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Application of quantitative pharmacology to inform clinical pharmacokinetic trials in the pediatric population

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Quantitative pharmacology brings important advantages to overcome some of the limitations of conducting pediatric clinical trials. As an example, optimal sampling strategies facilitate sparse sampling studies benefiting the design and conduct of pharmacokinetic (PK) trials while minimizing phlebotomy and burden to participating children. Additionally, the scientific community and regulatory agencies globally support the use of model-based approaches to select rationalize doses for pediatric trials. The objective of this work is to demonstrate the application of quantitative pharmacology to optimize pediatric trials using two examples. The first one comprises the application of a model-based approach to select doses and optimize the PK sampling scheme for the clinical evaluation of a novel oral suspension of spironolactone in pediatric patients with edema.

A population PK model was developed and qualified for spironolactone and its metabolite, canrenone, using data from adults and bridged to pediatrics (2-<17 years) using allometric scaling. The model was then used via simulation to explore different dosing and sampling scenarios. The second example aimed the application of a physiologically based absorption model, developed considering the nasal physiology and formulation properties, to support the dose selection of a novel nasal spray for a pediatric trial. The model was firstly developed and verified using data from adults, and then extrapolated to pediatrics (4- <18 years) using different scaling factors to account for differences in the physiology across these populations. Different doses were then simulated using the PBAM model extrapolated to pediatrics to compare systemic epinephrine exposures and select the more appropriate dose in different age groups for the trial.

Biography

Valvanera Vozmediano is Assistant Professor at the Center of Pharmacometrics & System Pharmacology, Department of Pharmaceutics, and University of Florida. She has been working as Principal Consultant with Dynakin's Drug Modeling & Consulting group, and has been the Director of the Research & Development Department of the same company since 2008.

She received her B.S. in Pharmacy from the University of Basque Country in Spain in 2006, and earned her Ph.D. in Pharmacology in 2011 at the same University. Her doctorate research was completed at Dynakin with the design of pioneering regulatory standard pediatric investigational plan (PIP) for a new H1 antihistamine drug applying state of the art modeling & simulation (M&S) techniques. Her research activity includes a postdoctoral internship as Marie Curie (B-MOB program) and authorship of peer-reviewed publications.

She is expert in the application of allometric and semi-mechanistic scaling as well as preclinical MIDD using population PK/PD methods specializing in translational development, mainly for the pediatric field. She has successfully completed several projects in that domain as an industrial consultant in FTIM questions, PIPs, and bridging studies, including support to successful filings for new drug applications. Valvanera is invited professor for the Master in Drug Development of the University of Basque Country, and she was also a tutor in the International Master of Pediatric Clinical Pharmacology from the Global Research in Pediatric Network of Excellence (GRIP).