most events mild (Grade 1) in severity and was similar between the PLG0206 treatment and placebo groups. There were no SAEs, life-threatening events or deaths throughout the study. IV PLG0206 exhibited linear PK over the dose range of 0.05 to 1 mg/kg. The median terminal half-life (t1/2) ranged from 7.37 to 19.97 hours. AUC0-∞ increased with increasing PLG0206 dose ranging between 1581.41 and 21141.52 ng/mL/hr. Cmax ranged between 256 and 2633 ng/mL. The mean apparent volume of distribution (Vz) increased between 25.49 and 94.2 L, mean clearance (CL) were similar across all and ranged from 2.42 to 4.18 L/hour.

Conclusion. Following single IV infusion to healthy volunteers, PLG0206 was safe and well tolerated across doses ranging from 0.05 to 1 mg/kg. IV PLG0206 exhibits linear PK over the dose range. These findings support the ongoing development of IV PLG0206 and will inform dosing regimens in future studies to investigate its utility as an antimicrobial agent.

Disclosures. Despina Dobbins, BS, Peptilogics (Employee) Parviz Ghahramani, PhD, PharmD, MSc, MBA, Peptilogics (Consultant) Jonathan Stockbeck, PhD, Peptilogics (Employee)

1099. Evaluation of the Safety and Pharmacokinetics (PK) following Administration of Single and Multiple Doses of Anti-Staphylococcal Lysin, LSVT-1701, in Healthy Adult Subjects

Mary Beth Wire, PharmD;3 Soo youn Jun, PhD;3 In-Jin Jany, PhD;3 Jun Gi Hwang, PhD;2 David Huang, MD, PhD, Peptilogics (Employee) Despina Dobbins, BS, Peptilogics (Employee) Parviz Ghahramani, PhD, PharmD, MSc, MBA, Peptilogics (Consultant) Jonathan Stockbeck, PhD, Peptilogics (Employee)

Methods. Study ITB-101-1b was a Phase 1, randomized, double-blind, placebo-controlled, multiple ascending dose study. Subjects were randomized 3:1 to active/placebo in each cohort. LSVT-1701 was administered as a 6 mg/kg single dose and twice daily (BID) doses of 1.5, 3.0, and 4.5 mg/kg for 4 days (24h between Doses 1-2, 12h between Doses 2-6). Study drugs were administered as a 1-hour IV infusion. Serial serum samples were collected over 24 hours following the first and last doses for measurement of LSVT-1701 concentrations by a validated ELISA method. PK analysis performed. AEs, and there were no severe AEs, no serious AEs, and no deaths. AEs were of mild (97%) to moderate (3%) intensity and were reported by all subjects in the LSVT-1701 6 mg/kg single dose group and 1-3 (17-50%) of subjects receiving 1.5 to 4.5 mg/kg BID or placebo. The most common AEs of headache, chills, rigors, and fever generally lasted for ≤2 days with or without acetaminophen treatment, and no clinically significant changes in blood pressure, heart rate, ECG, or clinical labs (other than transient increases in CRP) were observed. Infusion site reactions (erythema, pain, induration, warmth) were observed with BID administration of LSVT-1701, but not with the single 6 mg/kg dose or placebo. LSVT-1701 exposure increased greater than in proportion to dose and t1/2 was concentration-dependent, increasing with higher doses. No accumulation in LSVT-1701 exposure was observed.

