**Last-mile delivery: a reference plot to help non-pharmacometricians interpret population pharmacokinetics results**

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**BACKGROUND:** Although pharmacometricians have put great efforts into transitioning the modeling results via simulations to facilitate the appropriate dosing, there is still a knowledge gap for frontline practitioners to understand the raw results from population pharmacokinetics (PopPK) analysis and subsequently make a meaningful interpretation to guide clinical practice. A practical tool is warranted to fill up the gap, facilitating the last-mile delivery of modeling results to clinicians and clinical pharmacologists (especially those without pharmacometrics background).

**OBJECTIVES:** The overarching aim of this study was **(i)** to develop an interactive contour plot that links between-subject variability, therapeutic range, and probability of target attainment (PTA); **(ii)** to demonstrate the utility of the contour plot with four different motivating cases (i.e., flat dosing, covariate-based dosing, therapeutic drug monitoring (TDM), and handling inter-occasion variability (IOV) ).

**METHODS:** For the drugs with steady-state average plasma concentrations or area under the curve (AUC) as the therapeutic target, the in-theory best performance of the *a priori* covariate-based dosing regimen was derived given the information of unexplained between-subject variability from the PopPK analysis**.** A web-based interactive reference plot was implemented using the Shiny package in R.

**RESULTS:** With an equation derived for the maximum PTA, the interactive contour plot was subsequently implemented in a web-based interface.The tool we developed helps answer the questions about the choice of dosing strategy in clinical practice. Here, we demonstrated the utilities by having one practical case for each question(shown in **Figure 1**): **(i)** Is the one-dose-fits-all strategy suitable for pembrolizumab? **(ii)** How much can the *PTA* be bimproved at most if we use covariate-based dosing instead of one-dose-fits-all for mycophenomic acid? **(iii)** When do we need TDM for vancomycin? **(iv)** What is the impact of IOV for valganciclovir?

**CONCLUSION:** An interactive reference plot was developed to serve as a practical kit to assist non-pharmacometricians in better interpreting the result of PopPK analysis by establishing a performance window. In doing so, this “last-mile delivery” service not only provides an approachable tool for educational purposes but enhances the impact of model-based precision dosing strategy on decision-making in clinical practice.

**Figure 1** Reference plottings for demonstrated drugs. Solid triangles stand for final models or the model with IOV considered. Open triangles represent base models. Solid square presents the model without IOV considered.

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