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MEETING ABSTRACT

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Pharmacometrics – Opportunities in pharmacological research and clinical practice

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Pharmacometrics represents a multi-disciplinary research field that describes and quantifies (patho-)physiological processes in a system (*e.g.* a patient) and its interactions with drugs using mathematical and statistical models. These models are frequently developed to characterise time courses of drug exposure (pharmacokinetics), drug effects (pharmacodynamics) and/or disease progression, and enable conclusions on favourable or unfavourable drug responses. Thereby, data from different sources (***e.g.*** *in vitro* data and clinical data) can be analysed and jointly integrated.

Since its emergence in the 1970s, pharmacometrics has experienced a remarkable growth. Pharmacometrics has revolutionised rational decision-making in pharmaceutical industry across the value chain ('model-informed drug development'), but also in pharmacotherapy and patient care to tailor dosing strategies, improve therapeutic response and prevent toxicity ('model-informed precision dosing'). Apart from that, regulatory agencies like the U.S. Food and Drug Administration and the European Medicines Agency have strongly supported pharmacometric analyses and their inclusion in regulatory submission dossiers and even drug labels.

Nonlinear mixed-effects (NLME) models, often referred to as 'population (pharmacokinetic or pharmacodynamic) models', enable to simultaneously analyse data (***e.g.*** concentration–time profiles) of an entire population, while still not ignoring differences between individuals (***e.g.*** patients). On this basis, the typical representative of the data (*i.e.* the 'typical patient' in the population) can be described, together with different sources of variability (*e.g.* between-patient variability). Importantly, potential causes of this variability, ***e.g.*** patient- or disease-related factors ('covariates') like body weight, renal function or genetic polymorphisms, can be identified, which constitute the basis for dosing individualisation.

Once successfully developed and evaluated, pharmacometric models can be used for simulations to answer 'what-if' questions. For example, study scenarios not covered by the raw data (***e.g.*** new dosing regimens) as well as extrapolations to other study populations (***e.g.*** from preclinical species to humans), can be investigated. Simulations, specifically clinical trial simulations, can also serve to inform the design of future clinical trials in a resource-saving manner or to derive hypotheses for further studies.

This keynote lecture aims to outline the basic concepts of pharmacometrics and diverse applications and opportunities of this research area in preclinical and clinical research. Examples of past accomplishments of pharmacometrics will span different therapeutic areas with a focus on, but not limited to, antibiotic research and continuous data (*i.e.* time courses of observations). Last, an outlook of pharmacometric tools to individualise dosing in clinical practice and its role in therapeutic drug management will be given, together with further promising developments in this rapidly evolving field.

Keywords: pharmacometrics – population pharmacokinetic models – population pharmacokinetic/pharmacodynamic models – PK/PD – modelling and simulation – model-informed precision dosing

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