CHDR
Centre for Human Drug Research

Clinical pharmacokinetics and pharmacometrics

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Over the past decade, our pharmacometricians have provided in-depth pharmacokinetic (PK) and pharmacodynamic (PD) analyses to support critical decisions in the development of a range of drugs. Our team is adept at performing non-compartmental analyses and population PK/PD analyses for all types of clinical studies, at all phases of drug development. Our PK and pharmacometric expertise is especially extensive in the field of early clinical drug development.

CHDR's pharmacometrics team delivers a range of services, including:

- Timely **interim non-compartmental PK analyses** to inform decisions related to dose escalation alongside clinical trials. With direct access to Promasys®, our clinical data management system, and connections with external bioanalytical laboratories, we are able to relate drug concentrations to actual sampling times.

- **Final non-compartmental PK analyses** for all types of clinical trials. We deliver well-structured PK analysis reports on which to base your clinical study report.

- **Concentration-QTc analyses** to characterise the relationship between QTc interval and exposure, drawing on Holter ECG data. Insight into this relationship contributes to the understanding of the QT effect of novel compounds. Our analyses are reported according to regulatory requirements, and can form part of a TQT study waiver request.

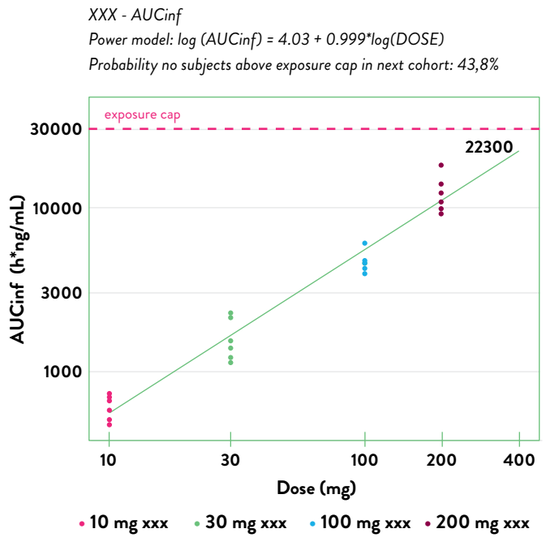

Figure 1: depicts the prediction of exposure (AUCinf) for a next cohort, based on non-compartmental analysis. The exposure can be assessed against a predefined exposure cap.

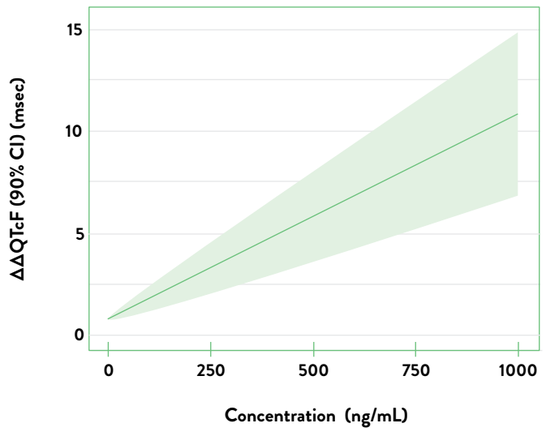

Figure 2: illustrates how a concentration-QTc model predicts placebo-corrected change from baseline in QTcF. To allow a TQT study waiver, the upper limit of the 90% confidence interval should not exceed 10 msec at the highest clinically relevant exposure.

- **Population PK/PD analyses and clinical trial simulations** to characterise the PK and the exposure-efficacy and/or exposure-safety relationship, as well as supporting future clinical trials.

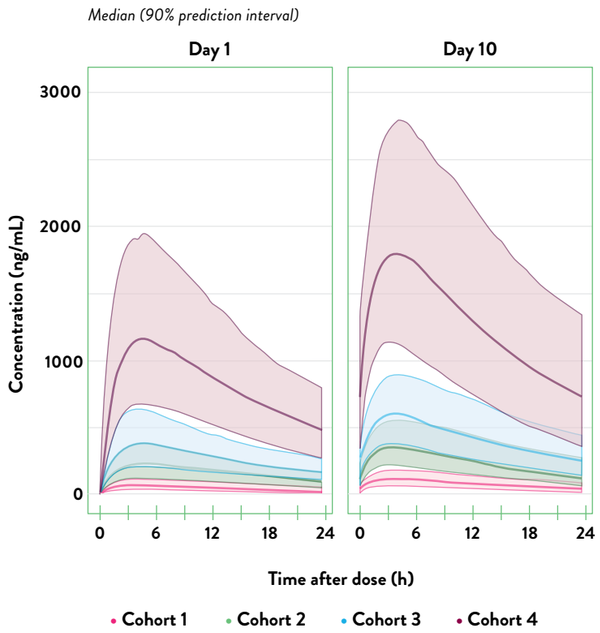

Figure 3: shows how concentration-time profiles following single and multiple dosing may be simulated.

