Joint BfArM/DIA Statistics Workshop

Event #12107
17-19 October 2012
Maritim Hotel Bonn, Bonn, Germany

Programme Co-Chairs

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Adjunct Professor for Biometry, Hannover Medical School, Germany

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Senior Director of Biostatistics, F. Hoffmann-La Roche AG, Switzerland

Tim Friede
Professor of Biostatistics, Chair, Department of Medical Statistics, University Medical Centre Göttingen, Germany

Andrew Thomson
Head of Epidemiology, Vigilance Risk Management of Medicines (VRMM), Medicines and Healthcare products Regulatory Agency (MHRA), UK

Sue Todd
Professor of Medical Statistics, University of Reading, UK

Joerg Zinserling
Senior Statistical Assessor, Federal Institute for Drugs and Medical Devices (BfArM), Germany

Overview

This 2.5 day event is the first joint workshop on statistical methodology in clinical research and development by DIA Europe and the Federal Institute for Drugs and Medical Devices (BfArM). Renowned statisticians from industry, regulatory bodies and academia will contribute to this workshop and share their expertise. The workshop will examine the increasingly important role of statistics in clinical R&D and will also explore new applications of statistical methods.

Key Topics

- Innovative clinical trial designs: Applications and regulatory reflections
- Model-based drug development
- Using observational data beyond randomised trials
- Statistical issues in the clinical development of oncology therapeutics
- Key topics in regulatory statistics

Who Will Attend

Professionals with an interest in the application of, and research into, statistics in the drug development process from the pharmaceutical industry, academia, regulatory and governmental agencies, as well as contract research organisations.

Objectives

- To provide a forum for lively and informative discussions about novel statistical methods and their application in clinical R&D
- To bring together professionals from all disciplines/areas of drug development to share experience and knowledge
- To provide up-to-date information on current regulatory topics in the field of statistics
- To explore progress in the use of new methodologies and other/new areas of interest for statisticians who work in the field or who want to develop their career into this area

Continuing Education

DIA meetings are generally approved by the SwAPP (Swiss Association of Pharmaceutical Professionals) Commission for Professional Development (CPD) and SGPM (Swiss Society of Pharmaceutical Medicine) and will be honoured with credits for pharmaceutical medicine. All participants are eligible for these credits and certificates are available on request from the registration desk. The Swiss Association of Pharmaceutical Professionals (SwAPP) and the Swiss Society for Pharmaceutical Medicine (SGPM) have accredited this workshop with 14.5 credits.

PRE-WORKSHOP TUTORIALS ON KEY STATISTICAL TOPICS IN DRUG DEVELOPMENT

Wednesday, 17 October 2012 I 09:00-12:30

Tutorial 1
VALIDATION OF SURROGATE ENDPOINTS

Tutorial 2
MISSING DATA IN CLINICAL TRIALS

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PRE-WORKSHOP HALF DAY TUTORIALS

08:30 **ARRIVAL & TUTORIAL REGISTRATION**

09:00 **TUTORIAL 1 / TUTORIAL 2**

10:30 - 11:00 **COFFEE BREAK**

Tutorial 1 I 09:00 – 12:30

VALIDATION OF SURROGATE ENDPOINTS

Tutorial Instructor:
Tomasz Burzykowski, Vice-President Research, IDDI, Belgium and Professor of Biostatistics, Hasselt University, Belgium

This tutorial will focus on the use of biomarkers and surrogate endpoints in drug development. We will formalise the concepts of prognostic/predictive biomarkers and surrogate endpoints and review the main issues related to their application. In particular, we will focus on approaches to validation of surrogate endpoints. All methods and concepts discussed will be illustrated with real-life examples from various areas of clinical medicine.

LEARNING OBJECTIVES

During this tutorial, attendees will learn about:

- the differences between biomarkers and surrogate endpoints, and between different types of biomarkers
- the implications of the differences for the application of biomarkers and surrogate endpoints in drug development
- the methods for validating surrogate endpoints for use in drug development

TARGET AUDIENCE

This tutorial will be of interest to researchers and members of clinical and statistical staff involved in planning and coordinating drug development programmes from pharmaceutical companies, biotechnology firms, academic research institutions.

