

Improving Predictability of Efficacy and Safety

Clinical Trial Simulation



Designing a Better Study

In the face of rising cost and scrutiny of clinical trials, modeling and simulation can test assumptions and make predictions that improve planning and decision-making across the full spectrum of therapeutic innovation. Drug safety and efficacy predictions are now used for clinical trial simulation (CTS) to inform individual trial design.

As more clinical teams better understand these techniques, the practice is rapidly growing in Regulatory, Scientific and Operational acceptance. Through CTS, Quintiles is diligently striving to improve the success rate of clinical trials.

An Experienced Partner

Since 1999, Quintiles has proactively addressed specific regulatory questions, helped design future studies and provided input on product labeling through broad model-based drug development experience involving more than:

- > 20 major submissions that included Population PK/PD analyses
- > 30 sponsors
- > 50 compounds in 13 therapeutic areas
- > 70 modeling projects (with up to 22 individual studies in a single meta-analysis)

Our Pharmacokineticists and Biostatisticians are trained in modeling and CTS methodologies and technologies, and senior staff members have extensive experience identifying expert knowledge gaps, imparting discipline on the design process across all parties and developing innovative options beneficial to similar studies in different patient populations.

Quantitative and Collaborative Edge

Modeling and simulation enables calculated decision-making. Clinicians, clinical pharmacologists and statisticians across Quintiles work with customers to better quantify problems and collaboratively assess results so all development options are well informed. This collaborative edge leads to smarter decisions and better outcomes.

Improved Success Rates and Greater Efficiencies

Quintiles CTS provides the ability to test multiple scenarios, predict the potential study outcomes for each and select the most advantageous study design. Before conducting a study, testing various trial designs through computer simulation can help improve the likelihood of a successful study. Quintiles' services also include clinical trial operational models that are important in helping optimize study conduct.

These statistical models have significantly improved efficiencies in identifying:

- > Geographic regions where patients cluster
- > Clinic recruitment rates
- > Clinical supplies
- > Monitoring patterns
- > Operational processes that inform simulations used in decision-making

Improving Safety and Reducing Risk

The FDA's 2009 *Guidance for Industry: End-of-Phase 2A Meetings* encourages sponsors to seek regulatory meetings to discuss quantitative modeling and trial simulations to improve dose selection and clinical trial design.¹ Quintiles can help avoid safety and efficacy issues sooner and reduce risk and cost involved with human testing by allowing a "test run" of designs.

Results from Quintiles CTS Services may help predict likely outcomes for a range of assumptions about trial size, dose selection and operational considerations, such as:

Study Specifics

- > *Benefits and trade-offs of different trial designs (parallel, cross-over, etc.)*
- > *Optimal dosing for each treatment arm to minimize overlap in exposures and subsequent responses*
- > *Anticipated patient exposures and responses for each treatment*
- > *The ideal sampling scheme*

Inclusion / Exclusion Criteria

- > *Optimal inclusion / exclusion criteria to capture the desired population that is driving the response*
- > *Effects of changes in recruitment rates and criteria on study timelines and results*

Safety and Efficacy

- > *Effects of protocol deviations and treatment compliance on safety and efficacy*

Study Results

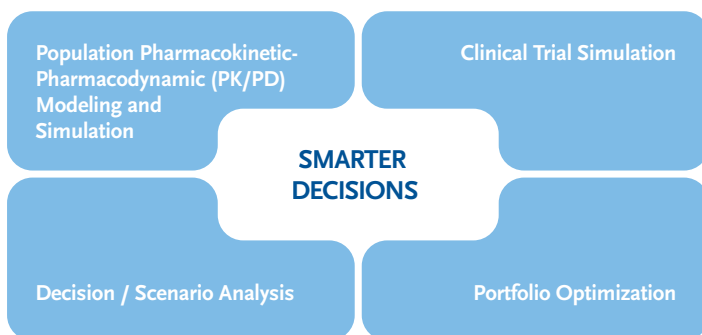
- > *Placebo effect on patients over time*
- > *How investigational drug compares to competitors' drugs*

Statistical Analysis

- > *Whether planned study analysis can detect statistical significance*

Quintiles Model-Based Drug Development

Let Quintiles help improve your decision-making by leveraging data to guide trial design conduct and analysis through clinical trial simulation.



Join us for success in the New Health.

We're here for you.

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Case Study

Quintiles Clinical Trial Simulation

Focus

Sponsor came to Quintiles to design a Phase 2 study to get as many patients to approximately 60-70% inhibition of an ion channel as quickly as possible to treat an acute condition.

Challenge

From the collected pharmacokinetic and pharmacodynamic (PK/PD) data in Phase 1, a long absorption phase and long elimination half-life were observed. This made it difficult to design a traditional dosing regimen for acute treatment.

Service

Based upon Quintiles Phase 1 PK/PD modeling, Clinical Pharmacologists and Biostatisticians across Quintiles and the sponsor prepared a simulation of several different dosing scenarios to help design the most efficacious study design.

Results

The sponsor's ability to make more informed decisions and more accurately predict efficacy earlier can significantly reduce time and cost of human testing. In this case, a clinical trial simulation demonstrated the 4x loading dose with a 1x maintenance dose provided the best coverage of at least 60-70% ion channel inhibition in most patients. This recommendation also provided over a 70% reduction in the time to onset of effect when compared to treatments that did not have a loading dose.

- 1 Center for Drug Evaluation and Research, FDA, September 2009. Guidance for industry: end-of-phase 2A meetings. As of June 1, 2012, available at: <http://www.fda.gov/DrugsGuidanceComplianceRegulatoryInformation/Guidances/default.htm>.