Bayesian Estimation of Vancomycin AUC_{0-24} in an Adult Population with Hematologic Cancer: What Would Be the Best Sampling Strategy?

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Background In accordance with the latest IDSA consensus on the therapeutic target of vancomycin, it is recommended to use the Bayesian approach to determine the area under the curve (AUC_{0-24}) [1]. Using a pharmacokinetic model developed through a population-based approach in a population of adults with hematologic cancer, estimating AUC_{0-24} would be feasible with samples collected during therapeutic monitoring [2]. The consensus recommends the use of post-dose concentration (C_{peak}) with pre-dose concentration (C_{trough}) for estimating AUC_{0-24}. However, other sampling strategies might be simpler and better suited for clinical practice. Therefore, the objective was to determine the best sampling time(s) to estimate AUC_{0-24} using the Bayesian approach.

Methods A virtual population (n=7000) was simulated based on the distribution of the significant covariates (ideal body weight and estimated glomerular filtration rate) from the population used to develop the previous pharmacokinetic model [2]. The dosing regimens from the Le Blanc et al. nomogram were used to generate, with NONMEM® (v.7.5), simulated PK profiles of one loading dose followed by three maintenance doses (steady-state). Three sampling strategies were explored: C_{peak} (1-hour post-dose) and C_{trough} (predose); C_{trough} only; and one single sampling taken at each hour between two dosing intervals. For each of these profiles, PK parameters were predicted and compared using the Bayesian approach. Simulated and predicted AUC_{0-24} at steady-state were calculated with Dose/clearance (CL) using R (v4.0.4).

Results Estimating AUC_{0-24} with the Bayesian approach in an adult population with hematologic cancer yields comparable results when using one or two samples compared to the full profile (R^2 = 0.88 vs. 0.85). C_{trough} remains the best single sampling time (R^2=0.85). However, collecting a sample at any time from 4 hours post-dose onwards would provide an estimation of AUC_{0-24} comparable in precision to that obtained from a sampling of C_{trough} only, regardless of renal function (R^2≈0.73-0.77).

Conclusion The use of the Bayesian model provides more flexibility in sampling practices during therapeutic monitoring. Comparing the model's performance on initial doses versus steady-state doses remains to be confirmed. Ultimately, utilization and clinical evaluation would confirm the results obtained with our virtual population.

Key words (up to 6): Vancomycin, Hematologic Cancer, Bayesian approach, Therapeutic Drug Monitoring, Sampling Strategy

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