Tutorial 2 I 09:00 – 12:30

MISSING DATA IN CLINICAL TRIALS

Tutorial Instructor:
Mike Kenward, Professor of Biostatistics, Department of Medical Statistics, London School of Hygiene and Tropical Medicine, UK

This tutorial will focus specifically on the handling of dropout in longitudinal experiments and trials. A clear distinction will be made between analyses in which the occurrence of dropout is classed as a particular outcome, and in which it is a nuisance preventing the collection of all the intended data. This workshop will concentrate on the latter setting. The central role of the estimand for analyses of incomplete clinical trial data will be explored, and linked to more familiar concepts like “intention to treat” and “per protocol” populations. The position of Rubin’s classification of missing value mechanisms will be assessed in the light of this. A range of analyses will be considered, ranging from simple ad hoc, to model-based. The comparative advantages and disadvantages of these approaches will be carefully explored, particularly in the light of the intended estimand. The concept of sensitivity analysis will be developed and some possible examples described. Those based on so-called “Pattern Mixture Models” will be given particular emphasis. The analyses discussed, both primary and sensitivity, will be illustrated using examples with accompanying SAS code.

LEARNING OBJECTIVES

At the conclusion of this tutorial, attendees will:

- be able to identify the main issues surrounding missing data in longitudinal clinical trials;
- be able to appreciate the main types of analysis appropriate for such settings, together with their advantages and disadvantages;
- be able to appreciate the role of sensitivity analysis for incomplete data;
- know how to approach a range of such primary and sensitivity analyses in practice.

TARGET AUDIENCE

This tutorial will be of interest to statisticians and statistically experienced clinicians involved in the design and analysis of longitudinal experiments and clinical trials.

WEDNESDAY | 17 OCTOBER 2012

START OF WORKSHOP

12:30 **REGISTRATION AND WELCOME COFFEE**

13:30 **Current Statistical Challenges in the US Regulatory Environment**
Lisa LaVange, Director, Office of Biostatistics, Office of Translational Sciences, CDER, FDA, USA

14:00 **Session 1**

INNOVATIVE CLINICAL TRIAL DESIGNS

Session Co-Chairs:
Tim Friede, Professor of Biostatistics, Chair, Department of Medical Statistics, University Medical Centre Göttingen, Germany
José Pinheiro, Senior Director of Quantitative Decision Strategies, Janssen Research & Development, LLC, USA

In this session we will hear from renowned speakers about the latest development in group-sequential and adaptive design methodology, highlighting recent developments in the use of short-term outcomes such as early read-outs of the primary endpoint for decision making in interim analyses.

In the second part, modelling and simulation approaches to drug development will be showcased.

Group Sequential Tests for Delayed Responses
Christopher Jennison, Professor of Statistics, University of Bath, UK (jointly with Lisa Hampson, Lancaster University, UK)

Using Surrogate Endpoints for Decision-Making in Adaptive Seamless Designs
Sue Todd, Professor of Medical Statistics, University of Reading, UK

Panel Discussion
Martin Posch, Professor of Medical Statistics, Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Austria
and session speakers

15:30 **COFFEE BREAK**

16:00 **Session 1 continued**

INNOVATIVE CLINICAL TRIAL DESIGNS

Session Co-Chairs:
Tim Friede, Professor of Biostatistics, Chair, Department of Medical Statistics, University Medical Centre Göttingen, Germany
José Pinheiro, Senior Director of Quantitative Decision Strategies, Janssen Research & Development, LLC, USA

Innovative Designs: Where practice meets theory
Filip de Ridder, Biostatistics and Programming, Janssen Pharmaceutica, Belgium

Adaptive Dose-ranging Study to Fully Characterise the Dose-response Relationship in Multiple Sclerosis
Francois Mercier, Senior Consultant, Pharsight, France

Panel Discussion
Mohamed Alosh, Statistics Team Leader, Division of Biometrics III, CDER, FDA, USA
and session speakers

