Berry Consultants
Statistical Innovation

FACTS

FACTS Fixed and Adaptive Clinical Trial Simulator

The Leading Edge of Trial Design

FACTS is a software system for simulating clinical trials, enabling biostatisticians to optimize and fully understand the trial design through the simulation process. FACTS was designed with input from leading industry biostatisticians and is licensed by major pharmaceuticals companies, CRO's and Biotechs, and over 20 academic and research organizations.

FACTS enables 'in silico' trial design. Unlike other trial design tools that simply use simulation as a form of integration to compute statistics. FACTS provides thorough and detailed trial simulation, taking into account time to endpoint, intermediate visits, dropouts, varying accrual rates etc..

Through the many operating characteristics that can then be estimated, the statistician has a "flight simulator" in which they can simulate a variety of different trial conditions and scenarios, creating a much more thorough understanding of the trial design's strengths and weaknesses. The simulation results are also much more comprehensible to non-statisticians than conventional statistics and can be used to provide them with clear picture of how the trial may perform.

The FACTS Engines

The FACTS simulation engines are grouped into 5 types: **Dose Escalation, FACTS Core** where 1 or more treatment arms are tested against one or two control arms, **Enrichment Designs** where the same treatment is tested in different patient populations or different indications, **Staged Designs** where FACTS simulates two trials that are run back to back such as a seamless Phase 2/3, and **Platform Trials** where multiple treatments are tested, with treatments exiting the trial and new ones entering over time.

All the engines are fronted by a common user interface (UI) that makes FACTS easy to learn and easy to use. As well as ease of use, FACTS is feature rich, flexible, fast and delivers extensive outputs and graphical summaries.

Feature Rich

FACTS has innovative features in each engine:

Dose Escalation: 3+3, mTPI, CRM, CRM targeting a toxicity band, 2D-CRM, overdose control, single subject run-in, categorical toxicity, toxicity and efficacy, joint modeling of 2 groups, continuous enrolment, backfilling, fine-grained dose selection, multiple dose escalation controls, multiple stopping rules.

Core Designs: Dose response modeling, 2D dose response modelling, longitudinal models, hierarchical priors for control, dose response adaptation, Bayesian and frequentist analysis, Bayesian predictive probabilities and user defined quantities of interest to be estimated in the MCMC sampling. The auto generation of a Report describing the design in MS Word.

Core Multiple Endpoint: A particularly powerful extension to the Core design simulators is the ability to simulate, analyze and act on up to four endpoints. These might be efficacy and tolerability endpoints, early and late endpoints, or primary and secondary efficacy endpoints or any combination of these.

Enrichment Designs: Hierarchical response modeling across the control arms and the estimate of the treatment effect, hierarchical priors for controls, longitudinal models, study and sub-group level adaptation.

Staged Designs: Simulate the treatment selection at the end of a phase and the decision whether to run the next stage or not and the impact this has on the next phase. Whether the stages are separate (such as separate phase 2 and phase 3 trials) or a seamless phase 2/3.

Platform Trials: Simulate from the start of a platform trial up to some point in its future (such as the first 5 years, the first 1,000 participants or first 10 treatments), with initial treatments at the outset and future treatments becoming available at some specified time window in the future (the exact time being sampled stochastically). A "maximum concurrent" number of treatments can be specified with future treatments potentially having to wait until there is a free slot in the trial. Available for continuous and dichotomous endpoints, with options for early stopping rules and response adaptive randomization and both Bayesian and frequentist analysis.

Flexible

FACTS is flexible – all these options are individually selectable and can be combined with the other options. This makes the range of study designs that FACTS can simulate enormous, but it also means that working in FACTS, a trial designer can build a trial design up incrementally starting with a straight forward design and explore the impact of each innovation one at time, selecting the best.

Fast

The trial simulators are all tightly coded in C++ and run 10-100 times faster than designs created within statistical programming environments. For many designs 1,000 simulations can be run in a few minutes or even seconds. We can also support licensees integrating FACTS with their computing grid facilities for running very large numbers of simulations of particularly demanding designs. Being able to get simulation results quickly transforms the experience of designing complex trials.

Full Output

The user has full access to all the simulation results including the final analysis of each simulated trial, every interim analysis of each simulated trial, and all the simulated subjects and their responses within each trial. The results are written out into CSV files that are easily loaded into other analysis tools. FACTS has extensive graphical support, allowing the simulation results to be visualized and easily presented including allowing the user to walk through the simulation of individual trials.

Detailed Simulation

FACTS allows detailed specification of the simulated data to be sampled in the simulations – properties such as the overall dose response, patterns of longitudinal responses, recruitment rates and dropout rates can all be specified. Designs can be specified, simulated, and analyzed in minutes rather than days.

It is also possible to load into FACTS a file of externally simulated subject responses, allowing complete control of the simulated patient population and their responses.

Design Variants

FACTS makes it easy to compare the performance of a design at different sample sizes, not just comparing the type-1 error and power but also the design's ability to make correct decisions such as selection of the best dose and identification of the correct treatment population or indication.

Analysis

All the engines support analysis of an externally provided dataset as well as simulation of trials. Giving a new way to evaluate designs and making it easier to use FACTS to implement the trial that has been designed.

A Platform for the Future

For designing adaptive trials, FACTS offers an unparalleled access to innovative trial design ideas, it is being actively developed by an expert team at Berry Consultants, overseen by our senior statisticians and advised by our licensees.

Actively Supported

As well as comprehensive documentation, all licensees are supported directly by the development team through a swift response to queries, a regular webinar schedule and an online training program.