Danish Society for Biopharmaceutical Statistics

Two-day DSBS Course

Group Sequential and Adaptive Methods in the Design of Clinical Trials

25-26 October 2022, hosted by Lundbeck A/S

Lecturer

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Dept of Mathematical Sciences, University of Bath

This course will comprise of two halves: In the first we shall review the methods and application of (now) standard group sequential designs. In addition, we shall discuss some of the more recent controversies and developments including: controlling bias when reporting results of a trial with early stopping; reporting of results on co-primary endpoints; and accommodating delayed observations ("pipeline" data) at interim analyses. The second half of the course will discuss adaptive designs and various applications including sample size re-estimation, enrichment designs and Phase II/III seamless designs.

Participants must bring their own laptop.

Venue Lundbeck A/S
Ottiliavej 9
2500 Valby

Registration

The course fee is 1200 DKK for the full course.

Deadline

Please register before

13-Oct-2022

To register, please send a mail to

commres1351@Lundbeck.com

Joint registration by department is warmly welcomed.

There is a limit of 30 attendees. The first come, first serve principle will be applied.

Group Sequential and Adaptive Methods in the Design of Clinical Trials

Formal data monitoring procedures are now a standard feature of the design and conduct of long-term clinical trials. A unified formulation of group sequential procedures allows a simple, powerful approach to their implementation with different types of stopping rule and a great variety of endpoints. We shall survey the main ideas of group sequential procedures including: superiority, non-inferiority and equivalence testing; normal, binary, survival, regression and longitudinal endpoints; inference on termination; nuisance parameters; trials with multiple arms or multiple endpoints.

More recently, methods have been proposed to allow modification of a trial in mid-course while still protecting the type I error. Possible modifications include enlarging the sample size to increase power, changing the study population (for example, enrichment), modifying the treatment, or reducing the number of treatment arms. These adaptations may follow rigid rules, pre-specified in the protocol; more flexible approaches permit unplanned changes at unplanned interim analyses. We shall describe these procedures in detail and discuss their benefits and limitations.

Statistical software will be used to illustrate the methods and examples.

Outline:

- Principles of group sequential methods; underpinning theory and computation; the general framework, including normal, binary and survival endpoints.
- Boundaries: efficacy, futility (binding and non-binding); error spending designs; the “pipeline” problem when there is a delayed response.
- Information monitoring and nuisance parameters; estimation and confidence intervals after a sequential trial; stochastic curtailment.
- Multiple endpoints
- From group sequential to adaptive designs: sample size modification to improve power.
- Methodology for adaptive designs: combination tests and testing multiple hypotheses.
- Adaptive enrichment designs: changing the target population.
- Trials with multiple treatments: seamless Phase II/III transition.
- Case studies and discussion: participants will be invited to discuss their experiences in implementing adaptive designs, interacting with regulators or serving on Data and Safety Monitoring Boards.

Prerequisites:

This course is aimed at Masters level statisticians who have some familiarity with clinical trials but not necessarily with the aspects of sequential monitoring or adaptive trial design.

Learning objectives:

By the end of the course, participants should be able to

- Assess whether a group sequential or adaptive design is appropriate for a clinical trial.
- Develop a group sequential design with a suitable number of interim analyses and maximum sample size, achieving the desired type I error rate and power.
- Implement a trial using error spending and information monitoring to cope with initially unknown parameters such as response variance or baseline hazard rate.
- Apply combination tests and multiple hypothesis tests as part of an adaptive trial in which observed responses are used to make choices on sample size modification, selecting one of several treatment arms, or focusing on a sub-population.
- Understand the potential benefits of adaptive clinical trials and how to assess these.