Venn Life Sciences
Think Research

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Listen Think Deliver

Pharmacometrics

Providing in-depth insight into PK-PD data

At Venn, our Pharmacometrics group has the expertise to deliver in-depth analysis of PK and PD data through predictive PK-PD modeling & simulation.

During drug development, pharmacokinetic (PK) and pharmacodynamic (PD) modeling & simulation (M&S) is applied to enhance decision making and study design. PK-PD M&S facilitates compound selection for clinical development, improved design of drug formulations and CMC processes, and optimizes study designs (e.g. dose selection). M&S enables understanding of variability in treatment response, between study populations (e.g. from adults to paediatrics) and facilitates strategic and critical project (go/no-go) decisions. M&S can be utilised at all stages of drug development, is an integral part of the regulatory dossier and is requested by agencies starting as early as pre-NDA.

Venn Expertise

Exploratory analysis for instant decision - making

To facilitate decision-making within a drug development program, Venn can perform exploratory analysis with rapid turn-around times. We can build models, based on interim data, to predict PK and/or PD for planned dose groups or for predictions to multiple dosing. This construction is typically used during early Phase I and Phase IIa studies, enabling solid decision making for dose setting and/or follow on clinical study designs

Cross-study population analyses including covariate analysis

Cross-study population analysis is performed to characterize the PK and PD of the candidate drug in the target population. The relationship between PK-PD and covariates (e.g. age, weight genotype, comedication and disease state) can be explored to explain parameter variability and to facilitate dose adjustment decisions. For subsequent studies, outcomes can be explained by the covariates included in the modeling exercise. Simulations can also be performed to explore the impact of the different covariates on the PK-PD. Such models are frequently used to support label claims.

Extrapolation to humans / paediatrics

In the absence of human data, non-clinical data can also be used to generate animal Pharmacometrics models. These models can be used to extrapolate to humans. This data can be used for the justification of dose selection for first in man clinical studies.

If human adult data is available, models can be built to enable extrapolation to paediatric populations. By using this model, dose adjustments can be derived resulting in appropriate exposure in children.

OPTIMISING DEVELOPMENT WITH PREDICTIVE MODELS

Translational	Clinical	Biometrics	Documentation & Scientific Presentations
(Population) PK & PK-PD (NONMEM) modeling	(Population) PK & PK-PD (NONMEM) modeling	Safety and Statistics Programming	
		TLF's programming (Tables Figures Listings)	Statistical analysis plan
	Describing complex absorption/release profiles	Exploratory efficacy analysis	
Inter-species scaling / modeling		Programming of nonmem inputs	Modeling plan
	Cross-study analysis (covariate analysis)	Macros for safety analysis	
Paediatric modeling		Programming in SAS, R	Pharmacometric report
	Modelling of biomarkers, disease progression	Data visualisation	
Quantitative systems pharmacology approaches		Sample size calculations	Posters / publication
	Trial Simulations	Statistical inference	

Bayesian Analysis

Bayesian analysis can be performed at different stages of drug development. If prior information is available, a Bayesian approach can be more appropriate for fitting of new datasets. Typical applications include determination of the next dose level in a dose escalation study, assessment of dose proportionality or extrapolation in paediatric studies.

Programming Datasets

Venn can support you with extensive experience and expertise in both modeling and programming. Datasets are programmed using SAS.

Quality

WinNonLin®, NONMEM® and R software are used for the different M&S projects. All work is performed following Standard Operating Procedures, thus ensuring integrity, traceability and reproducibility within the analysis.

Case Studies

Venn has been involved at all phases of drug development across many projects, including:

- Optimization of the release characteristics of a slow-release fixed dose combination product by comparing in vitro dissolution profiles with dog and human in vivo release profiles (IVIVC)
- Supporting dose selection in a 3-month toxicology study using simulations of plasma concentrations after multiple dosing with non-linear pharmacokinetic properties
- Determination of relevant start doses or target concentrations for first-in-man studies by interspecies scaling
- PK-PD model development of a drug exhibiting Target - Mediated Drug Disposition (TMDD)
- Optimizing the dose regimen at which the desired minimum decrease in viral load is achieved for an antiviral compound
- Optimization of a Phase III dosing schedule after characterisation of the relationship between plasma concentrations and the in vivo receptor binding to a CNS target
- Bayesian probability estimation of exceeding a predefined threshold exposure in Phase I tolerability studies

M&S can be utilised at all stages of drug development and is now an integral part of the regulatory dossier

Why Venn Life Sciences?

- Experienced team of Pharmacometricians
- Part of an integrated drug development team, including medical writers and regulatory expertise
- Rapid and well-founded decision making
- Broad experience in Pharmacometrics analysis and modeling
- Committed to delivering your project on time
- Flexible approach

For more visit www.vennlifesciences.com or email us at getintouch@vennlife.com