Exposure-response characterisation is an integral component of studies performed at CHDR. Using predictive PK/PD modelling and simulation at all stages of drug development, we aim to:

- support study design and dose selection for (first-in-human) clinical studies, drawing on pre-clinical or published data of existing compounds where appropriate
- gain an understanding of variability in exposure and treatment response
- establish the response profile of the drug based on measurements obtained using NeuroCart® and PainCart®
- optimise PK and PD sampling timepoints to reduce patient burden
- facilitate strategic and critical (go/no-go) project decisions
- optimise study designs for subsequent clinical studies (e.g. dose selection for a phase II trial)

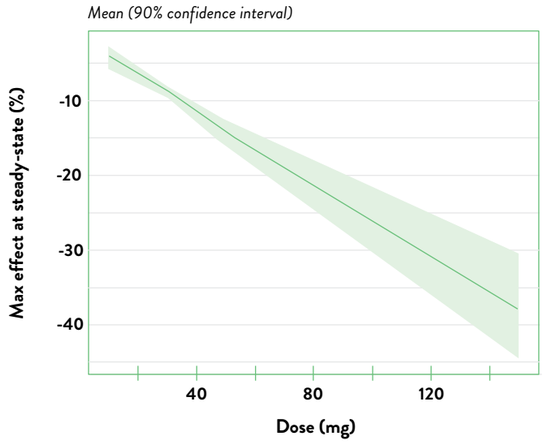

Figure 4: illustrates how the simulation of an effect at steady state for different dose levels can support dose selection.

Upholding high standards

All services are performed in accordance with international regulatory standards set by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) as well as abiding by ICH-GCP. All analyses are carried out using validated software, such as Phoenix WinNonlin for NCA analyses and NONMEM for modelling and simulation. Analyses are guided by Standard Operating Procedures (SOPs) and completed according to agreed timelines. Data and calculations are always checked by an independent reviewer before a report is finalised.

Why choose CHDR?

The Centre for Human Drug Research specialises in early-phase clinical drug research. CHDR's overall mission is to improve the drug development process by collecting as much information as possible regarding the candidate drug in the early phases of development. This information helps sponsors make informed decisions regarding the course of clinical development for their product.

Why choose CHDR?

Research at CHDR covers a wide range of fields, including the central nervous system (CNS) and pain, the cardiovascular system, haemostasis, immunology, and dermatology. In addition, CHDR is at the forefront in developing novel biomarkers and methods for measuring drug-related effects in all of these research areas.

Pharmacology matters

Whether studying a new cognitive-enhancing drug, a next-generation painkiller, or a new monoclonal antibody designed to treat rheumatoid arthritis, the goal is to determine how the compound's effects correlate with both the dose and blood concentration at any given moment. In addition, understanding which biological systems are activated is an essential first step towards quantifying this relationship. At CHDR, our focus on pharmacology is reflected clearly in what we call question-based drug development.

Question-based drug development

CHDR actively uses question-based drug development - or QBD - as a more rational approach to drug development compared to conventional approaches. QBD can be best described as a series of questions that are addressed throughout the process. These questions often seem simple enough, but failing to answer even one question - or even addressing the questions in the wrong order - can have dire consequences. Thus, using this approach can potentially save companies millions of dollars by helping predict a catastrophic issue early in the development process, before the more expensive latter stages (for example, large-scale clinical trials or the marketing phase).

From a general perspective, the most important questions are:

1. Does the biologically active compound and/or active metabolite(s) reach the intended site of action?
2. Does the compound cause its intended pharmacological and/or functional effect(s)?
3. Does the compound cause any unintended pharmacological and/or functional effect(s)?
4. Does the compound have a beneficial effect on the disease and/or clinical pathophysiology?
5. What is the compound's therapeutic window?
6. How does any variability with respect to the drug response in the target population affect the product's development?

Contact

To learn about CHDR's full range of services, contact us today.

+31(0)71 524 64 00

info@chdr.nl

www.chdr.nl