In critically-ill patients with confirmed ARC.

**Methods.** Infected patients in the intensive care unit with CrCl ≥130 mL/min received a single dose of I/R 1.25g as a 30min infusion. Blood samples were collected over 6 hours (hr) for IML and REL concentration determination by a validated LC/MS/MS assay. Protein binding was assessed at 0.5hr by ultrafiltration (UF). An 8hr urine creatinine (UCr) collection was performed to confirm ARC. IML and REL plasma concentrations were fitted to compartmental models in WinNonlin. Simulated concentration vs time profiles were used to assess attainment of pharmacodynamic (PD) targets for IML (30%+T >MIC) and REL (T/AUC/MIC) 18 at the susceptibility breakpoint of 2 mg/L.

**Results.** Five patients (60% female) completed the study. Mean (SD) age, weight, and APACHE II were 43 (14) years, 90 (15) kg, and 16 (6), respectively. All patients had confirmed ARC with CrCl of 160.6 ± 47.0 mL/min (range: 135-244mL/min) based on UCr. IML and REL concentrations fitted a 2-compartment better than 1-compartment model. IML PK was: clearance, 17.9 ± 8.7 L/hr; volume of central compartment, 15.6 ± 11.2 L; volume of peripheral compartment, 10.6 ± 5.4 L; and intercompartmental clearance, 16.6 ± 14.5 L/hr. REL PK parameters were 11.9 ± 7.5 L/hr; 17.0 ± 11.3 L; 13.5 ± 9.4 L; and 13.4 ± 11.1 L/hr respectively. Half-life was 1.5 ± 0.5 for IML and 2.8 ± 2.2 hr for REL. Protein binding for IML ranged from 0-10%, while REL was 0-14%. IML T >MIC ranged from 40-90%, and REL T/AUC/MIC ranged from 22.6-59.0.

**Conclusion.** These are the first data to describe IML and REL PK in critically-ill infected patients with ARC. Despite plasma clearance values greater than those reported in healthy volunteers and patients in clinical trials, I/R 1.25g as a 30 minute infusion provided optimal exposure in all patients for isolates with MICs ≤2 mg/L.

**Disclosures.** Donald P. Nicolau, PharmD, Abbvie, Cepheid, Merck, Paratek, Pfizer, Takeda, Shiongyi, Tetraphase (Other Financial or Material Support). I have been a consultant, speakers bureau member, or have received research funding from the above listed companies.

**Abstracts • OFID 2021:8 (Suppl 1) • 5635**
Background. ADG20 is a fully human IgG1 monoclonal antibody engineered to have potent, broad neutralization against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other SARS-like CoVs with pandemic potential as well as an extended-half-life. ADG20 is administered intramuscularly (IM). A QSP/PBPK model was constructed to support dose selection for a COVID-19 Phase 2/3 prevention trial (EVADE: NCT04859517).

Methods. A QSP/PBPK model and a CDC reference adult body weight distribution (45–150 kg) were used to simulate 1000 concentration-time profiles for candidate single-dose regimens of ADG20 (150–450 mg IM). As serum virus neutralizing antibody (sVNA) titers are reportedly a key correlate of protection from COVID-19, a regression equation between time-matched serum ADG20 concentrations (following a 300 mg IM dose) and sVNA titers was developed using measured titers against authentic SARS-CoV-2 determined by a plaque reduction neutralization assay. Projected ADG20 serum concentrations relative to neutralization potency in vitro (90% inhibitory concentration [IC90]) for authentic SARS-CoV-2 were also evaluated.

Results. The measured 50% neutralization titer (MN50; geometric mean [coefficient of variation, %]) was 1382 (32.7%) 13 days after a single 300 mg IM dose of ADG20. This was within the range of peak AVNA titers reported for COVID-19 vaccine recipients. Using the linear equation relating serum ADG20 concentration to time matched individual MN50 titers and the QSP/PBPK median PK prediction, the anticipated median MN50 exceeded the threshold for protection from SARS-CoV-2 infection established in a non-human primate adoptive transfer model for up to 52 weeks. Based on the QSP/PBPK median PK prediction, median ADG20 serum concentrations are projected to remain >10-fold above the ADG20 IC90 value of 0.011 mg/L against authentic SARS-CoV-2 for up to 52 weeks (Figure).

Conclusion. Following administration of a single 300 mg IM dose, sVNA titers and concentrations of ADG20 are projected to remain above thresholds anticipated to be required for protection against COVID-19 for up to 52 weeks. These data support the evaluation of a single ADG20 300 mg IM dose for the prevention of COVID-19.

Figure. QSP/PBPK model forecast of ADG20 300 mg IM in adults.

Predicted median serum ADG20 concentration is shown with the dotted line representing 100× in vitro IC90 of 0.011 mg/L or 1.1 mg/L; the solid black line represents the simulated median; the shaded area represents the 90% prediction interval. The projected median half-life of ADG20 300 mg IM exceeded 74 days. PBPK model inputs include Ln-normal Kd,FcRn of 9.55 nM (10% IIV); IM bioavailability of 100%; 15% IIV on muscle lymph RC; and Centers for Disease Control and Prevention weight inputs including first order pharmacokinetic (foPK) equations and Bayesian models. Most AUCs calculated by the three methods did not differ on average, but dosing recommendations for foPK at the patient level varied substantially compared to the Bayesian method. This difference is because Bayesian estimation incorporates actual patient exposures while foPK equations rely on idealized dose timing to predict AUCs.

Disclosures. Kimberly C. Claeyis, PharmD, GenMark (Speaker's Bureau) Marc H. Scheetz, PharmD, MSc, Nevakar (Grant/Research Support) SuperTrans Medical (Consultant/US Patent 10688195B2 (Other Financial or Material Support, Patent holder))

1091. Validation of an Allometrically Scaled Body Weight Equation to Predict Vancomycin Clearance and Guide 24-Hour Vancomycin AUC Dosing in Obese Patients

Brent Footer, PharmD, BCPs; Arthur Nguyen, PharmD; Meagan Greckel, PharmD; Colton Taylor, PharmD; Alyssa Christensen, PharmD, BCIDP; Gregory Tallman, PharmD, BCIDP; Greg Michalski, PharmD; Providence Portland Medical Center, Portland, Oregon; Providence Saint Vincent Medical Center, Portland, Oregon; School of Pharmacy, Pacific University, Portland, Oregon

Session: P-62. PK/PD Studies

Background. Accurately determining empiric vancomycin (VAN) doses in obese patients represents a clinical challenge. A recent population pharmacokinetic (PK) study provided an equation to estimate vancomycin clearance (CL) based on age, sex, serum creatinine (Scr), and allometrically scaled body weight. The purpose of this study was to validate this equation in a population of obese adults treated with vancomycin at eight community-based hospitals and use the CL estimate to guide empiric VAN dosing.

Methods. The study period was November 1, 2020 and March 30, 2021. Patients were included if they were ≥18-year-old with a body mass index (BMI) ≥30 kg/m², had an empiric dose targeting an AUC24 determined using the above referenced equation, and had a calculated AUC24. Only the first vancomycin course and AUC calculation for each patient were included. Patients with a creatinine clearance <30mL/min and pregnant women were excluded. AUC24 and other PK parameters were calculated using two levels and noncompartmental analysis. Observed versus predicted CL and AUC24 were plotted to determine correlation.

Results. Sixty patients were included, of which 60% were male and 33% had a confirmed methicillin-resistant Staphylococcus aureus infection. The mean age, BMI, and baseline Scr were 61.8 years, 37.8 kg/m², and 0.99 mg/dL, respectively. Fifty-three