

# A simulation of Bayesian adaptive seamless Phase 2/3 design at the planning and execution phases

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This presentation is a case study of how trial simulations can be used in the designing and planning of a clinical trial. Simulations were utilized extensively in both the design and planning phases for a novel Bayesian adaptive seamless Phase 2/3 design of an experimental drug to treat diabetes (AWARD-5), which was used for the US/EU NDA submissions. The simulation exercises required collaboration among experts in medicine, statistics, pharmacokinetics/pharmacodynamics, regulatory and cluster computing. We expect this presentation will encourage the use of trial simulations in order to enhance the new generation of clinical development programs.

Bayesian adaptive seamless Phase 2/3 trials (e.g., AWARD-5) introduce new challenges in both study design and implementation. Computer trial simulations must be used to assess the operating characteristics (determining the decision criteria of interim analyses, type I error and power, etc.). AWARD-5 involved selecting doses for a Phase 3 program (including AWARD-5 itself) based on interim data from adaptive randomized dose-ranging part (stage 1) in a seamless, blinded manner. Implementing such designs poses unique challenges from a business, logistical and regulatory perspective, and strongly requires collaboration among various internal and external expertise.

This case study, AWARD-5, is an example where trial simulations were necessary in the design and planning of the trial. The authors propose that trial simulations should be used even when designing and planning fixed trials where traditional statistical methods can be used to assess operating characteristics. Simulations can provide a more realistic assessment of the potential performance of a trial since they do not rely on often unrealistic or at least unverified assumptions needed for analytical approaches.

This presentation will cover the role of trial simulations in: a) determining adaptive design features of AWARD-5, b) planning the implementation of AWARD-5; c) establishing the operating characteristics of AWARD-5.

## References:

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