Pharmazie

Ronald Niebecker

Population Pharmacokinetic Modelling and Simulation of Monoclonal Antibodies Including the Impact of Immunogenicity and Importance of Study and Analysis Design Factors

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D 188 (Diss. Freie Universität Berlin)

Shaker Verlag
Aachen 2014

Bibliographic information published by the Deutsche Nationalbibliothek
The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available in the Internet at http://dnb.d-nb.de.

Zugl.: Berlin, Freie Univ., Diss., 2013

Printed in Germany.

ISBN 978-3-8440-2650-4
ISSN 0945-0939

Shaker Verlag GmbH • P.O. BOX 101818 • D-52018 Aachen
Phone: 0049/2407/9596-0 • Telefax: 0049/2407/9596-9
Internet: www.shaker.de • e-mail: info@shaker.de

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Dissertation zur Erlangung des akademischen Grades des
Doktors der Naturwissenschaften (Dr. rer. nat.)

eingereicht im Fachbereich Biologie, Chemie, Pharmazie
der Freien Universität Berlin

vorgelegt von
Ronald Niebecker
aus Rostock
2013

Diese Arbeit wurde von 2009 bis 2013 unter der Leitung von Prof. Dr. Charlotte Kloft am Institut für Pharmazie der Martin-Luther-Universität Halle-Wittenberg (bis Mai 2011) und der Freien Universität Berlin (ab Mai 2011) angefertigt.

1. Gutachter: Prof. Dr. Charlotte Kloft

2. Gutachter: Prof. Dr. Bernd Meibohm

Disputation am 29. Oktober 2013

Für meine Familie

Abbreviations and symbols

Abbreviation	Definition
AAA	Anti-adalimumab antibodies
AAPS	American Association of Pharmaceutical Scientists
AAR	Anti-antibody response
ABW	Adjusted body weight
ADA(s)	Anti-drug antibody/ies
ADME	Absorption, distribution, metabolism, excretion
ADR	Adverse drug reaction
ADVAN	PREDPP subroutine for general nonlinear models
AIC	Akaike information criterion
ATI	Antibodies to infliximab
AU	Arbitrary units
AUC(s)	Area(s) under the curve
BMI	Body mass index
BQL	Below lower limit of quantification
BSA	Body surface area
CD	cluster of differentiation
CDD	Case deletion diagnostics
CDR	Complementarity determining regions
CI	Confidence interval
CID	Chronic inflammatory diseases
CL_ADA	Clearance caused by ADAs
CLC	Central linear clearance (model developed in project I)
CLL	Linear clearance
CLNL	Intrinsic clearance, computed as VMAX/KM
C_{max}	Maximum plasma concentration
C_{min}	Minimum (trough) plasma concentration
%CV	% coefficient of variation
CWRES	Conditional weighted residuals
df	Degree(s) of freedom
DPP4	Dipeptidyl peptidase 4 (gene family)

continued...

Abbreviation	Definition
EBE	Empirical Bayes estimates
ECL	Electrochemiluminescence assay
ECM	Extracellular matrix
EDA	Exploratory data analysis
EGA	Exploratory graphical analysis
ELISA	Enzyme-linked immunosorbent assay
EMA	European Medicines Agency
EPAR	European Public Assessment Report
ES	Effect size
Fab	Fragment antigen-binding
FAP	Fibroblast activation protein
Fc	Fragment crystallisable
FcγR	Fc gamma receptor
FcRn	Neonatal Fc receptor
FDA	United States Food and Drug Administration
FFM	Fat-free mass
FO	First-order estimation method
FOCE	First-order conditional estimation method
FOCE+I	FOCE estimation method with interaction
GLS	Genealised least squares
HACA	Human anti-chimeric antibodies
HAFA	Human anti-fusion protein antibodies
HAGR	Human anti-globulin response
HAHA	Human anti-human antibodies
HAMA	Human anti-murine antibodies
HT	Height
IBW	Ideal body weight
Ig	Immunoglobulin
IIV	Interindividual variability
IM	Intramuscular
IOV	Interoccasion variability
ISV	Interstudy variability
IV	Intravenous
KM	Michaelis-Menten constant
LAP	Laplacian estimation method

continued...

