including vancomycin intermediate susceptible Staphylococcus aureus (VISA) and daptomycin non-susceptible strains (DNS). Lipoglycopeptides, notably dalbavancin (DAL), have been employed due to their ease of administration and enhanced activity against inherently resistant S. aureus. As previously demonstrated, the use of β-lactams, specifically ceftazidin (CFZ) in combination with anti-MRSA drug therapy has been effective in eradicating S. aureus complicated by increased resistance. The objective of this study was to evaluate the activity of DAL, VAN, and DAP, alone and in combination with CFZ in a pharmacokinetic/pharmacodynamic (PK/PD) model.

Methods. The well-characterized Denny VISA strain, D712, was evaluated in eight different regimens in duplicate via a one-compartment 7-day PK/PD model. The experimental regimens were as follows: D712 growth control, DAL 1500 mg given on day 1, VAN 2 g given every 12 hours, DAP 10 mg/kg once-daily, CFZ 2 g given every 8 hours and DAL, DAP, and VAN in combination with CFZ.

Results. The combination of DAL + CFZ, or VAN + CFZ, or DAP + CFZ demonstrated a significant log₂ CFU/mL reduction (more than 5 log₂ CFU/mL and up to detection limit), compared with each drug used as monotherapy (P < 0.001). Neither DAP nor VAN demonstrated sustained bactericidal activity (represented by a >3-log₃ CFU/mL reduction from baseline) and resulted in significant regrowth when admixed alone. However, the DAP + CFZ, and VAN + CFZ combination models demonstrated bactericidal activity at 4 hours and 24 hours, respectively. While DAL alone did not demonstrate bactericidal activity, the DAL + CFZ combination was more rapidly bactericidal, achieving a >3-log reduction from baseline in 8 hours vs. 48 hours (P < 0.05).

Conclusion. The combination of DAL, VAN, or DAP with CFZ demonstrated significantly improved activity against this multiple drug-resistant S. aureus strain. Further research is warranted, both in vivo and in vitro, to explore the synergistic capabilities of anti-MRSA drug therapy in combination with beta-lactams.

Disclosures. All authors: No reported disclosures.

1540. A Population Pharmacokinetic Model for Vancomycin in Korean Patients Receiving Extracorporeal Membrane Oxygenation Therapy: A Prospective Study Younghee Jung, MD; Dong-Hwan Lee, PhD; Hyoung Soo Kim, PhD; Hallym University Sacred Heart Hospital, Anyang-si, Kyonggi-do, Republic of Korea

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Background. There is no literature on population pharmacokinetics (PK) of vancomycin in Korean patients receiving extracorporeal membrane oxygenation (ECMO) therapy. The aim of this study was to develop a population PK model for vancomycin in Korean ECMO patients.

Methods. We prospectively enrolled adult patients who were undergoing ECMO and receiving vancomycin from July 2018 to April 2019. After initial dose of vancomycin was administered, serial blood samples (seven to nine times per patient) were drawn before the next dose. A population PK model for vancomycin was developed using a nonlinear mixed-effect modeling. Age, sex, creatinine clearance, and body weight were tested as potential covariates in the model. Model selection was based on log-likelihood test, model diagnostic plots, and clinical plausibility.

Results. Fourteen patients were included over the period. Ten received venovenous, three venoarterial, and one both type ECMO. Eleven were men and the median age was 54 (interquartile range 45–66.3). Mean estimated glomerular filtration rate (eGFR) was 69 ± 46 mL/minute/1.73m² by the modification of diet in renal disease equation. A total of 123 vancomycin concentrations from the patients were included in the analysis. The population PK of vancomycin was best described by a two-compartment model with a proportional residual error model. The typical value (% between-subject variability) for total clearance was estimated to be 3.43 L/h (21.6%), central volume of distribution was 9.22 L, the intercompartmental clearance was 10.75 L/h (49.9%), and the peripheral volume of distribution was 19.6 L (26.6%). The proportional residual variability was 8.81%. Creatinine clearance significantly influenced vancomycin clearance (CL). The proposed equation to estimate vancomycin clearance in Korean ECMO patients was CL = 4.33 × 0.199 × (eGFR – 56).

Conclusion. A two-compartment population PK model successfully describes vancomycin PK profiles in Korean ECMO patients. The model could be used to optimize the dosing regimen if more data become available from currently ongoing clinical study.

Disclosures. All authors: No reported disclosures.