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ePoster Viewing
PK/PD to improve treatment of critically ill patients

COMPARATIVE EVALUATION OF THE ACCURACY AND PRECISION OF PHARMACOKINETIC EQUATIONS TO PREDICT FREE MEROPENEM CONCENTRATIONS IN CRITICALLY ILL PATIENTS

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Objectives: Population pharmacokinetic analyses that quantify the effect of demographic, pathophysiological, and other drug-related factors on pharmacokinetic behavior are valuable for accurately predicting individualized and optimized doses for patients. The aim of this study was to establish the agreement between observed and population pharmacokinetic equations based predictions of concentrations to rank the predictive performance of available pharmacokinetic models.

Methods: Unbound meropenem concentrations were measured in critically ill patients as part of a clinical therapeutic drug monitoring (TDM) program. Published one and two compartment population models with covariate relationships were coded in the R language into Individually Designed Optimum Dosing Strategies – Scientific (ID-ODS - S®) and were used to predict meropenem concentrations. Difference plots were produced to visually evaluate the agreement between the observed and predicted concentrations. Absolute and relative bias and precision of the models as predictors of observed concentrations were determined. The clinical implications of the different results were evaluated according to whether the predicted concentration would have required dose adjustment for a target of 100% f T>MIC (chosen MIC = 2 mg/L).

Results: 157 free meropenem concentrations from 56 patients were available for analysis. Eight published pharmacokinetic models were evaluated using percentage difference plots. The models studied showed an absolute bias in predicting serum concentrations that ranged from a mean (95%CI) % difference of -108.6 (-119.91, -97.30) % to19.86 (7.26, 32.47) %, while absolute precision ranged from-249.13 (-263.42, -234.84) % to 31.91 (17.62, 46.21) % and -178.93 (-196.93, -160.93) to 175.04 (157.04, 193.04). A dose change prompted by individuals was required in 44% to 64% of the concentrations. When compared to an absolute standard, the one compartment model by Muro et al. developed in Japanese patients was found to be the least biased and most precise at predicting free meropenem concentrations.

Conclusion: Seven of the eight equations evaluated here are likely to under-predict free meropenem concentrations coupled with variable magnitudes of precision that prompted similar dosing decisions using four of the targeted models. When compared to the absolute standard, the model by Muro et al. ranked the highest at accurately and precisely predicting free meropenem concentrations. The calculated results of this dosing approach also led to similar choices of dose adjustments most often as compared to the results based on the observed concentrations. The best performed model thus may be adapted into a TDM program focusing on the optimal dosing of meropenem.