SMi present their 5th annual conference on...

Adaptive Designs in Clinical Trials

Monday 8th & Tuesday 9th April 2013
Copthorne Tara Hotel, London, UK

KEY SPEAKERS INCLUDE:

Christopher Jennison
Professor of Statistics
University of Bath

Frank Fleischer
Teamleader Clinical Biostatistics
Boehringer-Ingelheim

Micheal Krams
VP - Head of Neurology Franchise
Johnson & Johnson

Vladimir Anisimov
Senior Strategic Biostatistics Director
Quintiles

Thomas Jaki
Researcher, Department of Mathematics and Statistics
Lancaster University

Andy Kenwright
Project Statistician
Roche Products Limited

Martin Simán
Director
AstraZeneca

Emmanuel Pham
Snr. Director Global R&D Statistics
Ipsen

Jouni Kerman
Statistical Methodologist
Novartis

Alun Bedding
Director, Biostatistics and Programming
Development Partners
GlaxoSmithKline

WHY YOU SHOULD ATTEND THIS UNIQUE EVENT:

• It’s the only conference in Europe to focus specifically on adaptive designs
• Benefit from the first-hand experiences of speakers whose organisations have recently made breakthroughs in adaptive designs
• Hear the very latest on predictive analytical techniques for increasing efficiency of drug development
• Learn how to develop a normal standing clinical trial into an adaptive clinical trial
• Discover data software that supports the ever-increasing complexity of adaptive clinical trials by attending the post-conference workshop

PLUS AN INTERACTIVE HALF-DAY POST-CONFERENCE MORNING WORKSHOP

Wednesday 10th April 2013, Copthorne Tara, London, UK

Population Enrichment Designs with the ADDPLAN software

Workshop Leader:
Gernot Wassmer, PhD, Senior Vice President and Chief Software Architect, ADDPLAN
9.00pm – 1.00pm

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Adaptive Designs in Clinical Trials
Day One | Monday 8th April 2013

8.30 Registration and Coffee

9.00 Chairman’s Opening Remarks
Vladimir Anisimov, Senior Strategic Biostatistics Director, Quintiles

9.10 Exploratory dose finding in malaria
- Goal is characterisation of key aspects of drug PK/PD relationship in early phase trials
- Investigation of designs incorporating adaptive dose-allocation for this purpose
- Construction of candidate PK/PD models and simulation of operating characteristics
- Introduction of case study
Baldur Magnusson, Statistician, Novartis International AG

9.50 The motivation, promise, and success of Bayesian adaptive trial design
- Well-designed adaptive trials can mitigate the risk of a failed clinical trial
- Avoiding “anticipated regret” and avoiding undue focus on minor threats to trial success
- An adaptive trial “by design” all relevant statistical threats to trial validity must be addressed via simulation
- The productive use of adaptive trials is limited mostly by the conservative nature of those designing the trials
Roger Lewis, Senior Medical Scientist, Berry Consultants

10.30 Morning Coffee

11.00 Predictive analytical techniques for increasing efficiency of drug development
- Main uncertainties and interactions between adaptive trial design, patient recruitment, randomisation
- Adaptive patient recruitment prediction and trial cost modelling
- Data-driven predicting trial performance and site productivity
- Predictive event modelling and adaptive recruitment adjustment
- Optimisation of different stages of drug development
Vladimir Anisimov, Senior Strategic Biostatistics Director, Quintiles

11.40 An adaptive design to explore prevention therapies for Alzheimer’s Disease
- The research question – Alzheimer’s Disease
- Applying adaptive design methodology to the research question
- Biomarkers as enablers for the adaptive design
- Case Study
Michael Krams, VP - Head of Neurology Franchise, Johnson & Johnson

12.20 Networking Lunch

1.50 Designing multi-arm multi-stage clinical trials
- Two principle approaches for designing multi-arm multi-stage clinical trials
- Discussion: Options for selecting treatments
- Software to design such studies is presented
Thomas Jaki, Researcher, Department of Mathematics and Statistics, Lancaster University

2.30 Controlling the weighted sum of type I and type II errors and implications for the design and analysis of adaptive designs
- Hypothesis testing in clinical trials
- Should Type I error be fixed in drug development?
- An alternative to maximising power for fixed Type I error
- Traditional values for Type I and Type II error rates and implications for the relative costs of these errors
- An Alternative Form of the Neyman-Pearson Fundamental Lemma
- The Likelihood Principle and Adaptive Trials
Andy Grieve, Senior Vice President Clinical Trial Methodology, Aptiv Solutions

3.10 Afternoon Tea

3.40 Pediatric adaption: early (stage) we practice, later perhaps we practice less
- Examples of adaptive designs in early stage pediatric trials are documented and hopefully growing
- Late stage confirmatory trials examples
- Discussion of potential barriers to pediatric studies
- Late stage confirmatory trial case studies
Andy Kenwright, Project Statistician, Roche Products Limited

4.20 On the p-value in adaptive designs
- Understanding the adaptive p-value
- Comparing fixed vs adaptive p-values
- When is an adaptive p-value “better”
- A case study for the promising zone in asthma
Frank Fleischer, Teamleader Clinical Biostatistics, Boehringer-Ingelheim

5.00 Chairman’s Closing Remarks and Close of Day One

Who should attend this conference:
You should attend this event if you are a Director, Chief Executive, Chief Scientific Officer, Vice President, Head of Department, Principal Scientist or Statistician within the Pharmaceutical or Healthcare industry with responsibilities in the following areas:

- Biostatistics
- Adaptive Trials Design
- Regulatory Affairs
- Clinical Drug Development
- Contract Research
- Clinical Operations
- Research and Development
- Intellectual Property
- Legislation & Policy Advice
- Drug and Safety Assessment
- Clinical Pharmacology
- Experimental Medicine
- Clinical Trials
- Business Development

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Contact Cathy Bishop,
SMi Marketing on +44 (0) 20 7827 6134 or email: cbishop@smi-online.co.uk
8.30 Registration and Coffee

9.00 Chairman’s Opening Remarks
Vladimir Anisimov, Senior Strategic Biostatistics Director, Quintiles

9.10 From preclinical studies to adaptive designs - A path to the future
• Preclinical data is very often underused, whereas they can provide very valuable prior information for Bayesian approach
• Adaptive design can also be implemented in non-clinical studies to maximise the information extracted from the study
• This extended approach opens the way to a global approach of drug development; fully data driven and allowing early selection of a winning area for a project.
Emmanuel Pham, Senior Director, Global R&D Statistics, Ipsen

9.50 Session reserved for sponsor
• Developing adaptive designs
• New processes in preserving trial outcomes
• Comparison between design approaches
Senior representative from a sponsor

10.30 Morning Coffee

11.00 Adaptive trials in pre-clinical discovery
• What is important in pre-clinical trials
• How does pre-clinical differ from clinical
• How can we use adaptive designs to improve translation from animal to human
Alun Bedding, Director, Biostatistics and Programming Development Partners, GlaxoSmithKline

11.40 Bayesian model-guided first in human dose escalation trials in healthy volunteers
• Use a predictive model to provide supporting information for dose-escalation decisions for a data monitoring committee
• Design the model to provide high-quality predictions; the model must be fully trusted by the clinical team and hence based on prior information drawn from expert opinion and on prior research
• Case study illustrating design of such a model and use in practice
Jouni Kerman, Statistical Methodologist, Novartis

12.20 Networking Lunch

1.30 Decision support for design of clinical trial programmes
• Designing a clinical development programme
• Difficulties in multi-stage collaborative trials among various disciplines
• Framework and tools developed to transparently translate target product claims
• Study specifications, scientific questions and underlying risks defined
Martin Simán, Director, Design and Interpretation Centre of Excellence, AstraZeneca

2.10 Adaptive sample size and modification in clinical trials: Start small then ask for more?
• Methods for adaptive sample size re-estimation at interim analyses
• Understanding Mehta and Pocock’s “indifference zone” approach
• Improving Mehta and Pocock’s approach to make better use of additional sample size
• Use of group sequential stopping rules with a delayed response
Chris Jennison, Professor of Statistics, University of Bath

2.50 Afternoon Tea

3.20 From the idea to the publication in academic trials
• Protocol development
• Quality of data and monitoring
• Governing the logistics
• Chronology of the steps and critical points
Genevieve Depresseux, Academic Research Manager, Université Catholique de Louvain.

4.00 Bayesian Variable Selection (BVS) approach for dose-response modelling
• Introduction of BVS
• Application to dose-response modelling
• Comparison with other methods
• Case study
• Review and discussion
Adetayo Kasim, Research Statistician, Durham University

4.40 Chairman’s Closing Remarks and Close of Day Two
Overview of workshop
ADDPLAN is a comprehensive software package for designing and performing confirmatory adaptive clinical trials. A recent application of adaptive designs is to population enrichment designs in which subsets of patients can be selected at an interim analysis for the subsequent parts of the trial. The workshop provides a basic introduction to the underlying theory and a demonstration of software. Many examples will illustrate the use of the software some of which workshop attendees will be able to work on themselves.

Why you should attend:
- To learn about confirmatory adaptive designs
- To design and evaluate operating characteristics of population enrichment designs

Programme

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<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>9.00</td>
<td>Registration &amp; Coffee</td>
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<tr>
<td>9.30</td>
<td>Welcome &amp; Introductions</td>
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<tr>
<td>9.40</td>
<td>Theory of Adaptive Design</td>
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<td>10.20</td>
<td>Combination testing principle</td>
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<td>11.00</td>
<td>Afternoon Refreshments</td>
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<td>11.30</td>
<td>Closed testing Approach</td>
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<td>Basics of ADDPLAN</td>
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<td>• Simulation of specification in enrichment designs</td>
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<td>• Analysis in enrichment designs</td>
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<td>• Case Study</td>
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<tr>
<td>1.00</td>
<td>Close of Workshop</td>
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About the workshop host
Gernot Wassmer, PhD, is Senior Vice President and Chief Software Architect in ADDPLAN Inc, an Aptiv Solutions company. He is adjunct Professor for Biostatistics at the Institute of Medical Statistics, University of Cologne, Germany. He received his PhD 1993 at the University of Munich, Germany, and was a Research Fellow at the Institute of Statistics, University of Munich, at the Institute for Epidemiology, GSF Neuherberg, and at the Institute of Medical Statistics, University of Cologne. He also works as a statistical consultant for the pharmaceutical industry. His major research interest is in the field of statistical procedures for group sequential and adaptive plans in clinical trials. Dr. Wassmer is a co-founder of the ADDPLAN Software Corporation.
### JANUARY

- **Biomarkers Summit**  

- **Social Media in the Pharma Industry**  
  23 – 24 January 2013, London

- **Quality by Design**  
  23 – 24 January 2013, London

- **Pre-Filled Syringes**  
  28 – 29 January 2013, London

- **Pharmaceutical Microbiology**  

### FEBRUARY

- **Parallel Trade**  
  6 – 7 February 2013, London

- **Advances and Progress in Drug Design**  
  18 – 19 February 2013, London

- **Lyophilisation - Freeze Drying in Pharmaceuticals and Biopharmaceuticals**  
  25 – 26 February 2013, London

### MARCH

- **Superbugs & Superdrugs - A Focus on Antibacterials**  
  4 – 5 March 2013, London

- **Imaging in Cancer Drug Development**  
  13 – 14 March 2013, London

- **Controlled Release**  
  18 – 19 March 2013, London

- **Paediatric Clinical Trials**  
  20 – 21 March 2013, London

### APRIL

- **Adaptive Designs**  
  8 – 9 April 2013, London

- **Asthma & COPD**  
  15 – 16 April 2013, London

- **Pharmaceutical Portfolio & Lifecycle Management**  
  17 – 18 April 2013, London

### MAY

- **Generics, Supergenerics & Patent Strategies**  
  13 – 14 May 2013, London

- **Pain Therapeutics**  
  20 – 21 May 2013, London

- **ADC Summit**  
  20 – 21 May 2013, London

- **Clinical Trial Logistics**  
  22 – 23 May 2013, London

### JUNE

- **RNAi & Nanotechnology**  
  5 – 6 June 2013, London

- **Biobanking**  
  24-25 June 2013, London

- **Allergies**  
  26 – 27 June 2013, London

- **ADMET**  
  26 – 27 June 2013, London

### JULY

- **Pharmacovigilance**  
  1 – 2 July 2013, London

- **Cell Culture**  
  3 – 4 July 2013, London
DENNIS DESIGNS IN CLINICAL TRIALS

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Cardholder’s Name:
Signature: Date:

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