17:30 **DRINKS RECEPTION**

18:30 **END OF DAY ONE**

THURSDAY | 18 OCTOBER 2012

09:00 Session 2

STATISTICAL ISSUES IN THE CLINICAL DEVELOPMENT OF ONCOLOGY THERAPEUTICS

Session Co-Chairs:
Hans-Ulrich Burger, Senior Director of Biostatistics, F. Hoffmann-La Roche AG, Switzerland
Bertil Jonsson, Senior Expert, Medical Products Agency (MPA), Sweden

This session will highlight a number of areas of current interest in clinical development in oncology. Crossover of patients to active treatment and its impact on clinical endpoints, adequate timing of analyses, especially interim analyses related to the assessment of maturity of data, surrogate endpoints and their validation, as well as adequate descriptive statistics to assess the treatment effect in a "time to event" endpoint will be some of the topics discussed in this session from both a regulatory and industry point of view. A panel discussion with all speakers will provide further insight beyond the individual presentations.

How to Live with Crossover in Cancer Trials
Steven Tereenstra, Statistician, Medicines Evaluation Board (MEB), The Netherlands

Determination of Maturity in Survival Type Endpoints
Dominik Heinzmann, Biostatistician, F. Hoffmann-La Roche AG, Switzerland

Surrogate Endpoints in Oncology
Tomasz Burzykowski, Vice-President Research, IDDI, Belgium and Professor of Biostatistics, Hasselt University, Belgium

10:30 COFFEE BREAK

11:00 Session 2 continued

STATISTICAL ISSUES IN THE CLINICAL DEVELOPMENT OF ONCOLOGY THERAPEUTICS

Session Co-Chairs:
Hans-Ulrich Burger, Senior Director of Biostatistics, F. Hoffmann-La Roche AG, Switzerland
Bertil Jonsson, Senior Expert, MPA, Sweden

Multiple Endpoints Analyses using Gate keeping Procedure based on Graphical Approach – Application to a Phase III Study aiming to demonstrate the Efficacy of a targeted therapy in Breast Cancer
Nathalie Fretault, Novartis Pharma AG, Switzerland

Statistical Issues in PFS Assessment
Andreas Brandt, Federal Institute for Drugs and Medical Devices (BfArM), Germany
Ulrike Hermes, Federal Institute for Drugs and Medical Devices (BfArM), Germany

Measures to Assess Clinical Benefit in Time-To-Events Analyses
Hans-Ulrich Burger, Senior Director of Biostatistics, F. Hoffmann-La Roche AG, Switzerland

Panel Discussion
with session speakers

12:30 LUNCH

Unless otherwise disclosed, DIA Europe acknowledges that the statements made by speakers are their own opinion and not necessarily that of the organisation they represent, or that of the DIA Europe.

Speakers and agenda are subject to change without notice. Recording of any DIA Europe tutorial/workshop information in any type of media, is prohibited without prior written consent from DIA Europe.

14:00 Session 3

MODEL-BASED DRUG DEVELOPMENT

Session Co-Chairs:
Michael Branson, Global Franchise Head, Translational Sciences, Novartis Pharma AG, Switzerland
Efthymios Manolis, European Medicines Agency (EMA), EU

In this model-based drug development session we will focus on examples using empirical through to pharmacological (physiological) model-based approaches in drug development. We will also identify how these approaches can be coupled with simulations to develop robust approaches, through compared and contrast/scenario assessments, to support decision-making within clinical trials/programmes.

Model-based Approaches to Improve the Efficiency of Clinical Drug Development: Challenges and rewards
José Pinheiro, Senior Director of Quantitative Decision Strategies, Janssen Research & Development LLC, USA

Using Model-based Meta-analyses to Better Inform Decision-making for Proof of Concept Studies
Martin Boucher, Associate Director Global Pharmacometrics, Pfizer, UK

Model-Based Analyses for Pivotal Trials, with an Application to Biosimilarity Assessments in Rheumatoid Arthritis
Didier Renard,Cluster leader, Modeling and Simulation, Novartis Pharma AG, Switzerland

15:30 COFFEE BREAK

16:00 Session 3 continued

MODEL-BASED DRUG DEVELOPMENT

Session Co-Chairs:
Michael Branson, Global Franchise Head, Translational Sciences, Novartis Pharma AG, Switzerland
Efthymios Manolis, European Medicines Agency (EMA), EU

Drowning by Numbers or Surfing the Virtual Sea? Why I worry about simulation
Stephen Senn, Competence Center for Methodology and Statistics, CPR Santè, Luxembourg

Role of Modelling and Simulation (M&S) in EMA Submissions
Efthymios Manolis, European Medicines Agency (EMA), EU

Panel Discussion
with session speakers

17:30 END OF DAY 2

ABOUT DIA

The DIA is a global association of approximately 18,000 members who are involved in the discovery, development, regulation, surveillance or marketing of pharmaceuticals or related products. The DIA is committed to the broad dissemination of information on the development of new medicines or generics, biosimilars, medical devices and combination products with continuously improved professional practice as the goal.

The DIA is an independent non-profit organisation. The voluntary efforts of DIA members and speakers allow the DIA to organise conferences, workshops and training courses and provide publications and educational material.

DIA's headquarters are in Horsham, PA, USA, with the European office in Basel, Switzerland, and other regional offices in Tokyo, Japan, Mumbai, India, and Beijing, China.

For more information, visit www.diahome.org or call DIA Europe on +41 61 225 51 51.

FRIDAY I 19 OCTOBER 2012

08:30 Session 4

USING DATA BEYOND RANDOMISED TRIALS

Session Co-Chairs:
Andrew Thomson, Head of Epidemiology, VRMN, MHRA, UK
Juergen Kuebler, Global Head, Clinical Sciences, CSL Behring GmbH, Germany

Statisticians have not often had as much input into designing and analysing observational studies as they have had into confirmatory clinical trials. With more demands for integrating data across the product life-cycle for different authorities, and more possibilities for studies using large electronic health records, this session aims to examine both the need and opportunity for statisticians to become more involved with generating and analysing data from observational studies, and explore how these can be combined with data we are more used to seeing.

Looking at Safety with the Eyes of Janus: A retrospective and prospective observational safety study using electronic medical records and the US National Death Index
Tim Auton, Associate Director of Biostatistics, Astellas Pharma Europe BV, The Netherlands

Integrating Observational and Interventional Research alongside Clinical Care – the UK approach
John Parkinson, Director, General Practice Research Database Division, MHRA, UK

Strategically Combining Clinical and Observational Data – Steps towards a cross-source analysis plan
Yvonne Geissbuehler, Global Epidemiologist, Novartis Pharma AG, Switzerland

10:00 COFFEE BREAK

10:30 Session 4 continued

USING DATA BEYOND RANDOMISED TRIALS

Session Co-Chairs:
Andrew Thomson, Head of Epidemiology, VRMN, MHRA, UK
Juergen Kuebler, Global Head, Clinical Sciences, CSL Behring GmbH, Germany

Adding Statistical Value to Observational Data used to Support HTA Activities
Christine A. Fletcher, Director of Biostatistics, Amgen Ltd., UK

Adding Statisticial Value to Obervational Studies - A Regulatory Perspective
Andrew Thomson, Head of Epidemiology, VRMN, MHRA, UK

Panel Discussion
with session speakers

12:00 LUNCH

13:00 Session 5

KEY TOPICS IN REGULATORY STATISTICS

Session Co-Chairs:
Norbert Benda, Head of Biostatistics and Special Pharmacokinetics, Federal Institute for Drugs and Medical Devices (BfArM), Germany
Andy Grieve, Senior Vice President of Clinical Trial Methodology, Aptiv Solutions, Germany

In this session, regulatory statistical experts will present current statistical issues that are highly relevant in the drug approval process.

Regulatory Challenges in the Assessment of Subgroups in Randomised Clinical Trials
Armin Koch, Head of Institute of Biometry, Hannover Medical School, Germany

Statistical Considerations on Subgroup Analysis in Clinical Trials
Mohamed Alosh, Statistics Team Leader, Division of Biometrics III, CDER, FDA, USA

Covariate Adjustment in Regulatory Clinical Trials
Lisa LaVange, Director, Office of Biostatistics, Office of Translational Sciences, CDER, FDA, USA

14:30 COFFEE BREAK

15:00 Session 5 continued

KEY TOPICS IN REGULATORY STATISTICS

Session Co-Chairs:
Norbert Benda, Head of Biostatistics and Special Pharmacokinetics, Federal Institute for Drugs and Medical Devices (BfArM), Germany
Andy Grieve, Senior Vice President of Clinical Trial Methodology, Aptiv Solutions, Germany

Regulatory Issues in Adaptive Designs
Martin Posch, Professor of Medical Statistics, Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Austria

Panel Discussion
with session speakers

16:00 END OF WORKSHOP

HOTEL INFORMATION

The DIA has blocked a number of rooms at the:
MARITIM Hotel Bonn
Godesberger Allee
(Access: Kurt-Georg-Kiesinger Allee 1)
53175 Bonn
Phone: + 49 (0) 228 8108-0
Fax: + 49 (0) 228 8108-811
Reservation phone: + 49 (0) 228 8108-777
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Group Name: DIA

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IN CASE OF CANCELLATION:
Cancellations and modifications will be free of charge, if received no later than 6:00 PM local hotel time on day of arrival. Otherwise 90% of the full stay will be charged.

GUARANTEE POLICY:
Your reservation must be guaranteed by a valid credit card.

REGISTRATION FORM

Joint BfArM/DIA Statistics Workshop
17-19 October 2012 I Maritim Hotel Bonn, Bonn, Germany

ID #12107

If DIA cannot verify your membership upon receipt of registration form, you will be charged the non-member fee.
The fee is inclusive of lunch and coffee breaks of EUR 150.00 per day.

CATEGORY	Member (after 5 September 2012) Fee*	Non-Member Fee*
Industry	€ 1'050.00 ❑	€ 1'165.00 ❑
Government/Charitable/Non-profit/Academia (Full-Time)	€ 525.00 ❑	€ 640.00 ❑
I wish to attend tutorial no. _____	€ 350.00 ❑	
*All Fees will be subject to the local German VAT of 19%		

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TOTAL AMOUNT DUE: €_____ **NOTE: PAYMENT DUE 30 DAYS AFTER REGISTRATION AND MUST BE PAID IN FULL BY COMMENCEMENT OF THE EVENT**

SMEs, STUDENT RATES AND GROUP DISCOUNTS ARE AVAILABLE! PLEASE CONTACT THE DIA FOR MORE INFORMATION.

REGISTRANT

PLEASE COMPLETE IN BLOCK CAPITAL LETTERS OR MAKE REGISTRATION EVEN SIMPLER BY ATTACHING THE REGISTRANT'S BUSINESS CARD HERE

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Payments must be net of all charges and bank charges must be borne by the payer.

CANCELLATION POLICY

All cancellations must be in writing and received with DIA Europe by 17:00 CET on 10 October 2012

Cancellations received by the date above are subject to an administrative fee:
Full Meeting Cancellation: Industry (Member/non-member) = € 200.00. Government/Charitable/Non-profit/Academia (Member/non-member) = € 100.00. Tutorial cancellation: € 50.00. Registered attendees who do not cancel by the date above and do not attend, will be responsible for the full registration fee. Registered attendees are responsible for cancelling their own hotel reservations. DIA Europe reserves the right to alter the venue and dates if necessary. If an event is cancelled, DIA Europe is not responsible for airfare, hotel or other costs incurred by registered attendees.

Transfer Policy
You may transfer your registration to a colleague prior to the start of the event but membership is not transferable. Substitute attendees will be responsible for the non-member fee, if applicable. Please notify DIA Europe office of any such substitutions as soon as possible.

IMPORTANT: **Hotel and travel reservations should be made ONLY after receipt of written registration confirmation from DIA Europe. If you have not received your confirmation within five working days, please contact DIA Europe.**

HOW TO REGISTER

The DIA Europe Customer Services Team will be pleased to assist you with your registration. Please call us on +41 61 225 51 51 from Monday to Friday between 08:00 and 17:00 CET.

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