Summary of LSVT-1701 PK Parameters

**LVST-1701 Dose (mg/kg)**

| Day | ACCx (μg/mL) | Cmax (μg/mL) | t1/2 (h) |
|-----|-------------|-------------|---------|
| BID | 0.125 single (mg/kg) | 5.0 (1.35) | 4.9 (1.48) | 0.67 (0.21) |
| 0.3 single (mg/kg) | 7.0 (1.35) | 10.9 (1.48) | 0.67 (0.21) |
| 0.4 single (mg/kg) | 11.1 (1.35) | 13.1 (1.48) | 0.67 (0.21) |
| 0.6 single (mg/kg) | 20.6 (1.07) | 21.0 (1.93) | 0.67 (0.21) |
| 1.0 single (mg/kg) | 12.3 (0.67) | 19.0 (6.68) | 0.67 (0.21) |
| 1.5 single (mg/kg) | 5.0 (1.35) | 10.9 (1.48) | 0.67 (0.21) |
| 2.0 single (mg/kg) | 5.0 (1.35) | 10.9 (1.48) | 0.67 (0.21) |
| 3.0 single (mg/kg) | 5.0 (1.35) | 10.9 (1.48) | 0.67 (0.21) |
| 4.0 single (mg/kg) | 5.0 (1.35) | 10.9 (1.48) | 0.67 (0.21) |
| 4.5 single (mg/kg) | 5.0 (1.35) | 10.9 (1.48) | 0.67 (0.21) |
| 6.0 single (mg/kg) | 5.0 (1.35) | 10.9 (1.48) | 0.67 (0.21) |

**Summary of LSVT-1701 PK Parameters**

Conclusion. The safety and PK profile of LSVT-1701 is favorable for evaluation in patients with S. aureus infections, including bacteremia and infective endocarditis, for which new treatments are needed.

Disclosures. Mary Beth Wire, PharmD, Lysovant (Consultant) Soo youn Jun, PhD, iNtRON Biotechnology (Consultant) In-Jin Jany, PhD, iNtRON (Consultant) Jun Gi Hwang, PhD, Lysovant (Consultant) David Huang, MD, PhD, Lysovant (Consultant)

1100. A Prospective Evaluation of Neurotoxicity Among Patients Receiving Dose-Optimized Cefepime or Meropenem With Concomitant Therapeutic Drug Monitoring

Kathleen Smith, MD, PharmD;1 Ellen G. Kline, MS;1 Lori Shutter, MD, FNCx, FCCM;1 Joanne Fong-Iasarrivongwe, MD;2 Alexandre Urbán, MD;2 Holt Murray, MD;2 Karin Byers, MD, MS;2 Ryan K. Shields, PharmD, MS;2 1University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; 2University of Pittsburgh, School of Medicine, Pittsburgh, PA; 3University of Pittsburgh, Pittsburgh, Pennsylvania

Session: P-62. PK/PD Studies

Background. Cefepime (FEPI) induced neurotoxicity (NT) may have serious implications for patients (pts). Retrospective studies have employed variable definitions of NT, finding renal impairment and FEP trough concentrations (Cmin) > 20 mg/L as risk factors. Prospective studies comparing antibiotics have not been performed.

Methods. We conducted a prospective study of pts receiving FEP or meropenem (MEM) with neurologic evaluation and therapeutic drug monitoring (TDM). A NT advisory board (NTAB) was established to develop standardized definitions of possible, probable and definitive NT (Fig 1). Cases of potential NT were adjudicated by the NTAB who were blinded to study treatment. FEP and MEM midpoint and Cmin concentrations were measured at steady-state by validated methods.

Results. 127 patients were included (70 FEP, 57 MEM). Demographics and treatment characteristics were similar between groups (Fig 2); 63% were in the ICU. FEP and MEM Cmin varied from 1.9 – 140.5 and 0.6 – 31.3 mg/L, respectively. Median FEP Cmin and total exposures (AUC) were 23.1 mg/L and 347.6 hr*mg/L, respectively. Corresponding MEM values were 5.9 mg/L and 124.3 hr*mg/L, respectively. Cmin values were inversely correlated with renal function for both FEP and MEM (P < 0.001). Rates of possible, probable, or definitive NT were 10% and 5% for FEP and MEM, respectively (P=0.51; Fig 3). 16% and 3% of pts with FEP Cmin > 20 mg/L had NT, respectively (P=0.11; Fig 4). Median MEM Cmin were 12.3 and 3.4 mg/L among pts with and without NT, respectively (P=0.09; Fig 4). Pts of both groups did not vary by infusion length or by dose, and FEP and MEM exposures were similar between patients with (17%) or without (83%) microbiologic recurrence due to the same pathogen. FEP was discontinued in 4 pts due to NT; no pts stopped MEM due to NT.