A first application of population pharmacokinetics in feline therapeutics
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Objectives: In veterinary medicine, characterization of the pharmacokinetics is usually performed using a 2 stage approach, thereby limiting most of the analyses to rich datasets. This research aimed to model the PK of the NSAID robenacoxib using a NLME approach thereby leveraging all available information collected from various sparse and rich data sources with different dosing routes. Another objective was to demonstrate that using multiple samples from the posterior distribution of the random effects instead of just the mode leads to robust estimates of correlations between population parameters.

Methods: Data from 83 cats were pooled from 7 preclinical and 1 field robenacoxib PK studies. Cats received robenacoxib subcutaneously and/or intravenously. Data from both routes were modeled simultaneously using NLME in Monolix 4.3.2. The influence of parameter correlations and available covariates on population parameter estimates were evaluated by using the mode vs. multiple samples from the posterior distribution of the random effects.

Results: A two-compartment mammillary model with first-order absorption and elimination best described the PK of robenacoxib in blood. Simultaneous fitting of all dosing routes unveiled the flip-flop kinetics of robenacoxib for which no dosing adjustment seems necessary. Our results further showed that using several samples of the posterior distribution instead of just the mode allows for a more robust estimate of correlations between model parameters.

Conclusions: This work constitutes the first population PK analysis in a large scale of cats. Using several samples of the posterior distribution instead of the EBE allows for a robust estimation of the correlation between model parameters. This research illustrates the value of NLME for the reconciliation of diverse pharmacokinetic data in veterinary drug research and development.

References: