Bayesian concept for combined Phase 2a/b trials

Stefan Klein (Bayer AG, Berlin)

In many pharmaceutical trials, phase 2a and Phase 2b trials are performed as separate entities. Often, Phase 2a trials are performed as 2-armed trials comparing the highest safe dose of a new drug against placebo. After the end of Phase 2a, a Proof of Concept (=POC) decision will be made, based on the Phase 2a trial data. Following a positive decision a Phase2b dose finding trial is performed, usually applying (nonlinear) regression methodology.

In such a setting, information from Phase 2a is usually lost. This could be avoided using a Bayesian Phase 2 design, where the outcome of the PoC study is used as prior information for the dose finding study.

The technical difficulty of having different types of models in phase 2a and phase 2b, can be solved by exchanging the original parameters of the (nonlinear) dose response regression with expected value parameters for the doses used in phase 2a In such way, the information of phase 2a study can be easily incorporated into the dose response regression.

Using the examples of linear dose regression and a 3 parameter Emax model, this talk will provide simulation results for the proposed design: Results for the efficiency gain due to the use of prior information as well as for the robustness of the approach will be presented.