Abbreviation	Definition
LAP+I	LAP estimation method with interaction
LBM	Lean body mass
LL	Log likelihood
LLOQ	Lower limit of quantification
LLP	Log likelihood profiling
LOCF	Last observation carried forward
LRT	Likelihood ratio test
MAPE	Median absolute percent estimation error
ML	Maximum likelihood
MPE	Median percent estimation error
NCA	Non-compartmental analysis
NLME	Nonlinear mixed-effect(s)
NM-TRAN	NONMEM translator (part of NONMEM)
NONMEM	Nonlinear mixed-effect modelling software
OBJ_{ELS}	Extended least squares objective function
OFV	Objective function value
PBPK	Physiologically-based pharmacokinetics
PLC	Peripheral linear clearance (model developed in project I)
PNWT	Predicted normal weight
POCA	Power coefficient for nonlinear CL_ADA model (project III)
PPC	Posterior predictive check
PRED	Prediction subroutine (part of NONMEM)
PREDPP	Prediction for population pharmacokinetics (part of NONMEM)
PsN	Perl-speaks-NONMEM
Q	Intercompartmental clearance
R	Software for various data analyses
RIA	Radioimmunoassay
RIPA	Radioimmunoprecipitation assay
RME	Receptor-mediated endocytosis
RSE	Relative standard error
RSV	Residual variability
RU	Response units
SACA	Saturation parameter for nonlinear CL_ADA model (project III)
SC	Subcutaneous
SIGDIG	Number of significant digits

continued...

Abbreviation	Definition
SPR	Surface plasmon resonance
STS	Standard two-stage method
TALD	Time after last dose
t_{max}	Time of C_{max}
TMDD	Target-mediated drug disposition
TNF-α	Tumour necrosis factor alpha
TOL	Tolerance
ULOQ	Upper limit of quantification
ΔV_ADA	Increased distributional space caused by ADAs
VMAX	Maximum elimination rate achievable (Michaelis-Menten parameter)
VPC	Visual predictive check
Vss	Volume of distribution at steady-state
Vx	Volume of distribution of xth compartment
WRES	Weighted residuals
WT	Weight
Xpose	Graphic library for R

end

Symbol	Definition
$f()$	Function relating observations to model predictions
$g()$	Function relating model parameters to population parameters and covariates
P_{ki}	Individual parameter estimate for kth parameter and ith individual
$var(y_i)$	Variance-covariance matrix for y_i
x_{ij}	Model input for the ith individual at the jth time point, including all aspects of study design
y_i	Vector of the observations of the dependent variable for the ith individual
y_{ij}	Observations for the ith individual at the jth time point
$\hat{y}_i$	Vector of model predictions/expectations
z_i	Covariates observed in the ith individual
ϵ	Random-effects parameter, residual variability
ϵ_{ij}	Vector of residuals between observed values and model-predicted values, for the ith individual in the jth observation
η	Random-effects parameter, interindividual variability
η_i	Vector of interindividual random-effects in ith individual
Θ	Vector of typical population parameter estimates
θ	Typical population parameter estimate
κ	Random-effects parameter, interoccasion variability
κ_{im}	Vector of interoccasion random-effects in the ith individual at the mth occasion
π^2	Variance for κ
ρ	Correlation coefficient
Σ	Variance-covariance matrix for ϵs
σ^2	Variance for σ
$\sigma_i\sigma_j$	Covariance between two σs
ϕ_i	Model parameters of the ith individual
Ω	Variance-covariance matrix for ηs
ω^2	Variance for η
$\omega_i\omega_j$	Covariance between between two ηs

Contents